

Dietary Supplements and Oral Health



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Per 1994 Dietary Supplement Health Education Act

- A dietary supplement is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet.
- The "dietary ingredients" in these products may include: vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites.
- Dietary supplements can also be extracts or concentrates, and may be found in many forms such as tablets, capsules, softgels, gelcaps, liquids, or powders.

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- Since passage of DSHEA, the marketplace has grown from roughly 4,000 products to more than 29,000.
- The sheer number and variation in products makes it difficult for clinicians to counsel patients about DS use.

Tsourounis, et al. Clin Pharmacol Ther 2010; 87(2):147-9

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Do You Believe?

- Most Americans get all the micronutrients they need in their diet.
- Nutrient deficiencies are rare in the United States.
- The dental and medical communities are adequately trained to recognize nutrient deficiencies in their clinical practice.

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Food is Foundational



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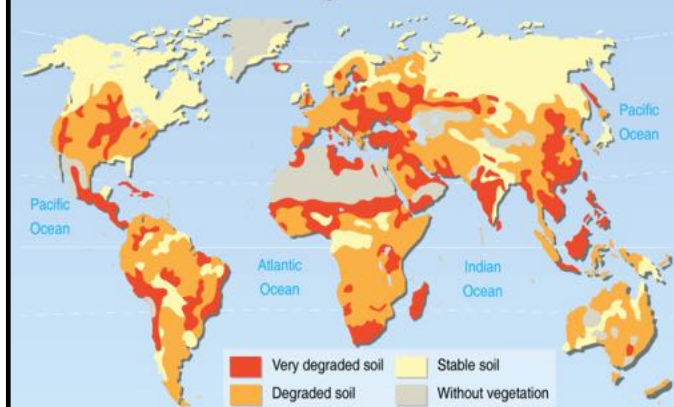
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Soil degradation



Source: UNEP, International Soil Reference and Information Centre (ISRIC), World Atlas of Desertification, 1997.

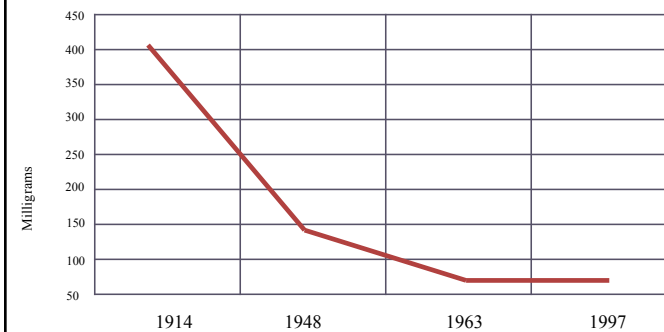
Philippe Rekacewicz, UNEP/GRID-Arendal

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Average Mineral Content in Selected Vegetables, 1914-1997

Sums of Average of Calcium, Magnesium, and Iron in Cabbage, Lettuce, Tomatoes and Spinach



Source: Lindlahr, 1914; Hamaker, 1982; US Department of Agriculture, 1963 & 1997

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Centers for Disease Control

- Recent findings have determined that *less than optimal biochemical levels* of vitamins and minerals are associated with risks of adverse health effects.
- “These health effects include cardiovascular disease, stroke, impaired cognitive function, cancer, eye diseases, poor bone health, and other conditions.”

CDC: 2nd National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population

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At Risk Populations

- Obesity (B1, B6, B12, D)
- Ethnic/racial minorities
 - Hispanics (B3, folate, D, magnesium, iron)
 - African Americans (iron, zinc, B6, D)
- Those with chronic disease
- Chronic medication use
- Families with food insecurity
- Those on restricted diets
 - Vegans - B6, B12, D, K, choline, iron, zinc, omega 3s



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Case 41-year old Female

- Strict vegan for 2.5 years. Disturbance of taste (unable to sense flavor of variety of fruits and vegetables), fatigue after simple daily activities, paresthesia of the anatomic structures innervated by the mandibular division of the trigeminal nerve on her left side, disturbance of memory and slowing mental faculty. No meds. No significant medical or dental history.

Pontes HA, et al. *J Can Dent Assoc* 2009; 75(7):533-7.

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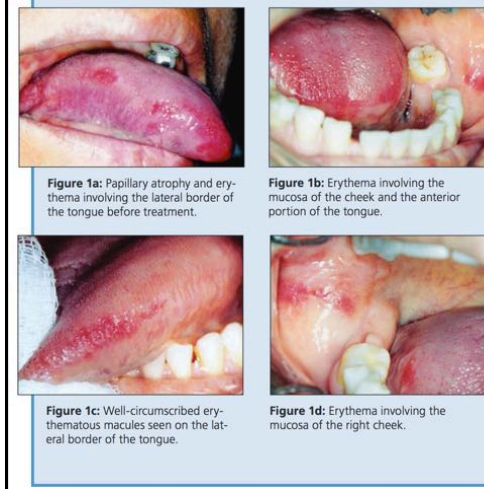


Figure 1a: Papillary atrophy and erythema involving the lateral border of the tongue before treatment.

Figure 1b: Erythema involving the mucosa of the cheek and the anterior portion of the tongue.

Figure 1c: Well-circumscribed erythematous macules seen on the lateral border of the tongue.

Figure 1d: Erythema involving the mucosa of the right cheek.

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Laboratory Tests

Test	Normal range (female)	Patient's values
RBC count (cells/ μ L)	3.90–5.03	1.63
Hemoglobin (g/dL)	12.0–15.5	7.2
MCV (fL)	80–100	144
Hematocrit (%)	36–45	23.4
RDW (%)	13 \pm 1.5	25
Serum folate (ng/mL)	3–16	7.73
Serum cobalamin (pmol/L)	118–716	71.8

MCV = mean corpuscular volume; RBC = red blood cell; RDW = red cell distribution width.

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Figure 2a: Dramatic resolution of erythema and all pathologic symptoms after 1 week of treatment with parenteral doses of cobalamin and folic acid.

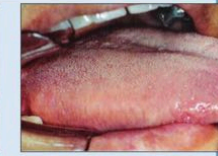


Figure 2b: Absence of papillary atrophy and erythema previously seen on the lateral border of the tongue.



Figure 2c: Tissue regeneration on the mucosa of the cheek appeared complete after 2 weeks of treatment.

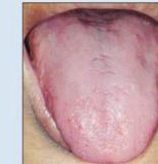


Figure 2d: Complete tissue regeneration on the tongue after treatment.

Patient treated with 1000 mcg B12 IM per week for 4 weeks and 1 mg folate daily.
Symptoms disappeared after 14 days of treatment.

