MICRONUTRIENTS

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- Required by the body in trace amounts
- Perform specific cellular functions

Micronutrients:

- Vitamins
- Minerals

After attending lectures on this topic, the student should be able to understand:

- Sources, daily requirements and deficiency of vitamins.
- Water-soluble vitamins: structure, biochemical role and nutritional disorders of riboflavin, niacin, pyridoxine, thiamine, pantothenic acid, cobalamin, biotin and folic acid.
- Fat-soluble vitamins: structure, biochemical role and nutritional disorders of vitamins A, D, E, and K.

VITAMINS

“Vitamine”

1912- Casimir Funk- “vital amine”

-from rice husks that cured beriberi

Nutritional-deficiency disease resulting in neural degeneration

Note: Few vitamins are amines

Amine-derivative of ammonia

- Classification:
  - Solubility
  - Functions in metabolism

Organic compounds

-Function in a wide variety of capacities in the body

-Most prominent function- serve as co-factors (co-enzymes)

Co-enzymes and Co-factors- molecules or ions that are used by enzymes to help catalyse reactions

- Co-enzymes-organic molecules that contain functionalities not found in proteins
- Co-factors are catalytically essential molecules or ions that are covalently bound to the enzyme

Micronutrients:

- Essential dietary factors
- Cannot be synthesized in the human body
- Must be provided in the diet

Absence results in deficiency diseases

- Previously:
  - Prevent acute deficiency diseases such as scurvy and beri-beri

- Recently:
  - Maintenance of optimal health
  - Prevention of chronic disease

  Prophylactic use: as focus shifts from treatment of acute disorders to prevention of chronic illnesses

Essential for the normal processes of:

- Metabolism
- Growth
- Maintenance of health

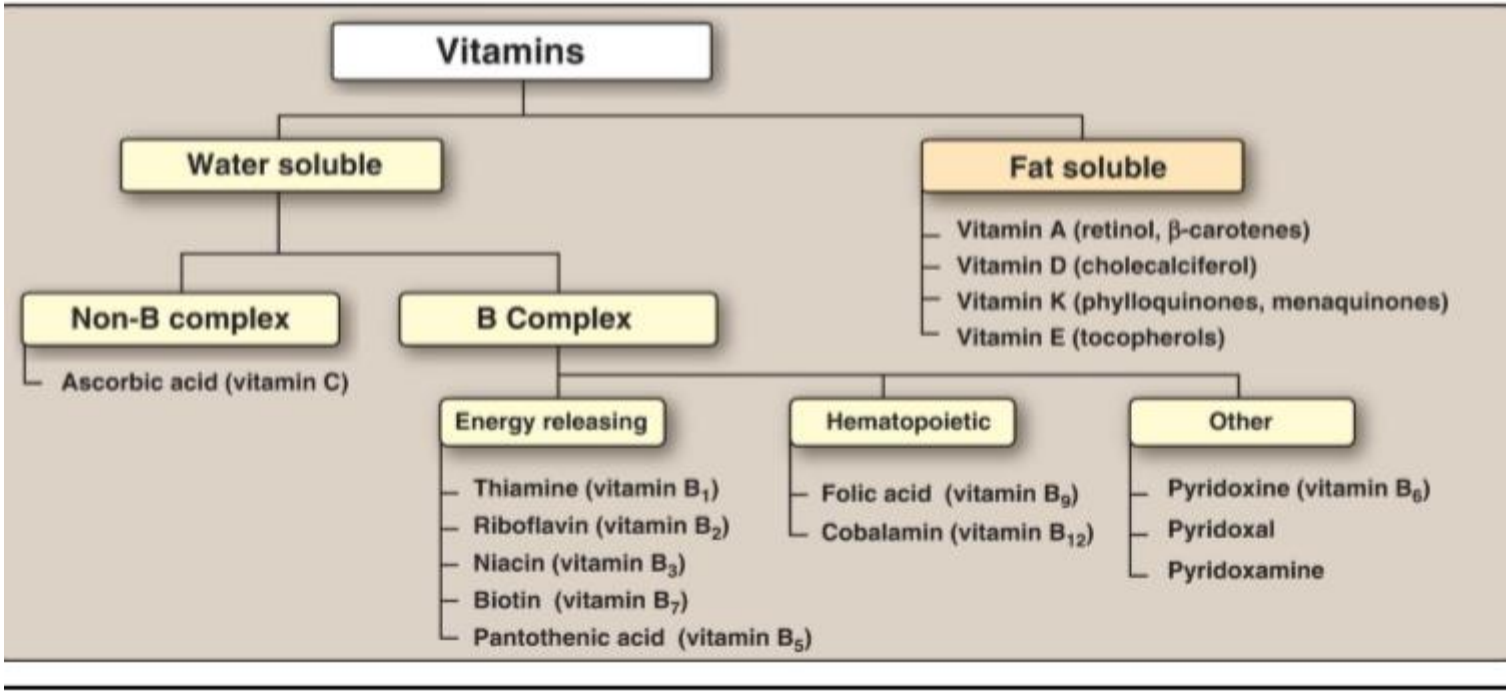
- Not in the group of essential nutrients, such as dietary minerals, essential fatty acids or essential amino acids
- Classified by their biological and chemical activity, not their structure

Diverse biochemical functions:

- Vitamin D-hormone-like-functions as regulators of mineral metabolism
- Vitamin A- regulators of cell and tissue growth and differentiation

- Vitamin E-function as antioxidants and sometimes vitamin C)
- The largest number of vitamin, B complex vitamins, function as precursors for enzyme cofactors

CLASSIFICATION



Water soluble

- B Vitamins and Vitamin C (non B-complex)
  - Share few common properties besides their solubility characteristics *Since they are water soluble excess can be excreted through urine (not stored in the body)*
- Continuous daily supply in diet

- Most of these vitamins act as coenzymes
- Some B vitamins-B_1, B_2 help in the process the body uses to make energy

Water soluble

- Thiamine (Vit B_1)
- Riboflavin (Vit B_2)
- Niacin (Vit B_3) (Nicotinic acid or Nicotinamide)
- Pantothenic acid (Vit B_5)
- Vitamin B_6 (Pyridoxine, pyridoxal, Pyridoxamine)
- Biotin (Vit B_7)
- Vitamin B_{12} (Cobalamin)
- Folic Acid (Vit B_9)
- Ascorbic Acid

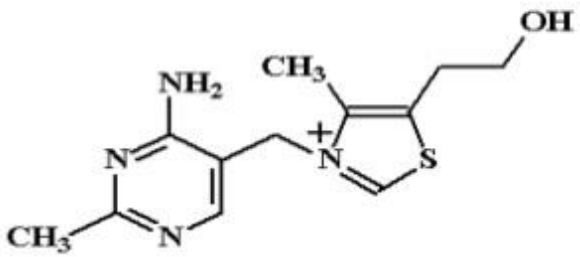
Thiamine (Vit B_1): occurs as coenzyme, Thiamine pyrophosphate (TPP)

TPP functions in the generation of activated aldehyde species

Enzymes that use TPP include: pyruvate decarboxylase, pyruvate dehydrogenase, branched chain α-keto acid dehydrogenase, α-keto glutarate dehydrogenase, transketolase

STRUCTURE

Thiamine - Structure

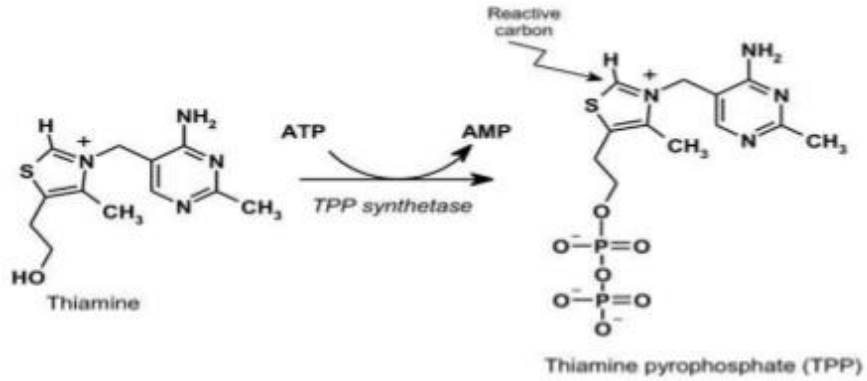


Thiamine

Thiamine contains a substituted pyrimidine ring (dimethyl 6-amino pyrimidine) connected to a substituted thiazole ring (Methyl hydroxy ethyl thiazole) by means of Methylene bridge.

STRUCTURE OF TPP

Activation of Thiamine



❑The active form of the coenzyme, **thiamine pyrophosphate (thiamine diphosphate, TPP), is synthesized by an enzymatic transfer** of **a pyrophosphate group from ATP to thiamine**).

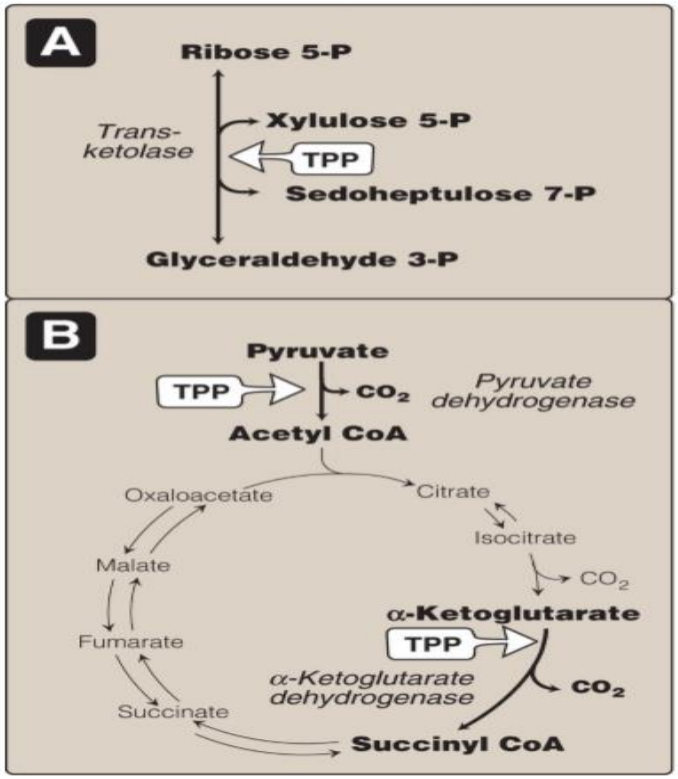


Fig: Reactions that use thiamine pyrophosphate

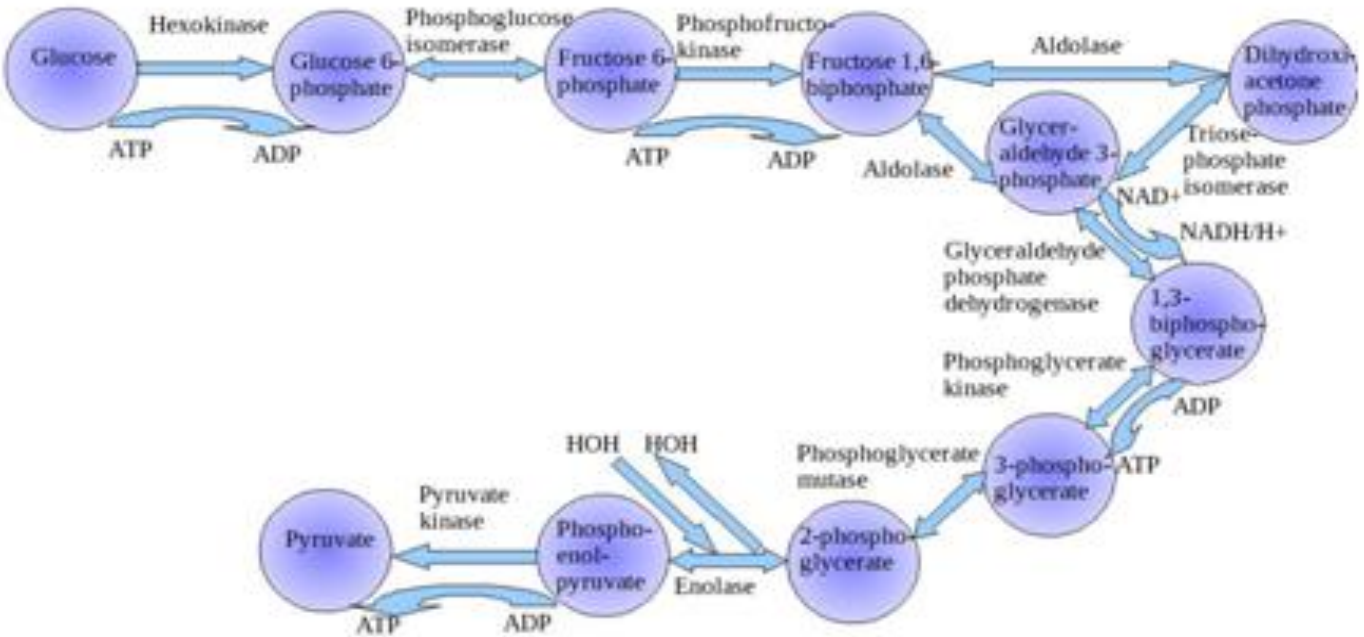
Metabolism

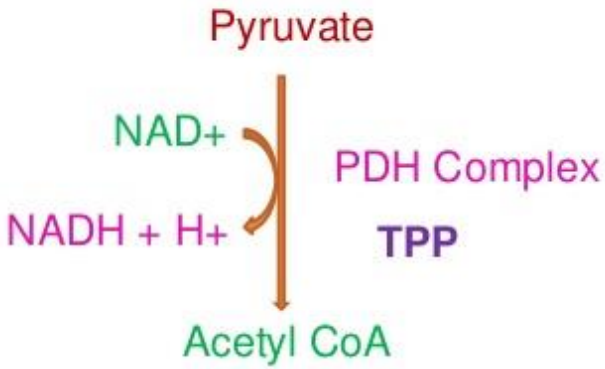
- Carried by the portal blood to tissues bound to albumin and other proteins
- Stored as thiamine pyrophosphate (80%)
  - Skeletal muscle, liver, heart, kidneys etc

- TPP connected with energy releasing reactions in carbohydrate metabolism
  - –Pyruvate dehydrogenase complex-irreversible conversion of pyruvate to acetyl CoA-essential for complete oxidation of glucose

Links glycolysis and TCA cycle

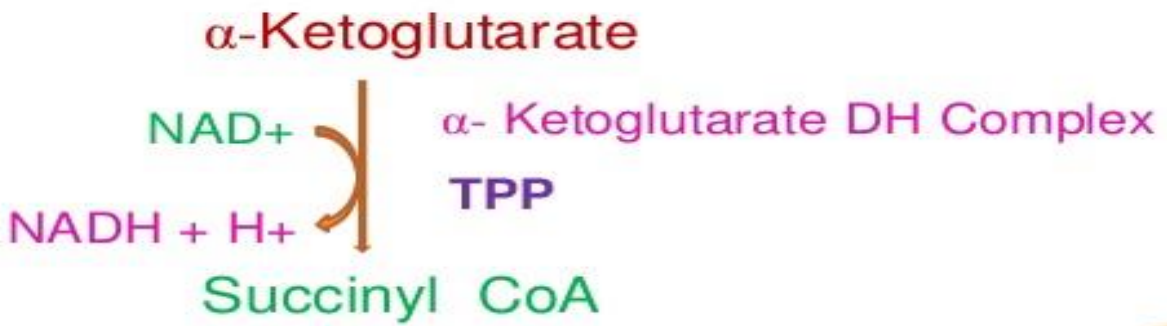
GLYCOLYSIS


Glucose
Hexokinase
Glucose 6-phosphate
ATP
ADP
Phosphoglucose isomerase
Fructose 6-phosphate
Phosphofructo-kinase
ATP
ADP
Fructose 1,6-biphosphate
Aldolase
Dihydroxy-acetone phosphate
Triose-phosphate isomerase
Aldolase
Glycer-aldehyde 3-phosphate
NAD+
NADH/H+
Glyceraldehyde phosphate dehydrogenase
1,3-biphospho-glycerate
Phosphoglycerate kinase
ADP
ATP
3-phospho-glycerate
Phosphoglycerate mutase
HOH
HOH
2-phospho-glycerate
Enolase
Phospho-enol-pyruvate
Pyruvate kinase
Pyruvate
ATP
ADP

