

Dietary Supplements: A Critical Review of the Evidence



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"*Healthy At Home*" and
"*Life Is Your Best Medicine*"

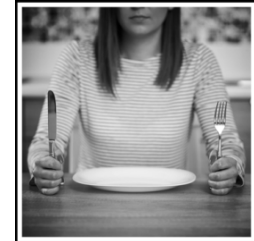
www.DrLowDog.com

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Real State of Our Nutrition

- **90 million** vitamin D deficient (using the Endocrine Society guidelines < 20ng/mL)
- **30 million** are deficient in vitamin B6
- **18 million** have B12 deficiency
- **16 million** have vitamin C deficiency
- **13% of Latinas and 16% of African American women (ages 12-49) are iron deficient**
- Women 25-39 overall have **borderline iodine insufficiency**



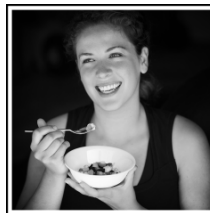
CDC: 2nd National Report on the Biochemical Indicators of Diet and Nutrition in the U.S. population

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Vitamin B6 (Pyroxidal-5-Phosphate)

- Involved in production of **serotonin, dopamine, melatonin, hemoglobin, protein metabolism, energy production, and more.**
- Deficiency: **depression; impaired cognition, attention, memory, and sleep.** Increased risk **heart disease, stroke and colorectal cancer.**
- **OTC analgesics and OCPs** lower B6 levels.
- **30 MILLION Americans** are deficient in B6. **Seldom ever tested.** Research shows ~6 mg/d to maintain normal serum level.



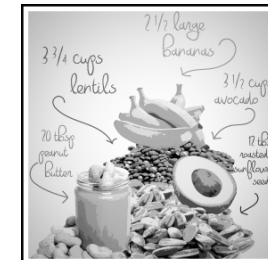
Larson SC, et al. *JAMA* 2010; 303(11):1077-83
Morris MS, et al. *Am J Clin Nutr* 2008; 87(5):1446-54
Urbek A, et al. *Am J Clin Nutr* 2014; 100(1):250-5

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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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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

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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

• **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.

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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 he has a beefy red and deeply fissured tongue and complains of 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?

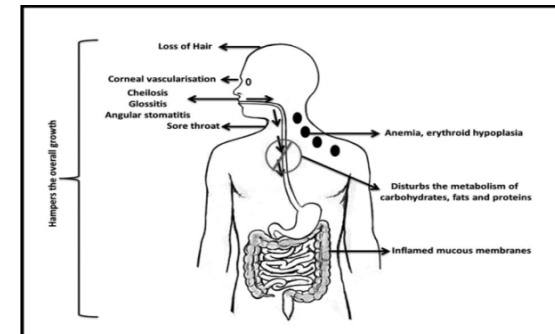
- A. Vitamin B2
- B. Vitamin B6
- C. Vitamin C
- D. Vitamin B12



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

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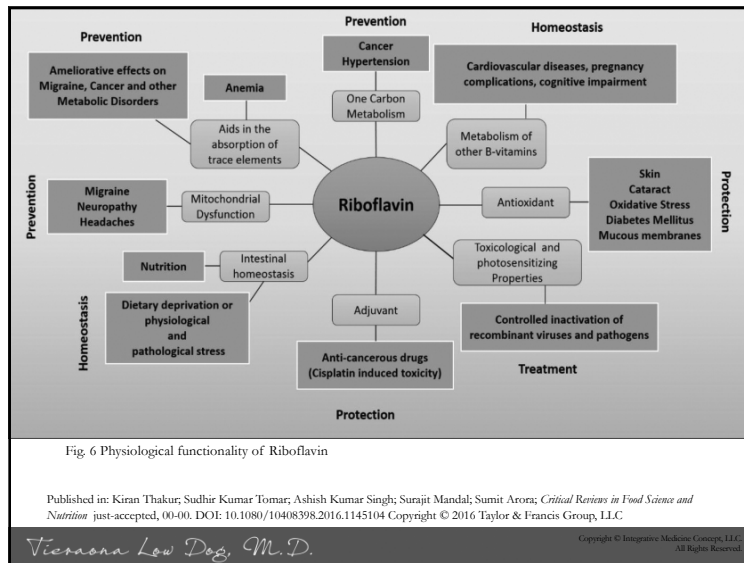
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Riboflavin (B2) deficiency causes ariboflavinosis, which manifests as cracked lips, inflammation of the tongue, dryness or burning of the oral cavity, and sore throat.

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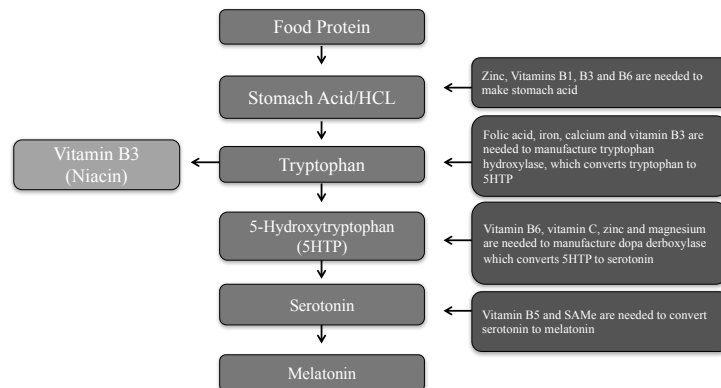
Riboflavin Deficiency: At Risk Groups