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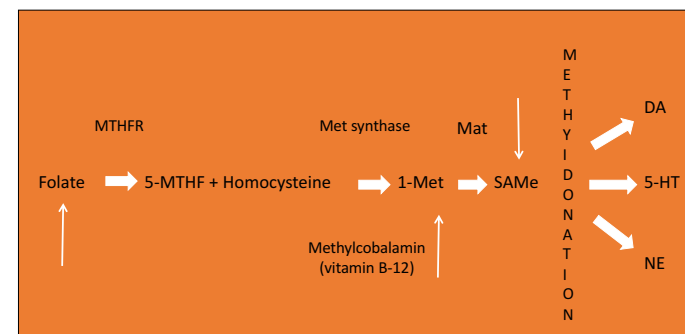
B-Vitamins

- The B-vitamins are important for the metabolism of carbohydrates, fats and proteins and play a vital role in the production of fuel and energy for the body.
- There are eight B-vitamins that partner together, which is why you almost always want to take them together in balanced amounts.



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Vitamin B12

- Found in animal and fortified foods. Key role in DNA synthesis, hematopoiesis and neurological function.
- Deficiency damages myelin sheath covering cranial, spinal, and peripheral nerves, resulting in neurological damage.
- Myelination primarily occurs during fetal development and early infancy but continues through early adulthood.
- Risk: inadequate intake, veganism, malabsorption, medications, obese, insulin resistant adolescents.
- MMA level > 271 nmol/L is most reliable measure of deficiency (aim for serum B12 500-800 pg/ml)

Niafar M, et al. Intern Emerg Med 2015; 10(1):93-102.

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PPIs and Metformin Both Deplete B12



Metformin With Proton Pump Inhibitors: A Polypharmacy Recipe for Neuropathy via Vitamin B12 Depletion
Zdilla MJ. Clin Diabetes 2015; 33(2):90-5.

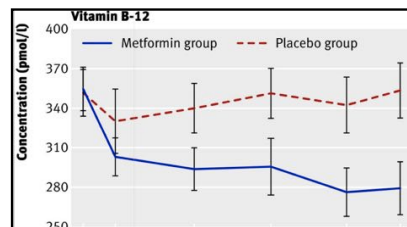
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Metformin and Vitamin B-12

Study of 390 patients with type 2 diabetes randomized to metformin (850 mg) or placebo T1D for 4.3 years.

Compared with placebo, metformin treatment was associated with a mean decrease in vitamin B-12 concentration of -19%.



De Jager, et al. BMJ 2010; 340:c2181

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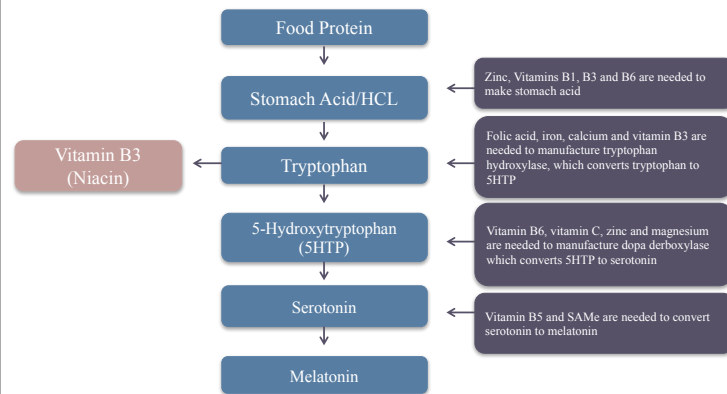
Metabolism of B12

- Protein enters stomach, HCL and pepsin separate B12 from protein in animal food
- Free B12 joined to protein called intrinsic factor (IF) made by parietal cells in stomach.
- B12-IF travels to ileum where, if calcium is adequate, it is absorbed.
- Atrophic gastritis is thought to affect 10%-30% of people over 60 years of age.
- Frequently associated with the presence of autoantibodies directed towards stomach cells and/or *H. pylori* infection.
- Diminished gastric function in individuals with atrophic gastritis can result in bacterial overgrowth in the small intestine and cause food-bound vitamin B12 malabsorption.

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Serotonin and Melatonin Pathways



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Vitamin B6 (Pyroxidal-5-Phosphate)

- Critically involved in production of serotonin, dopamine, melatonin, hemoglobin, protein metabolism, energy production, and more.
- Deficiency: depression; impaired cognition, attention, memory, and sleep. Increased risk for heart disease, stroke and colorectal cancer.
- Common OTC analgesics and oral contraceptives lower B6 levels. 30 MILLION Americans are deficient in B6.
- Serum PLP < 20 nmol/L = deficiency, PLP 20-30 nmol/L risk CVD/stroke.
- Need ~6 mg per day to maintain normal serum level.

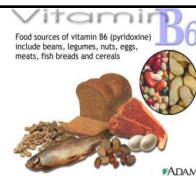


Larsson SC, et al. JAMA 2010; 303(11):1077-83
Morris MS, et al. Am J Clin Nutr 2008; 87(5):1446-54
Ulvik A, et al. Am J Clin Nutr 2014; 100(1):250-5

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Vitamin B6 Deficiency



- **30 million Americans are deficient (PLP < 20nmol/L)**
- Women twice as likely to be deficient and deficiency rates for blacks (15.7%) are higher than for whites (10.7%).
- NSAIDs and oral contraceptives interfere with B6 metabolism.
- NHANES (n=6000): *most OCP users had PLP < 20 nmol/L.*
- *Chronic inflammation increases B6 catabolism*
- Upper limit set at 100 mg per day.

CDC 2nd National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population
Morris MS, et al. Am J Clin Nutr 2008; 87(5):1446-54
Ulvik A, et al. Am J Clin Nutr 2014; 100(1):250-5

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To Get 1.5 mg B6 in Food

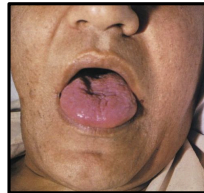
- 2.5 bananas
- 12 Tbsp. roasted sunflower seeds
- 8 ounces chicken breast
- 8 ounces sockeye salmon
- 3.5 cups raw diced avocado
- 3 cups sweet potatoes
- 15 cups of milk OR
- 20 Tbsp. peanut butter

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65-year old man complains of persistent tingling and numbness in his legs (bilateral) during a routine oral care visit. Dentist notes the he has a beefy red and deeply fissured tongue and complained of a sore throat. Other than cataract in his right eye, no known medical problems. Vegetarian and lactose intolerant. Which of the following nutrient deficiencies would best explain his symptoms?

- A. Vitamin B2
- B. Vitamin B6
- C. Vitamin C
- D. Vitamin B12

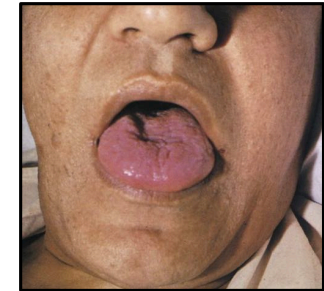


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Vitamin B2 Deficiency

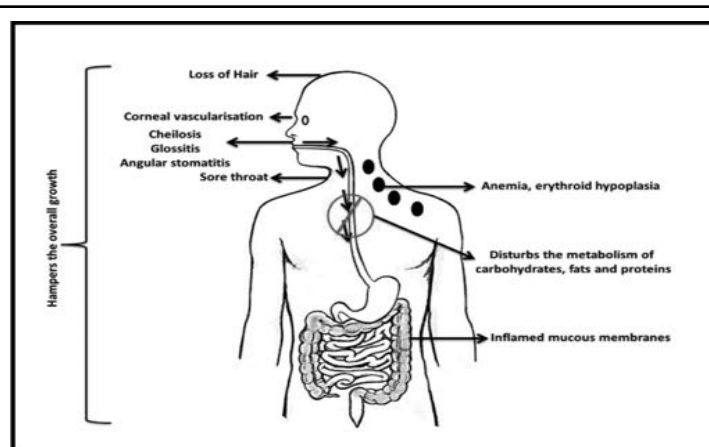
The best answer is A. Riboflavin deficiency causes ariboflavinosis, which manifests as cracked lips, inflammation of the tongue, dryness or burning of the oral cavity, and sore throat.