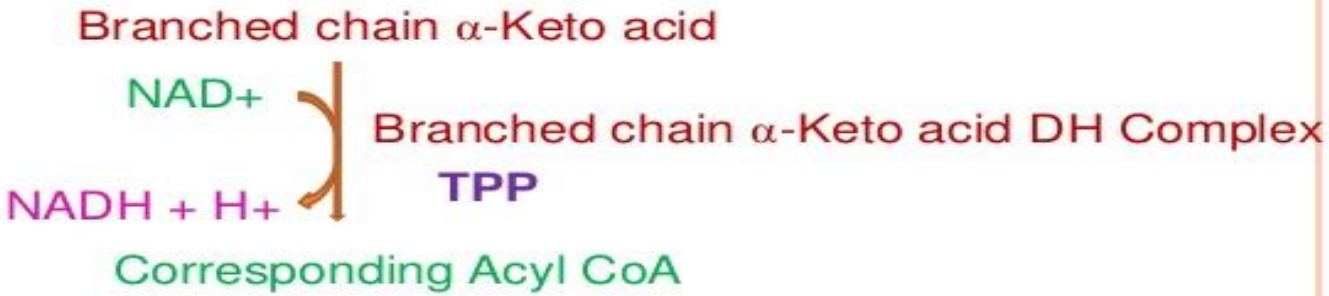


- Transketolase is dependent on TPP
- It is involved in HMP shunt

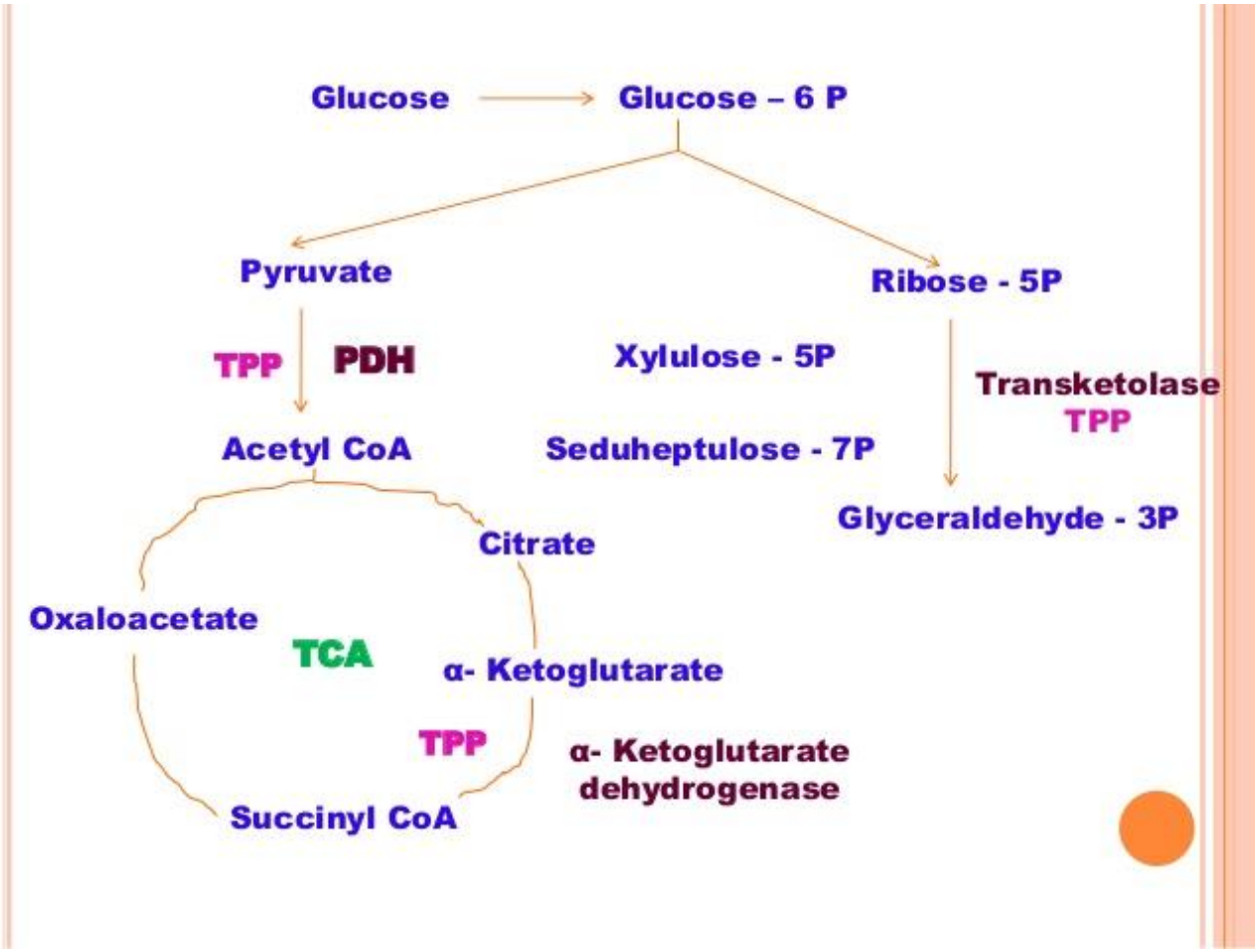
- ***α- Ketoglutarate dehydrogenase complex:***
- It converts α- Ketoglutarate succinyl CoA in TCA cycle



- ***The branched chain α-Keto acid dehydrogenase (decarboxylase):***
- It catalyses the conversion of α-keto acids to corresponding acyl CoA



- Essential for transmission of nerve impulse
- TPP is required for synthesis of **Acetylcholine**


Glucose
Glucose – 6 P
Pyruvate
Ribose - 5P
TPP
PDH
Xylulose - 5P
Transketolase
TPP
Acetyl CoA
Seduheptulose - 7P
Glyceraldehyde - 3P
Citrate
Oxaloacetate
TCA
α- Ketoglutarate
TPP
α- Ketoglutarate
dehydrogenase
Succinyl CoA

Sources:

seeds, nuts, wheat and lean meat etc

Biochemical changes in deficiency:

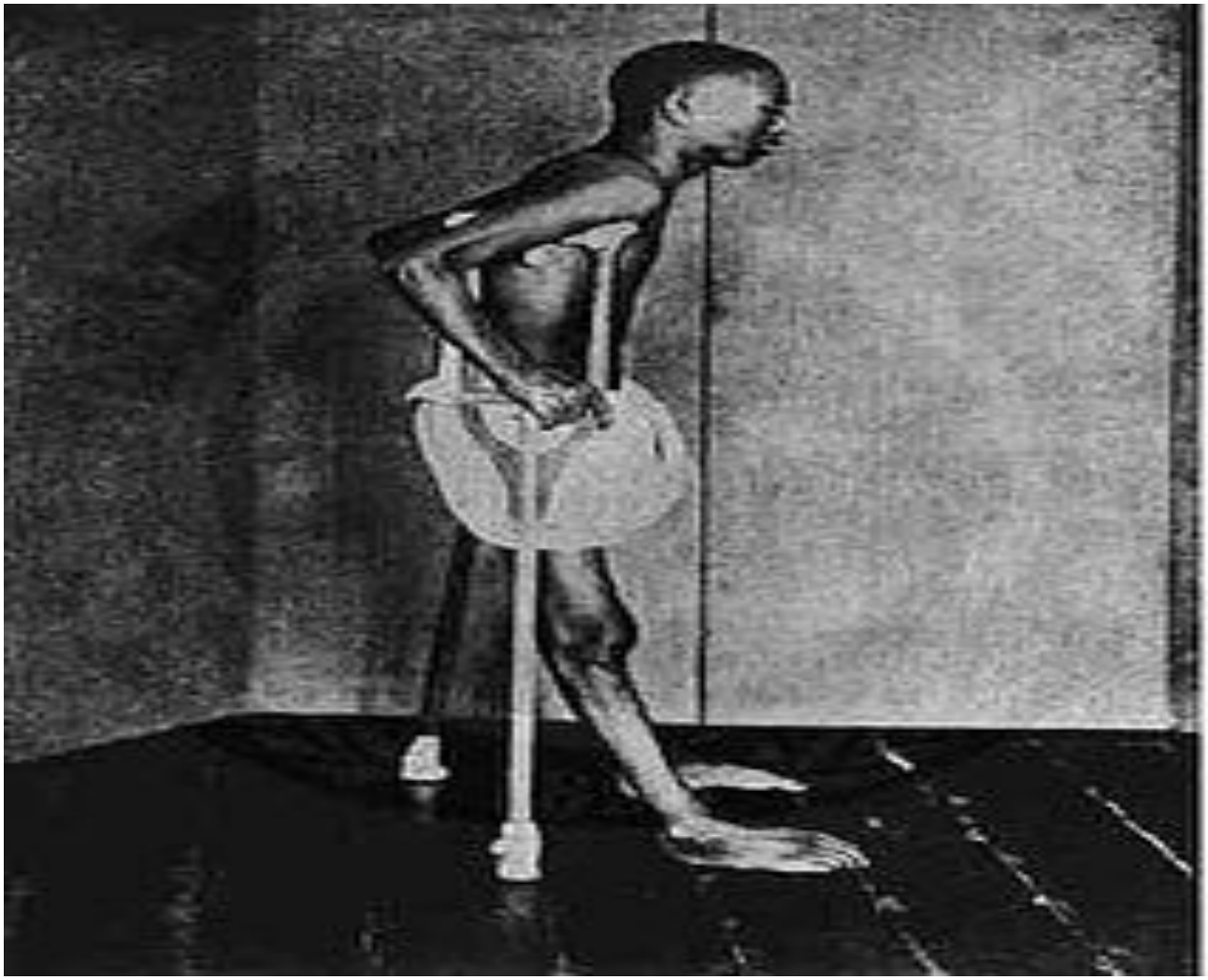
- Carbohydrate metabolism is impaired
- Accumulation of pyruvate in tissues
- Excretion of pyruvate in urine
- Alteration in Blood Brain Barrier (BBB) allows pyruvate into brain- disturbed metabolism
- Impairment in nerve transmission

Clinical condition-Beri-Beri

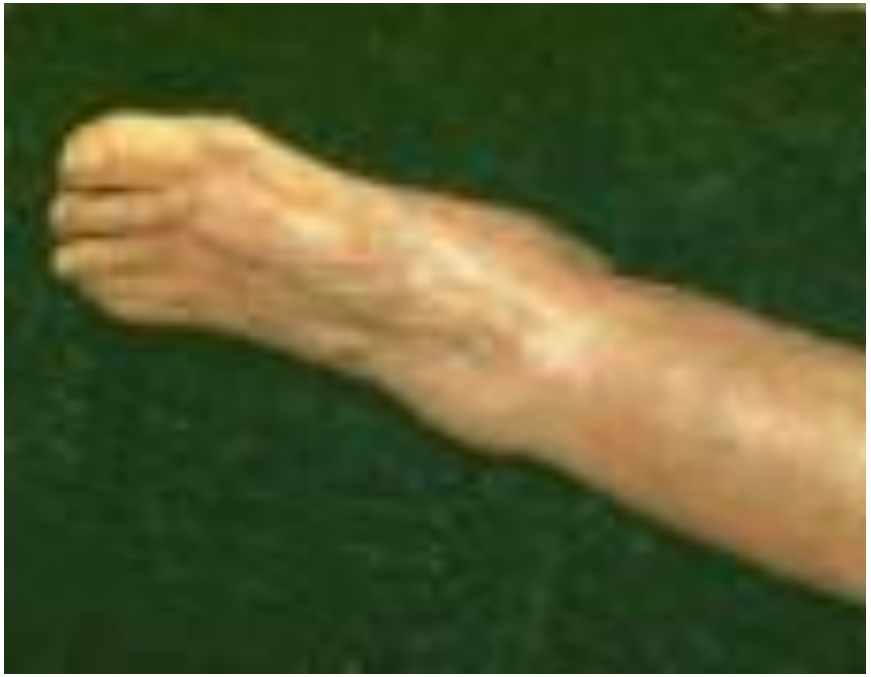
edema, cardiovascular disorders

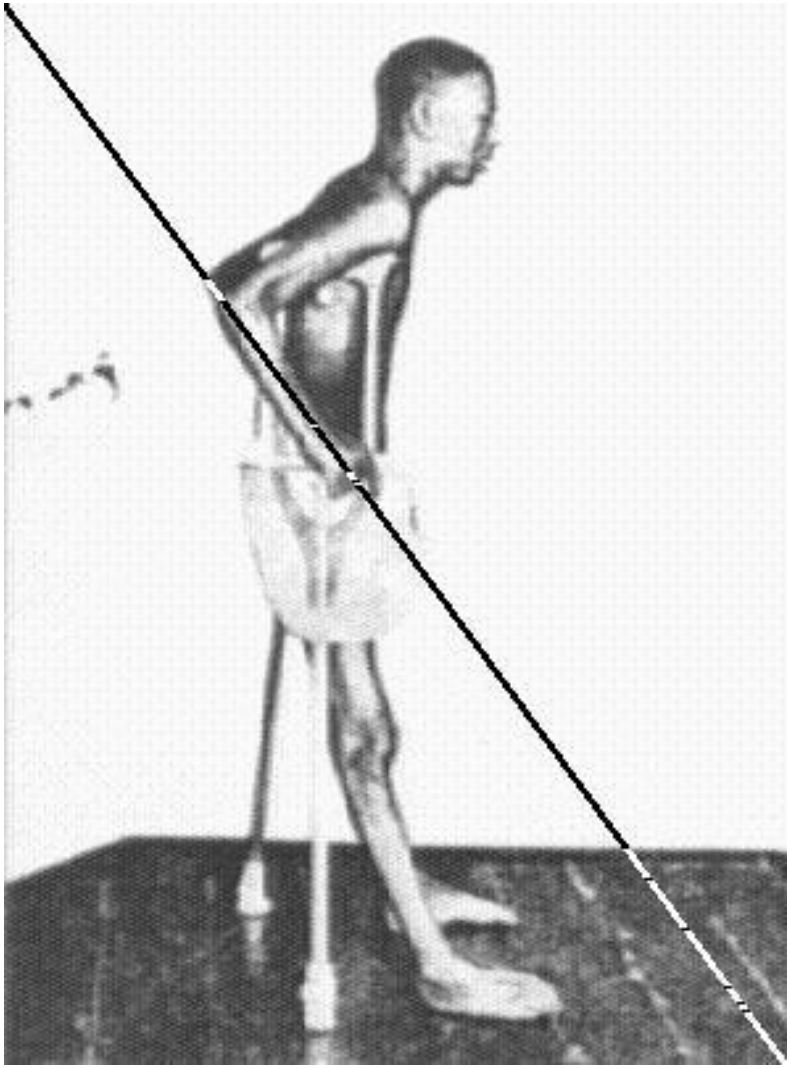
- Common in populations consuming exclusively polished rice as staple food

- Deficiency symptoms
  - Enlarged heart, cardiac failure
  - Muscular weakness
  - Apathy, poor short-term memory, confusion, irritability
  - Anorexia, weight loss



Wet and Dry BeriBeri





Beriberi: cluster of symptoms caused primarily by a nutritional deficit in vitamin B_1 (thiamine)

Alcoholics develop a syndrome

- Ethanol inhibits the active transport of thiamine
- Could be one of the causes of thiamine deficiency in alcoholics
- Thiamine intakes are usually also low because of their penchant for drinking but not eating

- **Wernicke-Korsakoff syndrome**. Acute stage of this disease, known as Wernicke's encephalopathy
- Characterized by mental derangement, delirium and ataxia.
- Chronic stage, known as *Korsakoff psychosis*- the patient has anterograde amnesia.

- ***Thiamine deficiency due to thiaminase:*** Thiamine can be destroyed if the diet contains *thiaminases*-cleave the pyrimidine ring from the thiazole ring.
- Enzymes are present in some ferns, raw fish and sea foods (thought to contribute to the incidence of beriberi in areas in Japan where raw fish (Sushi) is a common dietary constituent.

Absorption and Transport

- Dietary thiamine is absorbed readily from jejunum and proximal ileum and is transported to tissues where it is converted to the active form, thiamine pyrophosphate. Two different mechanisms are involved in absorption depending on the level of intake:

1. At levels below 5 mg/day, the absorption occurs by an active, ATP-dependent process, which is saturable at concentrations of 0.5-1.0 µmol/L.