- **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)

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Serotonin and Melatonin Pathways



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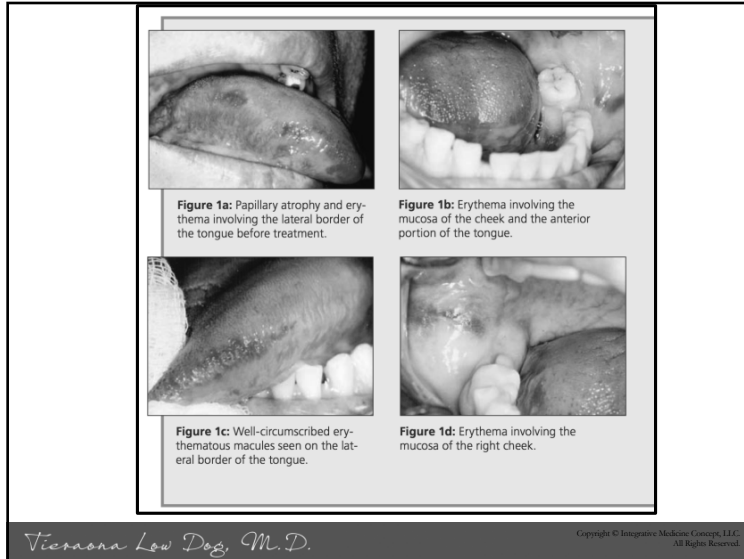
Case 41-year old Female

- 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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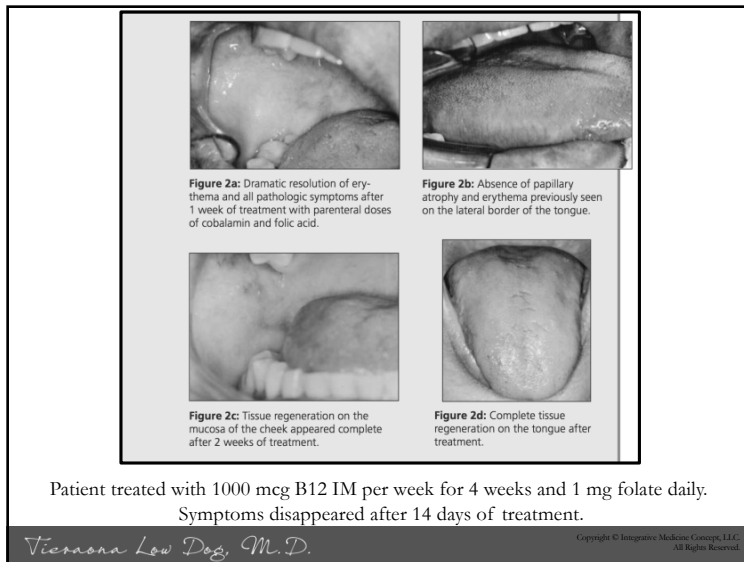


Laboratory Tests

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

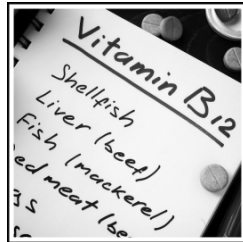
MCV = mean corpuscular volume; RBC = red blood cell; RDW = red cell distribution width.

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Metabolism of B12

- Protein enters stomach, **HCL/pepsin** separate from animal food
 - Free B12 joined to **intrinsic factor (IF)** made by parietal cells in stomach.
 - B12-IF travels to **ileum** where, if calcium is adequate, it's **absorbed**.
 - **Atrophic gastritis** affects 10%-30% of people over 60 years of age.
 - Atrophic gastritis can lead to **bacterial overgrowth in small intestine and cause food-bound vitamin B12 malabsorption**.
 - Frequently associated with the presence of autoantibodies directed towards stomach cells and/or *H. pylori* infection.
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Bied JK, et al. Risk of Deficiency in Multiple Concurrent Micronutrients in Children and Adults in the United States. *Nutrients* 2017; doi: 10.3390/nu9070655

Corugade R, et al. Prevalence and Prediction of Subclinical Micronutrient Deficiency in German Older Adults: Results from the Population-Based KOR-Age Study. *Nutrients* 2017; doi: 10.3390/nu9121276

Vitamin B12 Deficiency

- Risk for deficiency increases with age:
 - 7% those 51–70 years of age
 - 15% >70 years are B12 deficient
- Decline in gastric acid makes it hard to absorb food-bound B12.
- Institute of Medicine recommends adults > 50 get B12 from **fortified foods/supplements**
- Risks: **inadequate intake, malabsorption, medications, vegan, obesity, and aging.**

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Metformin and PPI Increase Risk for Low B12

- 2015 meta-analysis: **80% increased risk B12 deficiency after 10 months of regular proton pump inhibitor use.**
- Meta analysis: 29 studies: **245% increased risk B12 deficiency with metformin use.** Low B12 shown to **increase progression of diabetic neuropathy.**
- B12 deficiency can lead to **difficulty walking, tingling/numbness** in hands and feet, **fatigue**, shortness of breath, **loss of appetite, joint pain, depression, loss of taste and smell, cognitive impairment, and dementia.**
- **B12 should be monitored every 1-2 years if taking these medications.**