From McLaren DS: *A colour atlas and text of diet-related disorders*, ed 2, London, 1992, Mosby-Year Book.

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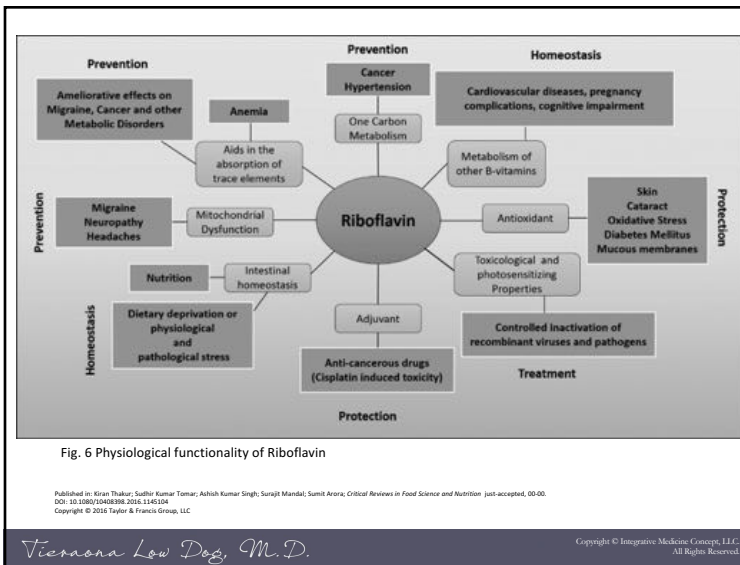
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Riboflavin Deficiency: At Risk Groups

- Alcoholics
- Those with chronic infection or liver disease (increased demand)
- Inflammatory bowel disease (decreased absorption)
- Diabetics (increased excretion)
- Elders (decreased absorption, dietary intake)
- Vegans (insufficient dietary intake)
- Pregnant and breastfeeding women (increased demand – low riboflavin increases risk for pre-eclampsia)
- Adolescents, particularly girls (increased demand)
- Athletes (increased demand)
- Hyperthyroidism (increased demand)
- MTHFR C667T genotype (increased demand)
- Brown-Vialetto-Van Laere syndrome genetic neurological disorder mutation in transporter: deafness, bulbar palsy, respiratory difficulties)

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Which of the following micronutrients is needed to convert vitamin B6 to the active form of pyridoxal 5 phosphate in the liver?

- A. Iron
- B. Zinc
- C. Riboflavin
- D. Vitamin A

- The correct answer is C.
- Riboflavin is needed to convert all forms of vitamin B6 to the active form of PLP. Zinc is needed by cells to take up PLP.

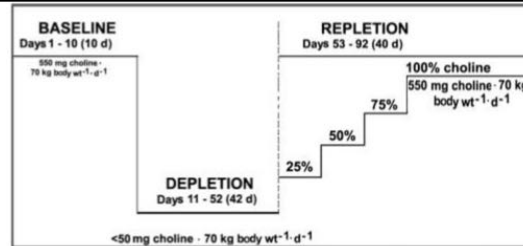
Choline: Related to B-Vitamins

- Choline deficiency causes abnormal deposition of fat in the liver, which results in a condition called nonalcoholic fatty liver disease.
- Necessary for healthy cell membranes and cognition as we age.
- Water soluble nutrient in the B-vitamin family that is particularly crucial during pregnancy and the first three years of a child's life.
- New daily value set in 2016: 550 mg per day

Jiang X, et al. Trends Endocrinol Metab 2014; 25(5):263-73.

Jiang X, et al. FASEB J. 2012;26(8):3563-3574.

Wozniak JR, et al. Nutr Res 2013; 33(11):897-904



- 57 healthy adults were fed choline-deficient diets under controlled conditions.
- Results showed that 77% of men, 80% of postmenopausal women, and 44% of premenopausal women developed fatty liver, liver damage, and/or muscle damage.
- Dysfunction corrected when choline was reintroduced into diet.

Fischer LM, et al. Am J Clin Nutr. 2007;85(5):1275-1285.

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Choline in Pregnancy

- Prospective study involving 154 healthy mother-infant pairs conducted in Vancouver, Canada (72% white, 15% Asian). All women were taking PNV.
- Maternal blood collected at 16 and 36 weeks gestation and infant neurodevelopment assessed at 18 months age for 154 mother-infant pairs. Babies were all singletons and full-term.
- Significant *positive* associations found between infant cognitive test scores and maternal plasma free choline and betaine ($p=0.009$) and a strong trend towards gross motor development.

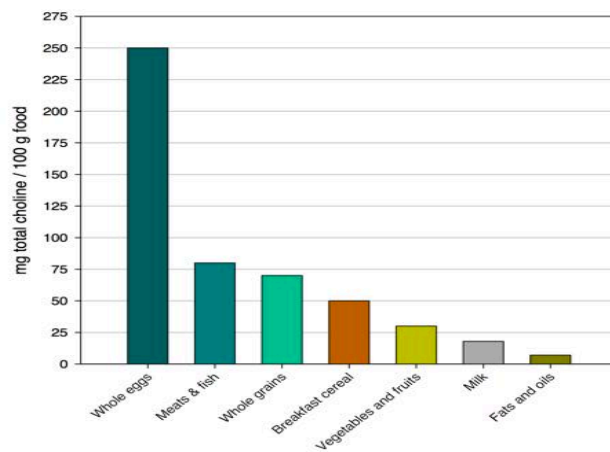


Wu BT, et al. PLoS One 2012; 7(8):e43448.

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Choline in Foods: <http://nalcd.nal.usda.gov/download/47335/PDF>



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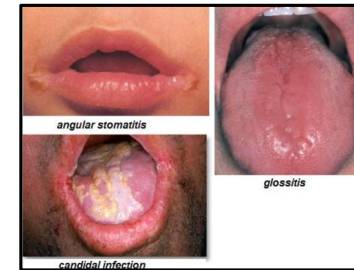
A 26-year old African American woman comes in for her routine dental exam. She mentions that she craves ice all the time, even in the winter. Dentist notes generalized oral mucosal atrophy and pallor. What nutrient deficiency is most likely?