2. At levels higher than this, the absorption occurs by passive diffusion.

Assessment of Thiamine Status

- Thiamine-Evaluated by estimating *urinary thiamine excretion* and *plasma levels of pyruvate and lactate*, particularly after an oral glucose load (these acids accumulate because of the decreased activity of *pyruvate dehydrogenase*).
- Determination of *erythrocyte transketolase activity*, which requires TPP as a coenzyme, confirms the deficiency

Thiamine in the human body has a half-life of 18 days and is quickly exhausted, particularly when metabolic demands exceed intake

Riboflavin (Vit B_2)-component of flavin coenzymes, FAD and FMN

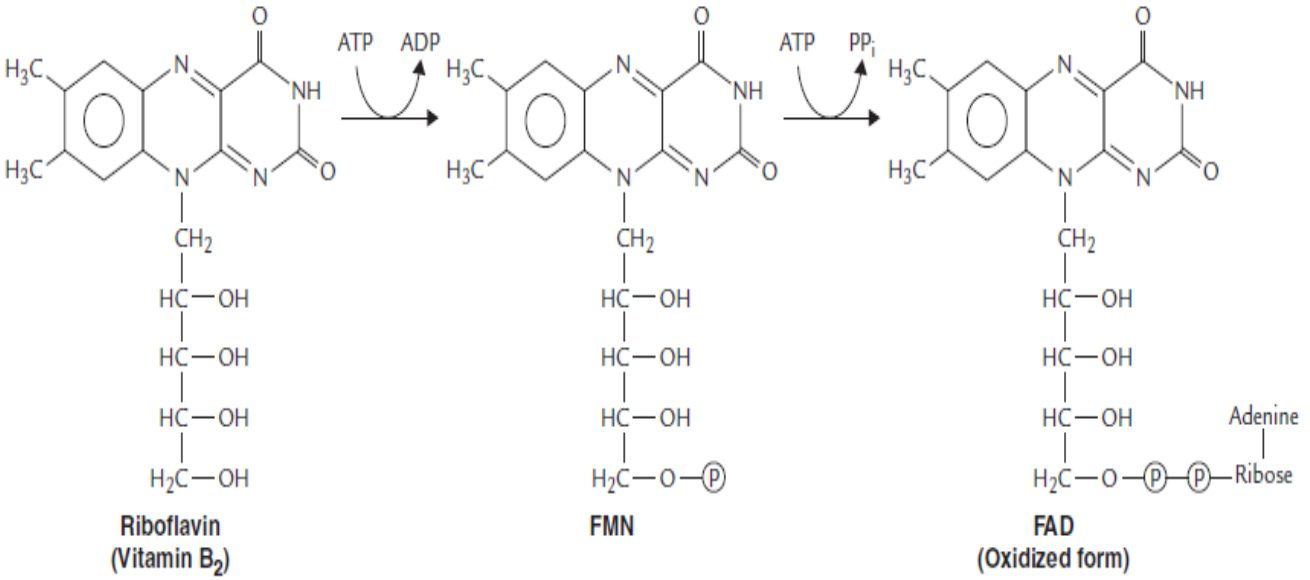


Fig. Synthesis of FMN and FAD from dietary riboflavin.

Coenzyme Activity

- Riboflavin-component of two coenzymes: flavin mononucleotide (**FMN**) and flavin adenine dinucleotide (**FAD**).
- Known as **flavin nucleotides**. FMN is formed (in intestine) by attachment of a phosphate group to the ribitol side chain. FAD, which contains adenosine linked via phosphate group to FMN, is formed by adenylation of the latter in liver.
- The flavin nucleotides serve as prosthetic groups for the enzymes called *flavin-dependent* (*flavoprotein*) *enzymes*. These enzymes remove a pair of hydrogen atoms from the substrate and thereby participate in a number of oxidation reduction reactions in metabolism

FMN-dependent enzymes:

- FMN is a cofactor for *L-amino acid oxidase*.
- The enzyme *NADH dehydrogenase,* of respiratory chain contains FMN.

FAD-dependent enzymes:

- FAD is a constituent of the Complex II of the respiratory chain.

FAD is a constituent of the *microsomal hydroxylase* system.

- FAD is a cofactor for several enzymes, e.g. *D-amino acid oxidase, succinate dehydrogenase, acyl CoA dehydrogenase, glycerol 3-phosphate dehydrogenase, xanthine oxidase, pyruvate dehydrogenase, α-ketoglutarate dehydrogenase,* etc.

- During oxidation process, FAD accepts two hydrogen atoms from substrate and gets reduced to $FADH_2$. The two nitrogen atoms of the isoalloxazine ring accept the hydrogen atoms.
- FMN is likewise reduced to $FMNH_2$.

Absorption, Transport and Storage

Ingested in form of flavoproteins. The FAD and FMN components are released from the protein complex in the stomach, and free riboflavin is released in the intestine, from which it is absorbed by an *active ATP dependent process*.

Activation of riboflavin via an ATP dependent enzyme system occurs next, resulting in the production of FMN and FAD.

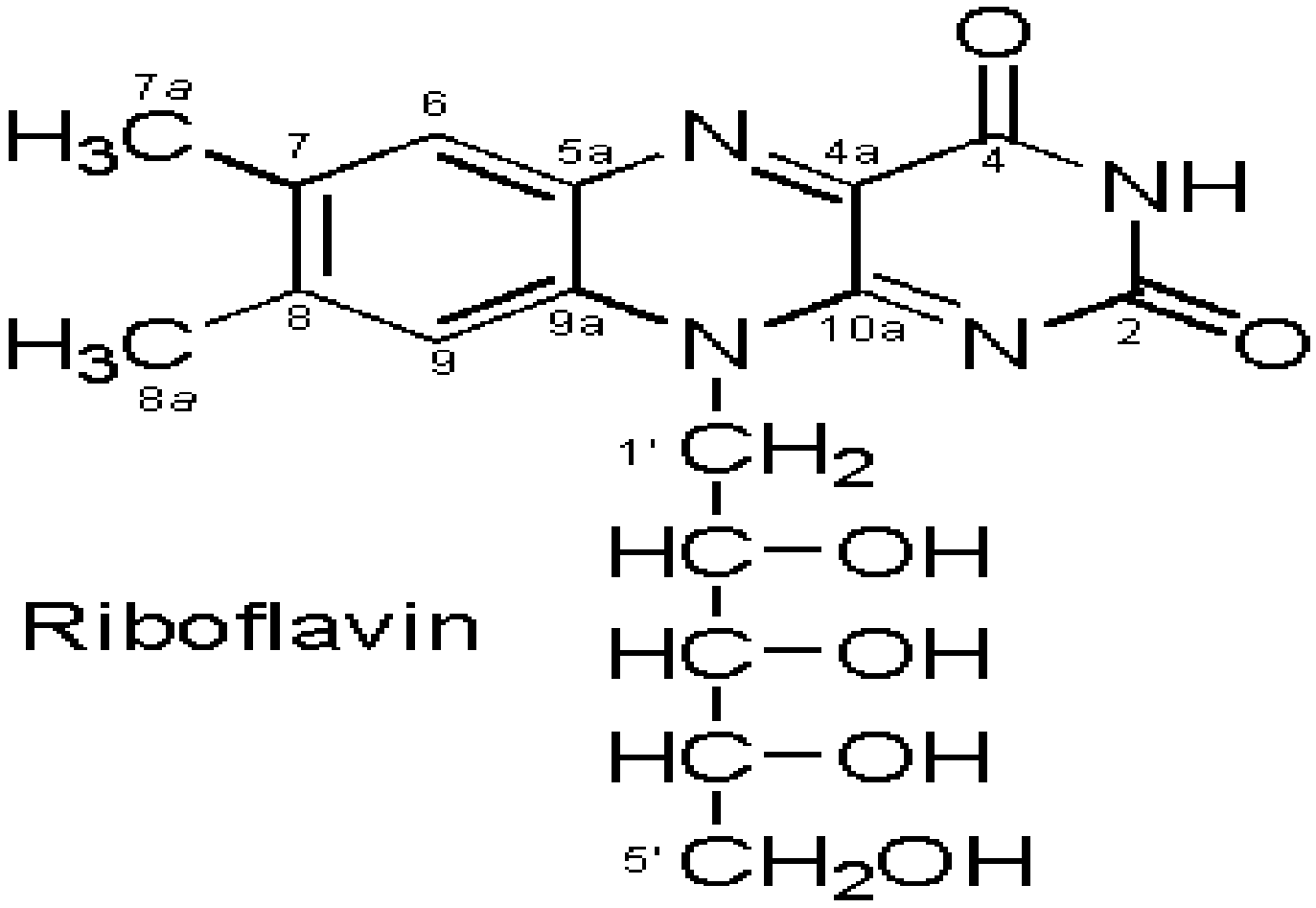
Main storage form of the vitamin, found mainly in the liver, is FAD.

Deficiency Manifestations

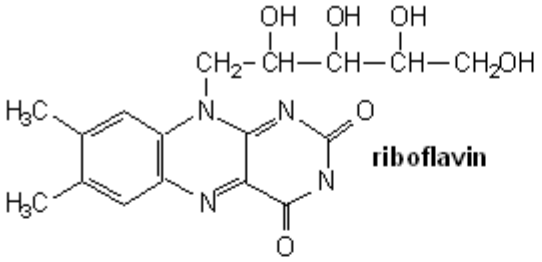
Symptoms confined to skin and mucous membranes.

- *Angular stomatitis* (inflammation of the mouth), *glossitis* (inflammation of the tongue), *cheilosis* (reddening of the mucous membrane of lips), *seborrheic dermatitis* (rough and scaly skin around nasolabial and scrotal areas), corneal vascularization, and a form of peripheral neuropathy are the prominent features.
- Condition is referred to as **ariboflavinosis**.

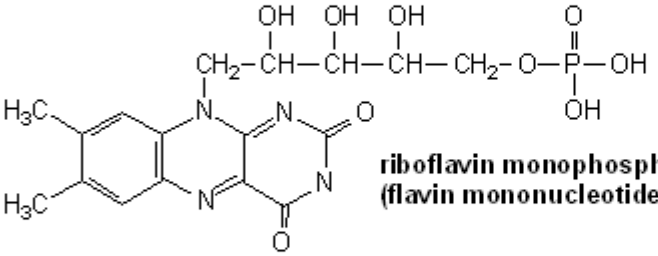
- Energy metabolism of both sugars and lipids
- Activation via an ATP-dependent enzyme system


7a
6
7
5a
N
4a
4
O
NH
H3C
8
9a
N
10a
N
2
O
H3C
9
8a
1'
CH2
HC
OH
HC
OH
HC
OH
5'
CH2OH

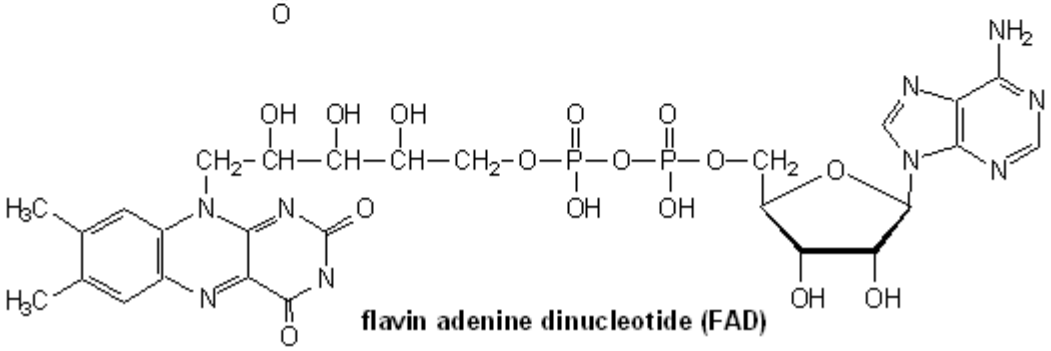
Riboflavin



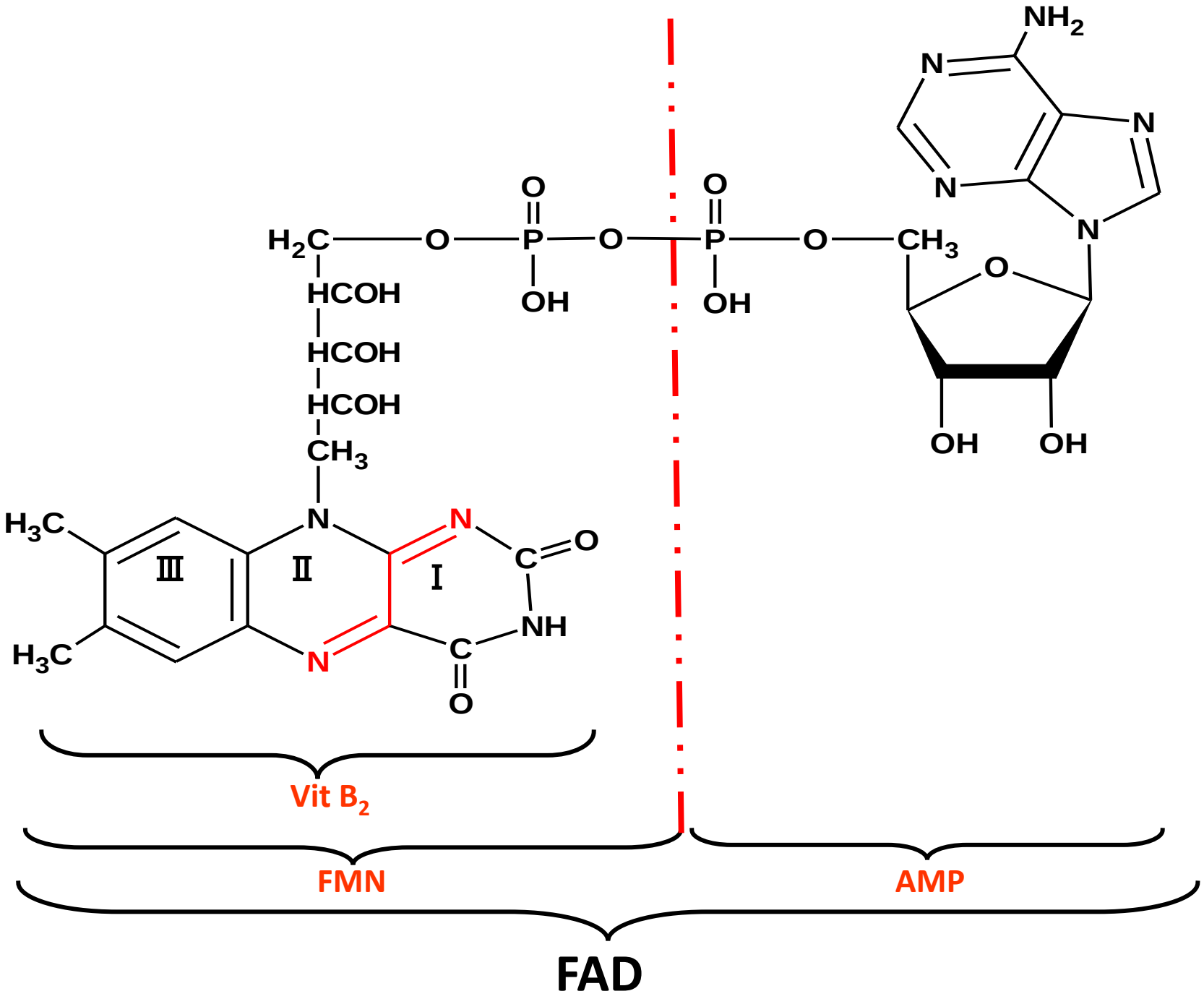
riboflavin



riboflavin monophosphate
(flavin mononucleotide, FMN)

