

The Water-Soluble Vitamins

Overview of Water-Soluble Vitamins

- Dissolve in water
- Generally readily excreted
- Subject to cooking losses
- Function as a coenzyme
- Participate in energy metabolism
- 50-90% of B vitamins are absorbed
- Marginal deficiency more common

Thiamine (Vitamin B1)

- Composed of an imidazole and pyrimidine ring, connect by a methylene link
- Destroyed by alkali, heat, sulfides, pasteurization and sterilization

Sources of Thiamine

- Unrefined or fortified cereal grains
- Enriched bakery products, organ meats (liver, kidneys) and legumes
- Asparagus, spinach, green peas
- Cauliflower, sunflower seeds
- Eggs
- Thiamine content in human milk is relatively low (16 ug/ml)

Absorption, Transport, Metabolism of Thiamine

- **Absorbed in the jejunum**
 - Active absorption – sodium ion dependent (if low thiamine)
 - Passive absorption – if excess thiamine
 - Absorption is inhibited by ethanol – physiologic dose is insufficient in the chronic alcoholic
- **Transported by RBC in the blood**
- **Excess quickly excreted in the urine**

Biologic action

- **Thiamine pyrophosphate (TPP) – an active form of thiamine**
 - As a cofactor for the oxidative decarboxylation of pyruvate to form acetyl-Co A (enters krebs cycle)
 - Essential for carbohydrate metabolism
 - As a coenzyme for transketolase, an enzyme of the pentose pathway

RDA (recommended daily allowance) For Thiamine

- Requirements depends on carbohydrate intake
- RDA 0.4 mg / 1000 kcal consumed
- Generally exceeds RDA in diet
- Surplus is rapidly lost in urine; non toxic

Who is at Risk For Deficiency?

- Poor
- Alcoholics
- Elderly
- Those who consume processed foods (polished rice)

Deficiency of Thiamine

- **Thiamine deficiency – Beriberi occurs if the intake is less than 1mg/day**
 - Dry beriberi - Weakness, nerve degeneration, irritability, severe muscle wasting poor arm/leg coordination, loss of nerve transmission
 - Wet beriberi - Edema, enlarge heart, heart failure, cyanosis, dyspnea and aphonia

Diagnosis

- Suspected in all cases of malnutrition
- **Confirmatory test – 24 hours urinary thiamine excretion**
 - Value less than 15 microgram / day – thiamine deficiency
 - Normal value – 40 – 100 microgram / day
- **Response of red cell transketolase to the addition of thiamine in vitro**
 - In thiamine deficiency – red cell response to thiamine is greater than those of normal
 - If increase in transketolase activity is <15 % - normal
 - If increase in transketolase activity is 15 % - 25% - mild
 - If increase in transketolase activity is >25% - severe

Treatment

- **Mild beriberi**
 - Oral 5 mg thiamine / day is satisfactory
- **Severe beriberi**
 - IV 10 mg thiamine twice daily
 - In fulminant heart disease – higher doses with vigorous treatment of congestive heart failure is necessary

Riboflavin (vitamin B2)

- It is a flavoprotein
- **Coenzymes:**
 - Flavin mononucleotide (FMN)
 - Flavin adenine dinucleotide (FAD)
- **Oxidation-reduction reactions**
- **Electron transport chain**
- **Citric Acid Cycle**
- **Catabolism of fatty acids**

Sources of riboflavin

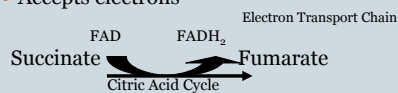
- Milk/products
- Enriched grains
- Meat, poultry fish
- Vegetables – broccoli, spinach etc
- Sensitive to uv radiation (sunlight)
- Stored in paper, opaque plastic containers
- Resistant to oxidation and to heat
- Not destroyed by pasteurization or evaporation
- Human milk contains 40 – 70 ug / 100 kcal

Absorption, Transport, & Metabolism of Riboflavin

- HCL (hydrochloric acid) in the stomach release riboflavin from its bound forms
- Absorption
 - Active or facilitated transport during low to moderate intake
 - Passive absorption during high intake
- Transported by a protein carrier in the blood
- Biliary obstruction, high dietary fiber, antacids – decrease the bioavailability

Biologic action

- Accepts electrons



- A number of important enzymes (eg. Glutathione reductase, xanthine oxidase etc) require flavin coenzymes
- The enzymes catalyzing the synthesis of niacin from tryptophan and the conversion of pyridoxal phosphate to an active coenzyme are flavin dependent

Biologic action

- Fatty acid synthesis
- Affects reactions involved in amino acid metabolism requiring this vitamin.

RDA for Riboflavin

- Requirements based on caloric intake
 - Infants – 0.4mg/1000 kcal
 - Children – 0.8 – 1.2 mg/1000 kcal
- Average intake is above RDA
- Toxicity not documented

Who is at Risk For Deficiency?

