Water-soluble Vitamins: Coenzymes

• water soluble vitamins - **most act as coenzymes**
  • enable enzymes to regulate metabolic reactions
• Vitamin C is an antioxidant, not coenzyme
• Generally readily excreted
• Subject to cooking losses

• “enzyme helpers”
• combine with protein portion of enzyme to make active form of enzyme

• **Fat soluble** (ADEK)
  • NONE are coenzymes

• **Water soluble** (Bs, C)
  • most function as coenzymes
Micronutrients

• Thiamin (B₁)
  • thiamin pyrophosphate (TPP)
    – Energy metabolism

- Scientists originally believed vitamin B was a single compound.
- Vitamin B = 8 compounds, including thiamin, riboflavin, niacin, vitamin B6, folate, B12, pantothenic acid, and biotin.
  • act primarily as coenzymes

• Functions of Thiamin
  • vitamin component of coenzyme TPP - thiamin pyrophosphate
  • works in reactions that produce energy
    • helps break down glucose (necessary for conversion of pyruvate to acetyl CoA, and another step of Kreb’s), make RNA and DNA, or produce energy-rich molecules that power protein synthesis
  • [also necessary for neurotransmitter synthesis (present in membranes of nerve cells)]
  • Absorbed in the jejunum by a carrier-mediated system
  • Transported by RBC in the blood
  • Excess quickly excreted in the urine

Food source of thiamin
  • Wide variety of food
  • White bread, pork, hot dogs, luncheon meat, cold cereal
  • Enriched grains/ whole grains
Thiamin deficiency, toxicity

• **Beriberi**
  - Occurs where polished rice is the only staple
  - Peripheral neuropathy
  - Occurs within 7 days on a thiamin deficient diet
• **Dry beriberi**
  - Weakness, nerve degeneration, irritability, poor arm/leg coordination, loss of nerve transmission
• **Wet beriberi**
  - Edema, enlarge heart, heart failure
• **Wernicke-Korsakoff**
  - Mainly in alcoholics
    - Alcohol diminishes thiamin absorption
    - Alcohol increases thiamin excretion
    - Poor quality diet
  - Involuntary eye movement; double vision
  - Ataxia: staggering, poor muscle coordination
  - Mental confusion, “drunken stupor”
Riboflavin (B₂)

- electron carriers
  - FAD
  - FMN

Functions of riboflavin
- part of two enzymes: FAD & FMN
  - these enzymes required in reactions that extract energy from glucose, fatty acids, and amino acids
- [supports antioxidant activity of gluthione peroxidase]
- HCl in the stomach release riboflavin from its bound forms
- Absorption
  - Active or facilitated transport during low to moderate intake
  - Passive absorption during high intake
  - Increase with intake
- Transported by a protein carrier in the blood
- Small amount stored in liver, excess excreted
- Food sources of riboflavin
  - Milk/products
  - Enriched grains
  - Liver
  - Oyster
  - Brewer’s yeast
  - Sensitive to uv radiation (sunlight)
  - Stored in paper, opaque plastic containers
Riboflavin deficiency, toxicity

- **Ariboflavinosis**
  - Glossitis, cheilosis, seborrheic dermatitis, stomatitis, eye disorder, throat disorder, nervous system disorder

- Occurs within 2 months
- Who’s at risk for deficiency?
- **Usually in combination with other deficiencies**
  - Rare
  - Low milk/dairy intake
  - Alcoholics
  - Long term phenobarbital use
Niacin (B₃)

- **Names**
  - Nicotinic acid = niacin
  - Nicotinamide = niacinamide

- **Coenzymes**
  - NAD⁺
  - NADP⁺

- **Functions**
  - energy metabolism
  - fatty acid synthesis

**Functions of niacin**

- **two compounds**: Nicotinic acid (niacin) & nicotinamide (niacinamide)
- forms a part of crucially important coenzymes that participate in at least 200 metabolic pathways
- plays a major role in energy metabolism
- synthesize fatty acids

**Coenzymes**

- Nicotinamide adenine dinucleotide (NAD)
- Nicotinamide adenine dinucleotide phosphate (NADP)