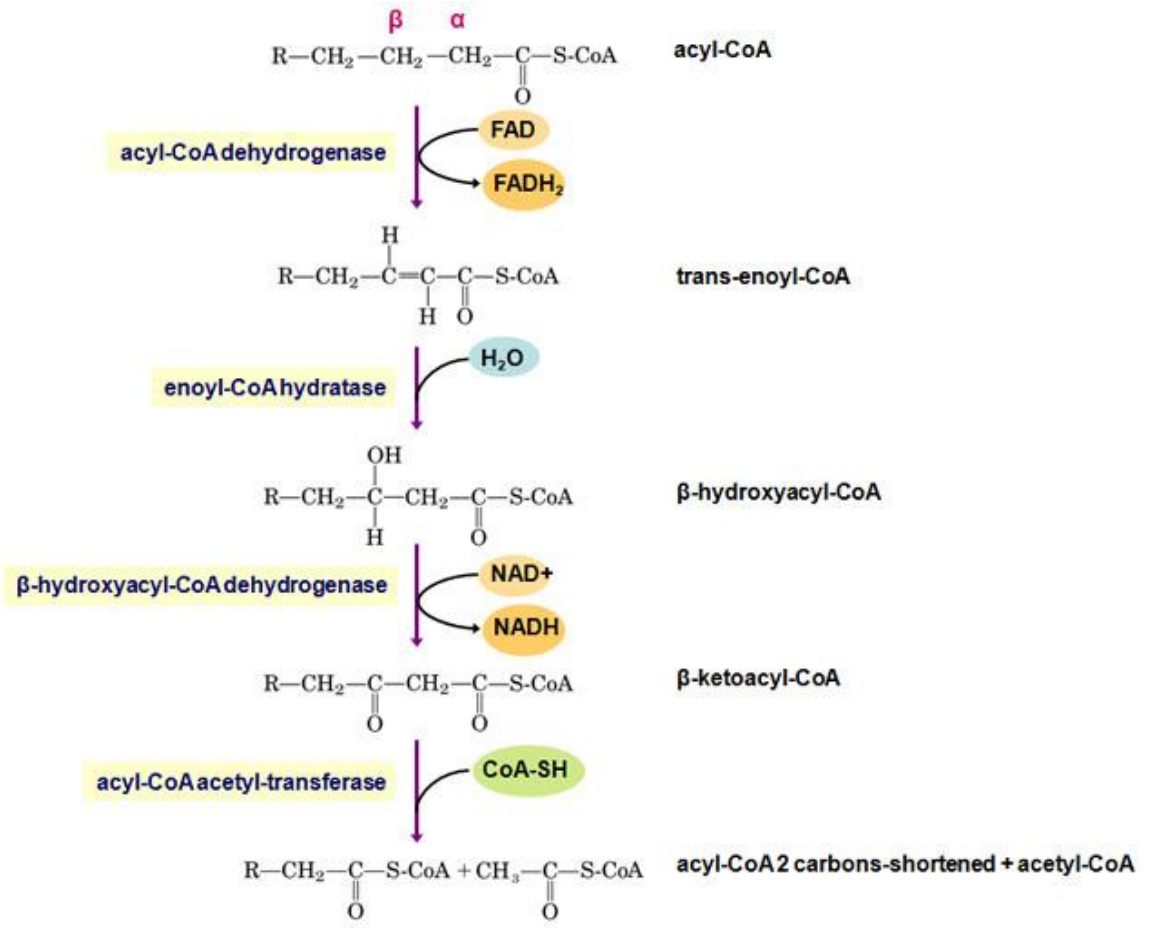


flavin adenine dinucleotide (FAD)


NH2
N
N
N
N
O
O
H2C
O
P
O
P
O
CH3
OH
OH
HCOH
HCOH
HCOH
CH3
O
OH
OH
H3C
H3C
N
N
C
O
NH
C
O
N
Ⅲ
Ⅱ
Ⅰ
Vit B2
FMN
AMP
FAD

- Produce energy
- Antioxidant working to rid the body of free radicals
- Change vitamin B_6 and folate into usable forms
- Body growth and red blood cell production

Beta Oxidation

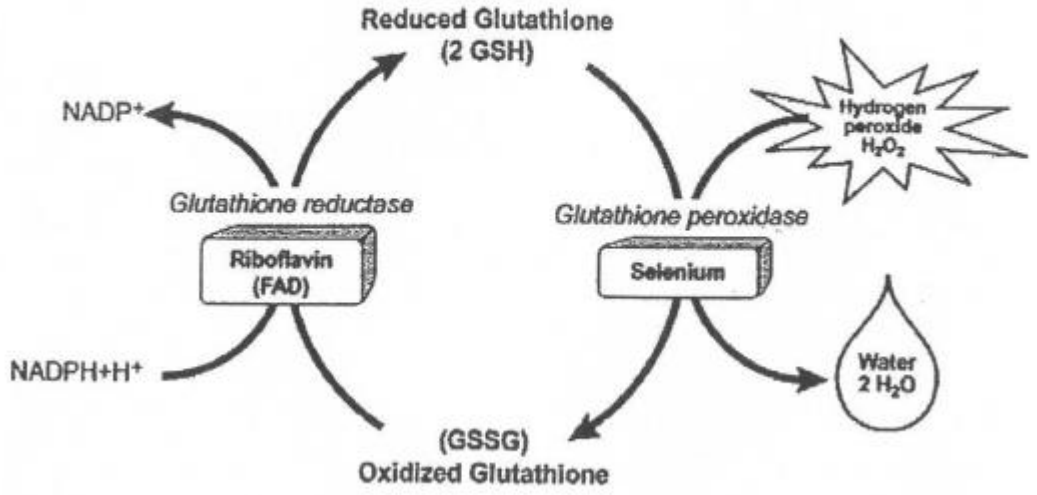


Energy production and metabolic processes in the body require the use of oxygen, however oxygen containing molecules can be highly reactive and can cause harm to many structures in the body, including blood vessel linings and joint tissues

A small protein-like molecule called glutathione helps to prevent this damage

Glutathione must be constantly recycled and vitamin B_2 allows this to happen, as it is a cofactor for the enzyme glutathione reductase, which reduces the oxidized form of glutathione back to its reduced form

The Glutathione Oxidation Reduction (Redox) Cycle



Riboflavin deficiency is quite common if dietary intake is lacking, as it is continuously excreted in the urine

Note: Riboflavin deficiency is always accompanied by a deficiency of other vitamins

- Riboflavin is light sensitive
- Phototherapy for jaundice may induce transient riboflavin deficiency in infants

Riboflavin deficiency:

- Primary-Diet poor in vitamin B_2
- Secondary-Another reason for the deficiency:

  -such as conditions that affect absorption in the intestines

  -body not being able to use the vitamin, or an increase in the excretion of the vitamin

Preventing cataracts, migraine headaches: Vitamin B_2, along with other nutrients, is important for normal vision

Sources: meat, nuts, legumes, milk, fish etc

Deficiency-Non fatal syndrome of inflammation

Diagnosis: Glutathione reductase enzyme activity

Niacin (Vit B_3)

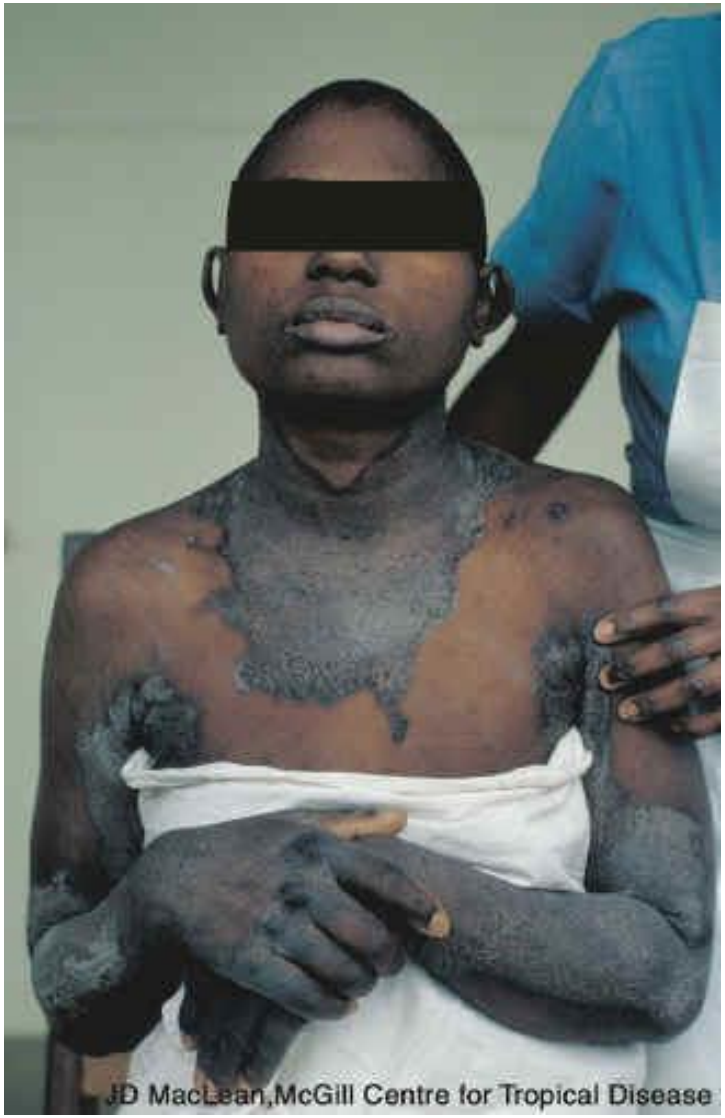
-Part of the coenzyme nicotinamide adenine dinucleotide (NAD^+) and nicotinamide adenine dinucleotide phosphate ($NADP^+$)-participate in oxidoreductase reactions

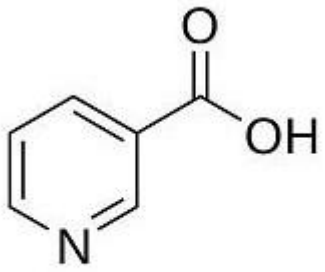
Synthesis from tryptophan not efficient

Severe deficiency (Three Ds)

- Diarrhoea
- Dermatitis
- Dementia
- Isoniazid predisposes niacin deficiency

Pellagra





Niacin

Nicotinamide

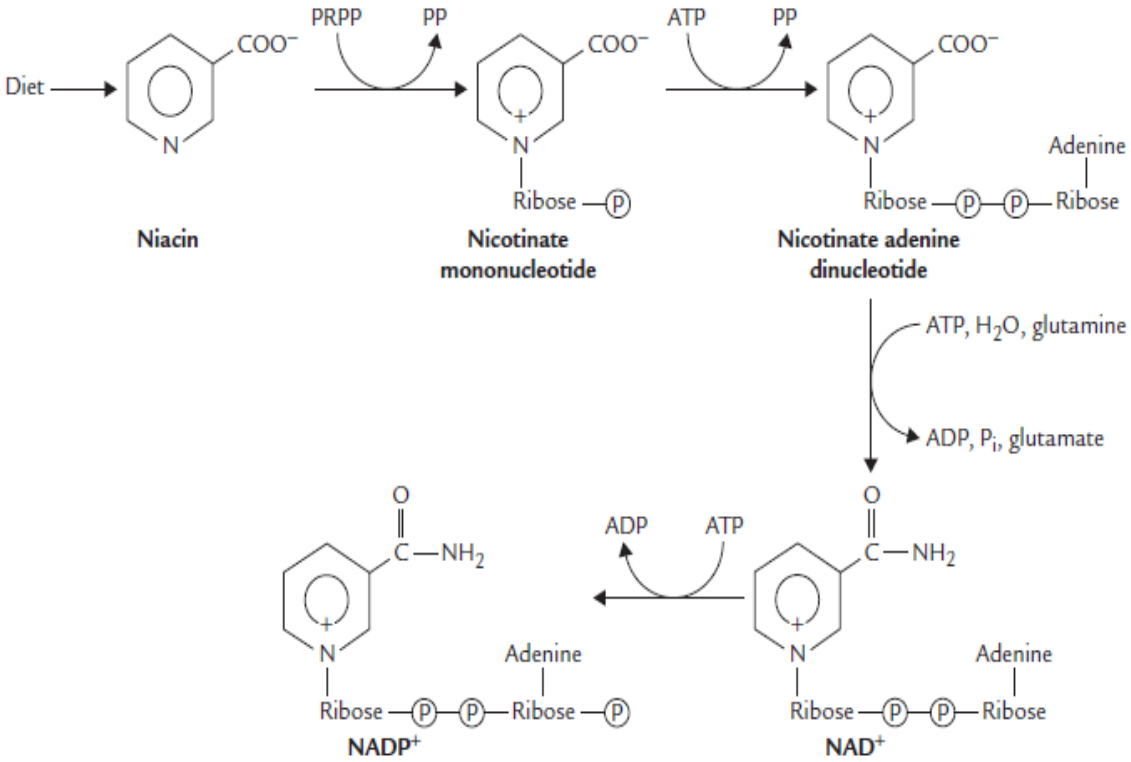
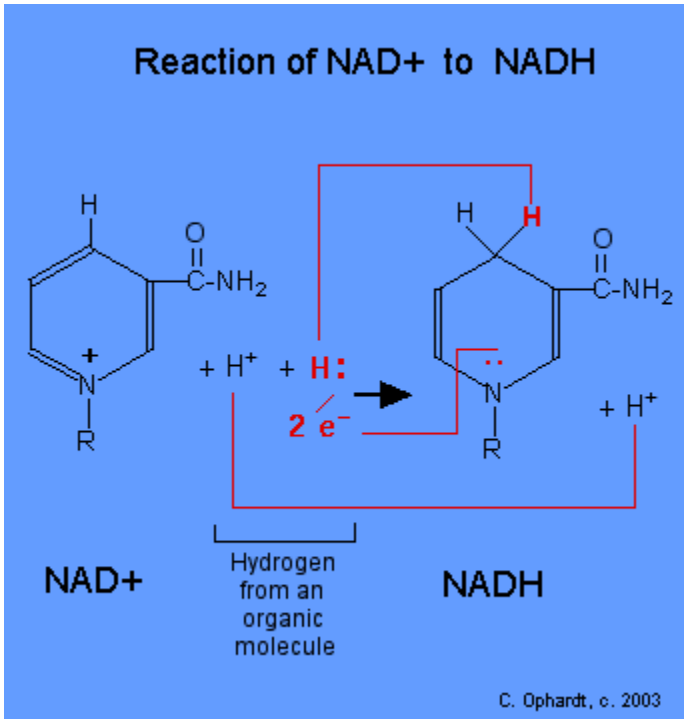
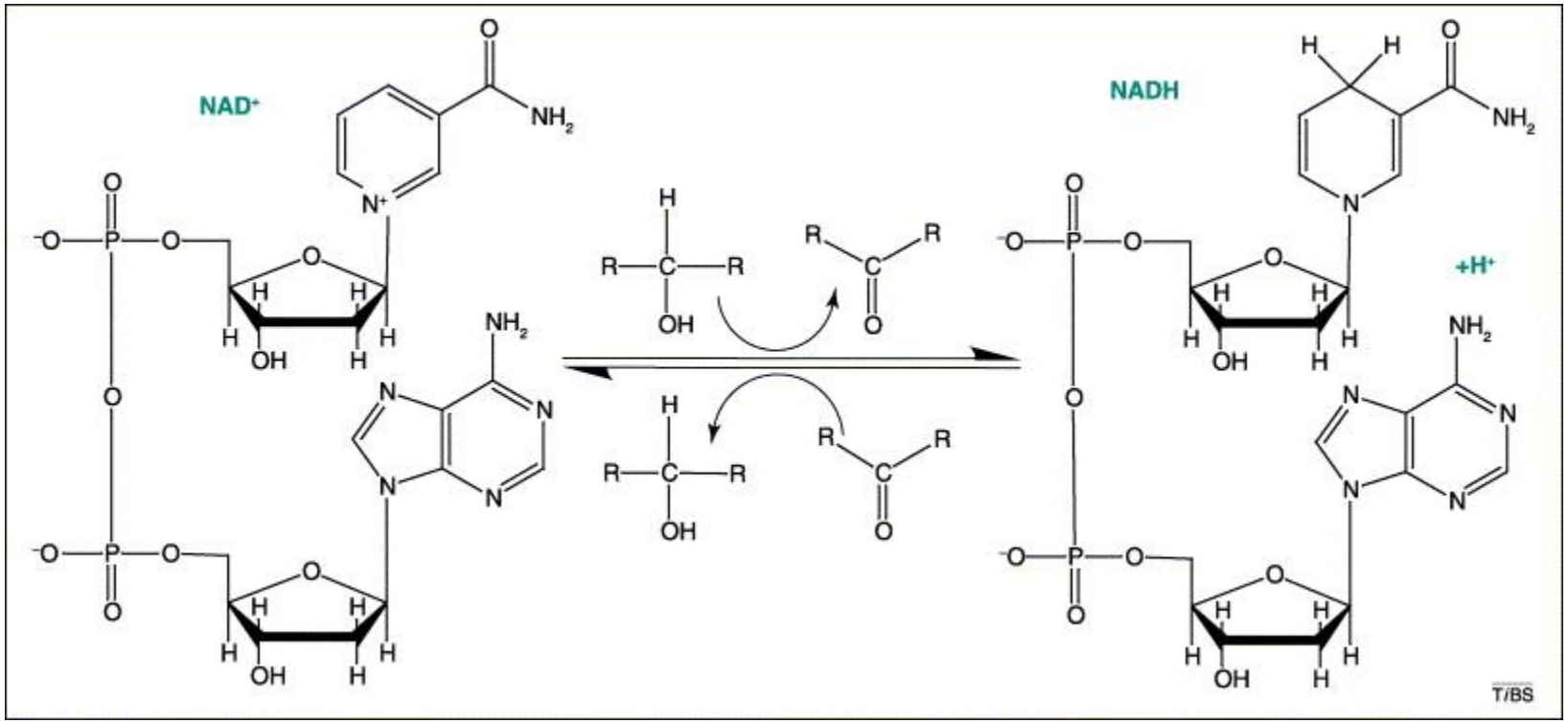


Fig: Synthesis of nicotinamide adenine dinucleotide (NAD). Attachment of a phosphate group to a 2–OH in the NAD yields NADP


Reaction of NAD+ to NADH
H
O
C-NH2
+
N
R
+ H+
+ H:
2 e−
H
H
O
C-NH2
N
R
+ H+
Hydrogen from an organic molecule
NAD+
NADH
C. Ophardt, c. 2003


NAD+
NADH
+H+
T/BS

Pyridoxine (Vit B_6)

- Mixture of pyridoxine, pyridoxal, pyridoxamine and their 5' phosphates
- Active form is Pyridoxal phosphate

-Role in amino acid metabolism implies requirements increase with increase in protein intake

- ***Absorption, Transport and Excretion***

Rapidly absorbed from the intestine by *passive diffusion*. Absorption is highly efficient: about 80% of the ingested vitamin is absorbed. Phosphorylated pyridoxine vitamers are hydrolyzed by intestinal membrane *alkaline phosphatase* and dephosphorylated forms are absorbed.

