Vitamins

MAIN QUESTIONS TO ANSWER:

• What is a vitamin?

• For each vitamin,
  – what are the best food sources?
  – what are the physiological functions?
  – what are the results of deficiency?
  – what are the results of excessive intake?

...Vitamins

• Organic micronutrients required for reproduction, development, growth, & maintenance of body functions.

• Vitamins have many regulatory functions in the body:
  – example: regulate enzyme activities (co-enzymes)
  – example: regulate the expression of genes
  – metabolites of the food-form of the vitamin often perform the functions

• Fat-soluble vitamins: A, D, E, K
  – May be stored in lipid-rich compartments...greater potential toxicity than water soluble vitamins

• Water-soluble vitamins: C, and the eight B vitamins (Thiamin, Riboflavin, Niacin, Pantothenic acid, B6, Biotin, Folate, B12)
  – Can function as co-enzymes.....B’s involved in energy-production reactions (DRI can be expressed per 1000 dietary kcal consumed)

Stages of vitamin nutrition, metabolism, and activity

Food form of vitamin

Intake from diet

Transport through body and cells

Structural changes in metabolism
Vitamin A

• Retinoids and Carotenoids:
  – Retinoid names: retin-...al, -ol, -oic/oate, -yl
  – Retinoids are present in dietary animal products
  – Some carotenoids can be converted in the body to retinoids

• Intake recommendations:
  – Unit: retinol activity equivalents (1 RAE = 1 mcg retinol ≥ 12 mcg β-carotene)
  – Typical adult RDA, 700-900 RAE (f-m), higher during lactation

• Major dietary sources & availability:
  – Fruits & vegetables (orange color), meats, fortified dairy products…Canadian diet, typically sufficient; <1/2 of dietary carotenoids absorbed

• Storage and mobilization from stores:
  – Liver, main storage for retinyl esters [FA, retinol (R) linked to a fatty acid (FA)]
  – Mobilization: R-FA converted R (also carotenoid sources); circulatory carriers deliver R throughout body; R converted to bioactive retinoids in cells

Vitamin A (biologically active derivatives):

• Functions of vitamin A:
  – Two main functions at molecular level: light absorption (retinal) & control of gene expression (retinoic acids)
  – Regulation of gene expression accounts for many effects of retinoids upon health and disease

• Deficiency of vitamin A (rare in developed countries):
  – Typically a result of chronic low intake; may also result from low storage/mobilization capacity; e.g., liver diseases
  – May cause eye diseases: night-blindness, or more severe, xerophthalmia
  – May compromise immune & epithelial tissue function, & increase risk of some cancers?
  – May cause reproduction & developmental problems

• Toxicity of vitamin A:
  – High retinoid intake in early pregnancy may cause developmental malformations (not carotenoid intake)....also, >UL: skin, bone, liver toxicity

Vitamin D

• Intake recommendations:
  – Typical young adult AI, 5 mcg/d cholecalciferol (depends on sun exposure; higher AI for older...)

• Major dietary sources & availability:
  – Fatty fish, fortified milk, also produced in skin exposed to sun/UV light
  – Canadian diet is typically sufficient (increased risk for children, older adults, people with darker skin, winter time...)

• Forms & mobilization:
  – Cholecalciferol (D3) can be made by body from cholesterol (7-dehydro; with UV)
  – Reactions in liver and kidney lead to successive activation of D3, to 25-hydroxy-D3, and to 1,25-dihydroxy-D3
  – Circulatory carrier delivers 25-hydroxy-D3 throughout body
Vitamin D

- **Functions of vitamin D:**
  - Form with most biological activities: 1,25 dihydroxy-D3 (vitamin D₃ hormone)
  - Active form is involved in control of gene expression
    - accounts for many effects of ‘vitamin D’ in health and disease
  - Important for bone health and many other functions
    - Can ↑ blood Ca (and P) levels and ↓ loss of calcium from body

- **Deficiency of vitamin D:**
  - may result from: low dietary intake & low sun exposure; low fat intake or absorption; liver diseases
  - can lead to bone weakness (rickets, osteomalacia)
  - may increase risk of other diseases...