- A. Folate
- B. Iron
- C. Calcium
- D. Selenium

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- Review of Systems May Yield
 - Shortness of breath
 - Fatigue
 - Sensitivity to cold
 - Muscular weakness
 - Low blood pressure
 - Restless legs
 - Pica (chew ice or non-food items)
- Physical Exam Findings
 - Angular cheilitis
 - Atrophic glossitis
 - Generalized oral mucosal atrophy
 - Candida infections
 - Mucosal pallor
 - Stomatitis
 - Nonspecific pallor of the mucous membranes



Correct answer is B: Iron

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Iron

WHO: Iron deficiency most common nutrient deficiency in world, affecting 2 billion people.

- Iron deficiency anemia accounts for 20% of all global maternal deaths.
- Necessary for growth and development and essential component of hemoglobin.
- Iron promotes resistance to disease; improves health of the teeth, skin, and bones; maintains energy
- Meta-analysis found that iron supplementation *improved attention, concentration, and IQ.*
- Iron deficiency increases the risk of lead toxicity



Falkingham M, et al. *Nutr J* 2010; 25:9-4.
Calarge C, et al. *J Child Adolesc Psychopharmacol.* 2010;20(6):495-502

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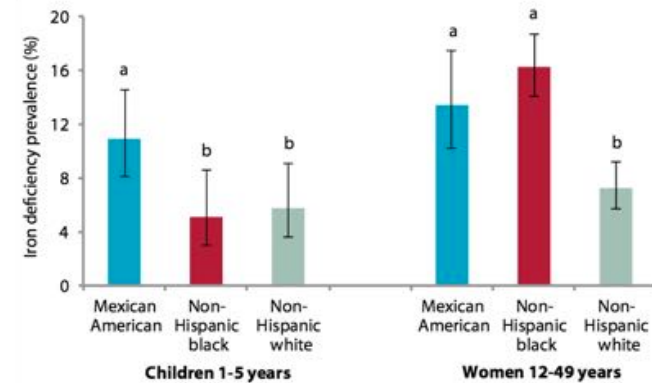


Figure H.3.a. Age-adjusted prevalence estimates of low body iron stores (<0 mg/kg) in U.S. children and women by race/ethnicity, National Health and Nutrition Examination Survey, 2003-2006.

Error bars represent 95% of confidence intervals. Bars not sharing a common letter differ within children and women ($p < 0.05$). Age adjustment was done using direct standardization.

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To Get 18mg of Iron in Food

- 4 cups of raisins
- 3-5 cups instant oatmeal
- 3 cups Special K cereal**
- 3 cups cooked lentils
- 2.2 cups canned white beans
- 10 ounce beef liver
- 45 ounce chicken breasts
- 15 cups broccoli OR
- 3 cups cooked spinach



Non heme iron absorption is 2- to 3-fold higher with co-ingestion of 25 to 75 mg of vitamin C

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Note: Hemochromatosis

- The gene for familial hemochromatosis (*HFE* gene) affects 8% of the US white population.
- Excess body iron is postulated to be important in the etiology of CAD, strokes, certain cancers, and neurodegenerative disorders because iron is important in free radical formation.
- Iron absorption is highly regulated to prevent excess, no physiologic pathway for ridding the body of iron exists.
- People NOT at risk of iron deficiency (teenage boys, adult men, women with infrequent menstrual cycles, and postmenopausal women) should NOT take multivitamins that contain iron or iron supplements unless instructed to do so by their health care provider.

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Food Fortification

- Many cereals fortified with vitamins B1, B2, B3, B5, B9, B12, and C; iron and calcium.
- Both an *upside and downside* (potential nutrient excess (e.g., iron in men, deficiency in women and children)
- Further complicating the issue: most non-GMO and/or organic cereals are not fortified.



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Vitamin C Deficiency



- Malaise and lethargy early symptoms.
- Then shortness of breath and muscle/bone pain.
- Skin changes, easy bruising, gum disease, loose teeth, slow healing wounds, dry mouth, dry eyes. emotionally labile.
- Weakened capillaries. Hemorrhage is hallmark of scurvy and hair follicles are common site of cutaneous bleeding.
- Inflammation of interdental and marginal gingiva followed by bleeding, ulceration, and bad breath.
- Swelling of periodontal membranes occur, followed by loss of bone and loosening of the teeth.

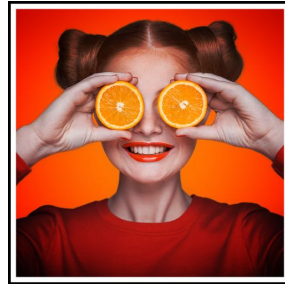
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Vitamin C

- Potent antioxidant, activates folate, needed to convert tryptophan to serotonin, cofactor in synthesis of carnitine, thyroxine, norepinephrine, dopamine and immune cells
- Vitamin C levels decline rapidly during periods of emotional and physical strain, and illness.
- Given the consistent effect of vitamin C on the duration and severity of colds in the regular supplementation studies, and the low cost and safety, it may be worthwhile for common cold patients to test on an individual basis whether therapeutic vitamin C is beneficial for them."



Hemila H, et al. Cochrane Database Syst Rev 2013; Jan 31;1:CD 000980

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Pregnancy and Smoking

- Giving pregnant smokers (9969 women) vitamins C and E starting at 9-16 weeks gestation reduced risk of placental abruption (40%) and preterm birth (30%) compared to placebo.
- 500 mg/d vitamin C improved newborn PFT results and decreased wheezing through 1 year compared to placebo in 150 pregnant smokers.



McEvoy CT, et al. JAMA 2014; ;311(20):2074-82.
Gandley R, et al. Pregnancy Hypertens 2012; 2(3):331-2

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Sperm

- Seminal fluid rich in vitamin C, acts as a potent antioxidant and helps to maintain the quality and function of sperm.
- Fertile men have significantly higher seminal vitamin C levels compared to infertile men.
- May improve sperm concentration and mobility.

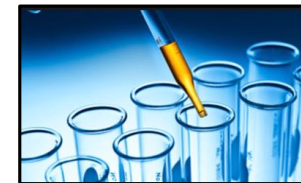


Rafice B, et al. Urol J 2016; 13(2):2635-9.

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Lab Tests



- Ascorbic acid levels can be determined by with a fasting blood sample.
- Serum or plasma levels less than 11.4 $\mu\text{mol/L}$ indicate deficiency.
- Levels between 11.4 and 50 $\mu\text{mol/L}$ indicate suboptimal status.

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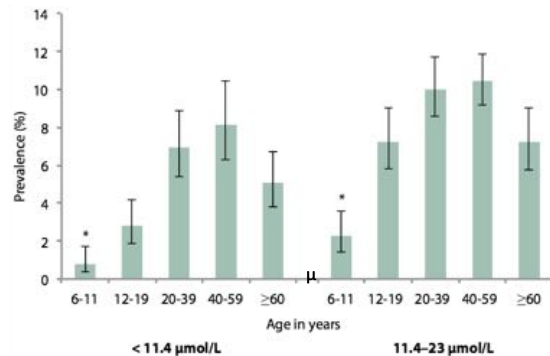


Figure H.1.f. Prevalence estimates of vitamin C deficiency (serum concentrations less than 11.4 $\mu\text{mol/L}$) and low vitamin C concentrations (11.4-23 $\mu\text{mol/L}$) in the U.S. population aged 6 years and older by age group, National Health & Nutrition Examination Survey, 2003-2006.