Major circulating form of vitamin B_6 is pyridoxal phosphate (PLP). Produced from the absorbed pyridoxine and pyridoxamine. Pyridoxic acid is the principal excretory form of the vitamin in urine. Its formation is catalyzed by *aldehyde oxidase*.

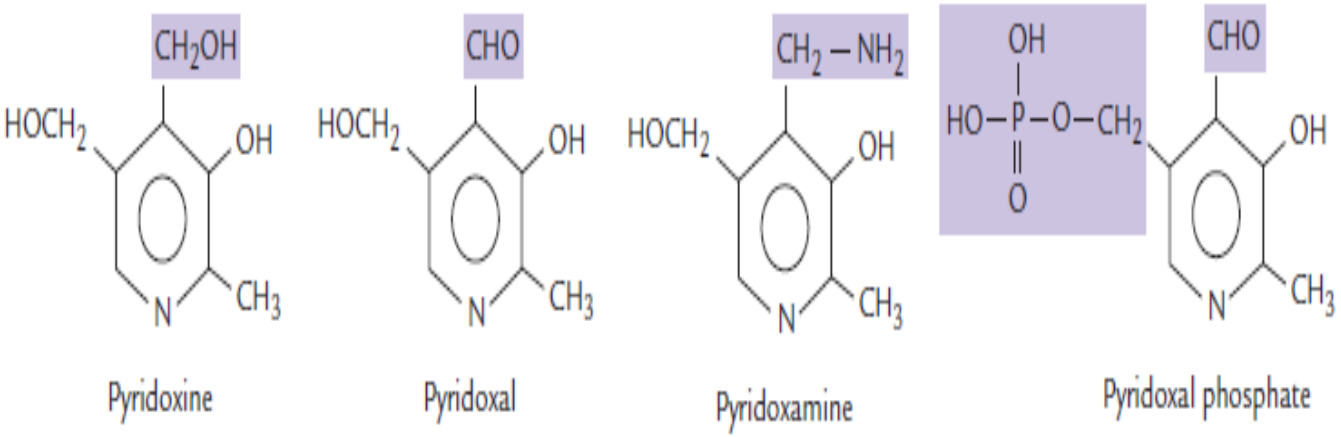


Fig. Structures of B6 vitamins. Pyridoxine is primary alcohol, pyridoxal is an aldehyde, and pyridoxamine is an amine.

Coenzyme Functions

Pyridoxal phosphate serves as a coenzyme for a broad range of reactions in intermediary metabolism, especially of amino acid metabolism where it seems to play a central role. For this reason, *requirement of B6 also increases with protein intake*. Some of the more important PLP-dependent reactions are:

1. *Transamination*: PLP is a coenzyme for *transaminases*, where it acts as an amino group carrier.

2. *Decarboxylation*: All decarboxylation reactions of amino acid metabolism require PLP. Particularly important in this respect are *glutamate decarboxylase* and *DOPA decarboxylase*. These enzymes are involved in the production of -aminobutyric acid (GABA) and catecholamine neurotransmitters (epinephrine, norepinephrine, dopamine) respectively in the nervous system.

- ***Condensation*:** Enzyme 8-*aminolevulinic acid synthase* that catalyzes joining of glycine and succinyl CoA in the haem biosynthetic pathway requires PLP as a cofactor.
- This accounts for anaemia seen in B_6 deficiency

Clinical Deficiency

Deficiency of vitamin B_6 is rare because of its widespread distribution in a variety of foodstuffs. Deficiency symptoms are most often seen in *alcoholics*, women taking oral contraceptives, and in infants fed with formula diet low in this vitamin. Probably the commonest cause of deficiency is drug antagonism. **Isoniazid**, an antitubercular drug, reacts with PLP to form a hydrazone that is biologically inactive, rapidly excreted in urine, and also inhibits *pyridoxal kinase*. Penicillamine, used in the treatment of Wilson's disease and rheumatoid arthritis, also combines with PLP to render it unavailable.

Major symptoms of B_6 deficiency include neural dysfunction and anaemia. The former is accounted by an impairment in the synthesis of neurotransmitters such as norepinephrine and serotonin. Anaemia is accounted by impairment of haem biosynthesis. Other features of B_6 deficiency include lesions of the skin and mucosa, *sideroblastic anaemia* and personality changes.

In rare instances, vitamin B_6 can be toxic and cause convulsions at very high levels. Possible mechanism is by enhancing decarboxylation of L-DOPA in several tissues. In patients treated for parkinsonism, efficiency of DOPA is thereby reduced

- Diagnosis
  - –Aspartate transaminase in RBCs

- Severe deficiency-Anemia

- Biotin
  - Intestinal flora
  - Co-enzyme in multienzyme complexes involved in carboxylation reactions
    - Lipogenesis-formation of fatty acids from acetyl coA
    - Gluconeogenesis

- Avidin in raw eggs binding to biotin
- Inherited single or multiple carboxylase deficiencies
- Immunodeficiency disease

Deficiency: Prolonged use of antibacterial drugs

- Sources: Normal bacterial flora of the gut
- Ubiquitously distributed- plants, animal tissues-Liver, yeast, peanut, soybean, milk, egg yolk

Cobalamin (Vitamin B_{12})

Contains one Cobalt atom coordinated with 4 pyrrole rings

Function related to that of folate

Deficiency produces same signs and symptoms

Found only in foods of animal origin

Ascorbic Acid (Vitamin C)

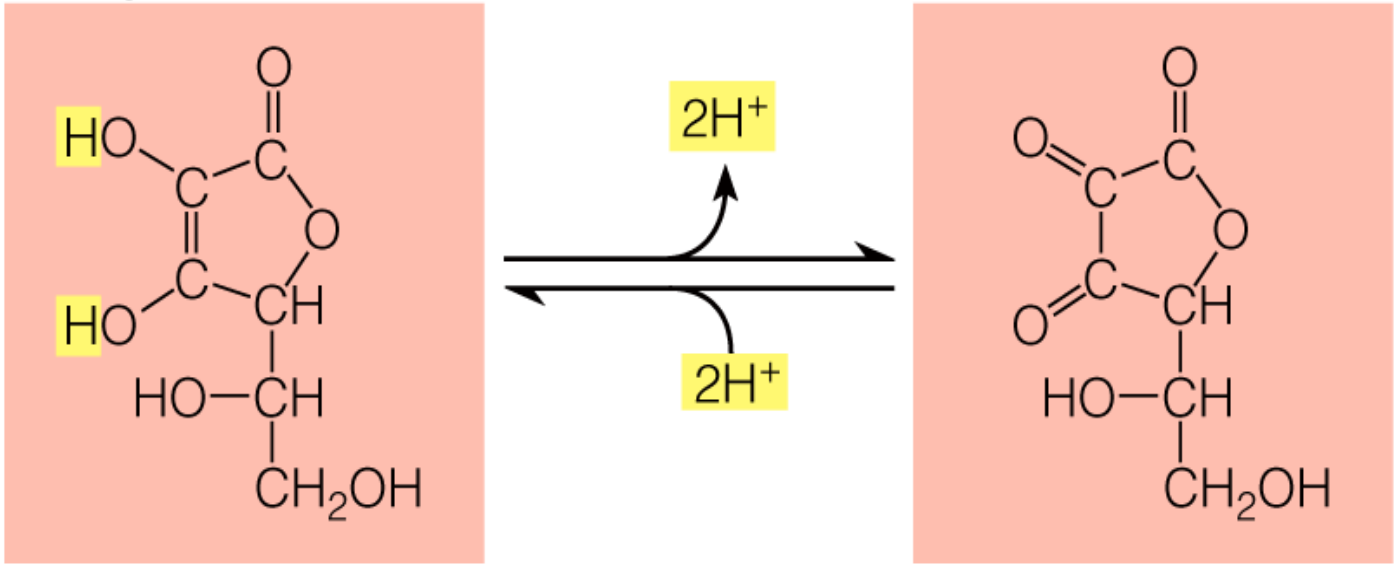
Easily destroyed by heat, alkali and storage

Process of cooking 70% of vitamin C is lost

Structural formula closely resembles that of carbohydrates. Reducing property depends on double bonded carbons

Only L has activity

- Man, higher primates, guinea pigs and bats unable to synthesize ascorbic acid from glucose because of block in gulonolactone oxidase step



Ascorbic acid protects against oxidative damage by donating its two hydrogens with their electrons to free radicals (molecules with unpaired electrons). In doing so, ascorbic acid becomes dehydroascorbic acid.

Dehydroascorbic acid can readily accept hydrogens to become ascorbic acid. The reversibility of this reaction is key to vitamin C's role as an antioxidant.

- Functions
  - Collagen synthesis (strengthens blood vessel walls, provides matrix for bone growth)-post-translational hydroxylation of proline and lysine
  - Antioxidant-prevents cancer formation
  - Steroid synthesis-Initial step stimulated by the vitamin C

- Amino acid metabolism-hydroxylation of tryptophan to 5-hydroxyl tryptophan- formation of serotonin.
- Oxidation of parahydroxyphenyl pyruvate to homogentisic acid
- Helps in absorption of iron-Reduces ferric acid to ferrous state

- Strengthens resistance to infection- Stimulates phagocytic action of leukocytes and formation of antibodies
- Cataract- Regular intake reduces the risk of cataract formation

- Hemoglobin metabolism- reconversion of met-hemoglobin to hemoglobin
- Folic acid metabolism-Folate reductase to reduce folic acid to tetrahydrofolic acid

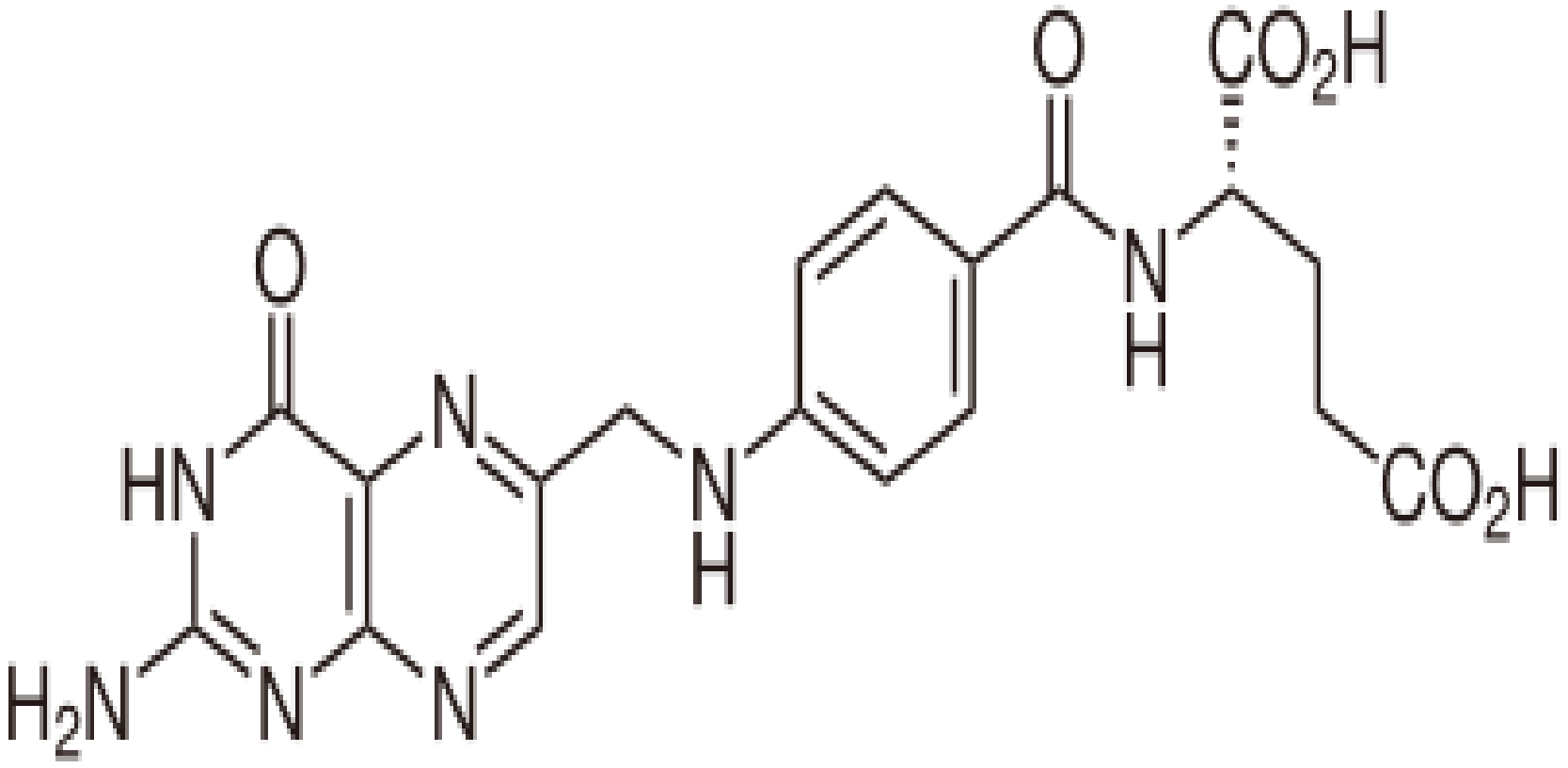
- Food Sources
  - Citrus fruits (oranges, grapefruits, tangerines, lemons, limes)
  - Cabbage-type of vegetables; Dark green vegetables (such as bell peppers and broccoli)
  - Strawberries and other berries, melons, papayas, mangoes, potatoes and tomatoes

- Deficiency-scurvy-defective collagen synthesis
- Collagen gives tensile strength to fibers- necessary for normal production of supporting tissues

Symptoms

- Anemia, atherosclerotic plaques, pinpoint hemorrhages
- Bone fragility, joint pains
- Poor wound healing, frequent infections
- Bleeding gums, loosened teeth
- Muscle degeneration and pain
- Hysteria, depression
- Rough skin, blotchy bruises

FOLIC ACID



- DNA synthesis, repair DNA, and methylate DNA as well as a coenzyme in certain biological reactions

- Aiding in rapid cell division and growth, such as in infancy and pregnancy

(Children and adults both require folate to produce healthy red blood cells and prevent anemia)

