A Vitamin A Day Keeps The Pharmacist Away

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Objectives

• Which vitamins, supplements might you actually need to add to your diet
• Noteworthy supplements and whether or not they really work
• Interactions to be wary of
• What should you look for when reading about new products, new uses for vitamins
• Good sources of information
We LOVE Our Supplements

• >30% of Americans take a multivitamin-mineral product
  – $5.5 billion spent each year
• Nonvitamin, nonmineral dietary supplements are the most commonly used complementary health approach by U.S. adults
  – ~18% of almost 90,000 Americans polled
  – <5% used complementary medicine INSTEAD OF traditional medicine
Vitamins

- Vitamin D
  - Helps absorb calcium
  - Antioxidant – helps protect our cells from damage
- Calcium
  - Required for helping our blood clot
- Vitamin A
  - Supports structure and function of bones and teeth
- Vitamin E
  - Important for vision
- Vitamin K
Minerals

Minerals: Inorganic elements that come from soil, water – absorbed by plants

- Iron
- Zinc
- Selenium
- Chromium
- Copper
- Iodine
Recommended Dietary Allowance (RDA): Average daily level of intake sufficient to meet the nutrient requirements of nearly all healthy individuals

Table 1: Recommended Dietary Allowances (RDAs) for Vitamin C [8]

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Pregnancy</th>
<th>Lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 months</td>
<td>40 mg*</td>
<td>40 mg*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7-12 months</td>
<td>50 mg*</td>
<td>50 mg*</td>
<td></td>
<td></td>
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<tr>
<td>1-3 years</td>
<td>15 mg</td>
<td>15 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-8 years</td>
<td>25 mg</td>
<td>25 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-13 years</td>
<td>45 mg</td>
<td>45 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14-18 years</td>
<td>75 mg</td>
<td>65 mg</td>
<td>80 mg</td>
<td>115 mg</td>
</tr>
<tr>
<td>19+ years</td>
<td>90 mg</td>
<td>75 mg</td>
<td>85 mg</td>
<td>120 mg</td>
</tr>
<tr>
<td>Smokers</td>
<td>Individuals who smoke require 35 mg/day more vitamin C than nonsmokers.</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

* Adequate Intake (AI)

Daily Value (DV)
Developed by FDA to help consumers compare the nutrient contents of products within the context of a total diet

If actual amount not listed, look for >20% daily value
Foods containing >20% DV are considered high in the nutrient

Nutrition Facts

<table>
<thead>
<tr>
<th>Amount Per Serving</th>
<th>% Daily Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories 90</td>
<td>Calories from Fat 30</td>
</tr>
<tr>
<td>Total Fat 3g</td>
<td>5%</td>
</tr>
<tr>
<td>Saturated Fat 0g</td>
<td>0%</td>
</tr>
<tr>
<td>Trans Fat 0g</td>
<td>**</td>
</tr>
<tr>
<td>Cholesterol 0mg</td>
<td>0%</td>
</tr>
<tr>
<td>Sodium 300mg</td>
<td>13%</td>
</tr>
<tr>
<td>Total Carbohydrate 13g</td>
<td>4%</td>
</tr>
<tr>
<td>Dietary Fiber 3g</td>
<td>12%</td>
</tr>
<tr>
<td>Sugars 3g</td>
<td></td>
</tr>
<tr>
<td>Protein 3g</td>
<td></td>
</tr>
</tbody>
</table>

Vitamin A 80% • Vitamin C 60%
Calcium 4% • Iron 4%

* Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs:
Calories 2,000 2,500
Total Fat Less than 65g 80g
Sat Fat Less than 20g 25g
Cholesterol Less than 300mg 300mg
Sodium Less than 2,400mg 2,400 mg
Total Carbohydrate 300g 375g
Fiber 25g 30g
Calories per gram:
Fat 9 • Carbohydrate 4 • Protein 4

* Intake of trans fat should be as low as possible
Vitamins

What you may want to consider adding into your regimen
Calcium

• 99% of body’s calcium is in our bones
• RDA
  – Adolescents: 1300 mg/day
  – Adults: 1000 mg/day
  – Postmenopausal women: 1200 mg/day
  – Anyone >70 years old: 1200 mg/day
Calcium

• Food sources
  – Milk: 299 mg in 8 ounces
  – Yogurt: 415 mg in 8 ounces
  – Kale: 100 mg per cup
  – Soymilk: 299 mg per 8 ounces IF calcium-fortified
Calcium