Error bars represent 95% of confidence intervals. *Prevalence in children is significantly lower than prevalence in persons 20 years and older ($p < 0.05$).

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Supplement Form

- Numerous forms of supplements available: calcium and mineral ascorbates, Ester-C, ascorbic acid and natural acerola/rose hips.
- Studies have not found significant differences between the different forms.
- Oral dosing under tight control.
- Single doses > 200 mg are not well absorbed.



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Which of the following nutrients would be most beneficial for someone who has idiopathic taste disorders?

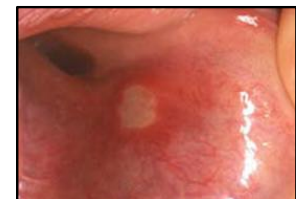
- Magnesium
- Vitamin C
- Zinc
- Biotin

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Zinc and Oral Health

- A review of clinical trials found “moderate quality evidence that zinc supplements improve overall taste improvement in patients with zinc deficiency/idiopathic taste disorders.”
- Zinc deficiency detected in 28% of recurrent aphthous stomatitis patients compared to controls.



Nagraj SK, et al. Cochrane Database Syst Rev 2014; 2014 Nov 26;11:CD010470.

Ozler GS. J Laryngol Otol 2014; 128(6):531-3

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Zinc and the Senses

- Zinc is necessary for sense of smell, which accounts for about 80% of your sense of taste!
- Also important for oral health; one sign of zinc deficiency is red, swollen, and tender gums that may bleed after brushing.
- Zinc helps protect cells that line the mouth in those undergoing chemotherapy or radiation.



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Zinc and Taste

- Study found half of women undergoing chemotherapy for gynecological cancer experienced altered taste.
- Serum zinc level consistently below lower limit of normal.
- RDBPCT of adult patients with head and neck cancers received zinc sulfate (50 mg, three times a day) or placebo at start of radiation through one month post. Zinc prevented radiation induced taste alterations.

Nishijima S, et al. Gynecol Oncol 2013; 131(3):674-8.

Najafizade N, et al. J Res Med Sci 2013; 18(2):123-6

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Zinc

- Zinc plays a vital role in our immune response.
- Marginal zinc deficiency lowers activity of important immune cells such as macrophages, neutrophils, and natural killer cells.
- WHO estimates marginal zinc status results in the deaths of > 780,000 children under the age five every year from diarrheal diseases, pneumonia, and malaria.
- Not effectively stored, must be continuously replaced in the diet.



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Zinc Deficiency in Children

Prevalence of zinc deficiency high in low-income minority children in the US, especially among African Americans and Hispanic adolescents:

- 28.4% females)
- 24.5% males



Brown KH, et al. Food Nutr Bull 2009; 30(1S):S12-40
Cole CR, et al. Am J Clin Nutr 2010; 91(4):1027-34.
De la Cruz-Gongora V, et al. Salud Publica Mex 2012; 54(2):135-45.

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Zinc in Children

- Meta-analysis concluded zinc supplementation reduces frequency, severity, and duration of diarrheal episodes in children under five years of age.
- Zinc supplementation in children (2-59 months) reduced incidence and prevalence of pneumonia.
- When supplemented for at least five months, zinc reduces cold incidence, school absenteeism and prescription of antibiotics in children.



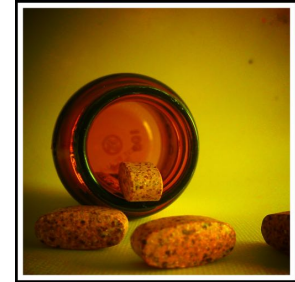
Aggarwal R, et al. Pediatrics. 2007;119(6):1120-1130
 Lassi ZS, et al. Cochrane Database Syst Rev 2010; 8:12:CD005978
 Singh M, et al. Cochrane Database Syst Rev 2011; 16:2:CD001364

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Zinc

- Zinc concentrations high in prostate gland, testes, and sperm. Deficiency might contribute to lower testosterone and infertility in men.
- Vegetarians need 50% more zinc due to lower absorption of zinc from plant foods. DV= 15 mg
- ACE inhibitors and thiazides deplete zinc
- Take 2 hours apart from medication, especially quinolones and tetracycline antibiotics.
- Do not take > 40 mg/d for more than a couple of months without supplementing copper.



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Table 2. Some Food Sources of Zinc

Food	Serving	Zinc (mg)
Oysters	6 medium (cooked)	27-50
Beef	3 ounces* (cooked)	3.7-5.8
Crab, Dungeness	3 ounces (cooked)	4.7
Pork	3 ounces (cooked)	1.9-3.5
Turkey (dark meat)	3 ounces (cooked)	3.0
Beans, baked	½ cup	0.9-2.9
Chicken (dark meat)	3 ounces (cooked)	1.6-2.7
Yogurt, fruit, nonfat	1 cup (8 fl. oz.)	1.8
Cashews	1 ounce	1.6
Chickpeas (garbanzo beans)	½ cup	0.5-1.3
Milk	1 cup (8 fl. oz.)	1.0
Almonds	1 ounce	0.9
Peanuts	1 ounce	0.9
Cheese, cheddar	1 ounce	0.9

*A three-ounce serving of meat is about the size of a deck of cards.

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For every 2000 mg of sodium intake, it takes this much daily calcium, on average, to maintain calcium balance.

- A. 200 mg
- B. 500 mg
- C. 1000 m
- D. 1500 mg

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Calcium Calculator: A Quick Estimate

Food	# Servings/Day	Estimated Calcium per serving, in mg	Calcium in mg
Milk (8 ounces)		X 300	=
Yogurt (6 ounces)		X 300	=
Hard Cheese (1 ounce)		X 200	=
Soy milk, fortified (8 ounce)		X 300	=
Orange juice, fortified (8 ounce)		X 300	=
Tofu, firm calcium set (4 ounces)		X 300	=
All foods not included above		X 250	=
		Total Calcium	=
AI for your gender and age group		Subtract your total calcium from AI	= Supplement this amount

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Deficiency



- One of the first signs of calcium deficiency is muscle cramping.
- Muscle aches of thighs and arms, with minimal exertion, could indicate a deficiency of calcium, vitamin D, and/or magnesium.
- Long term deficiency leads to poor bone development/loss of bone mineral density.
- If supplementing, calcium citrate or chelate better option for most people.
- Do not take calcium supplements at the same time as other medications (thyroid, bisphosphonates, phenytoin, tetracycline) or multivitamin/mineral.

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Calcium Requirements



- The RDA is 1,000 mg/day for children ages 4 to 8 years and 1,300 mg/day for boys and girls ages 9 to 13 years.
- Calcium intake recommendations are higher in children ages 9 to 13 to account for increased needs during puberty.
- Adults RDA is 1000 mg per day
1200 mg for women over 50 and
1200 mg for men over 70 years.