- Niacin is rapidly absorbed in the proximal small intestine by passive diffusion
- Transported from the liver to all of the tissues where it is converted to the coenzymes
- Niacin can be synthesized from tryptophan, but tryptophan is an essential amino acid that cannot be synthesized
Food sources of niacin

- **MEAT**: Beef, chicken, turkey, fish
- (Mushroom)
- Enriched grains
- Niacin is extremely stable to heat, light, acid, alkali, and oxidation; little cooking loss

**BODY CAN MAKE FROM TRYPTOPHAN**

- 60mg tryptophan can be converted into 1 mg niacin
- Estimate by dividing the total gram of protein by 6
Deficiency:

**Pellagra**

- 4 Ds (dementia, diarrhea, dermatitis, death)
- Occurs in 50-60 days
- Decrease appetite & weight
- Prevented with an adequate protein diet
- Enrichment Act of 1941
- Only dietary deficiency disease to reach epidemic proportions in the U.S.

**Who is at risk?**

- (Untreated) corn as main staple, poor diet, Hartnup disease, alcoholics
Vitamin B₆, Pyridoxine

- **Coenzyme**: pyridoxal phosphate (PLP)
- **Other forms**
  - Pyridoxal
  - Pyridoxamine
- **Functions**
  - Protein, carb metabolism
  - RBCs
  - Neurotransmitter synthesis
  - Homocysteine metabolism

The three major forms of vitamin B-6 are pyridoxine, pyridoxal, and pyridoxamine, which, in the liver, are converted to pyridoxal 5'-phosphate (PLP) — a cofactor in many reactions of amino acid metabolism. PLP also is necessary for the enzymatic reaction governing the release of glucose from glycogen.

**vitamin B6 = group of 6 compounds**
- liver converts all to PLP
- **Pyridoxal phosphate (PLP)** = primary active form
- stored in muscle tissue!
  - is co-enzyme for > 100 different enzymes more notably playing an active role in protein, amino acid metabolism
  - necessary for synthesis of nonessential amino acids
- involved in supporting white & red blood cells
  - needed for hemoglobin synthesis
- [lower homocysteine levels
  - homocysteine = amino acid, associated with fatal cardiac arrest
  - B6 helps convert it to other amino acids (B12 and folic acid also help)]
• Meat, fish, poultry
• Whole grains (not enriched back)
• Banana
• Spinach
• Avocado
• Potato
• Heat and alkaline sensitive
Micronutrients

**Vitamin B₆ deficiency, toxicity**

- **Deficiency**
  - Microcytic hypochromic anemia
  - Seborrheic dermatitis
  - Convulsion, depression, confusion
  - Reduced immune response

- **Toxicity potential**
  - Can lead to irreversible nerve damage with > 200 mg/day

- One cause of vitamin B6 deficiency is the use of the tuberculostatic medication *isoniazid*, and for this reason, it is recommended to supplement with vitamin B6 when using this drug.

- In women, another potential cause for vitamin B6 deficiency is use of oral *contraceptives* and other medications containing estro-progestational hormones (such as those prescribed as part of *Hormone Replacement Therapy*). Other contraceptive medications that may cause vitamin B6 deficiency include: the patch (Ortho Evra), vaginal ring (Nuvaring), hormonal IUD (Mirena) and shot (Depo Provera). Specifically, habitual use of estro-progestational hormones inhibit absorption of vitamin B6 (due to a disturbance of tryptophan metabolism), necessitating a larger daily dosage of B6 into the bloodstream. Signs of a Vitamin B6 deficiency include: depression, anxiety, loss of libido, insomnia, water retention, inability to process glucose (weight loss/gain).
Vitamin B₉: Folic Acid

- **Coenzymes**
  - Tetrahydrofolate
  - Dihydrofolate

- **Functions**
  - DNA synthesis
  - Homocysteine metabolism

- several related compounds
- **folic acid** most stable form, most often used in supplements
- **coenzyme forms** = tetrahydrofolate (THF) and dihydrofolate (DHF)

**Functions of folate**
- crucial to DNA synthesis & cell division,
- amino acid metabolism,
- maturation of red blood cells, other cells
- Good folate status in early pregnancy reduces risk of a group of birth defects called neural tube defects (NTD).
- lowers colon & breast CA risk in women
- activated BY B₁₂, and necessary for activation of B₁₂! They activate each other)

**Sources of folate**
- Liver
- Fortified breakfast cereals
- Grains, legumes
- Foliage vegetables
- Susceptible to heat, oxidation, ultraviolet light
• Signs of **folic acid deficiency**:
  • Diarrhea,
  • loss of appetite
  • weight loss
  • weakness
  • sore tongue
  • headaches
  • heart palpitations
  • irritability
  • behavioral disorders

• Women with folate deficiency who become pregnant are more likely to give birth to low birth weight and premature infants, and infants with neural tube defects.