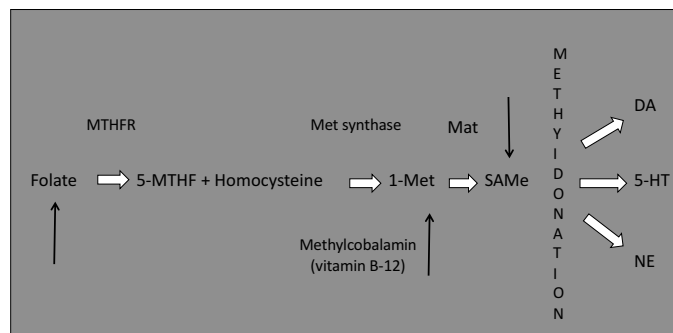
Jung SB, et al. Association between vitamin B12 deficiency and long-term use of acid-lowering agents: a systematic review and meta-analysis. *Intern Med J* 2015; 45(4):409-16.

Out M, et al. Long-term treatment with metformin in type 2 diabetes and methylmalonic acid: Post hoc analysis of a randomized controlled 4.3year trial. *J Diabetes Complications* 2018; 32(2):171-178.

Niafar M, et al. *Intern Emerg Med* 2015; 10(1):93-1026

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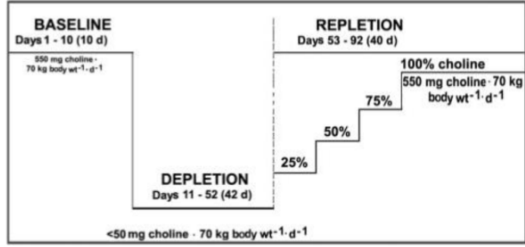
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Folate

- Women who are of reproductive age need **400 mcg/day of folate** at least 2-3 months before pregnancy to reduce the risk of neural tube defects.
- Folic acid received through food fortification in the US **is less than 130 mcg/day**, making supplementation vitally important.
- Given that many women are **avoiding gluten** containing foods, the contribution from fortified foods is likely even lower.
- **10-20% of individuals have abnormality in the MTHFR enzyme**, which is involved in the metabolism of folate, leading to low levels of folate in spite of intake. This is why a number of supplement companies now use **L-methylfolate** (the active form) instead of folic acid.

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- 57 healthy adults **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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THE FASEB JOURNAL

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Research
Maternal choline supplementation during the third trimester of pregnancy improves infant information processing speed: a randomized, double-blind, controlled feeding study

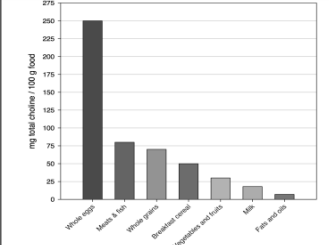
Marie A. Caudill, Barbara J. Strupp, Laura Muscalu, Julie E. H. Newins, and Richard L. Canfield

Published Online: 29 Mar 2018 | <https://doi.org/10.1096/fj.201700692R>

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- Critical during fetal development, influencing mood regulation, cognitive development, stress regulation and memory function.
- Suboptimal intakes present across many life-stage subpopulations and pregnant women in U.S.
- Only 8-10% of adults or pregnant women meet AI.
- Those eating eggs had highest levels.
- Look for prenatal with 200-300 mg

Choline



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

Blusztajn JK, et al. Neuroprotective actions of dietary choline *Nutrients* 2017; Jul 28;9(8). pii: E815.

Wallace TC, et al. *Nutrients* 2017 Aug 5;9(8). pii: E839.

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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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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?

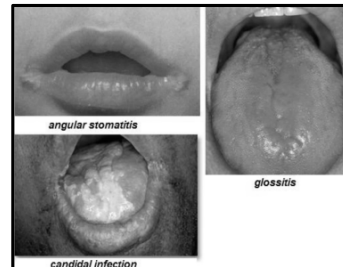
- A. Folate
- B. Iron**
- C. Calcium
- D. Selenium

Pica is symptom of iron deficiency (chew ice or non-food items)

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- Review of Systems May Yield
 - Shortness of breath, fatigue
 - Sensitivity to cold
 - Muscular weakness
 - Low blood pressure
 - Restless legs
- Physical Exam Findings
 - Angular cheilitis
 - Atrophic glossitis
 - Generalized oral mucosal atrophy
 - Mucosal pallor
 - Stomatitis
 - Nonspecific pallor of the mucous membranes



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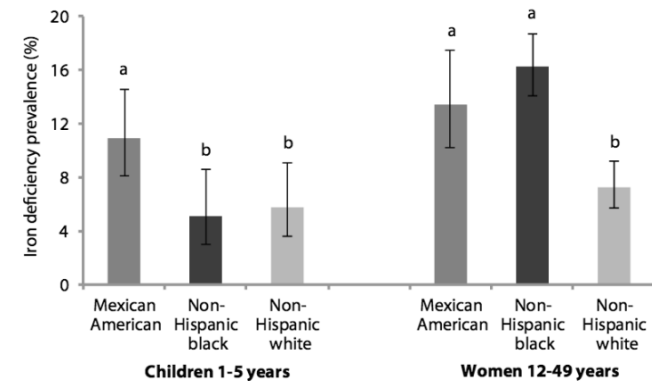


Figure H.3.a. Age-adjusted prevalence estimates of low body iron stores (<0 mg/kg) in U.S. children and women by race/ethnicity, National Health and Nutrition Examination Survey, 2003-2006.