The National Academies Press; 2011:345-402.

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Drug Induced Osteoporosis

These drugs include:

- Glucocorticoids (steroids) – 1:5 cases of osteoporosis
- Aromatase inhibitors (breast cancer)
- Anti-androgen therapy (prostate cancer)
- Proton pump inhibitors (heartburn)
- Antiretroviral drugs (HIV, hepatitis)
- SSRIs (antidepressants) and antipsychotics
- Anticonvulsants (epilepsy)
- Loop diuretics (e.g. lasix)
- Heparin and oral anticoagulants

Mazziotti G, et al. Am J Med 2010; 123:877-84

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Vitamin D

- Vitamin D interacts with more than 1000 genes
- Vitrally important for calcium regulation (bones, heart, etc.)
- Higher blood levels improve breast cancer survival and reduce risk of colorectal cancer.
- Low vitamin D in adults causes muscle weakness and lower back and hip pain.
- Children with insufficient vitamin D at risk of developing hypomineralized dental enamel, increasing susceptibility to caries
- Obesity increases the risk of deficiency..



Kim Y, et al. Br J Cancer 2014; 110(11):2772-84.
Ma Y, et al. J Clin Oncol 2011; 29(28):3775-82

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Vitamin D Deficiency and Obesity

Sample 6-18 year olds from 2003-6 NHANES

- Prevalence of vitamin D deficiency (<20 ng/mL):
 - Healthy-weight (21%)
 - Overweight (29%)
 - Obese (34%)
 - Severely obese children (49%)
- Prevalence of vitamin D deficiency in severely obese white (27%), Latino (52%), and African-American (87%) children.



Turer CB, et al. *Pediatrics* 2013; 131(1):e152-61

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Endocrine Society Guidelines

- Serum 25(OH)D level used to evaluate high-risk folks
 - Insufficiency defined as 21-29 ng/mL
 - Deficiency defined as <20 ng/mL
- **66.8 million Americans** 1 year and older had vitamin D levels between 12-20 ng/ml
- **23 million Americans** 1 year and older had serum levels less than 12 ng/ml
- Most at risk were women and non-Hispanic blacks.

CDC 2nd *National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population*
Holick MF, et al. J Clin Endocrinol Metab 2011; 96(7):1911-30

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Endocrine Society Guidelines

“For clinical care, it appears that all current (testing) methodologies are adequate if one targets a 25(OH)D value higher than current cut points; for example, a value of **40 ng/ml (100 nmol/L)** is without toxicity and virtually ensures that the individuals ‘true’ value is greater than 30 ng/ml (75nmol/L).”

Holick MF, et al. J Clin Endocrinol Metab 2011; 96(7):1911-30

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Endocrine Society Guidelines for Treating Deficiency

All adults who are vitamin D deficient should be treated with 50,000 IU of vitamin D2/D3 once per week for 8 weeks or 6000 IU of vitamin D2/D3 daily to achieve a blood level of 25(OH)D *above 30 ng/ml, followed by maintenance therapy of 1500–2000 IU/d.*



Holick MF, et al. J Clin Endocrinol Metab 2011; 96(7):1911-30

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Vitamin D

To get 600 IU/d Vitamin D3:

- 3-4 ounces sockeye salmon, cooked
- 11.4 ounces water-packed tuna
- 26 oil-packed sardines
- 15 large eggs
- 6 cups fortified milk OR
- 30-45 ounces yogurt



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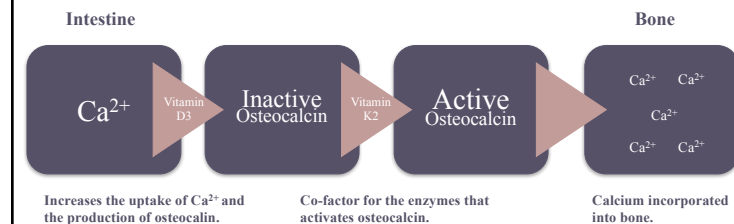
Vitamin K

- There are two main forms of vitamin K.
 - Phylloquinone, or vitamin K1, is synthesized by plants and makes up 90% of the vitamin K obtained in the diet. Best sources are green leafy vegetables. Fat-soluble so should be eaten with some healthy fat.
 - Menaquinone, vitamin K2, is result of bacterial action in GI tract converting K1 to K2 or obtained directly from food sources such as meat, egg yolks, fermented dairy and soy (e.g., miso, natto).



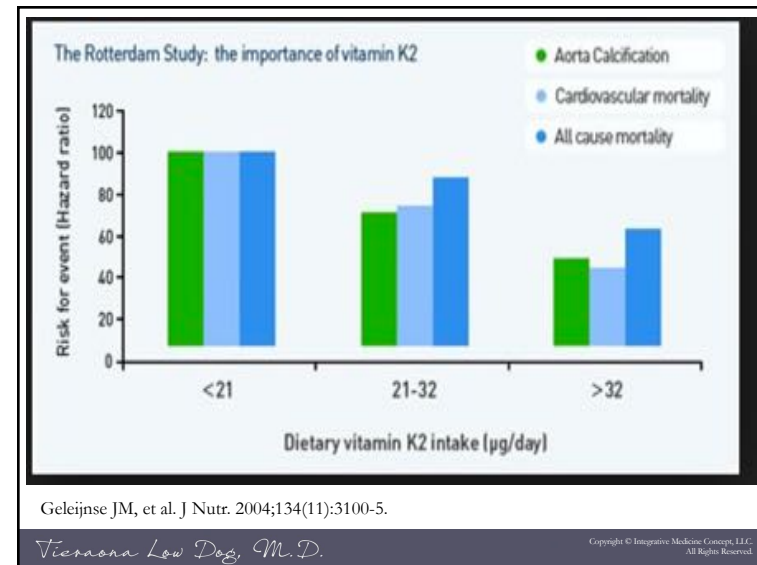
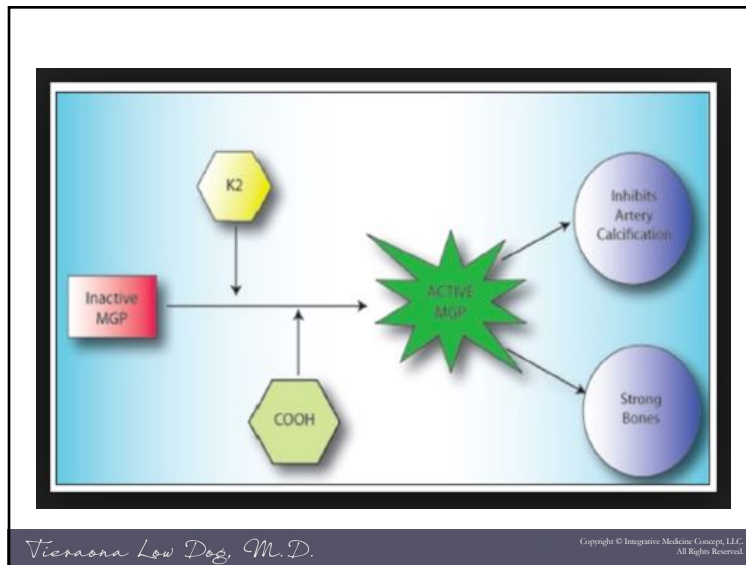
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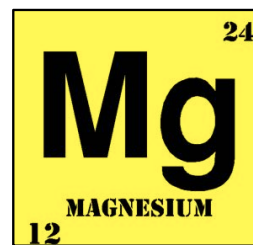
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Geleijnse JM, et al. J Nutr. 2004;134(11):3100-5.