• Some situations that increase the need for folate include:
  • pregnancy and lactation (breastfeeding)
  • alcohol abuse
  • malabsorption, including celiac disease
  • kidney dialysis
  • liver disease
  • certain anemias.

• Medications can interfere with folate utilization, including:
  • anticonvulsant medications (such as phenytoin, and primidone)
  • metformin (sometimes prescribed to control blood sugar in type 2 diabetes)
  • sulfasalazine (used to control inflammation associated with Crohn's disease, ulcerative colitis and rheumatoid arthritis)
  • triamterene (a diuretic)
  • methotrexate, an anti-cancer drug also used to control inflammation associated with Crohn's disease, ulcerative colitis and rheumatoid arthritis.

• tolerable upper intake level (UL) for folate of 1,000 µg for adult men and women
• Supplemental folic acid should not exceed the UL to prevent folic acid from masking symptoms of vitamin B12 deficiency
Folic acid is very important for all women who may become pregnant. Adequate folate intake during the periconceptional period, the time just before and just after a woman becomes pregnant, helps protect against a number of congenital malformations including neural tube defects. Neural tube defects result in malformations of the spine (spina bifida), skull, and brain (anencephaly). The risk of neural tube defects is significantly reduced when supplemental folic acid is consumed in addition to a healthy diet prior to and during the first month following conception. Women who could become pregnant are advised to eat foods fortified with folic acid or take supplements in addition to eating folate-rich foods to reduce the risk of some serious birth defects. Taking 400 micrograms of synthetic folic acid daily from fortified foods and/or supplements has been suggested. The Recommended Dietary Allowance (RDA) for folate equivalents for pregnant women is 600 micrograms.
Vitamin B₁₂: Cyanocobalamin

- “cobalamin”
- Folate activation
- Myelin sheath maintenance
- Homocysteine metabolism

**Vitamin B₁₂**
- don’t get from plants—plants and animal cannot make B₁₂—only bacteria and archae can synthesize it

- body DOES store large amounts (liver)
- group of compounds = cobalamin

**Functions of vitamin B₁₂**
- transforms folate into an activated form
- helps maintain myelin sheath
- Sources
  - Animal products
  - Organ meat (liver)
  - Seafood (shellfish)
  - Eggs
  - Hot dogs
  - Milk
- inadequate or unreliable sources include spirulina (an algae), nori (a seaweed), barley grass, and human gut bacteria.

- vegan sources of substantial B₁₂:
  - multivitamin supplements
  - fortified foods
  - Chinese herb *Dang Gui (Angelica sinensis)*
  - certain brands of fortified nutritional yeast


**B₄ deficiency, toxicity**

- **Excess**
  - None recognized

- **Adequate intake**

- **Deficiency**
  - Pernicious anemia (Megaloblastic anemia)
  - Nerve degeneration

- **Pernicious anemia (megaloblastic anemia + nerve degeneration)**
  - Nerve degeneration, weakness
  - Tingling/numbness in the extremities (parasthesia)
  - Paralysis and death
  - Looks like folate deficiency
  - Usually due to decreased absorption ability
Vitamin B₅ : Pantothenic acid

- **Coenzyme A (CoA)**
  - energy extraction
  - fatty acid synthesis

*pantothen* means "from everywhere"

- **Functions of pantothenic acid**
  - component of coenzyme A (CoA), which is part of acetyl CoA
  - critical to extraction of energy from nutrients and for building new fatty acids.