- **Toxicity of vitamin D:**
  - High dietary intake may lead to high blood calcium...nausea, confusion, loss of appetite...extreme: can lead to tissue calcification...& can be fatal

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Vitamin K

- **Intake recommendations:** Typical adult AI, 90-120 mcg/d (f-m)
- **Major dietary sources & availability:**
  - green leafy vegetables, some made by intestinal bacteria...less than % of the amount present in plants foods is normally absorbed during digestion
- **Forms, storage & mobilization:**
  - K: koagulation (historical); forms: Phylloquinone (K, K1, plants); Menaquinone (K2); Menadione (K3, synthetic)
  - Low storage in liver...increased susceptibility to consequences of deficiency
- **Functions of vitamin K:**
  - molecular level: coenzyme; helps regulate blood coagulation reactions; bone health and other functions
- **Deficiency of vitamin K:**
  - Rare with typical diets and normal intestinal flora...newborns are susceptible
  - Increased risk of hemorrhage
- **Toxicity of vitamin K:** Low (...reported with high doses of K3)

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Vitamin E

- **Intake recommendations:** Typical adult RDA 15 mg/d alpha-tocopherol
- **Major dietary sources & availability:** plant oils, nuts, whole grains/wheat germ, some vegetables...susceptible to light, air, heat
- **Forms & mobilization:**
  - food-form (d-alpha-tocopherol) and synthetic forms; circulatory transport by specific carrier proteins and lipoproteins
- **Functions of vitamin E:**
  - At molecular level: antioxidant (protects lipoproteins, cellular membranes & other lipid-rich compartments)
- **Deficiency of vitamin E:** ↑ oxidative damage & ↓ protection against toxins (e.g., in foods and smoke); severe deficiencies with some rare diseases...
- **Supplementation with E:** under research
- **Toxicity of vitamin E:** low relative to A and D...under research
(Water soluble vitamins…)

**Vitamin C**

- **Intake recommendations**: typical adult RDA = 75-90 mcg/d
- **Major dietary sources & availability**: fruits & vegetables…susceptible to heat & oxygen
- **Functions of vitamin C**:
  - molecular level: antioxidant; Coenzyme in collagen formation...
  - can lead to increased iron absorption
  - can 'reactivate' vitamin E...
- **Deficiency of vitamin C**: Scurvy (chronic); other health problems...
- **Supplementation with vit. C**: extra protection against oxidative damage?
- **Toxicity of vitamin C**: low (excess readily excreted); >1 g/day may cause GI problems.....also, too much iron may be absorbed...

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**Oxidative stress & Antioxidants**

Normal energy metabolism (oxygen)
Also, drugs and other chemicals, radiation

![Diagram of oxidative stress and antioxidants]

**Thiamin & Riboflavin & Niacin**

**Thiamin**

- **Intake & major dietary sources**: typical adult RDA, 1.1-1.2 mg/d (f~m;~0.5 mg/1000 kcal; most Canadians get ~2xRDA); foods: pork, whole grain products, enriched cereal, some vegetables…susceptible to heat; absorption ↓ by alcohol
- **Forms & functions**: dietary thiamin converted to active TPP form; body has some TPP reserves; TPP is a coenzyme in many decarboxylation reactions.... carbohydrate metabolism (helps body get energy from dietary carbohydrates)
- **Deficiency & Toxicity**: can lead to neurological disorders (low energy production, beriberi; low neurotransmitter levels); deficiency rare in Canada....chronic alcoholics; **toxicity**: low (excess readily excreted)

**Riboflavin**

- **Intake & major dietary sources**: adult RDA, 1.1-1.3 mg/d (f~m;~0.5 mg/1000 kcal; most get ~2xRDA); foods: dairy & other animal products, some veg...light-sensit.
- **Forms & functions**: Riboflavin converted to FAD, FMN active forms; FAD, FMN are coenzymes for energy production
- **Deficiency & Toxicity**: neurological symptoms (low energy production), skin inflammation; deficiency rare in Canada....alcoholics; **toxicity**: low (none reported)
Niacin

- **Intake recommendations:** typical adult RDA, 14-16 mg/d (f-m; ~7 mg/1000 kcal; most Canadians get ~2xRDA)
- **Major dietary sources & availability:** fortified bread, wheat bran, mushrooms, peanuts, animal products...relatively heat-stable
- **Forms and functions of niacin:**
  - some can be made by the body; niacin is converted to active forms, NAD+ & NADP+, that participate in 100's of metabolic reactions as coenzymes (e.g., energy, ATP, production reactions)
- **Deficiency of niacin:** the 3 d’s, skin lesions (dermatitis), diarrhea; Low energy production (neuro. symptoms: dementia)….pellagra
- **Supplementation with niacin:** under research for atherosclerosis; possible side effects for some people...not generally recommended
- **Toxicity:** at >20 x DRI, skin irritations, nausea, possible liver damage