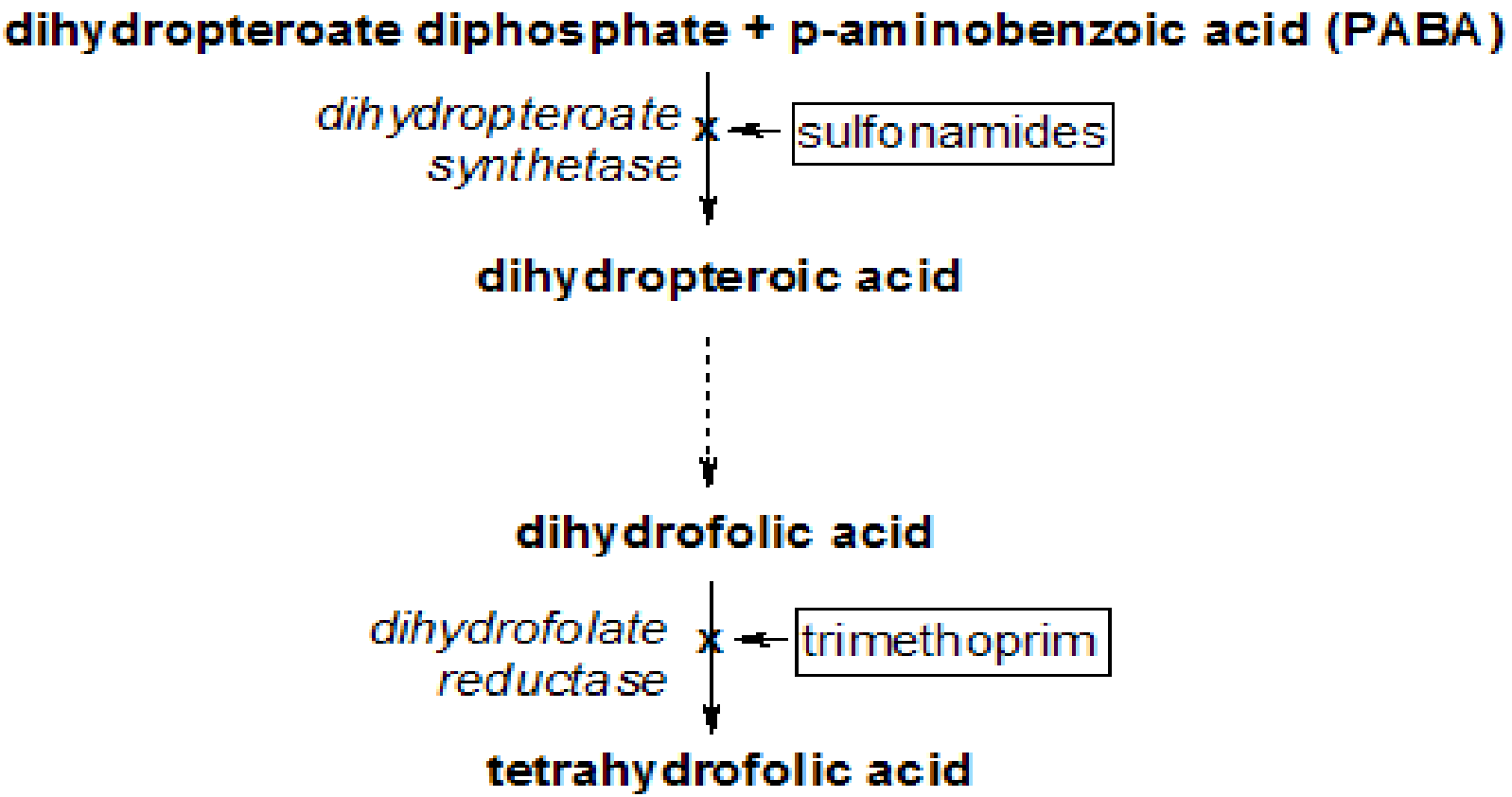
Deficiency:

- Neural tubule defects in developing embryo
- Nerve damage and limb numbness

Folate is important for cells and tissues that rapidly divide

Cancer cells divide rapidly, and drugs that interfere with folate metabolism are used to treat it

The anti-folate, methotrexate, is a drug often used to treat cancer because it inhibits the production of the active form of THF from the inactive dihydrofolate (DHF)


dihydropteroate diphosphate + p-aminobenzoic acid (PABA)
dihydropteroate synthetase
sulfonamides
dihydropteroic acid
dihydrofolic acid
dihydrofolate reductase
trimethoprim
tetrahydrofolic acid

However, methotrexate can be toxic, producing side effects, such as inflammation in the digestive tract that makes it difficult to eat normally. Also, bone marrow depression

Vitamins

- Most metabolic processes require vitamins
  - Many co-enzymes are composed of vitamins that help enzymes function

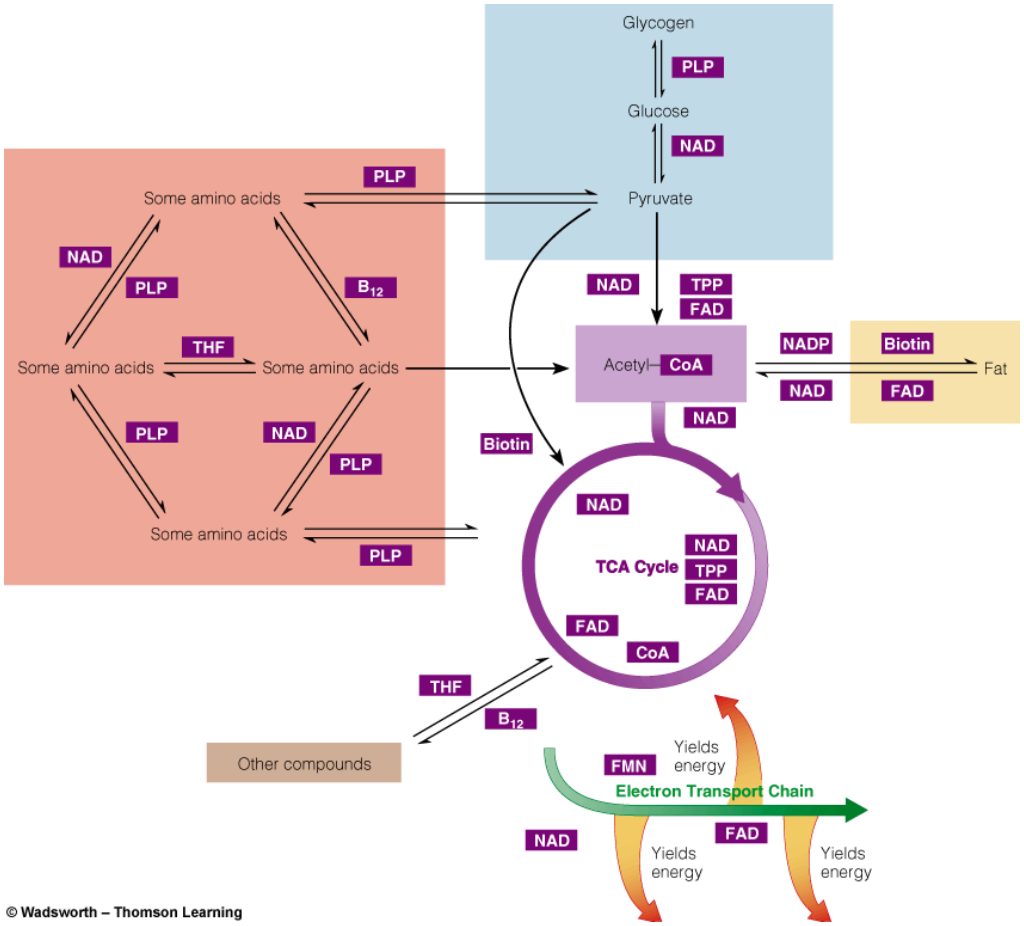


TABLE 8.9 Water-Soluble Vitamins

Vitamin	Coenzyme	Typical reaction type	Consequences of deficiency
Thiamine (B_1)	Thiamine pyrophosphate	Aldehyde transfer	Beriberi (weight loss, heart problems, neurological dysfunction)
Riboflavin (B_2)	Flavin adenine dinucleotide (FAD)	Oxidation–reduction	Cheliosis and angular stomatitus (lesions of the mouth), dermatitis
Pyridoxine (B_6)	Pyridoxal phosphate	Group transfer to or from amino acids	Depression, confusion, convulsions
Nicotinic acid (niacin)	Nicotinamide adenine dinucleotide (NAD^+)	Oxidation–reduction	Pellagra (dermatitis, depression, diarrhea)
Pantothenic acid	Coenzyme A	Acyl–group transfer	Hypertension
Biotin	Biotin–lysine complexes (biocytin)	ATP-dependent carboxylation and carboxyl-group transfer	Rash about the eyebrows, muscle pain, fatigue (rare)
Folic acid	Tetrahydrofolate	Transfer of one-carbon components; thymine synthesis	Anemia, neural-tube defects in development
B_{12}	5′-Deoxyadenosyl cobalamin	Transfer of methyl groups; intramolecular rearrangements	Anemia, pernicious anemia, methylmalonic acidosis
C (ascorbic acid)		Antioxidant	Scurvy (swollen and bleeding gums, subdermal hemorrhages)

Name	Daily requirement	Deficiency disease	Dietary sources
Water-soluble			
• Vitamin B_1 (Thiamine)	1.0–1.5 mg	Beriberi and Wernicke–Korsakoff syndrome	Legumes, pork, liver, nuts, the germ of cereals, yeast and outer layers of seeds.
• Vitamin B_3 (Niacin)	12–20 mg	Pellagra	Unrefined grains, yeast, liver, legumes and lean meat.
• Vitamin B_2 (Riboflavin)	1.1–1.5 mg	Ariboflavinosis (rare)	Milk, eggs, liver, and green leafy vegetables.
• Vitamin B_6 (Pyridoxine)	1.6–2 mg on a 100 g protein diet	Rare	Whole-grain cereals, wheat, corn, nuts, muscle meat, liver and fish.
• Pantothenic acid	5–10 mg	Rare	Yeast, liver and eggs
• Vitamin B_7 (Biotin)	5 µg/1000 kcal	Rare	Liver, kidney, milk, egg yolk, corn, and soya milk.
• Vitamin B_{12} (Cyanocobalamin)	3 µg	Pernicious anaemia	Liver, kidney, meats and milk
• Folic acid	400 µg	Megaloblastic anaemia	Liver, yeast and green vegetables.
• Vitamin C (Ascorbic acid)	45 mg	Scurvy	Citrus fruits, potatoes, particularly the skin, strawberries, raw or minimally cooked (green) vegetables and tomatoes; amla is the richest source.

Table: Dietary sources and daily requirement of vitamins and the attendant deficiency diseases

Name	*Co-enzyme form*	*RDA*	*Main reaction using the co-enzyme*	*Deficiency disease*
Folic acid	Tetrahydrofolic acid (THFA)	200 µg	One carbon group carrier	Macrocytic anemia Hyperhomocysteinemia
Cyanocobalamin (B_{12})	Adenosyl B_{12}, methyl cobalamin	1–2 µg	Isomerization of methyl malonyl, CoA, remethylation of homocysteine to methionine	Megaloblastic anemia, subacute combined degeneration, methylmalonic aciduria, hyper-homocyeinemia
Ascorbic acid	No specific form	75 mg	Antioxidant property due to its reducing action, hydroxylation of collagen	Scurvy

Note: The requirements are significantly higher in pregnancy and lactation. See also Table 37.1 for other water soluble vitamins.

TABLE: Summary of water soluble vitamins

Fat soluble

- Vitamin A, D, E and K
  - Contain rings and long aliphatic side chains
  - Hydrophobic
  - Absorbed in the intestines
  - Differ widely in their functions
  - Research on mechanisms slow

- Not readily absorbed or extracted from the diet
- Ample amounts stored in tissues
- Not act as coenzymes except Vitamin K

Vitamin A- 20 carbon molecule

- Exists as retinol, retinal and retinoic acid
- All found in animals
- Stored in the liver as esters of fatty acids

- Three forms of Vitamin A-important biological functions
  - –Retinol and Retinoic acid-signal compounds, bind receptor proteins inside cells
    - Ligand-receptor complex regulate gene expression during cell differentiation

  Retinal-light sensitive-important role in vision

Antioxidant role prevents the development of diseases in which the action of free radicals is implicated

Plays a protective role against cancer and cardiovascular disease

Vitamin A is necessary for vision mediated by the rod cells,

Deficiency often presents as “Night blindness,” the first symptom of Vitamin A deficiency

- Role in reproduction-in rats
- Role in epithelialisation
  - Dry skin, conjuctivae, cornea (xerophthalmia)

  Role in respiratory tract- dry tract leads to susceptibility to infection and lowered resistance to disease

  Role in Urinary tract

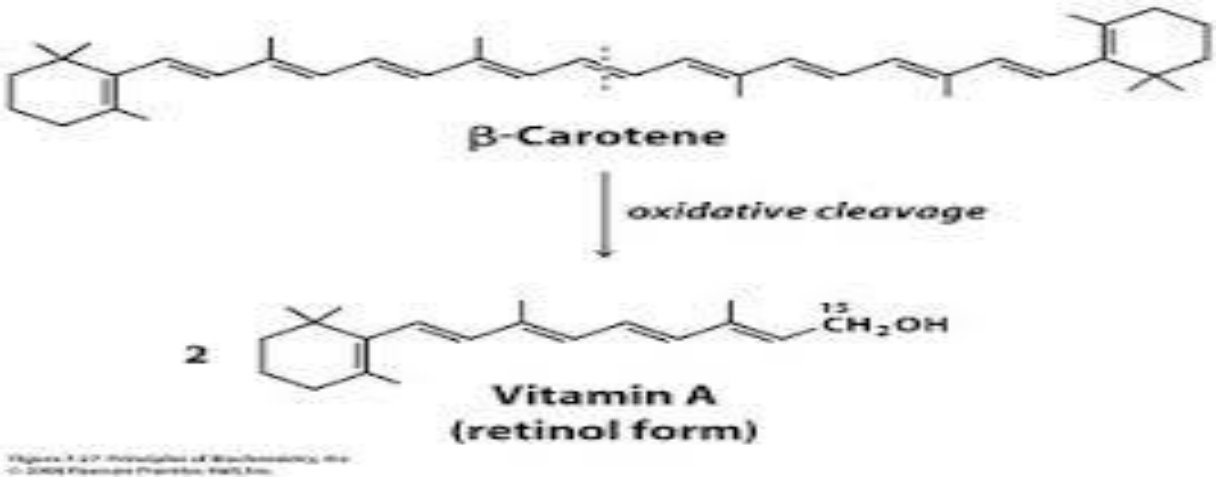
  Role in bone and teeth formation, growth, metabolism of DNA

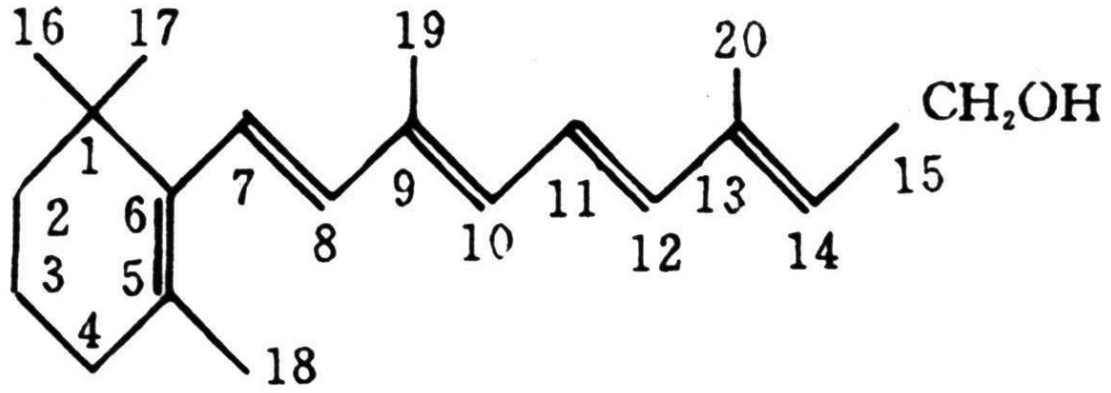
- Hypervitaminosis
  - Alteration of the skin
  - Hepatic dysfunction etc

Common cause of blindness in the world

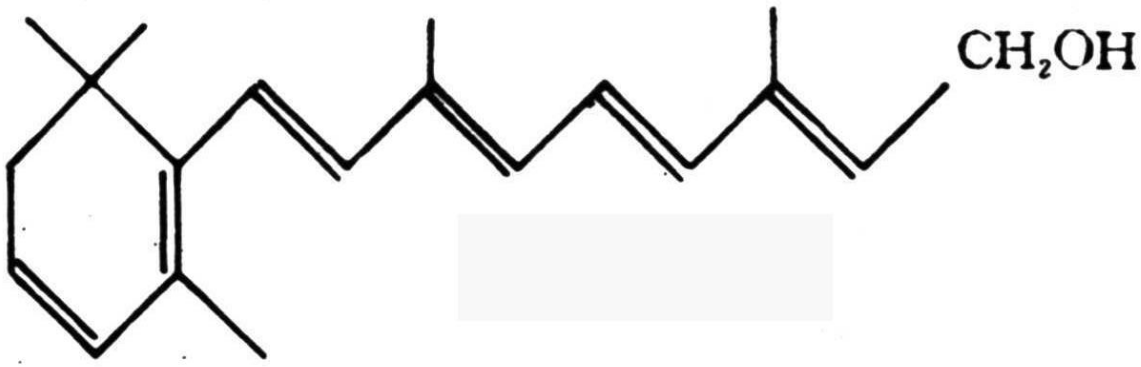
- Sources: liver, egg yolk, milk products
- Carrots and yellow vegetables rich in β-carotene (40-carbon plant lipid)