Found in almost every food, thus it’s name “pantothenic” acid (from everywhere)

- **Food sources**
  - Meat
  - Milk
  - Mushroom
  - Liver
  - Peanut
  - Adequate Intake = 5 mg/day
  - Average intake meets AI
Micronutrients

Excess
None reported

Adequate intake

Deficiency (RARE!)
Weakness
Fatigue
Impaired muscle function

• Extremely rare: only known from some studies with animals and a few volunteer clinical trials and with victims of starvation
• Symptoms noted when experimentally induced deficiency
• Fatigue, allergies, nausea, and abdominal pain

• Mouse models identified skin irritation and loss of hair color as possible results of severe pantothenic acid deficiency. As a result, the cosmetic industry began adding pantothenic acid to various cosmetic products, including shampoo. These products, however, showed no benefits in human trials. Despite this, many cosmetic products still advertise pantothenic acid additives

• No reliable studies to indicate a role in treating acne
Biotin (aka vitamin B7, or vitamin H)

• coenzyme involved in MANY reactions

• Sources
  • whole grains, eggs, nuts, legumes
  • vary in concentration
  • also synthesized by GI bacteria but bioavailability unknown

• energy metabolism
• gluconeogenesis
• fatty acid metabolism
• amino acid metabolism
• DNA synthesis
Micronutrients

Biotin deficiency, toxicity

• deficiency rare because
  • gut bacteria produce more than the body requires
  • many foods contain adequate amounts
  • the body effectively scavenges and recycles biotin from bodily waste

Signs:
• Dry skin
• Seborrheic dermatitis
• Fungal infections
• Rashes including erythematous periorofacial macular rash
• Fine and brittle hair
• Hair loss or total alopecia
• If left untreated, neurological symptoms can develop, including:
  • Mild depression, which may progress to profound lassitude and, eventually, to somnolence
  • Changes in mental status
  • Generalized muscular pains (myalgias)
  • Hyperesthesias and paresthesias

• Biotin supplements are often recommended as a natural product to counteract the problem of hair loss in both children and adults. There are, however, no studies that show any benefit in any case where the subject is not actually biotin deficient. The signs and symptoms of biotin deficiency include hair loss which progresses in severity to include loss of eye lashes and eye brows in severely deficient subjects. Some shampoos are available that contain biotin, but it is doubtful whether they would have any useful effect, as biotin is not absorbed well through the skin
Vitamin C: Ascorbic Acid

- **Functions**
  - antioxidant
  - collagen synthesis
  - synthesis of dopamine, noradrenaline and adrenaline

Vitamin C

- two forms: ascorbic acid, dehydroascorbic acid (oxidized form)
- most animals can make their own but humans, apes, guinea pigs, fruit bats and some trout can’t
- does **not** act as a coenzyme but DOES help enzymes

- an important participant in many reactions
- also has antioxidant activities.
  - helps protect cells from oxidative damage
  - may reduce risk of heart disease, certain types of cancer
- needed to form collagen (most abundant protein in body-part of connective tissues)

- synthesis of dopamine, noradrenaline and adrenaline
- also plays role in other essential compounds such as thyroid hormone, steroid hormones, bile acids, serotonin, parts of DNA molecule
• **Scurvy**
  • Deficient for 20-40 days
  • Fatigue, pinpoint hemorrhages
  • Bleeding gums and joints, hemorrhages
  • Associated with poverty
Choline

- **Functions**
  - Precursor: acetylcholine
  - Precursor: phospholipids
  - Precursor: betaine

- precursor for phosphatidylcholine, sphingomyelin, acetylcholine and the methyl donor betaine

- Acetylcholine - neurotransmitter
- Precursor to forming phospholipids (e.g. lecithin)
- Betaine needed to form methionine from homocysteine

- **Sources:**
  
The foods richest in phosphatidylcholine, the major delivery form of choline, are beef liver, egg yolks and soya. Beef liver, iceberg lettuce, peanut butter, peanuts and cauliflower are some foods that contain free choline.
Micronutrients

Choline deficiency, toxicity

- **Choline Excess**
  - fishy body odor comes from excretion of a choline metabolite

- **Choline deficiency**
  - doesn’t occur naturally - body can make more than enough (USUALLY)
  - considered “conditionally essential” - not sure what problems might necessitate intake
  - Liver damage, fatty liver