

***Fortify Your Life:
The Case for Dietary Supplements***



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Financial Disclosures

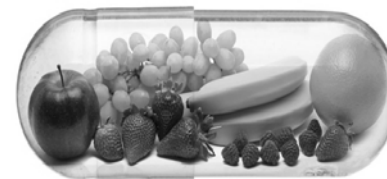
- Tieraona Low Dog, MD has the following disclosures to make:
 - President, Dr. Low Dog's Apothecary
 - Health Advisory Board, Pharmaca
 - Spokesperson, FoodState
 - Director, Scientific & Regulatory, Healthy Lifestyle Brands

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**Let your food be your medicine,
and your medicine be your food.**



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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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Food Insecurity

- Food insecurity is a serious public health problem associated with poor cognitive and emotional development in children and with depression and poor health in adults.
- Prevalence rate 30.2% food insecurity in female-headed households ~ 3 times the national average, more than 12.4 million children.
- Even mildest form of food insecurity is associated with risk of poor cognitive, social, and emotional development of children younger than 3 years.

Chilton M, et al. Am J Public Health 2009; 99(7): 1203–1211

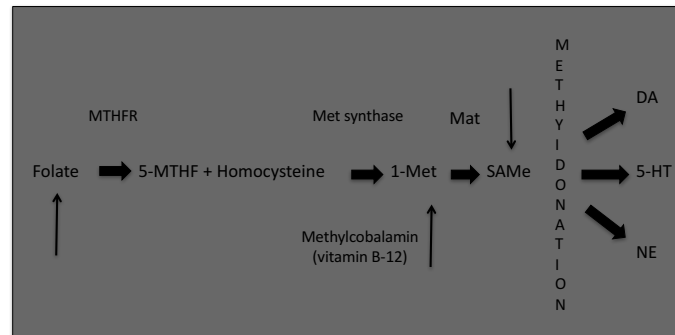
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B-Vitamins

- 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.

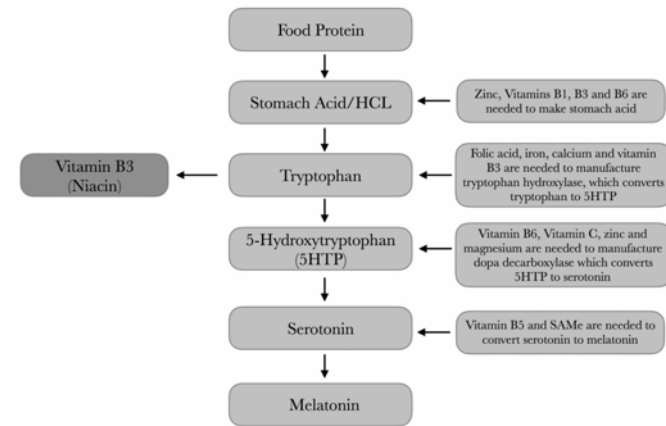
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The “Stress” B- Vitamins



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Serotonin and Melatonin Pathways



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The B-vitamins

- Vitally important for production of energy, maintenance of a healthy brain and nervous system and healthy function of the cardiovascular system.
- Low levels of vitamin B6 and B12 increase risk for *depression and impair cognition, attention, and memory*.
- Subset of women taking birth control pills shown to be low in vitamin B6.
- 2/3rd of those with B12 deficiency are over age 40.
- Women who do not eat fortified foods may not be getting sufficient folate, significant if pregnancy occurs.

Chitayat D, et al. J Clin Pharmacol 2016 Feb;56(2):170-5.

Rios-Avila L, et al. Am J Clin Nutr 2015; Sep;102(3):616-25.

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

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Food Fortification


- Many cereals are fortified with vitamins B1, B2, B3, B5, B9, B12, and C, as well as iron and calcium.
- This has both an upside and downside (potentially getting too much a nutrient; for instance iron in adult men).
- Further complicating the issue: **most non-GMO and/or organic cereals are not fortified.**

Kashi®
GoLean Crunch!®
Honey Almond Flax

Nutrition Facts
Serving Size 2/3 Cup (53g/1.9 oz.)