• Supplements
  – Most contain carbonate or citrate
  – Carbonate needs acidic environment for absorption, best taken with food

• Different brands, forms contain varying amounts of calcium
  – Check the label for how much *elemental* calcium is included

• Amount of calcium absorbed decreases with doses >500 mg
  – If taking 1,000 mg per day, split into multiple doses
Calcium

- Interactions: MANY!
  - Bisphosphonates - Fosamax, Actonel
  - Antibiotics
    - Fluoroquinolones - Cipro, Levaquin, Avelox
    - Tetracycline
  - Levothyroxine
  - Phenytoin
  - Thiazide diuretics - increased risk of hypercalcemia and hypercalciuria
  - Other antacids containing aluminum and magnesium - increase urinary excretion
  - Mineral oil and other stimulant laxatives decrease absorption
  - Steroids (glucocorticoids) - when taken for long periods of time can cause calcium depletion and bone loss
Calcium

• Side effects
  – Gas, bloating constipation
  – Carbonate >> citrate
  – Can be alleviated by taking smaller doses multiple times per day and taking with food

• Kidney stones
  – Increased risk with larger doses of *supplemental* calcium (higher amounts of dietary calcium did not show correlation)
  – Low fluid intake and high amounts of oxalate in your diet are of greater risk BUT beware of these things in combination with each other
Calcium Controversies

• In combination with Vitamin D, prevents fractures due to osteoporosis
  – TRUE!

• Decreases risk for colorectal cancer
  – QUESTIONABLE
    – Large, long-term studies show no significant difference compared to placebo
    – Observational, experimental studies while inconsistent, highly suggestive of protective effect
Calcium Controversies

• Increased risk of prostate cancer
  – Signs point to...POSSIBLY
  – Total daily calcium intake >1500 mg, compared to lower daily intake of 500-1000 mg

• Cardiovascular disease
  – Conflicting over the years
  – More recent data suggests an increased risk exists with higher doses in SUPPLEMENTS
  – Higher doses cause acute elevations in circulating blood levels which can cause changes to vasculature leading to cardiovascular problems
  – Evidence in question – these findings are often secondary in studies, and not the PRIMARY endpoint of the study
Calcium Controversies

• Calcium supplementation is often necessary (and beneficial!) for many adults
  – Check the labels of any multivitamins or supplements you take
  – Be aware of how much you are taking – if you have concerns about the amount, talk to your pharmacist or doctor
  – Keep drinking that milk and eating that cheese!!
Vitamin D

• Maintains calcium homeostasis
  – Increases calcium absorption in the gut

• Vitamin D from sun exposure and food sources requires conversion to active form in the body

Table 2: Recommended Dietary Allowances (RDAs) for Vitamin D [1]

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Pregnancy Lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12 months*</td>
<td>400 IU (10 mcg)</td>
<td>400 IU (10 mcg)</td>
<td></td>
</tr>
<tr>
<td>1-13 years</td>
<td>600 IU (15 mcg)</td>
<td>600 IU (15 mcg)</td>
<td></td>
</tr>
<tr>
<td>14-18 years</td>
<td>600 IU (15 mcg)</td>
<td>600 IU (15 mcg)</td>
<td>600 IU (15 mcg)</td>
</tr>
<tr>
<td>19-50 years</td>
<td>600 IU (15 mcg)</td>
<td>600 IU (15 mcg)</td>
<td>600 IU (15 mcg)</td>
</tr>
<tr>
<td>51-70 years</td>
<td>600 IU (15 mcg)</td>
<td>600 IU (15 mcg)</td>
<td></td>
</tr>
<tr>
<td>&gt;70 years</td>
<td>800 IU (20 mcg)</td>
<td>800 IU (20 mcg)</td>
<td></td>
</tr>
</tbody>
</table>

* Adequate Intake (AI)
Vitamin D

• Food Sources – very few natural sources
  – Swordfish, salmon: >400 units in 3 ounces
  – Most other sources provide <50% of daily value
  – Milk, yogurt, cereal: often fortified

The body itself makes vitamin D when it is exposed to the sun.
Vitamin D

• Supplements
  – Most exist over the counter as Vitamin D2 or Vitamin D3
    • Considered essentially equivalent although at higher doses D3 may be more potent
  – Available in multiple forms and doses
  – U.S. and Canada mandate that all infant formulas are fortified with Vitamin D
    • American Academy of Pediatrics recommends exclusively and partially breastfed infants receive supplements
Vitamin D