Magnesium

- Low magnesium intakes and low blood levels have been associated with type 2 diabetes, metabolic syndrome, elevated CRP, hypertension, atherosclerotic vascular disease, sudden cardiac death, osteoporosis, migraine headache, asthma, and colon cancer.
- 48% of US population consumes less than the required amount of daily magnesium.



Rosanooff A, et al. Nutr Rev 2010; 70(3):153-64.

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Magnesium and the Heart

- Low serum magnesium levels associated with higher all-cause and cardiovascular mortality.
- Review of 44 studies shows Mg supplements enhance blood-pressure lowering effect of BP medications in stage 1 hypertension when given 230-460 mg/d.
- Nurses Health Study (88,375 women) found that for every 0.25-mg/dL increment in plasma magnesium –41% lower risk of sudden cardiac death. Women with lowest levels of magnesium also had significantly increased risk of stroke.

Reffelmann, et al. Atherosclerosis 2011 Nov;219(1):280-4.

Rosanooff, et al. Magnes Res 2010 Mar;23(1):27-40.

Chiuve, et al. Am J Clin Nutr. 2011;93(2):253-60.

Akarolo-Anthony SN, et al. Stroke 2014; 45(10):2881-6

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Ulcer/GERD Medications

Drug Classification	Nutrient Depletion
Proton pump inhibitors	Magnesium, iron, calcium, vitamin B12, folic acid, zinc, vitamin C, vitamin D (?)
H2 antagonists	folic acid

- There were 118.5 million prescriptions for PPIs in 2010 with roughly \$11.4 billion in sales. These numbers do not include over-the-counter sales for PPIs.
- esomeprazole magnesium (Nexium)
- pantoprazole sodium (Protonix)
- lansoprazole (Prevacid)
- omeprazole and sodium bicarbonate (Zegerid)
- omeprazole (Prilosec)
- rabeprazole sodium (Aciphex)
- dexlansoprazole (Dexilant)

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FDA Safety Advisory

- FDA issued MedWatch warning and label change for PPIs due to low magnesium levels associated with long-term use.
- “Those taking medications, generally more than one year, may end up with low magnesium, which can put them at risk for seizures, irregular heartbeats, and muscle spasms.”
- Review of nine studies (n=115,455) found that the odds of *developing hypomagnesia increased by 75% if taking PPIs.*
- FDA advises magnesium levels be checked before and periodically during treatment.

Park CH, et al. PLoS One 2014; Nov 13;9(11):e112558.

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Magnesium for Migraines

- Studies show that migraineurs have low brain Mg during migraine attacks and may have systemic Mg deficiency.
- Mg reduces recurrent pediatric migraine and tension headaches.
- Canadian Headache Society gave magnesium citrate a strong recommendation for prophylaxis of migraine.
- Dose generally 300-400 mg/d. Diarrhea most common side effect (glycinate and citrate forms less GI complaints than oxide).



Sun-Edelstein C, Mouskop A. Clin J Pain. 2009 Jun;25(5):446-52.
Pringsheim T, et al. Can J Neurol Sci 2012; 39(2Suppl):S1-S9.
Mouskop A, et al. J Neural Transm 2012; 119(5):575-9.

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Iodine in Pregnancy

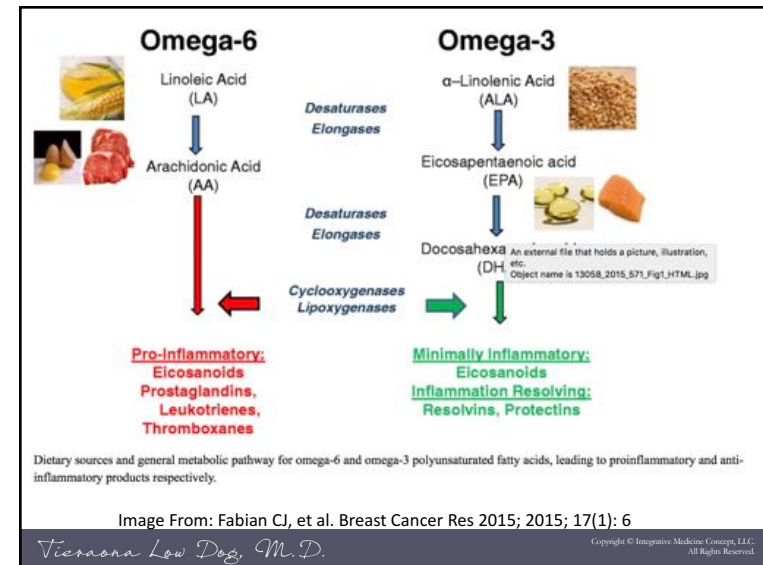
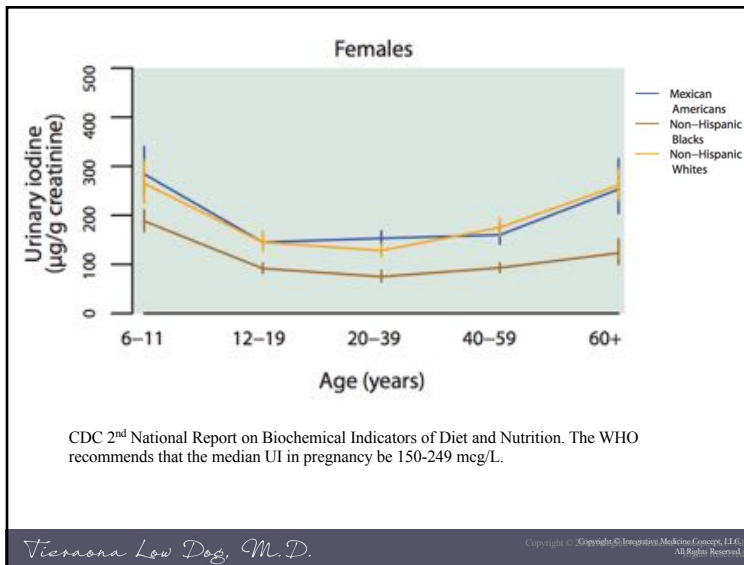
- Many reproductive aged women in US have marginal iodine status; salt in processed foods is not iodized.
- Deficiency associated with pregnancy loss and prematurity, and neurocognitive defects in the baby.
- Iodine deficiency now accepted as the most common cause of preventable brain damage in the world.
- Mild to moderate iodine deficiency associated with higher incidence of ADHD and lower IQ in the baby.
- American Thyroid Association recommends pregnant/lactating women supplement: 150 mcg/d potassium iodide.