Amount Per Serving	% Daily Value*
Calories 200 Calories from Fat 45	
Total Fat 5g	8%
Saturated Fat 0.5g	3%
Trans Fat 0g	
Polyunsaturated Fat 2g	
Monounsaturated Fat 2.5g	
Cholesterol 0mg	0%
Sodium 140mg	6%
Potassium 330mg	9%
Total Carbohydrate 35g	12%
Dietary Fiber 8g	32%
Soluble Fiber 4g	
Insoluble Fiber 4g	
Sugars 12g	
Protein 9g	13%
Vitamin A 0%	Vitamin C 0%
Calcium 2%	Iron 8%

*Percent Daily Values are based on a diet of other people's secrets.



Nutrition Facts
Serving Size 1/4 cup (30g)
Servings Per Container about 7

Amount Per Serving	% Daily Value*
Calories 210	
Calories from Fat 45	45
Total Fat 4.5g	7%
Saturated Fat 1g	6%
Trans Fat 0g	
Polyunsaturated Fat 2g	
Monounsaturated Fat 1.5g	
Cholesterol 0mg	0%
Sodium 150mg	6%
Potassium 150mg	4%
Total Carbohydrate 30g	13%
Dietary Fiber 4g	16%
Sugars 14g	
Other Carbohydrate 22g	
Protein 5g	
Vitamin A 0%	4%
Vitamin C 0%	0%
Calcium 2%	15%
Iron 6%	6%
Vitamin D 0%	10%
Thiamin 6%	10%
Riboflavin 2%	10%
Phosphorus 10%	25%
Magnesium 8%	10%
Zinc 4%	8%

*Percent Daily Values are based on a diet of other people's secrets.

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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Metformin With Proton Pump Inhibitors: A Polypharmacy Recipe for Neuropathy via Vitamin B12 Depletion

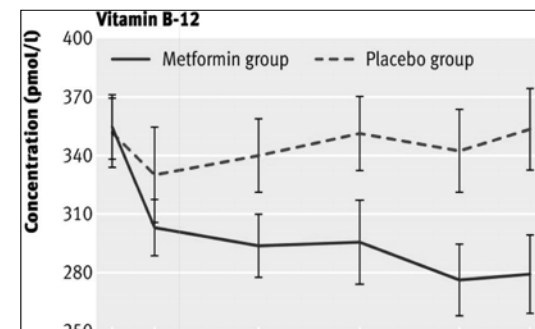
Zdilla MJ. *Clin Diabetes* 2015; 33(2):90-5.



MANY MEDICATIONS INTERFERE WITH NUTRIENT ABSORPTION AND UTILIZATION

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- Study of 390 patients with type 2 diabetes randomized to metformin (850 mg) or placebo TID 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

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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Metabolism of B12

- 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.

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Choline

- Water soluble nutrient in the B-vitamin family that is particularly crucial during pregnancy and the first three years of a child's life.
- Deficiency may be associated with permanent changes in brain function that negatively impact intelligence, memory, mood regulation, and stress response.
- Preclinical studies show choline partially ameliorates memory and learning deficits from prenatal alcohol exposure.
- RDA: 450 mg per day Breastfeeding: 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

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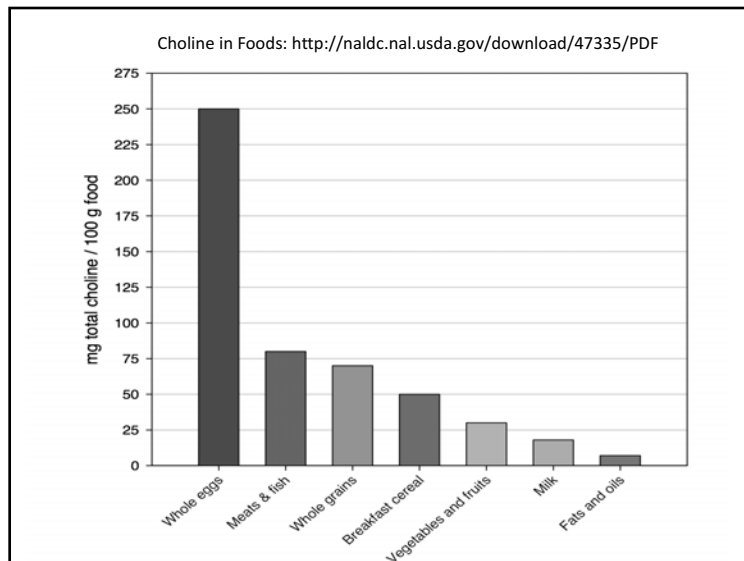
Choline and Cognition