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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Recommended dietary allowances for iron for infants, children, and adult women

Age	Infants and children	Women	Pregnant	Breastfeeding
7 to 12 months	11 mg	n/a	n/a	n/a
1 to 3 years	7 mg	n/a	n/a	n/a
4 to 8 years	10 mg	n/a	n/a	n/a
9 to 13 years	8 mg	n/a	n/a	n/a
14 to 18 years	n/a	15 mg	27 mg	10mg
19 to 50 years	n/a	18 mg	27 mg	9 mg
51+ years	n/a	8 mg	n/a	n/a

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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** important in etiology of CAD, strokes, certain cancers, and neurodegenerative disorders.
- Iron absorption is **highly regulated** to prevent excess, **no physiologic pathway for ridding body of iron**.
- 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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Zinc and Oral Health

- Zinc necessary for **sense of smell, which accounts for about 80% of your sense of taste!**
- Review of clinical trials found “moderate quality evidence that **zinc supplements improve overall taste improvement in patients with zinc deficiency/idiopathic taste disorders.**”
- Important for oral health; one sign of zinc deficiency is **red, swollen, and tender gums that may bleed after brushing.**



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 Taste

- Zinc helps **protect cells that line the mouth in those undergoing chemotherapy or radiation.**
- 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

- Concentrations in **prostate, testes, and sperm are high.** Deficiency might contribute to lower testosterone and infertility in men.
- **Vegetarians need 50% more zinc** due to lower absorption from plants.
- **ACE inhibitors, diuretics deplete zinc**
- **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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Calcium

- Adults RDA is **1000 mg per day 1200 mg for women over 50 and 1200 mg for men over 70 years.**
- First sign of deficiency is **muscle cramping/aches.**
- Long term deficiency leads to **poor bone development/loss of bone mineral density, numbness and tingling in the fingers, convulsions, lethargy, poor appetite, and abnormal heart rhythms.**



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Calcium and Vitamin D: Fracture

- Meta-analysis by National Osteoporosis Foundation: eight studies (n= 30,970 participants) found that **all studies showed calcium plus vitamin D supplementation produced a statistically significant 15 % reduced risk of total fractures and 30% reduced risk of hip fractures.**



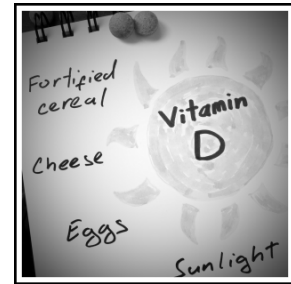
Weaver CM, et al. *Osteoporosis Int* 2016; 27: 367–376.

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Vitamin D

- Important for **calcium** regulation
- Higher blood levels **improve breast cancer survival and reduce risk of colorectal cancer.**
- Low vitamin D causes **muscle weakness, lower back and hip pain.**
- **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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- Deficiency can cause **osteomalacia** leading to **musculoskeletal pain** in the pelvis, shoulders, low back, and proximal muscles.
- Children at risk of **developing hypomineralized dental enamel, increasing susceptibility to caries**
- As age advances, intestinal resistance to 1,25(OH)₂D **impairs the uptake of calcium and a decline in renal function reduces activation of vitamin D.**

Vitamin D



Wintermeyer E, et al. Crucial Role of Vitamin D in the Musculoskeletal System. *Nutrients* 2016; Jun 1;8(6). pii: E319.

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Vitamin D: Bones and Balance

- Low vitamin D increases risk of **falls and gait instability.** Exercise, calcium and vitamin D supplementation all decrease falling in elders.
- Meta-analysis National Osteoporosis Foundation: **calcium plus vitamin D supplementation produced a significant 15 % reduced risk total fractures and 30% reduced risk hip fracture.**



Tricco AC, et al. Comparisons of Interventions for Preventing Falls in Older Adults: A Systematic Review and Meta-analysis. *JAMA* 2017; Nov 7;318(17):1687-1699.

Weaver CM. Calcium plus vitamin D supplementation and risk of fractures: an updated meta-analysis from the National Osteoporosis Foundation. *Osteoporosis Int* 2016 Jan;27(1):367-76

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Vitamin D and Respiratory Infection



Martineau AR, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ* 2017; 356: i6583.

- Acute respiratory infection kills ~2.65 million people/year.
- A review of 25 randomized controlled trials found that vitamin D supplementation reduced risk of acute respiratory infection among all participants and those who were deficient experienced the most benefit (NNT=4).
- Why not screen those at high risk?

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Vitamin D and Asthma



Jolliffe DA, et al. Vitamin D supplementation to prevent asthma exacerbations: a systematic review and meta-analysis of individual participant data. *Lancet Respir Med* 2017 Nov;5(11):881-890. Martineau AR, et al. Vitamin D for the management of asthma. *Cochrane Database Syst Rev*. 2016 Sep 5;9(9):CD011511.

- Viral respiratory infections major cause of **asthma exacerbations**.
- Systematic review and meta-analysis of 8 RCTs found **vitamin D supplementation reduced rate of asthma exacerbation requiring systemic corticosteroids** with greatest benefit seen in those with low baseline levels of vitamin D.

