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.

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.

• 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.

Food is Foundational

Average Mineral Content in Selected Vegetables, 1914-1997

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

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

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

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.

Laboratory Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Normal range (male)</th>
<th>Patient’s values</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC count (cells/μL)</td>
<td>3.90–5.03</td>
<td>1.63</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>12.0–15.5</td>
<td>7.2</td>
</tr>
<tr>
<td>MCV (fl)</td>
<td>80–100</td>
<td>144</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>36–45</td>
<td>23.4</td>
</tr>
<tr>
<td>RDW (%)</td>
<td>13±1.5</td>
<td>25</td>
</tr>
<tr>
<td>Serum folate (ng/mL)</td>
<td>3–16</td>
<td>7.73</td>
</tr>
<tr>
<td>Serum cobalamin (pmol/L)</td>
<td>118–716</td>
<td>71.8</td>
</tr>
</tbody>
</table>

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

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.

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

- Found in animal and fortified foods. Key role in DNA synthesis, hemapoiesis 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)


Metformin and Vitamin B-12

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%.


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.

PPIs and Metformin Both Deplete B12

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

Serotonin and Melatonin Pathways

Vitamin B3 (Niacin) → Food Protein → Stomach Acid/HCL → Tryptophan → 5-Hydroxytryptophan (5HTP) → Serotonin → Melatonin

Zinc, Vitamins B1, B3 and B6 are needed to make stomach acid.

Folic acid, iron, calcium and vitamin B3 are needed to manufacture tryptophan hydroxylase, which converts tryptophan to 5HTP.

Vitamin B6, vitamin C, zinc and magnesium are needed to manufacture dopa decarboxylase which converts 5HTP to serotonin.

Vitamin B5 and SAMe are needed to convert serotonin to melatonin.

Vitamin B6
(Pyridoxal-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.

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

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

Larsson SC, et al. JAMA 2010; 303(11):107783
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 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

Vitamin B2 Deficiency

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

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 C667TT genotype (increased demand)
- Brown-Vialetto-Van Laere syndrome genetic neurological disorder mutation in transporter: deafness, bulbar palsy, respiratory difficulties
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

• 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.


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.

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

- 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

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

Figure H.3a. 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 are not sharing a common letter differ within children and women (p < 0.05). Age adjustment was done using direct standardization.
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.

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.

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.

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.
**Vitamin C**

- Potent antioxidant, activates folate, needed to convert tryptophan to serotonin, cofactor in synthesis of carnitine, thyroxin, 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."


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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.


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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.


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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 µmol/L indicate deficiency.
- Levels between 11.4 and 50 µmol/L indicate suboptimal status.
Which of the following nutrients would be most beneficial for someone who has idiopathic taste disorders?

A. Magnesium  
B. Vitamin C  
C. Zinc  
D. Biotin

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.

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.
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.

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.


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.

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
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.


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.

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 mg
- D. 1500 mg

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving</th>
<th>Zinc (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oysters</td>
<td>6 medium (cooked)</td>
<td>27-50</td>
</tr>
<tr>
<td>Beef</td>
<td>3 ounces* (cooked)</td>
<td>37-58</td>
</tr>
<tr>
<td>Crab, Dungeness</td>
<td>3 ounces (cooked)</td>
<td>4.7</td>
</tr>
<tr>
<td>Pork</td>
<td>3 ounces (cooked)</td>
<td>1.9-35</td>
</tr>
<tr>
<td>Turkey (dark meat)</td>
<td>3 ounces (cooked)</td>
<td>3.0</td>
</tr>
<tr>
<td>Beans, baked</td>
<td>¼ cup</td>
<td>0.9-3.9</td>
</tr>
<tr>
<td>Chicken (dark meat)</td>
<td>3 ounces (cooked)</td>
<td>1.6-27</td>
</tr>
<tr>
<td>Yogurt, fruit, nonfat</td>
<td>1 cup (8 fl oz)</td>
<td>1.8</td>
</tr>
<tr>
<td>Cashews</td>
<td>1 ounce</td>
<td>1.6</td>
</tr>
<tr>
<td>Chickpeas (garbanzo beans)</td>
<td>¼ cup</td>
<td>0.5-1.3</td>
</tr>
<tr>
<td>Milk</td>
<td>1 cup (8 fl oz)</td>
<td>1.0</td>
</tr>
<tr>
<td>Almonds</td>
<td>1 ounce</td>
<td>0.9</td>
</tr>
<tr>
<td>Peanuts</td>
<td>1 ounce</td>
<td>0.9</td>
</tr>
<tr>
<td>Cheese, cheddar</td>
<td>1 ounce</td>
<td>0.9</td>
</tr>
</tbody>
</table>

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

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.