- 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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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.
- 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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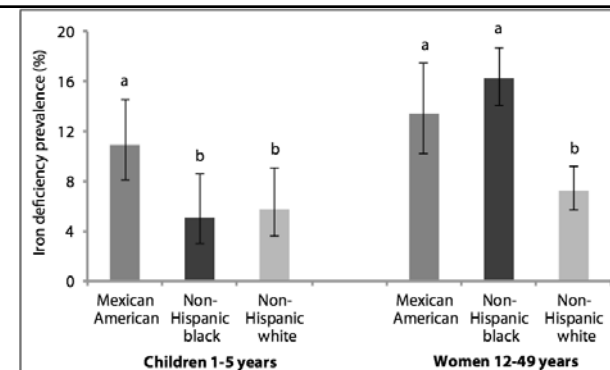


Figure H.3.a. Age-adjusted prevalence estimates of low body iron stores (< 0 mg/kg) in U.S. children and women by race/ethnicity, National Health and Nutrition Examination Survey, 2003–2006.

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

To Get 18 mg of Iron in Food

- 4 cups raisins
- 3–5 cups instant oatmeal
- 3 cups Special K cereal
- 3 cups cooked lentils
- 2.2 cups canned white beans
- 10 ounces beef liver
- 45 ounces chicken breast
- 15 cups broccoli
- 3 cups cooked spinach

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Warning: Iron

- People who are 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.
- When taking supplements: Look for iron bisglycinate, ferrous bisglycinate, or iron glycinate on the label. Take with vitamin C and NOT with calcium.

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Vitamin C



- Plays a role in activating folic acid, assists in conversion of tryptophan to serotonin, and is a cofactor in synthesis of carnitine, thyroxine, norepinephrine, and dopamine.
- Vitamin C levels decline rapidly during periods of emotional and physical strain, and illness.
- As levels fall, collagen synthesis is impaired: bruise more easily, skin becomes thick and dry, wounds take longer to heal, joints hurt, fatigue.
- 15.7 million Americans have vitamin C deficiency.

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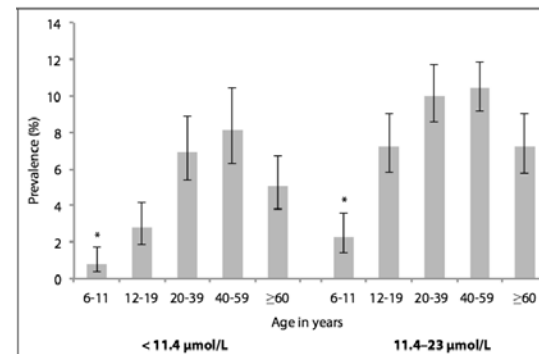


Figure H.1.f. Prevalence estimates of vitamin C deficiency (serum concentrations less than 11.4 µmol/L) and of low vitamin C concentrations (11.4–23 µmol/L) in the U.S. population aged 6 years and older by age group, National Health and Nutrition Examination Survey, 2003–2006.

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

Zinc

- Zinc plays a vital role in our immune response.
- Need zinc to activate T-lymphocytes, immune cells responsible for destroying cells infected with viruses or bacteria, or cancerous.
- Marginal zinc deficiency can also diminish the activity of other 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 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 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) and 24.5% (males) had zinc deficiency.

Brown KH, et al. Food Nutr Bull 2009; 30(15):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 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 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



- Zinc deficiency: loss of appetite; lack of taste or smell; poor wound healing; acne; hair loss; lack of menstrual period; night blindness; and depression
- Vegetarians need as much as 50% more zinc due to lower absorption of zinc from plant foods. DV= 15 mg
- ACE inhibitors and thiazide diuretics deplete zinc
- Best absorbed on empty stomach. Do not take more than 40 mg per day for more than a few days without medical supervision. Take 2 hours apart from medication, especially quinolones and tetracycline antibiotics.

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Life Stage Group	Calcium			Vitamin D		
	Estimated Average Requirement (mg/day)	Recommended Dietary Allowance (mg/day)	Upper Level Intake (mg/day)	Estimated Average Requirement (IU/day)	Recommended Dietary Allowance (IU/day)	Upper Level Intake (IU/day)
Infants 0 to 6 months	*	*	1,000	**	**	1,000
Infants 6 to 12 months	*	*	1,500	**	**	1,500
1-3 years old	500	700	2,500	400	600	2,500
4-8 years old	800	1,000	2,500	400	600	3,000
9-13 years old	1,100	1,300	3,000	400	600	4,000
14-18 years old	1,100	1,300	3,000	400	600	4,000
19-30 years old	800	1,000	2,500	400	600	4,000
31-50 years old	800	1,000	2,500	400	600	4,000
51-70 year old males	800	1,000	2,000	400	600	4,000
51-70 year old females	1,000	1,200	2,000	400	600	4,000
>70 years old	1,000	1,200	2,000	400	800	4,000
14-18 years old, pregnant/lactating	1,100	1,300	3,000	400	600	4,000
19-50 years old, pregnant/lactating	800	1,000	2,500	400	600	4,000