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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 had vitamin D levels between 12-20 ng/ml
- 23 million Americans had serum levels less than 12 ng/ml
- 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.**

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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Vitamin D

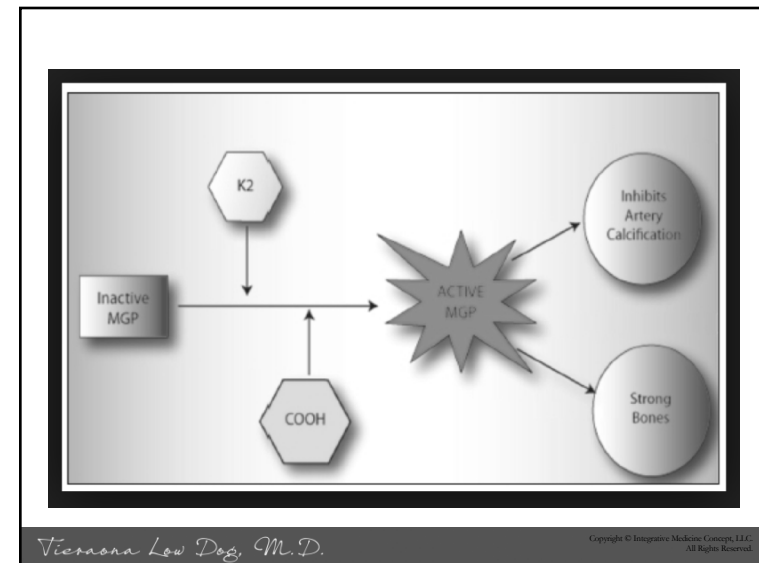
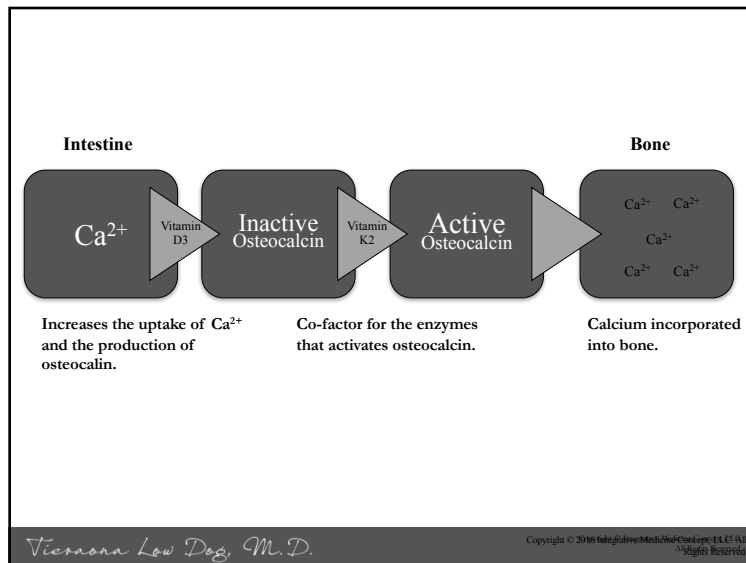
To get 600 IU/d Vitamin D3:

- 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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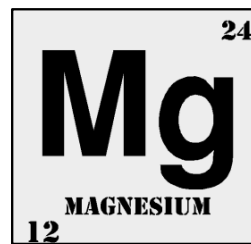
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Magnesium

- Low magnesium intake 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

- Low levels associated with higher **all-cause and CVD mortality.**
- Review of 44 studies shows supplements enhance **blood-pressure lowering effect of medications** 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.**
- Magnesium supplementation** has been shown to **improve glucose metabolism and insulin sensitivity** in those with type-2 diabetes.

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

Rosanooff, et al. *Magn 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

Gommers LM, et al. Hypomagnesemia in Type 2 Diabetes: A Vicious Circle? *Diabetes*, 2016; 65(1):3-1

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Ulcer/GERD Medications

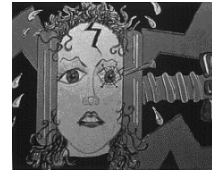
Drug Classification	Nutrient Depletion
Proton pump inhibitors	Magnesium, iron, calcium, vitamin B12, folic acid, zinc, vitamin C, vitamin D (?)
H2 antagonists	folic acid

- 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.

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Magnesium for Migraines



- Canadian Headache Society: strong recommendation for prophylaxis of migraine (also for riboflavin). American Academy of Neurology gave level B – probably effective.
- Magnesium dose 300-400 mg/d, though some need up to 600 mg per day.
- Diarrhea most common side effect (glycinate and malate forms less GI complaints).
- Caution with supplementation in those with poor kidney function.

Rajapakse T, et al. Nutraceuticals in Migraine: A Summary of Existing Guidelines for Use. *Headache* 2016; 56(4):808-16.

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Inappropriate Use



“Proton pump inhibitors (PPIs) are a class of medications that reduce acid secretion and are used for treating many conditions such as gastroesophageal reflux disease (GERD), dyspepsia, reflux esophagitis, peptic ulcer disease, and hypersecretory conditions (e.g. Zollinger-Ellison syndrome), and as part of the eradication therapy for *Helicobacter pylori* bacteria.

However, *approximately 25% to 70% of people are prescribed a PPI inappropriately. Chronic PPI use without reassessment contributes to polypharmacy and puts people at risk of experiencing drug interactions and adverse events (e.g. Clostridium difficile infection, pneumonia, hypomagnesaemia, and fractures).*”

Boghossian TA, et al. *Cochrane Database Syst Rev* 2017; Mar 16;3:CD011969.