- Enzymatic oxidative cleavage



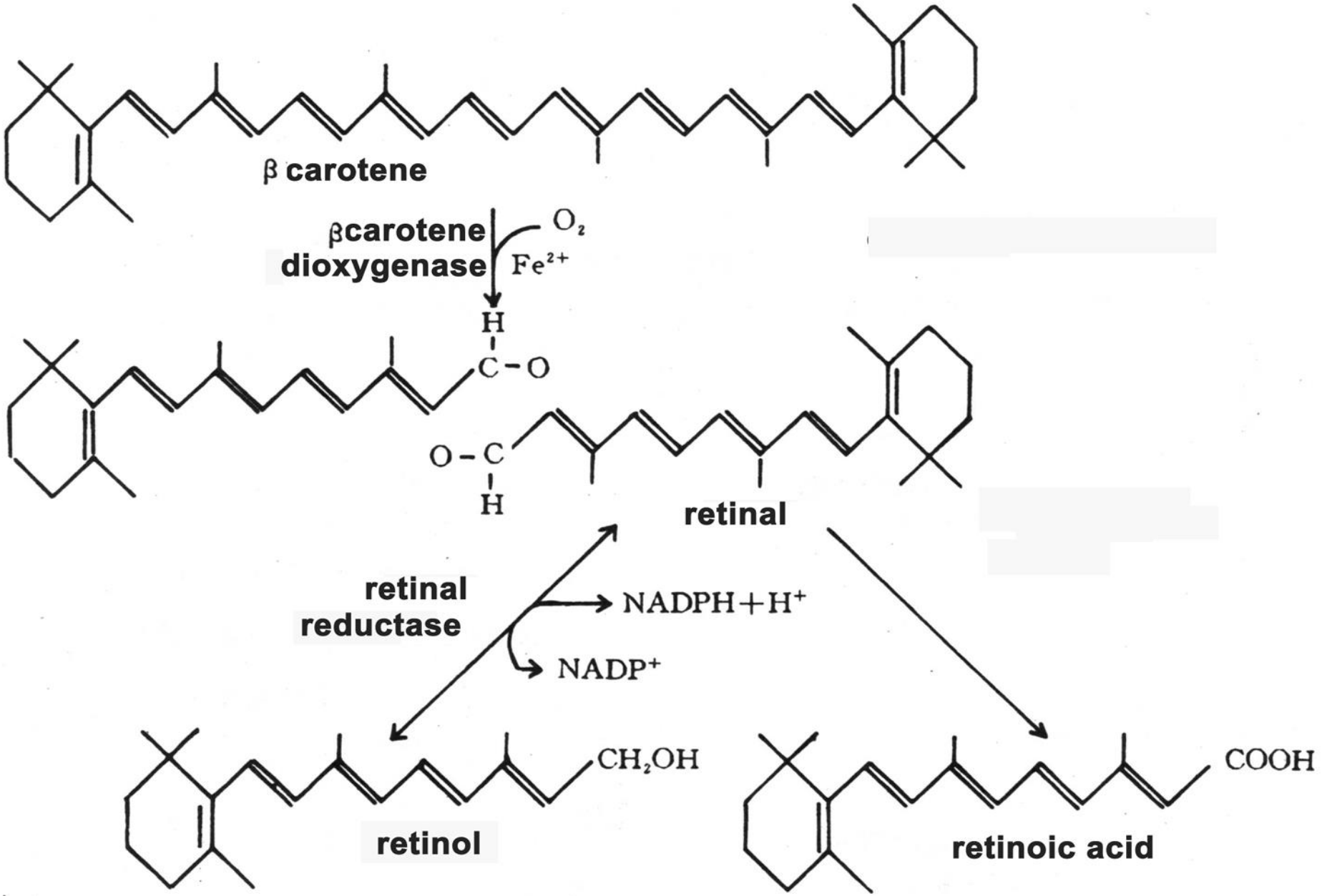


retinol (vitamin A_1)



3-dehydro-retinol (vitamin A_2)

Chemical structure of vitamin A1 and vitamin A2



oxidation of carotene to retinal in intestine and conversion to retinol and retinoic acid

- Vitamin D: Group of related lipids.
  - Human exposure to sufficient sunlight- Vitamin D_3 (cholecalciferol)
  - 7-dehydrocholesterol formed from cholesterol in the intestinal mucosa and liver
  - Passed on to the skin-undergoes activation to vitamin D3

- Two hydroxylation reactions of D_3 gives 1, 25-dihydroxycholecalciferol (activated)
- Both 1, 25-dihydroxycholecalciferol and D_2 are hormones- help control Ca^{2+} utilization in humans- regulates both intestinal absorption of calcium and its deposition in bones

Usually, deficiency due to insufficient exposure to sunlight

-inadequate dietary intake, GI disorder

Rickets-characterized by the production of soft pliable bones due to defective mineralization secondary to calcium deficiency

Osteomalacia- soft bones in adults

Vitamin D deficiency is also characterized by low concentration of calcium in blood in association with increased serum alkaline phosphatase

Vitamin E (α-tocopherol)- Anti-sterility vitamin

Deficiency is rare, except in pregnancy and the new born, where it is associated with hemolytic anemia

- Nature’s most potent and most abundant biological antioxidant (membrane antioxidant)

Main function of Vitamin E is as an antioxidant (prevention of hemolysis of RBC by hydrogen peroxide)

may be located near enzyme complexes that produce free radicals, such as *NADPH-dependent oxidase* systems

- Anti-atherogenic role: Inverse relationship between Vitamin E intake and incidence of morbidity and mortality from coronary artery disease
- Retards oxidation of LDL- decreasing production of pro-atherogenic ox LDL
- Impedes various cellular signaling pathways

- Boosts immune response
- Slows aging process
- Appears to offer protection against Alzheimer’s disease

- Defective lipid absorption and transport may cause deficiency

Vitamin K

- –Only one that acts as coenzyme among fat soluble vitamins
- -Involved in the clotting of blood (coagulation)
- Posttranslational processing of several proteins required in coagulation cascade

- Formation of mature clotting factors requires that glutamyl residues of precursor proteins be converted to γ-carboxylglutamate residues by addition of carboxylate group. Reaction dependent on Vitamin K which serves as a coenzyme

Deficiency: Rare

Causes:

- Due to treatment that eliminates normal intestinal flora
- Fat malabsorption syndromes
- Liver diseases
- Vitamin K antagonists-dicoumarin or warfarin (competitive inhibitors of Vitamin K)

New born: Hemorrhagic disease- most common nutritional deficiency in new borns because of inadequate vitamin K stores

TABLE 8.10 Fat-soluble vitamins

Vitamin	Function	Deficiency
A	Antioxidant	Inhibition of sperm production; lesions in muscles and nerves (rare)
D	Regulation of calcium and phosphate metabolism	Rickets (children): skeletal deformaties, impaired growth Osteomalacia (adults): soft, bending bones
E	Roles in vision, growth, reproduction	Night blindness, cornea damage, damage to respiratory and gastrointestinal tract
K	Blood coagulation	Subdermal hemorrhaging

The function and deficiency of A and E are switched.

MINERALS

Students should be able to understand:

- Absorption, transport and excretion of minerals.
- Mineral deficiency or excess: causes and consequences.
- Sources and daily requirements of minerals.
- Major elements: physiological role of sodium, potassium, magnesium.
- Trace elements: physiological role and deficiency disorders of iron, copper, magnesium, zinc, selenium, and molybdenum.

One of the 2 major classes of biologically critical micronutrients

Required for normal health and development

Need both macro and micronutrients for maintenance of all metabolic and developmental processes

Correlation between micronutrient deficiency and development of chronic metabolic disruption

- Supplementation with vitamins-deficiencies reduced and less common
- Minerals too, although not rigorously supplemented

Functions are numerous:

- Either quite broad or highly specific
- Activators of complex biochemical reactions in tissues
- Cofactors for enzymes

Inorganic elements

Serve a variety of functions:

- -cofactors in enzyme catalysed reactions
- -regulation of acid-base balance
- -nerve conduction and muscle irritability
- -structural elements in the body

- Macrominerals (Major)>100mg/day
- Microminerals (Minor) (Trace minerals)<100mg/day

Macrominerals

- Calcium
- Potassium
- Sodium
- Magnesium
- Chloride
- Phosphate
- Sulphur

Trace minerals

- Copper
- Iodine
- Iron
- Manganese
- Selenium
- Zinc

- Intestinal absorption difficult
  - Complex with phytates or fibres
  - Special carrier proteins needed
  - Synthesis of carrier proteins serves as an important mechanism for control of mineral levels

– A few minerals circulate in free unbound form- others require specific binding proteins

- Transferrin for Iron circulation
- Apoferritin protein for storage of Iron

Excretion- renal or the hepato-biliary route

Deficiency or Excess-Potentially hazardous

- Circulating levels: net result of absorption, utilization, storage and excretion
- Loss of control leads to deficiency or excess

Iron deficiency may be due to:

- Reduced dietary intake
- Decreased intestinal absorption
- Excessive loss due to bleeding

- Iron deficiency- Microcytic hypochromic anaemia
- Excess iron-Functional impairment of the liver and pancreas (hemochromatosis)
- Copper overload-Wilson’s disease

Sodium

Principal cation of the extra-cellular compartment

About *50 mmol/kg body weight* of sodium present in human body

- 50% is present in bones
- 40% in extracellular fluids
- 10% in soft tissues
- Plasma-135-145 mmol/L. Other extracellular fluids are also rich in sodium.
- Intracellular fluid concentration-about 35 mmol/L

Biochemical Functions

- Maintenance of irritability of excitable tissues
- Regulation of osmotic pressure and pH of body fluids and in membrane transport.

Neuromuscular excitability: Sodium, together with potassium (the other monovalent cation), increases the neuromuscular excitability; this is counterbalanced by the effect of the divalent cations, calcium and magnesium. The cations are distributed across the cell membrane of nerve fibres in such a way that the membrane exterior is slightly positive compared to the interior. This sets up a potential difference, known as the *resting potential*.

- When a stimulus is applied, the localized area becomes permeable to sodium, resulting in inward movement of these ions. Such an influx of positive ions results in the interior becoming slightly electropositive in relation to the exterior (i.e. *action potential*).

Fluid balance: Being the major cation of extracellular fluid, sodium plays an important role in maintenance of osmotic pressure, and thus helps to retain water in ECF.

Acid-base balance: In form of sodium bicarbonate, sodium is a component of the bicarbonate buffer. The latter is the chief buffer system in the extracellular fluid. The sodium-potassium exchange in renal tubules helps to acidify urine.

Membrane transport: Active absorption of a number of substances across the membranous barrier requires sodium cotransport. This is termed the secondary active transport

Absorption and Elimination

- Sodium absorption occurs throughout the small and the large intestine. Because sodium concentration in the intestinal fluid (145 mmol/L) is several folds higher than that in the intestinal mucosal cells (10 mmol/L), sodium passively diffuses into the cell. The intracellular sodium is then actively moved into the plasma by sodium pump through expenditure of ATP energy.

Sodium is eliminated from the body via urine. It is a meticulously regulated process, in which *mineralocorticoids* (e.g. aldosterone) play a major role: they act at distal convoluted tubules to cause retention of sodium and loss of potassium from the body. *Glucocorticoids* and *sex hormones* also have the same effect, but they are far less potent than aldosterone.

Requirement and Dietary Sources

- Normal diet contains sodium, mainly in form of table salt (sodium chloride), though meat, fish, eggs, milk, cheese, cauliflower, spinach, legumes and nuts are also good sources. **Excessive intake must be guarded against since it has been shown to lead to hypertension.**

Disturbances of Serum Sodium

Hyponatraemia: Serum sodium level falls below normal. It can be caused by (a) excess sodium loss or it may be (b) secondary to excessive water retention (*dilutional hyponatraemia*).

Hypernatraemia: Condition in which serum sodium level is elevated. It may occur as a result of excessive loss of water relative to the sodium loss in the body. Some more common conditions are Cushing's disease, hyperaldosteronism, prolonged cortisone therapy, dehydration and nephrogenic diabetes insipidus.

Raised blood pressure and blood volume are important manifestations of hypernatraemia

Potassium

- Potassium-chief intracellular cation. Body content of potassium is about 40 mEq/kg body weight, nearly 98% of which is located intracellularly. The extracellular concentration is much smaller (about 5 mmol/L) than the intracellular concentration of 145 mmol/L (Table).

	Na^+ (chief EC cation)	K^+ (chief IC cation)
Extracellular (EC) concentration	140 mmol/L	5 mmol/L
Intracellular (IC) concentration	35 mmol/L	145 mmol/L

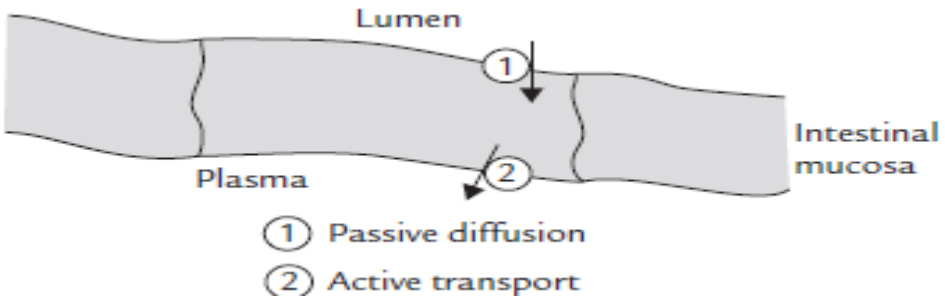


Table. Distribution of Na^+ and K^+ (cations) in body fluids. Concentration of these cations are given in mmol/L (mean values)

Biochemical Functions

Functions of potassium in the body include regulation of neuromuscular excitability, contraction of the heart, intracellular fluid volume and hydrogen ion concentration.

Neuromuscular excitability: Together with sodium, potassium helps maintenance of normal excitability of nerves and ensures smooth conduction of nerve impulses.

Contraction of heart: The potassium concentration in the ECF has a major influence on the contraction of cardiac muscles. A high concentration leads to slowing of heart rate, electrocardiographic abnormalities and possibly cardiac arrhythmia. These may be due to lowering of the membrane potential, which decreases the cell's action-potential intensity.

A low concentration of K increases the membrane potential, decreases irritability, and produces other ECG abnormalities and muscle paralysis. The heart may cease to contract in extreme cases.

- ***Intracellular fluid volume:*** Potassium in the cell maintains intracellular osmotic pressure and hence, intracellular fluid volume. Nearly half the ICF osmolarity is due to potassium.
- ***Hydrogen ion concentration:*** The potassium concentration has a significant influence on hydrogen ion concentration in the blood. Movement of K^+ into a blood-cell is normally counter-balanced by movement of H^+ out of the cell. In hypokalaemia (low serum potassium), these counter-balanced movements are decreased, and less H^+ moves out of cell. The hydrogen ion concentration is, therefore, decreased in serum, resulting in alkalosis

- ***Secondary active transport*:** Like sodium, potassium is also involved in secondary active transport of many substances.
- The sodium pump that is involved in active transport of glucose, galactose amino acids, etc. is actually a sodium-potassium pump: it causes active efflux of sodium and influx of potassium.

Dietary Sources, Absorption and Elimination

Potassium is abundant in foodstuffs of plant and animal origin since it is the principal intracellular cation.

Daily requirement of about 4 g can be easily met and so dietary deficiency is rarely seen.

Food sources are meat, fish, cereals, vegetables, oranges and peaches.

Potassium absorption occurs by passive diffusion along a concentration gradient in both small and large intestine. Excretion mainly occurs through renal route.

Disturbances of Serum Potassium

Hypokalaemia: Fall in serum potassium levels ***below 3 mmol/L.*** It may occur when excess potassium is lost from the body, when there is a reduced dietary intake, or when potassium is redistributed within the body.

- (a) Loss of potassium may occur via gastrointestinal route, in renal tubular acidosis, K-losing nephritis, hyperaldosteronism, etc.
- (b) Decreased dietary intake occurs with chronic starvation or anorexia nervosa.

(c) Hypokalaemia due to redistribution may be caused by insulin: insulin induces potassium to move into the cells. Magnesium deficiency may also lead to potassium deficiency.

Manifestations of hypokalaemia: Muscular weakness, confusion, irregular heart beat, tachycardia, and altered ECG pattern (flattening of ECG waves)

- ***Hyperkalaemia:*** Although less common, hyperkalaemia (***serum potassium 5.5 mmol/L***) is dangerous because of its effect on cardiac muscles. It may be caused by:
- (a) ***Failure of the kidneys to excrete potassium***, as in Addison's disease, in which low aldosterone production prevents potassium excretion. Renal failure can cause hyperkalaemia when daily urine output drops below 400–500 mL per day.
- (b) ***Redistribution of potassium***, which occurs in acidosis and crush injuries. These conditions lead to hyperkalaemia even though total body potassium is not increased. In acidosis, potassium moves out of the cells as hydrogen ions move in, and in crush injuries, the damaged tissues release their potassium content into blood circulation.
- (c) ***Others****:* Dehydration, massive blood transfusion and indiscriminate potassium therapy are other important causes of hypokalaemia.