*For infants, Adequate Intake is 200 mg/day for 0 to 6 months of age and 260 mg/day for 6 to 12 months of age.
**For infants, Adequate Intake is 400 IU/day for 0 to 6 months of age and 400 IU/day for 6 to 12 months of age.

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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.

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Calcium Supplements

- You need roughly 1000 mg per day of calcium **from all sources**, depending upon age.
- Chelated calcium (citrate, malate)
 - Best for those over 50 years old or those taking drugs to suppress stomach acid
- Do not take at the same time as other medications (thyroid, bisphosphonates, phenytoin, tetracycline)



Spence LA, et al. Nutr Rev 2013; 71(1):15-22

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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
- Vitally important for calcium regulation (bones, heart, etc.)
- Review of 30 studies show that high vitamin D status is strongly associated with better *breast cancer survival*.
- Review ~ 1,000,000 participants found 10 ng/mL increment in blood 25(OH)D level conferred a *26% reduction in risk* for colorectal cancer
- Obesity increases the risk of deficiency.....
- Endocrine Society: serum 25(OH)D level:
 - Insufficiency defined as 21-29 ng/mL
 - Deficiency defined as <20 ng/mL

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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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

“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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To Get 600 IU Vitamin D in Food

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

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American Endocrine Society



- All adults who are vitamin D deficient should be treated with 50,000 IU of vitamin D2/D3 once a week for 8 weeks or its equivalent of 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 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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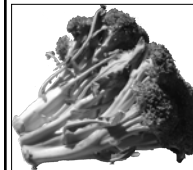
Endocrine Society Guidelines

- Obese children and adults should be given at ***least twice or three times*** the vitamin D requirements previously specified, as should all individuals taking anticonvulsant medications, glucocorticoids, antifungals such as ketoconazole and medications for HIV/AIDS.