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Rebound Acid Production

- DBPCT of **120 healthy volunteers randomized to 12 weeks of placebo or 8 weeks of esomeprazole 40 mg/d followed by 4 weeks of placebo.**
- Gastrointestinal Symptom Rating Scale (GSRS) was filled out weekly.
- **44% of those randomized to PPI reported ≥1 relevant, acid-related symptom in weeks 9–12 compared with 15% in placebo group ($P < .001$).**
- Proportion reporting dyspepsia, heartburn, or acid regurgitation in the PPI group was **22% at weeks 10 and 11, and 21% at week 12.**
- Corresponding figures in the placebo group were **7% at week 10, 5% at week 11, and 2% at week 12.**

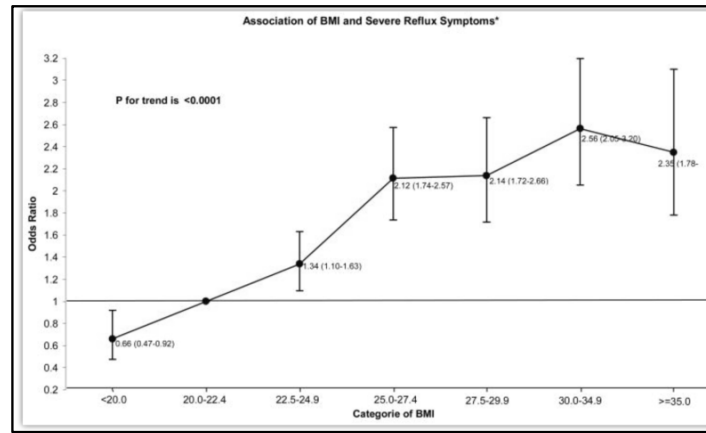


Reimer C, et al. *Gastroenterology* 2009; 137(1):80-7

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INCREASING BMI ASSOCIATED WITH GERD SYMPTOMS



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Melatonin

- **Melatonin** detected in enteroendocrine cells of gastrointestinal wall.
- Studies show that **patients with GERD and recurrent duodenal ulcers have lower melatonin concentrations** than healthy subjects.
- **Melatonin prevents gastric damage:** more effective than ranitidine but less effective than omeprazole in preventing stress ulcer. However, melatonin allows lower dose of omeprazole to be used.
- **Short term use of melatonin at even very high doses has not been associated with any significant side effects.**
- **Long-term treatment is not associated with any significant side effects, comparable to placebo.**

Kandil TS, et al. *BMC Gastroenterology* 2010;10:7
Andersen LP, et al. *Clin Drug Investig* 2015; Dec 21

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Melatonin for GERD

- Melatonin produced in GI mucosa plays important role in the protection against noxious agents, contributing to the maintenance of GI integrity, esophageal protection, gastroprotection and ulcer healing.
- Study of **60 patients with GERD by endoscopy** compared to controls. Received:
 - **3 mg melatonin**
 - **20 mg omeprazole**
 - **3 mg melatonin + 20 mg omeprazole**
- **Heartburn/epigastric pain decreased after 4 weeks and completely resolved in 8 weeks in all three groups.**
- Only groups with melatonin had improved LES function.

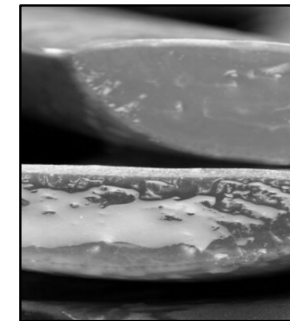
Kandil TS, et al. *BMC Gastroenterol* 2010; 10:7.
Brzozowska I, et al. *Curr Pharm Des* 2014; 20(30):4807-15

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Aloe Vera

- 79 people with GERD (endoscopy) given either:
 - 10 ml/d aloe vera syrup (standardized to 5.0 mg polysaccharide per mL of syrup)
 - Omeprazole capsule (20 g/d)
 - Ranitidine tablet (150 mg in fasted state in am and 150 mg 30 min before sleep) for 4 weeks.
- Frequencies of eight main symptoms of GERD (heartburn, food regurgitation, flatulence, belching, dysphagia, nausea, vomiting and acid regurgitation) were assessed at weeks 2 and 4 of the trial.
- **Significant benefit seen in all three groups.**



Santhosh Kumari CH, et al. *Int J Pharma Bio Sci* 2010; 1(2): 124.
Keshavara Z, et al. *Avicenna J Phytomed* 2014; 4(2): 137-143.
Panahi Y, et al. *J Tradit Chin Med* 2015; Dec;35(6):632-6.

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NO! THIS CONTAINS LATEX

Supplement Facts
Serving Size 1 Capsule
Servings Per Container 100

Amount Per Serving	% Daily Value
Aloe ferox (latex)	200 mg **
Beet (root)	150 mg **
Fennel (seed)	150 mg **
Aloe barbadensis (leaf)	50 mg **

**Daily Value not established.

Other ingredients: Plant-derived capsule, Magnesium stearate, Silica

YES! NO LATEX. 60 MG POLYSACCHARIDES

Supplement Facts
Serving Size: 2 fl oz. (59 ml)
Serving Per Container: 16

	Amount Per Serving	% Daily Value*
Calories	4	
Sodium	30 mg	1%
Total Carbohydrates	1 g	<1%
Calcium	25 mg	2%
Magnesium	4 mg	1%
Organic Aloe Vera Fillet Juice	58 ml	†
Organic Polysaccharide Rich Alosorb	60 mg	†


* Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not Established.