- Low milk/dairy intake
- Alcoholics
- Long term phenobarbital use

Deficiency of Riboflavin

- **Ariboflavinosis**
 - Glossitis, cheilosis, photophobia, seborrheic dermatitis, stomatitis, eye disorder (cataracts), throat disorder, nervous system disorder
- **Non specific symptoms**
 - Anorexia, weakness, weight loss, dizziness, confusion
- **Occurs within 2 months**
- **Usually in combination with other deficiencies**

Glossitis



Diagnosis

- **Dietary history**
- **24 hours urinary excretion of vitamins – usually not done**
- **Measurement of activity glutathione reductase in the red cells provides a functional index of flavin coenzyme activity**
 - If a flavin coenzyme (FAD) induced increase of 20% above the basal level is indicative of deficiency

Treatment

- **Children – 1 mg TDS for several weeks**
- **Infants – 0.5 mg BD**

Niacin (vitamin B₃)

- **Nicotinic acid (niacin) & nicotinamide (niacinamide) – are biologically equivalent vitamins (both referred to niacin)**
- **Coenzyme**
 - Nicotinamide adenine dinucleotide (NAD)
 - Nicotinamide adenine dinucleotide phosphate (NADP)
- **Oxidation-reduction reaction**
- **Metabolic reactions**
- **Tryptophan → nicotinic acid**

Sources of Niacin

- **Milk, cereals**
- **Leafy vegetables**
- **Fish**
- **Tea, coffee**
- **Human milk contains 30 mg / 100 kcal**
 - **More in compare to cow milk**
- **Heat stable; little cooking loss**

Absorption, Transport and Storage of Niacin

- Readily absorbed from the stomach and small intestine
- Absorption: active transport and passive diffusion
- Absorbed niacin is incorporated into two bioenergetic coenzymes (nicotinamide adenine dinucleotide (NAD) and its phosphate (NADP))
- Excess niacin is methylated in the liver, forming N1-methylnicotinamide
- Methylnicotinamide and its oxidation products are two major niacin metabolites found in urine

Biological action

- NAD and NADP are coenzymes for oxidation – reduction reactions, for obtaining energy from protein and in excision – repair mechanisms of DNA

RDA for Niacin

- 6.4 – 8 NE / 1000 cal
- High dose of nicotinic acid (not nicotinamide) reduces serum cholesterol and triglyceride.
- Side effects – skin flares, hyperuricemia, hyperglycemia, abnormal LFT
- NE – niacin equivalents
 - 1 NE = 1 mg of niacin or 60 mg of tryptophan

Deficiency of Niacin

- Pellagra
 - 3 Ds (dermatitis, diarrhea, dementia)
 - Occurs in 50-60 days
 - Decrease appetite & weight
- Characteristic red coloration of the tongue
- Neurologic symptoms
 - Apathy, headache, memory loss
- In severe and chronic cases – neurologic lesions persist even after adequate treatment

Dermatitis of Pellegra



Treatment

- Dose – 10 times of RDA
- Oral nicotinamide is preferred over nicotinic acid to avoid unpleasant side effects like flushing, tachycardia
- Parental therapy is considered when GI absorption is deficient.

Vitamin B6: Pyridoxine

- Main coenzyme form: pyridoxal phosphate (PLP)
- Activate enzymes needed for metabolism of fat , protein
- Synthesis of hemoglobin and oxygen binding and white blood cells
- Synthesis of neurotransmitters

Sources of pyridoxine

- Yeast, sunflower seeds
- Wheat germ, soya beans, walnuts
- Heat and alkaline sensitive

Absorption and Metabolism of Vitamin B-6

- Absorbed passively
- Vitamin B6 are phosphorylated in the liver
- Binds to albumin for transport in the blood
- B-6 is stored in the liver and muscle tissue
- Excess is excreted in urine

Biologic action

- Protein and fat metabolism
- Activates many enzyme systems and involves in the production of antibodies against bacterial diseases
- Prevents dandruff, eczema and psoriasis.
- Required for the absorption of Vitamin B12 and for the production of hydrochloric acid (HCl) and magnesium.
- Required for the production of neurotransmitters like serotonin, dopamine, noradrenaline, adrenaline

Deficiency of Vitamin B-6

- Microcytic hypochromic anemia
- Seborrheic dermatitis
- Convulsion, depression, confusion
- Reduce immune response
- Peripheral nerve damage
- Sore mouth, skin problems

- Vitamin B6 is given 10-50 mg/day to the patients on isoniazide to prevent peripheral neuropathy.