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

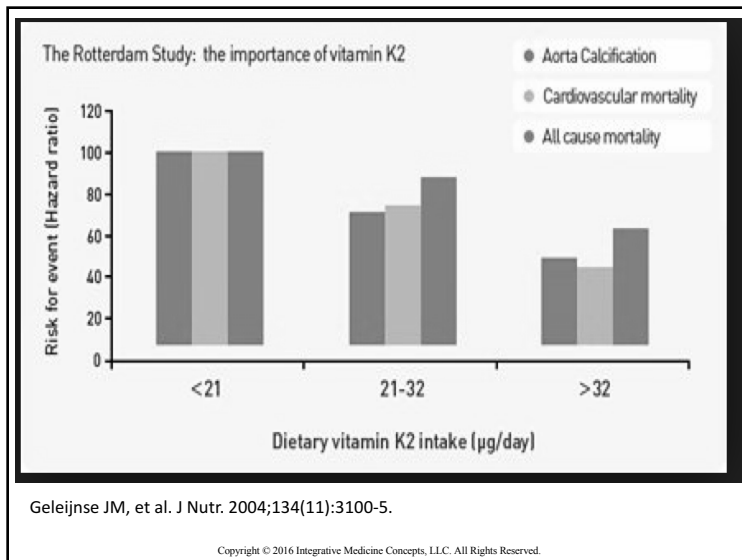
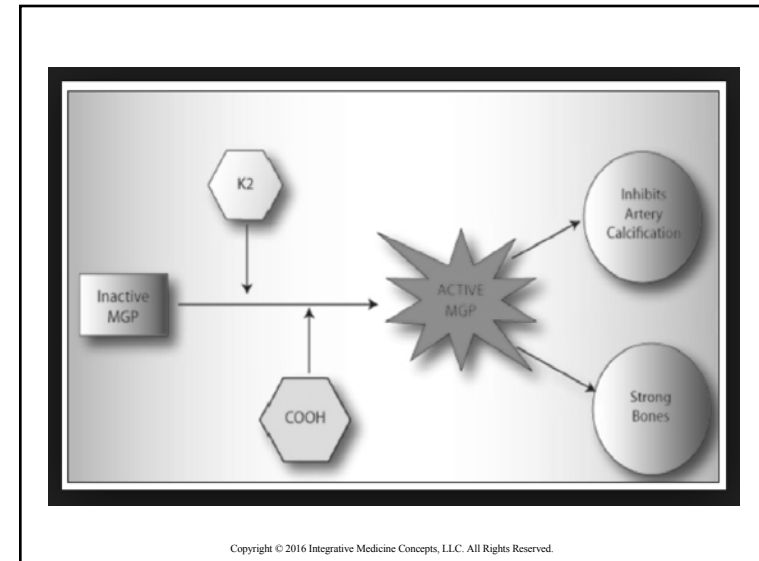
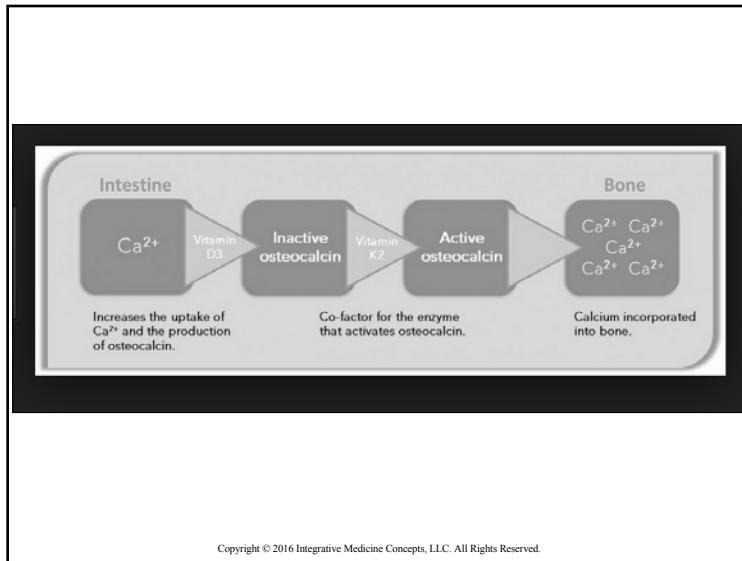
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Vitamin K



- 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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Magnesium

Mg
24
12
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.

Rosanoff 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.

Reffellmann, et al. Atherosclerosis 2011 Nov;219(1):280-4.
 Rosanoff, 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) - omeprazole (Prilosec)
 - pantoprazole sodium (Protonix) - rabeprazole sodium (Aciphex)
 - lansoprazole (Prevacid) - dexlansoprazole (Dexilant)
 - omeprazole and sodium bicarbonate (Zegerid)

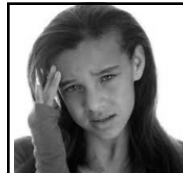
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FDA Safety Advisory

- 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, Mauskop A. Clin J Pain. 2009 Jun;25(5):446-52.
 Pringsheim T, et al. Can J Neurol Sci 2012; 39(2Suppl) S1-S9
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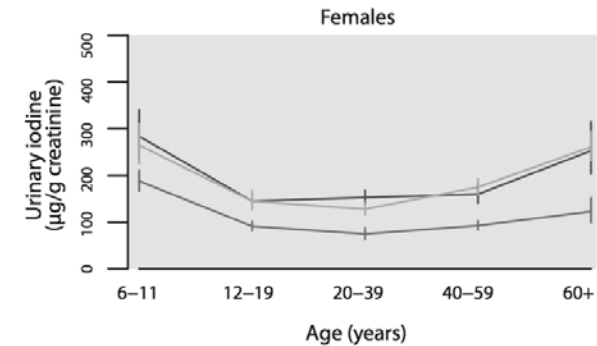
Iodine in Pregnancy



- Many reproductive aged women in US have marginal iodine status; salt in processed foods is not iodized.
- Deficiency associated with pregnancy loss and prematurity, cretinism, and neurocognitive defects in the fetus.
- 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.

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— Mexican Americans
— Non-Hispanic Blacks
— Non-Hispanic Whites
— Whites

CDC 2nd National Report on Biochemical Indicators of Diet And Nutrition. The WHO recommends that the median UI in pregnancy be 150-249 mcg/L.

Resources

- *Fortify Your Life*, Tieraona Low Dog, MD with National Geographic
- Dietary Supplement Label Database: dssl.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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