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Iodine in Pregnancy

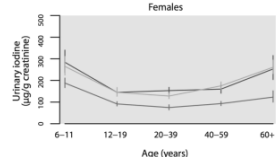
- Many reproductive aged women have **marginal iodine status**; salt in processed foods not iodized.
- Deficiency associated with **pregnancy loss, prematurity, and neurocognitive defects in baby.**
- Most common cause of preventable brain damage in the world. Mild to moderate deficiency associated with **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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Iodine Intake Pregnancy and Breastfeeding



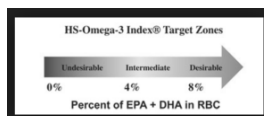
- Data from National Health and Nutrition Examination Survey 2011-2014 found that the **use of iodine containing dietary supplements among pregnant and lactating women remains low** in contrast with current recommendations.
 - Among **pregnant** women, 72.2% used any dietary supplement; however, **only 17.8% used a dietary supplement with iodine.**
 - Among **lactating** women, 75.0% used a dietary supplement; however, **only 19.0% used a dietary supplement with iodine.**

Gupta PM, et al. Use of Iodine-Containing Dietary Supplements Remains Low among Women of Reproductive Age in the United States. *Endocrine*. 2015;51(2):201-206. doi:10.1007/s12005-015-0422-2. Epub 2015 Mar 29. PMID: 25814222.

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Omega 3 Index



- Omega-3 Index indicates % of EPA+DHA in RBC.**
- Mean Omega-3 Index of Canadians aged 20-79 was 4.5%. **Fewer than 3% had levels associated with low CHD risk; 43% had levels associated with high risk.**
- Should we assess omega 3 fatty acid level to optimize levels in those with heart disease, periodontitis, chronic pain, etc?
- Most benefit from 800-1000 mg EPA and 300-500 mg DHA day
- Order your own omega 3 test at requestatest.com

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

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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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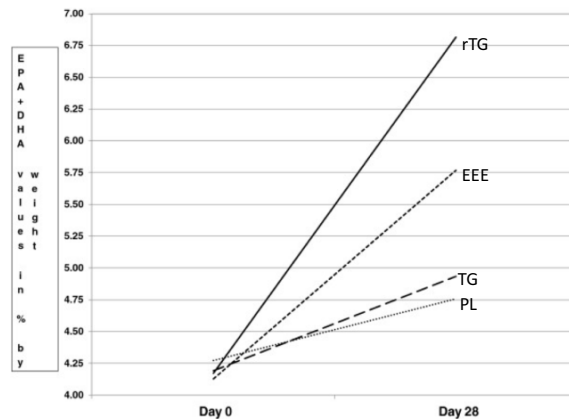
Dosing According to Manufacturer's Recommendations

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	
	Wholemeg® 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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Mean levels of EPA + DHA for four supplement groups at Day 0 and Day 28.

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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.”**

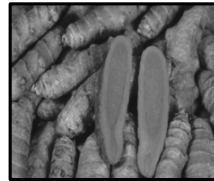
EFSA Journal 10(7): doi:10.2903/j.efsa.2012.2815

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Turmeric Rhizome (*Curcuma longa* and others)

- Rhizomes provide bright yellow-orange culinary spice and dye.
- Yellow pigments = **curcuminoids**
- Long history of **medicinal use for respiratory, skin, digestive and inflammatory conditions in India.**
- More than 65 clinical trials have shed light on its potential role in **CVD, diabetes, cancer, fatty liver, arthritis, neuro/psych disorders.**



Kunnumakara AB, et al. *Be J Pharmacol* 2016; Sep 17.
doi: 10.1111/bjph.13621.

Prasad S, et al. *Biotechnol Adv*
2014; 32(6):1053-1064

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Turmeric for Arthritis?

- **Laboratory, translational and clinical trials, in general, support use of curcumin for osteoarthritis.**
- 13 randomized clinical studies of varying methodological quality show turmeric/curcumin at sufficient dosing and in optimal preparations can **reduce pain and improve the functionality of patients with knee osteoarthritis.**



Chin K-Y. *Drug Des Dev Ther* 2016; 10: 3029-3042

Peddada KV, et al. *Orth Surg* 2015; 7(3):222-31

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Turmeric for Depression?

- Mini meta-analysis of 6 studies found curcumin reduced **depression symptoms, particularly in middle-aged patients when given at higher doses for longer periods of time.**
- Authors concluded, **“there is supporting evidence that curcumin administration reduces depressive symptoms in patients with major depression.”**
- Is this an impact on **microbiome**? Is it due to reduction in **inflammation**? **Is it real? More research needed.**



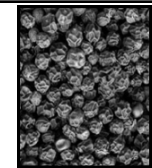
Al-Kawari D, et al. *Phytother. Res* 2016;
30(2):175-83

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“Cancer Prevention in 21st Century”

Absorption and Safety Issues



- **Low aqueous solubility of curcumin and its rapid metabolism and elimination from the body have constituted *major obstacles* to clinical use.**
- **Nanoencapsulation, curcumin complexed with phosphatidylcholine, and black pepper alkaloid, piperine, enhance tissue distribution and bioavailability.**
- **Note: Piperine causes inhibition of CYP3A4 and doses of 20 mg can cause *clinically relevant drug interactions* especially for drugs with narrow therapeutic indices.**
- **Dose in clinical trials generally 1000-1500 mg per day of turmeric extract standardized to 95% curcumin, taken in divided doses.**