Council on Environmental Health, et al. Pediatrics 2014; 133(6):1163-6.

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Omega 3 Fatty Acids – Bone/Muscle



- In animal studies, marine omega 3 attenuates bone loss associated with estrogen loss; EPA enhances calcium absorption, reduces calcium excretion and increases calcium deposition in bone.
- Marine omega 3 acids tend to have positive effects on bone if ingested for ≥ 18 months and given along with calcium.
- Omega-3 fatty acids stimulate muscle protein synthesis in older adults and may be useful for the prevention and treatment of sarcopenia.

Fernandes G, et al. *Prostaglandins Leukot Essent Fatty Acids*. 2003;68(6):361-372

Orchard TS, et al. *Br J Nutr*. 2012;107:S253-S260

Smith GI, et al. *Am J Clin Nutr* 2011; 93(2): 402-412

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Omega 3 and Prostate Cancer?

- SELECT trial raised concerns about potential link between omega 3s and increased prostate cancer/aggressive cancer.
- European Food Safety (EFSA) concluded, “there is no evidence for a role of EPA and/or DHA intake in the development of prostate cancer.”
- Also, “supplemental intake of EPA and DHA combined at doses up to 5 g/d does not give rise to safety concerns for adults.”

EFSA Journal 10(7): doi:10.2903/j.efsa.2012.2815

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Different Types of Fish Oil

- Supplementation is an alternative to eating fish; however, not all supplements are equal.
- Randomized, crossover study of 35 healthy individuals compared four popular brands/types of omega 3 fatty acids:
 - Concentrated triglyceride (rTG)
 - Ethyl ester (EE)
 - Phospholipid krill oil (PL)
 - Triglyceride salmon oil (TG)

Laidlaw M, et al. Lipids Health Dis 2014; 13:99

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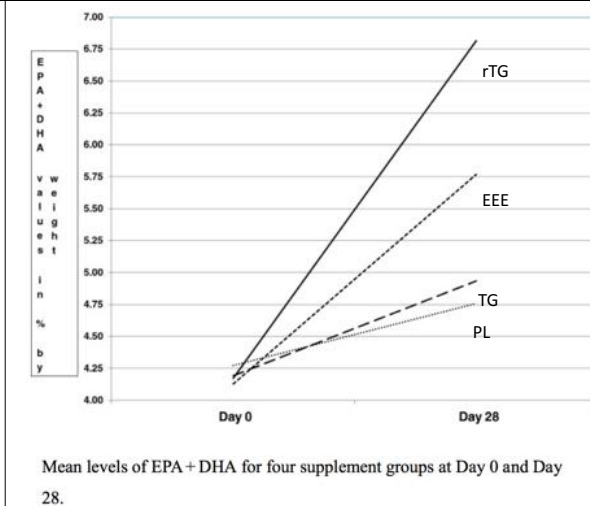
Dosing According to Manufacturer's Recommendations

TRT	Product	EPA & DHA per capsule*	Tested values	Label use: caps/day	Daily dosage of EPA + DHA
rTG	Nordic Naturals ProOmega®	325 mg EPA	329.6 mg EPA	2	EPA: 650 mg
	Triglyceride	225 mg DHA	226.0 mg DHA		DHA: 450 mg
EE	Minami MorEPA®	756 mg EPA	774.2 mg EPA	1	EPA: 756 mg
	Platinum Ethyl Ester	228 mg DHA	233.7 mg DHA		DHA: 228 mg
PL	Source Naturals ArcticPure®	75 mg EPA	78.0 mg EPA	2	EPA: 150 mg
	Krill Oil Phospholipid	45 mg DHA	46.7 mg DHA		DHA: 90 mg
TG	New Chapter			2	
	Wholemega® Salmon	90 mg EPA	96.4 mg EPA		EPA: 180 mg
	Oil Triglyceride	110 mg DHA	109.5 mg DHA		DHA: 220 mg

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Canadians and Omega 3

- The Omega-3 Index indicates the percentage of EPA+DHA in red blood cell fatty acids.
- Canadian government found that the mean Omega-3 Index level of Canadians aged 20-79 was 4.5%.
 - Levels higher for women, older adults, Asians and other non-white Canadians, omega-3 supplement users, and fish consumers; levels lower for smokers and people who were obese.
- Fewer than 3% of adults had levels associated with low CHD risk; 43% had levels associated with high risk.

Langlois K, et al. Health Rep 2015; Nov 18;26(11):3-11

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Evidence Based Products for Oral Health

INDICATION FOR ADULT HEALTH

Brand Name	Probiotic Strain	Dosage Form	CFU/Dose	No of Doses/Day	ID	AAD	CDAD	TD	C	FAP	IBS	IBD-UC	IBD-P	HP	OH	LDL-C	CID
Dentag™ Oral and ENT Health Probiotic Complex	<i>S. salivarius</i> BAA-1024 <i>L. plantarum</i> SD-5870 <i>L. reuteri</i> SD-5885 <i>L. acidophilus</i> SD-5212 <i>L. salivarius</i> SD-5208 <i>L. paracasei</i> SD-5275	Lozenge	1B/lozenge	2 lozenges											140-44		
Gum® PerioBalance®	<i>L. reuteri</i> ATCC 55730 100M <i>L. reuteri</i> ATCC PTA 5289 100M	Lozenge	200M/lozenge	2 lozenges											52,53		
OralBioica™ (BLIS K12)	<i>Streptococcus salivarius</i> K12	Lozenge	1B/lozenge	1-5 lozenges											50,51		

† - Product requires refrigeration

usprobioticguide.com

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Evidence Based Products for Oral Health

INDICATION FOR PEDIATRIC HEALTH

Brand Name	Probiotic Strain	Dosage Form	CFU/Dose	No of Doses/Day	Regurg/GvMot	Colic	ID	AAD	CDAD	IBD-UC	HP	C	FAP	IBS	CID	NI	CE/AD	OH
Dentag™ Oral and ENT Health Probiotic Complex	<i>S. salivarius</i> BAA-1024 <i>L. plantarum</i> SD-5870 <i>L. reuteri</i> SD-5885 <i>L. acidophilus</i> SD-5212 <i>L. salivarius</i> SD-5208 <i>L. paracasei</i> SD-5275	Lozenge	1B/lozenge	2 lozenges														140-44
OralBioica™ (BLIS K12)	<i>Streptococcus salivarius</i> K12	Lozenge	1B/lozenge	1-5 lozenges														50,51

† - Product requires refrigeration

usprobioticguide.com

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Resources

- *Fortify Your Life*, Tieraona Low Dog, MD with National Geographic
- Dietary Supplement Label Database: dslid.nlm.nih.gov
- NIH National Center for Complementary and Integrative Health (NCCIH): nccih.nih.gov
- Office of Dietary Supplements: ods.od.nih.gov
- Linus Pauling Institute: lpi.oregonstate.edu
- Consumer Labs: www.ConsumerLabs.com
- Natural Medicines Comprehensive Database: NaturalDataBase.com

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