Vitamin B6

- **Intake recommendations:** typical adult RDA, 1.3 mg/d (↑ for elderly)
- **Major dietary sources & availability:** fruits & vegetables, dairy & other animal products, cereals, yeast products...up to ½ may be destroyed by cooking
- **Forms and functions of vitamin B6:**
  - Phosphate forms such as PLP are active; PLP is a coenzyme in many metabolic reactions, e.g., for production of non-essential amino acids
  - other functions: synthesis of hemoglobin, neurotransmitters, niacin; conversion of HCO to C; gluconeogenesis; white blood cell (WBC) function
- **Deficiency of vitamin B6:**
  - neurological symptoms (e.g., ↓ neurotransmitter production); microcytic hypochromic anemia (low hemoglobin); immunodeficiency (↓ WBC)
- **Toxicity of vitamin B-6:** Nerve damage reported with chronic, high doses

Biotin & Pantothenic acid

**Biotin**

- **Intake & major dietary sources:** typical adult AI, 30 mcg/d; foods: egg yolks, liver, peanuts, cheese...some synthesized by intestinal bacteria...about ½ may be destroyed by cooking
- **Forms & functions:** active as biocytin BCY, attached to protein lysines; enzymatic (biotinidase) cleavage of BCY to biotin for absorption; BCY is a coenzyme in many reactions, e.g., production of fatty acids (anabolic) & use of carbohydrates & fat for energy (catabolic); novel, chromatin structure, functions under research...
- **Deficiency & Toxicity:** rare genetic deficiency (low biotinidase); deficiency can also be caused by some medications such as anti-convulsants; some signs of deficiency include neurological symptoms (e.g., from excess lactate) and skin problems (e.g., from fatty acid deficiencies); toxicity: very low (none reported)

**Pantothenic acid** ([AI, 5 mg/d, widespread food sources...])
Folate

- **Intake recommendations:** Typical adult RDA, 400 mcg/d (pregnancy, 600 mcg)
- **Major dietary sources & availability:** legumes & some other vegetables & fruits, liver, fortified cereals... heat-sensitive...Canadian diet typically deficient
- **Forms and functions of folate:**
  - Pteridine-PABA-glutamic acid: monoglutamylfolate (mGF; called folic acid); dietary polyGF converted to mGF in gut, for increased absorption
  - Biologically active THFA (tetrahydrofolic acid) form functions as coenzyme in many reactions, e.g., synthesis of DNA in cell division, conversion of hC to C, production of neurotransmitters; epigenetic effects under research
- **Deficiency of Folate:**
  - Slow or defective DNA synthesis: severe def. leads to megaloblastic (macrocytic) anemia with large rbc precursors, ↓body growth, ↑inflammation; ↑risk of some cancers(?); neurological symptoms (low neurotransmitters); high hC
  - Increased risk of spontaneous abortion and birth defects (esp. neural tube)
- **Toxicity of Folate:** Not well documented...skin irritations, respiratory distress

**Vitamin B12**

- **Intake recommendations:** Typical adult RDA, 2.4 mcg/d
- **Major dietary sources & availability:** animal products...release from food is required for absorption (↑ absorption from supplement sources); typical Canadian non-vegetarian diet provides > 2xRDA; absorption ↓ with aging
- **Forms, mobilization & functions of vitamin B12:**
  - Two factors (salivary R-protein & stomach intrinsic factor) aid in protection/absorption of B12 in body; B12 Absorbed in small intestine & delivered throughout body by carrier protein; liver stores supply for several years
  - Active forms include methylcobalamin; functions in DNA synthesis through THFA production; hC to M conversion; nerve cell integrity and function
- **Deficiency of vitamin B-12:**
  - Chronic: pernicious anemia...neurodegeneration, potentially fatal
- **Toxicity of B12:** very low

**Diet and Cancer**

CANCER is a group of diseases characterized by cells that have escaped normal growth & death controls; these abnormal cells have high rates of division (proliferation) & often invade & colonize other tissues (malignancy, metastasis)

- The development of many cancers is influenced by genetics as well as environmental factors such as diet
  - In terms of diet, cancer risk may be influenced by deficiencies of protective nutrients/phytochemical and excesses of harmful (carcinogenic) substances
- Are there dietary factors that may be help decrease the risk of cancers? Under research...
  - ↑Intake of....fruits/vegetables; vitamins B12 & folate; vit. A & D; vit. C, E, and other dietary antioxidants; other vitamins/ minerals/ fibre/ phytochemicals;
- Dietary factors that may increase the risk of some cancers
  - Deficiency of potentially protective factors (above); high caloric intake; high intake of fats/red meats; chronic high alcohol consumption; other toxins/carcinogens.........cooking methods