Gurley BJ, et al. *Planta Med* 2012; 78(13):1490-514

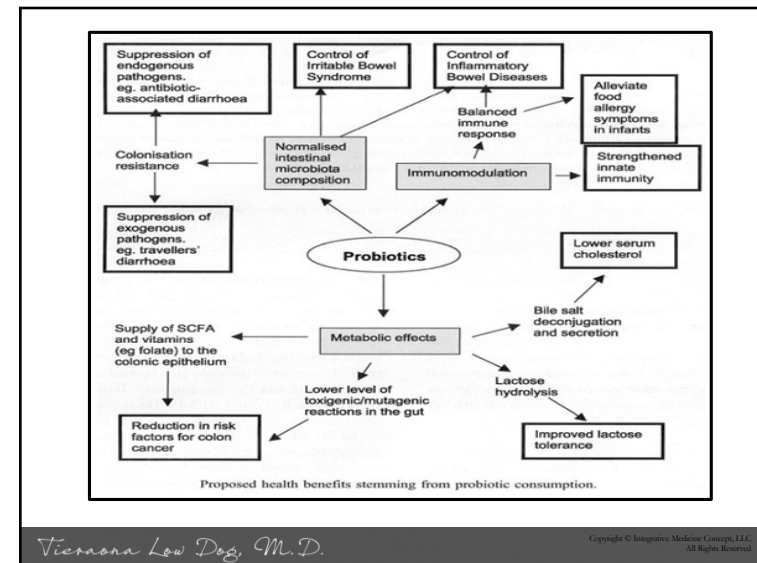
Bedada SK, et al. *Drug Res* 2016; Oct 24

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Supplement Facts		Supplement Facts	
Serving Size: 1oz. Servings Per Container: 16		Serving Size: Two Capsules Serving Per Container: 60	
Amt. Per Serving	% Daily Value	Two Capsules Contain:	
Organic Turmeric Root Extract (Supercritical CO ₂ Extraction)			
500mg *	*	Amount	% DV
Organic Black Pepper Fruit Extract (Standardized to 95% Piperine)		Per Serving:	
10mg *	*	Curcumin Phytosome† (Curcuma longa extract (root) / Phospholipid complex from Sunflower)	500 mg *
		* Daily Value (DV) not established. † This product uses Indena S.p.A.'s curcumin phytosome (Meriva). ‡ Curcumin Phytosome (Meriva) complexed with Time-Sorb, a time-release matrix.	
Supplement Facts			
Serving Size: 1 Veg Capsule			
	Amount Per Serving	%Daily Value	
Turmeric Root Extract (Curcuma longa) [Standardized to min. 95% Curcuminoids (630 mg) (including Curcumin, Demethoxycurcumin and Bisdemethoxycurcumin)]	665 mg *	*	
* Daily Value not established.			

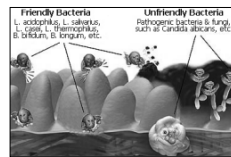
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Make Friends with Your Microbes!



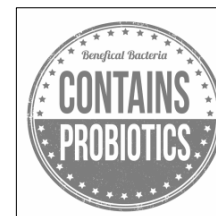
- Gastrointestinal
 - Reduce symptoms of irritable bowel syndrome
 - Reduce incidence of antibiotic associated diarrhea
- Genito-urinary
 - Reduce the risk of recurrent bladder infections
 - Help reduce recurrent yeast infections
- Pregnancy
 - Reduce allergies and eczema in high risk children, especially if born by Cesarean section, if taken last 2 months of pregnancy.

Grin PM, et al. *Cas J Urol* 2013 Feb;20(1):6607-14; Ford AC, et al. *Am J Gastroenterol* 2014; 109(10):1547-1561Copyright © Integrative Medicine Concepts, LLC.
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Probiotics

Hao Q, Dong BR, Wu T. Probiotics for preventing acute upper respiratory tract infections. *Cochrane Database Syst Rev*. 2015 Feb 3;(2):CD006895.

- Probiotics **modulate innate and adaptive immunity in elderly and also reduce length of respiratory/flu infection in children and adults**
- Review of 12 studies with 3720 participants found moderate-quality evidence shows number of **people who develop URTI is reduced when taking probiotics and probiotics reduce duration of URTI by ~ 2 days.**

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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	GID
Dentax™ Oral and ENT Health Probiotic Complex	<i>S. salivarius</i> BAA-1024 <i>L. plantarum</i> SD-5570 <i>L. reuteri</i> SD-5965 <i>L. acidophilus</i> SD-5212 <i>L. salivarius</i> SD-5208 <i>L. paracasei</i> SD-5273	Lozenge	1B/lozenge	2 lozenges											II 40-44		
Gum® PerioBalance®	<i>L. reuteri</i> ATCC 55730 100M <i>L. reuteri</i> ATCC PTA 5289 100M	Lozenge	200M/lozenge	2 lozenges											II 52,53		
OralBioics™ [BLIS K12]	<i>Streptococcus salivarius</i> K12	Lozenge	1B/lozenge	1-5 lozenges											II 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: dstd.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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