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

Vitamin D

- Vitamin D interacts with more than 1000 genes
- Vitaly 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.

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.

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.

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 (75 nmol/L).”

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.


Vitamin D

To get 600 IU/d Vitamin D3:

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

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).

Intestine

\[ \text{Ca}^{2+} \xrightarrow{\text{Vitamin D}} \text{Inactive Osteocalcin} \xrightarrow{\text{Vitamin K2}} \text{Active Osteocalcin} \]

Increase the uptake of \( \text{Ca}^{2+} \) and the production of osteocalcin.
Co-factor for the enzymes that activates osteocalcin.
Calcium incorporated into bone.

Bone
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.

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 a 41% lower risk of sudden cardiac death. Women with lowest levels of magnesium also had significantly increased risk of stroke.

References:
Ulcer/GERD Medications

<table>
<thead>
<tr>
<th>Drug Classification</th>
<th>Nutrient Depletion</th>
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<tbody>
<tr>
<td>Proton pump inhibitors</td>
<td>Magnesium, iron, calcium, vitamin B12,</td>
</tr>
<tr>
<td></td>
<td>folic acid, zinc, vitamin C, vitamin D</td>
</tr>
<tr>
<td>H2 antagonists</td>
<td>folic acid</td>
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</table>

- 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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Brand Name</th>
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<tbody>
<tr>
<td>Esomeprazole magnesium</td>
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<tr>
<td>Omeprazole</td>
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<td>Lansoprazole</td>
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<td>Dexlansoprazole</td>
<td>Dexilant</td>
</tr>
<tr>
<td>Omeprazole and sodium</td>
<td>Zegerid</td>
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</tbody>
</table>

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.


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).

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.
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.


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.”
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)


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.


Dosing According to Manufacturer’s Recommendations

<table>
<thead>
<tr>
<th>Product</th>
<th>EPA &amp; DHA per capsule*</th>
<th>% EPA + DHA (%)</th>
<th>Labeled use cap/day</th>
<th>Daily dosage of EPA + DHA (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nordic Naturals ProOmega®</td>
<td>325 mg EPA</td>
<td>92.6%</td>
<td>2</td>
<td>EPA: 605 mg, DHA: 450 mg</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>225 mg DHA</td>
<td>226.8 mg DHA</td>
<td></td>
<td>DHA: 450 mg</td>
</tr>
<tr>
<td>Minami MxEPA®</td>
<td>756 mg EPA</td>
<td>774.2 mg EPA</td>
<td>1</td>
<td>EPA: 756 mg</td>
</tr>
<tr>
<td>Platinum Ethyl Ester</td>
<td>228 mg DHA</td>
<td>233.7 mg DHA</td>
<td></td>
<td>DHA: 228 mg</td>
</tr>
<tr>
<td>Source Naturals Antarctic®</td>
<td>75 mg EPA</td>
<td>78.0 mg EPA</td>
<td>2</td>
<td>EPA: 150 mg</td>
</tr>
<tr>
<td>Krill Oil Phospholipid</td>
<td>45 mg DHA</td>
<td>46.7 mg DHA</td>
<td></td>
<td>DHA: 90 mg</td>
</tr>
<tr>
<td>New Chapter</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wholesome® Salmon</td>
<td>90 mg EPA</td>
<td>96.4 mg EPA</td>
<td>2</td>
<td>EPA: 180 mg</td>
</tr>
<tr>
<td>Oil Triglyceride</td>
<td>110 mg DHA</td>
<td>109.5 mg DHA</td>
<td></td>
<td>DHA: 220 mg</td>
</tr>
</tbody>
</table>
Evidence Based Products for Oral Health

Resources

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