Cobalamine (vitamin B12)

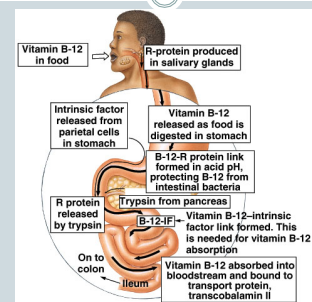
- Cyanocobalamin, Methylcobalamin, 5-deoxyadenosyl cobalamin are 3 forms of vit B12
- Folate metabolism
- Maintenance of the myelin sheaths
- Rearrange 3-carbon chain fatty acids so can enter the Citric Acid Cycle

Food Sources of Vitamin B-12

- Synthesized by bacteria, fungi and algae
- (Stored primarily in the liver)
- Animal products
- Organ meat (liver, kidneys, heart)
- Clams and oysters

Absorption of Vitamin B-12

- A specific, receptor mediated process operates at the ileum, involving a glycoprotein – intrinsic factors (IF).
- Cobalamin undergoes enterohepatic circulation – this process accounts for the very long half life of the vitamin



Biologic action

- Helps convert methylmalonyl CoA to succinyl CoA (citric acid cycle)
- RBC formation
- Nerve functions
 - Maintains myelin sheath
- Prevents Megaloblastic anemia

Deficiency

- Peripheral neuritis
- Methylmalonic aciduria
- Megaloblastic anemia

RDA for vitamin B12

- Infants – 0.3 ug/day
- Children – 0.5 – 1.5 ug/day
- Adolescents - 2 ug/day

Folic acid (pteroylglutamic acid)

- Coenzyme form: tetrahydrofolic acid (THFA)
- Vitals for the reproduction of the cell within the fetus
- Essential for normal growth and maintenance of all cells

Sources

- Leafy vegetables – spinach, turnip greens, lettuces
- Dried beans and peas
- Fortified cereals
- Sunflower seeds

Absorption, Metabolism

- Absorbed in the monoglutamate form with help of folate conjugase
- Actively absorbed during low to moderate intake
- Passively absorbed during high intake
- Delivered to the liver where it is changed back to the polyglutamate form
- Mostly stored in the liver
- Excreted in the urine and bile (enterohepatic circulation)

Biologic action

- DNA and RNS synthesis
- Homocysteine metabolism in collaboration with vit B12 – lowers the risk of heart diseases
- Neurotransmitter formation – serotonin, which regulate mood, sleep and appetite
- Cell division and protein synthesis

Deficiency

- Similar signs and symptoms of vitamin B-12 deficiency
- Pregnant women – neural tube defect
- Affects normal growth and repair of all cells and tissues

Megaloblastic Anemia

Cells divide normally
Folate and vitamin B-12 adequate
Normal blood cells in the bloodstream. The size, shape, and color of the red blood cells show that they are normal. Mature red blood cells have lost their nuclei.

Red blood cell precursor (stem cell)
Folate or vitamin B-12 deficient
Cells are unable to divide
Megaloblastic blood cells seen here in the bone marrow are arrested at an immature stage of development. They still have their nuclei and are slightly larger than normal red blood cells.

Neural Tube Defects

- Spina bifida
- Anencephaly
- Importance of folate before and during pregnancy

RDA

Age	Micrograms / day
Infants	70
1 -3 years	100
4-6 years	150
7-9 years	200
10-12 years	250
13-15 years	300
Pregnant & lactating women	400

- To reduce the risk of having a fetus with neural tube defect – supplementation of folic acid a month before conception and at least 3 months afterward is recommended.

Toxicity

- Epilepsy
- Skin, respiratory disorder

Vitamin C

- Ascorbic acid (reduced form), dehydro ascorbic acid (oxidized form)
- Synthesized by most animals (not by human)
- Absorbed by a specific energy dependant transport system
- Passive transport if intake is high
- Excess excreted

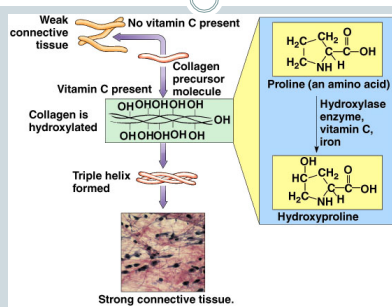
Sources

- Citrus fruits
 - Potatoes
 - Green peppers
 - Cauliflower
 - Broccoli
 - Strawberries
 - lettuce
 - Spinach
- Easily lost through cooking
 - Sensitive to heat
 - Sensitive to iron, copper, oxygen

Biologic action

- Reducing agent (antioxidant)
- Iron absorption
- Immune functions
- Collagen synthesis
- Wound healing, detoxification

Collagen synthesis



RDA

- Infants – 30 -40 mg / day
- Children – 40 – 70 mg /day

Deficiency

- Scurvy
 - Infancy (Barlow's disease) –
 - × anorexia, irritability, diarrhea, pallor
 - × susceptibility to infections
 - × sub-periosteal hemorrhage and long bone tenderness
 - × radiologic abnormalities are most frequent manifestations
 - Older children –
 - × hemorrhagic signs (bleeding of gum, conjunctiva and the intestinal tract)

Diagnosis

- Clinical features
 - History of inadequate dietary intake
 - X-rays of long bones
- Vitamin C therapy often results in dramatic improvement within 24-48 hours