Clinical manifestations: The symptoms of hyperkalaemia are similar to those of hypokalaemia in that myocardial irritability, irregular heartbeat, ECG changes, and muscle weakness may occur in either condition. *The greatest danger, however, is the possibility of cardiac arrest at levels greater than 7.0 mmol/L.*

Calcium

- Of all nutritionally important minerals, calcium occurs in largest amount in the human body: a 70 kg adult male contains 1.0-1.4 kg (25-33 g/kg of fat-free tissue) of calcium.
- Over 99% of the total body calcium present in bones and teeth, and about 1% in various body fluids.
- *Extracellular calcium represents physiologically active fraction* being involved in a number of critical functions.

A. Nutritional Requirement and Sources

- Daily dietary requirement about 400-500 mg. This replaces the daily loss of 300-400 mg calcium in urine and an additional loss in faeces and sweat. In the growing age group (12–20 years), about *1200* mg per day is required.
- **Recommendation**: Daily intake in the post-menopausal women must be higher (around 1500 mg) since they are at risk of developing osteoporosis, a condition characterized by loss of bone organic matrix as well as progressive demineralization.

Several other factors influence the dietary requirement. Vitamin D is required for the optimal utilization of calcium, and therefore, adequate supply of this vitamin decreases the dietary requirement of calcium.

Excess dietary proteins, on the other hand, may upset calcium balance by causing rapid excretion of this element.

- Exercise increases efficiency of calcium utilization.
- The calcium balance studies carried out on people, who have extensive exposure to sunlight, perform adequate exercise and subsist on low protein, vegetarian diet, indicate a need of only 300-400 mg of calcium per day.

***Sources*:**

- Milk and milk products richest sources
- Beans, cabbage, egg, fish and leafy vegetables are some other sources.

B. Functions

- In Bone

Calcium contributes enormously to the physical strength of bones (and teeth). Within the bone matrix, type I collagen is the major protein (90%) and calcium-rich crystals of hydroxyapatite [$Ca_{10}(PO4)_6(OH)_2$] are found on the collagen fibres.

The crystals are very small (less than 0.1 nm long) and are surrounded by a hydration shell of water. Smaller amount of the bone calcium is present in form of calcium phosphate and calcium carbonate and some other calcium salts. Together, all these minerals constitute about 50% of the total skeletal mass; the rest is made up of organic elements.

The calcium stores in bones are in a dynamic equilibrium with the surrounding extracellular fluid. As much as 700 mg of calcium may leave or enter the bones each day. ***Thus, bones serve as prime reservoir of body calcium.***

Deposition of calcium in bones depends on serum concentration of calcium (and phosphate). A value above 70 mg/dL reflects tendency of soft tissue calcification and below 20 mg/dL, it reflects defect of bone mineralization.

In Ionic Form

The calcium present in the body fluids, though extremely small in amount compared to that in bones, mediates a large number of physiological functions:

1. *Muscle contraction*: Calcium mediates excitation and contraction of muscle fibres. Contraction of striated muscles requires binding of calcium to troponin on thin filaments. The calcium-troponin interaction enhances reaction between actin and myosin, which triggers muscle contraction. In addition, calcium stimulates *ATPase*.

Smooth muscles do not have troponin. Their contraction is also calcium-dependent, but the calcium-sensing protein in smooth muscle is calmodulin, and not troponin.

***Blood coagulation*:** Coagulation of blood occurs through a cascade of reactions, most of which require calcium.

***Nerve excitability*:** Excitability and conductivity of nerves depends upon a number of cations, including calcium.

A raised plasma calcium level decreases and a low plasma calcium level increases the excitability of nerves.

***Activation of enzymes*:** Calcium causes direct activation of a number of enzymes, such as *succinate dehydrogenase, ATPase* and *pancreatic lipase.* Intracellularly, it interacts with **calmodulin**, a calcium-binding regulatory protein, and the calcium-calmodulin complex activates certain enzymes (Table below).

• Adenylate *cyclase*	• Guanylate *cyclase*
• *Phosphorylase kinase*	• Glycogen *synthase*
• Calcium-magnesium ATPase	• Phospholipase A_2
• Pyruvate *carboxylase*	• Pyruvate *dehydrogenase*
• Calcium-phospholipid-dependent protein *kinase*	• *Myosin kinase* • Cyclic nucleotide *phosphodiesterase*

Table: Enzymes regulated by calcium/calmodulin

As Intracellular Messenger

- Cytoplasmic calcium is an important intracellular signal.
- It is referred to as a “second messenger” because it mediates cellular response to a wide range of stimuli in a manner analogous to cAMP. For example, it acts as a second messenger for epinephrine or glucagon in hepatic glycogenolysis.
- Considered as the second messenger in phosphoinositide system, and as a third messenger for some hormones, such as ADH

Other Functions

Neuromuscular transmission: Neuromuscular transmission occurs through release of acetylcholine from the motor end plate, which requires calcium.

Membrane integrity and permeability: Transport of a number of substances across the membranous barrier is influenced by calcium.

Action on heart: Cardiac muscles are dependent on calcium for the generation of rhythmic impulses. Increased calcium concentration increases myocardial contractility and vice versa.

Secretory processes: Secretion of water-soluble products by *exocytosis* is triggered by calcium. Examples include the release of zymogens by pancreas, insulin from -cells, histamine from mast cells and neurotransmitters from nerve terminals. Endocytosis–exocytosis, cell motility and other such processes mediated via microtubules microfilaments are also regulated by calcium.

C. Metabolism

Absorption

Dietary calcium is absorbed in the duodenum and proximal jejunum through mediation of an intestinal **calcium binding protein (CBP)**. This protein transfers the luminal calcium across the intestinal mucosal cell by an energy dependent active process.

- ***Factors promoting absorption:*** Synthesis of CBP is enhanced by 1,25-dihydroxycholecalciferol, i.e. calcitriol, the activated form of vitamin D. This accounts for stimulation of intestinal calcium absorption by *calcitriol.*
- ***Factors inhibiting absorption:*** Calcium absorption is inhibited by certain compounds such as *oxalates*, *phytates*, and *phosphates*. These compounds form insoluble calcium salts. The undigested *dietary fats* also impair calcium absorption by forming insoluble calcium soaps. Dietary *fibres* also interfere with the absorption. Thus, a large part of dietary calcium is not absorbed and is eliminated in faeces.

Plasma Calcium

- Following absorption, calcium gets into blood plasma.

Factors increasing absorption
Calcitriol
PTH (acts by enhancing calcitriol production)
Acidity (low pH)
Growth hormone
Pregnancy, lactation
Lactose, arginine, lysine
Factors decreasing absorption
Oxalates and phytates
High dietary fats and fibres
Phosphates
Alkalinity
Chronic renal failure (leads to impaired activation of vitamin D)

Table: Factors affecting intestinal calcium absorption

Total plasma calcium is 9-11 mg/dL, and it exists in three forms:

- ***Ionized calcium:*** It is the biologically active fraction of the calcium in plasma. Maintenance of its concentration within tight limits (4.5–5.0 mg/dL) is required for nerve function, membrane permeability, muscle contraction and glandular secretion.
- ***Protein bound calcium:*** The majority of the remaining calcium is mainly bound to negatively charged albumin.
- ***Calcium complexed to substances such as citrate and phosphate*****:** It constitutes a small fraction (10% of total)

Serum calcium (9–11 mg /dL)

- 50% – Ionized Calcium
- 40% – Protein-bound Calcium
- 10% – Calcium complexed with citrate, phosphate, bicarbonate

Excretion

Excreted through the following routes:

- A large amount (200 mg/day) is secreted into the intestinal lumen and lost in faeces.
- About 300-400 mg/day is lost in urine; the kidneys start filtering calcium when the plasma levels exceed 7.0 mg%.
- A smaller amount is lost in sweat.

Fecal calcium excretion varies widely in response to diet, whereas elimination through other routes remains relatively constant.

- Critical mineral
- Involved in vast array of biochemical processes
  - Neural signalling, cell proliferation, cardiac function, digestive system
  - Storage–ER and other microsomal compartments

- Role in the release of parathyroid hormone
  - Fall in extracellular calcium levels triggers release of the hormone-increase in absorption of calcium in kidneys
  - Decrease in absorption of phosphate
  - Increase in synthesis of vitamin D

- Effect on Calcitonin:
- Rise in extracellular calcium:
  - Secretion of calcitonin leads to decrease in plasma calcium levels

Osteoporosis:

- Age 40-45 years- reduction in calcium absorption and increased calcium excretion leading to demineralization
- Above 60 years-reduced bone strength and increased risk of fractures
  - Calcium supplementation reduces the risk of fracture due to bone loss

Phosphorous

- Mainly intracellular ion
- Seen in all cells
- Inverse relationship with calcium
- Level regulated by excretion through urine

1. Formation of bone and teeth
2. Production of high energy phosphate. compounds, such as ATP, CTP, GTP, creatine phosphate, etc.
3. Synthesis of nucleoside co-enzymes, such as NAD and NADP
4. DNA and RNA synthesis, where phosphodiester linkages form the backbone of the structure
5. Formation of phosphate esters, such as glucose-6-phosphate, phospholipids
6. Formation of phosphoproteins, e.g. casein
7. Activation of enzymes by phosphorylation
8. Phosphate buffer system in blood. The ratio of Na_2HPO_4: NaH_2PO_4 in blood is 4:1. This maintains the pH of blood at 7.4.

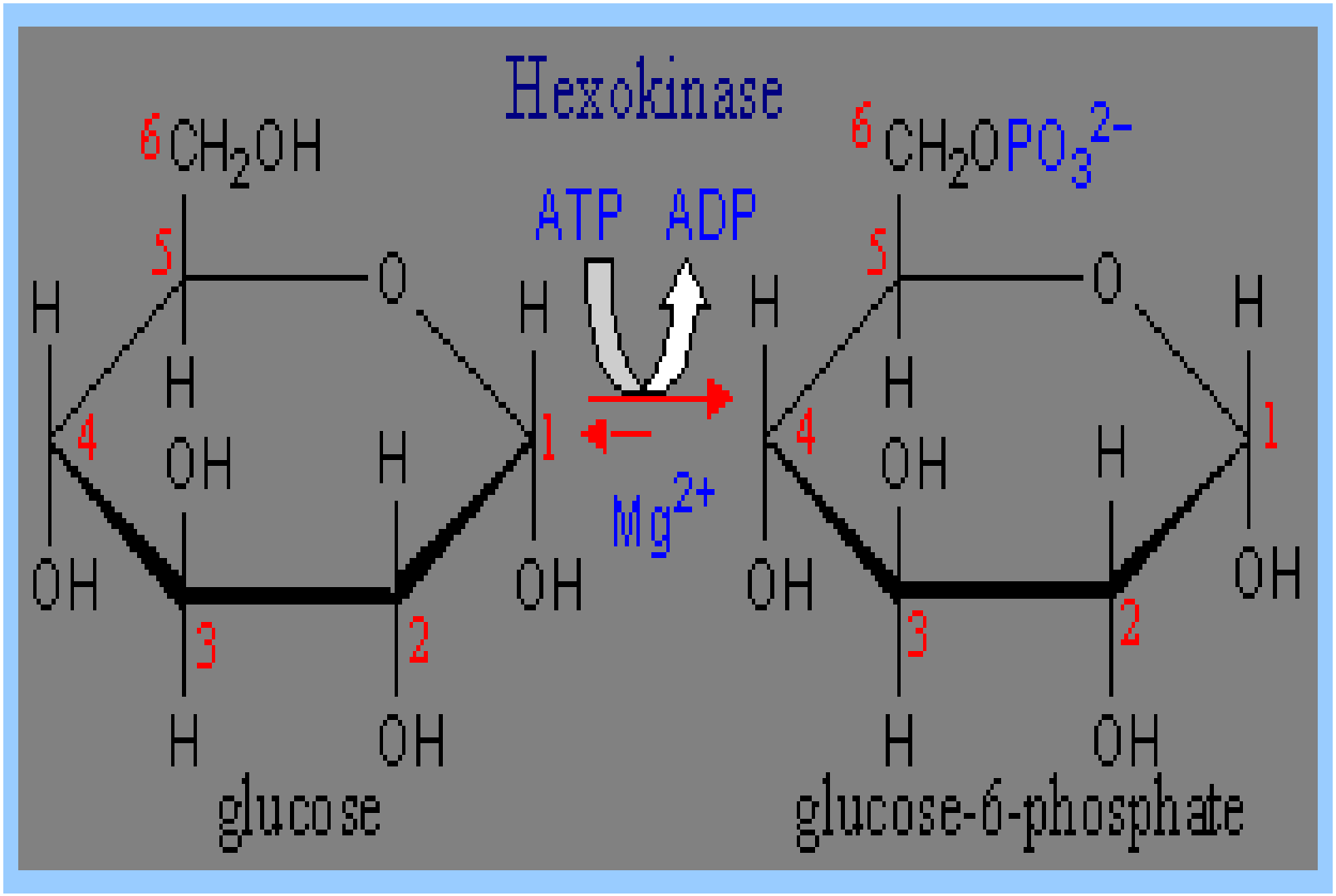
Table: Functions of phosphate ions

Magnesium

- Mainly in intracellular fluid
- Homeostasis maintained by intestinal absorption and excretion by kidneys

Magnesium

- Activator of > 300 enzymes
- All enzymes that utilise ATP as substrate
- Interacts with DNA to stabilise structure
- Nucleotide repair excision enzyme
- Protein synthesis-stabilises ribosomes


Hexokinase
6CH2OH
ATP ADP
6CH2OPO3 2-
Mg2+
glucose
glucose-6-phosphate

TRACE MINERALS

Copper

-critical to the proper production of connective tissue-collagen, elastin

-production of red blood cells

The copper-dependent enzyme, cytochrome *c* oxidase, plays a critical role in cellular energy production.

By catalyzing the reduction of molecular oxygen (O_2) to water (H_2O), cytochrome *c* oxidase generates an electrical gradient used by the mitochondria to create the vital energy-storing molecule, ATP

Wilson’s disease

- Ceruloplasmin level reduced. Promotes oxidation of ferrous ion to ferric form which is incorporated into transferrin

- Defect in the gene encoding copper binding ATPase in cells (ATP7B gene in liver cells)

Menke’s kinky hair syndrome

X-linked (affects only male child)

Dietary copper absorbed but not transported to blood due to absence of an intracellular copper binding ATPase

Melanin

- Copper in tyrosinase-an enzyme necessary for melanin formation

Iodine

- Component of thyroid hormone, thyroxine (T4), Triiodothyronine (T3).
  - Important role in regulation of energy metabolism via thyroid hormone functions

- Goiter
- Cretinism

  Pregnant women, lactating mothers, and young infants are among the most vulnerable to iodine deficiency due to their special requirements during these life stages

- Selenium
  - Refer to the previous slide under Vitamin B_2 -the Glutathione molecule

Zinc

- Co-factor in a number of enzymes
- Involved in a variety of biochemical processes
- Interacts with insulin

SUMMARY

1. Vitamins are all organic nutrients with various essential metabolic functions, required in small amounts in the diet because they cannot be synthesized by the body

2. Apart from vitamin C, the water-soluble vitamins are all members of the B complex and act as enzyme cofactors

3. Thiamine is a cofactor in oxidative decarboxytion of α-keto acids and of an important enzyme in the Pentose Phosphate Pathway, transketolase

4. Riboflavin and Niacin are each important cofactors in oxido-reduction reactions. Riboflavin is present as prosthetic groups in flavoprotein enzymes flavin mononucleotide and flavin adenine dinucleotide, whereas niacin is present in the NAD and NADP cofactors of many dehydrogenase enzymes.

5. Pantothenic acid is present in coenzyme A and acyl carrier protein, which act as carriers for groups in many important reactions, whereas pyridoxal phosphate is the coenzyme for several enzymes of amino acid metabolism including the transaminases.

6. Biotin is the coenzyme for several carboxylase enzymes, including acetyl-CoA carboxylase, the rate controlling enzyme in lipogenesis, and pyruvate carboxylase, important in gluconeogenesis**.**

7. As well as having separate functions, vitamin B_{12} and folic acid take part in providing one-carbon residues for nucleic acid synthesis.

8. Ascorbic acid is a water-soluble antioxidant that maintains many metal cofactors in the reduced state

9. Absence of the water-soluble vitamins from the diet provokes multiple deficiency states. Absence of a single vitamin leads to a characteristic deficiency syndrome.

END