• Side effects
  – Most concerning come from resulting increase in calcium: headache, nausea, vomiting, lethargy
    • Serious: Abnormal heart rhythm, kidney function decline

• Interactions
  – Weight loss drug orlistat (Xenical, Alli) and cholestyramine (cholesterol-lowering drug): reduce absorption
  – Phenobarbital and phenytoin (antiseizure) increase metabolism resulting in reduced calcium absorption
Vitamin D Benefits

• Prevention of rickets and osteomalacia
  – Once major issues in infants and children, significantly improved with fortified milk program in the mid-1900’s

• Osteoporosis
  – Result of long-term calcium and Vitamin D deficiency
  – Important: all studies showing benefit are in combination with CALCIUM
    • Vitamin D alone shows no benefit
Vitamin D Benefits

• Cancer Prevention
  – Largest investigation to date (36,000 postmenopausal women) found no differences in risk of colorectal cancer
  – Smaller study showed lower risk of cancerous lesions on colonoscopy
  – Question of increased risk of pancreatic cancer
  – Does Vitamin D deficiency increase cancer risk, does supplementation provide greater protection, does exposure pose increased risk?
  • TBD
Vitamin D Benefits

• The amount generally recommended is known to benefit in prevention of osteoporosis (WITH CALCIUM!) and support normal bone growth (WITH CALCIUM!)
  – Cannot specifically comment on cancer effects but normal doses likely to not increase risk
Iron

• RDA - varies depending on age, gender
  – Meat eaters
    • Males: 8 mg
    • Females: 18 mg
  – Non meat eaters: 1.8 times higher

• Some literature to suggest that elderly (>65 years old) are more likely to have chronic elevated total body iron than iron deficiency
Iron

• Food sources
  – Spinach: 3 mg per half cup
  – Lentils: 7 mg per cooked cup
  – White beans: 8 mg per cooked cup
  – Oysters: 8 mg per 3 ounce serving
  – Beef: 3 mg per 3 ounce serving

• Non-meat sources contain nonheme iron, meat sources contain heme and nonheme
  – Heme iron is more bioavailable than nonheme
  – Meat, poultry and seafood help absorption of nonheme iron
Iron

• Supplements
  – Multivitamin/multimineral w/iron: 18 mg
    • These are usually designed specifically for women
  – Those designed for men or seniors: less or no iron
  – Iron supplements: 65 mg

• Side effects (more common over 45 mg/day)
  – Constipation
  – Nausea

• Calcium may interfere with absorption of iron
  – Generally recommended to take separate supplements at different times of the day
Iron

• Interactions
  – Levodopa
    • Iron can decrease absorption
  – Levothyroxine
    • Iron can decrease absorption
    • Do not take within 4 hours of each other
  – Proton Pump Inhibitors (Nexium, Prevacid, Prilosec)
    • Stomach acid important for absorption of nonheme iron, these medications decrease acid production
    • No significant effect if normal iron stores
    • Those taking supplements for iron deficiency may have decreased effect from iron supplements
Herbal Supplements
Zinc

• Cold preparations
  – Multiple studies show a decrease in duration and severity of cold symptoms
  – Multiple studies show no difference
  – Most recent large review of literature done supports benefit

• Lozenges >>>>> Nasal products
  – Multiple case reports of anosmia (loss of smell)
  – 3 products recalled in 2009

• If needed, use the lozenges and use sparingly
  – No specific data to support recommendations on doses, length of treatment
Fish Oil

• Well established: primary and secondary prevention studies show reduction in all-cause mortality and cardiovascular disease outcomes such as sudden death, cardiac death, myocardial infarction
  – Best evidence: fish and fish oil supplements

• Lower triglyceride levels

• Small beneficial effect on blood pressure
# Fish Oil – Impact on Other Diseases

<table>
<thead>
<tr>
<th>Inconclusive</th>
<th>Greater Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Asthma</td>
<td>– Rheumatoid arthritis</td>
</tr>
<tr>
<td>– Inflammatory bowel disease</td>
<td></td>
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<tr>
<td>– Renal disease</td>
<td></td>
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<tr>
<td>– Lupus</td>
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<tr>
<td>– Bone density</td>
<td></td>
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<tr>
<td>– Diabetes</td>
<td></td>
</tr>
<tr>
<td>– Cognitive function</td>
<td></td>
</tr>
</tbody>
</table>
Fish Oil Products

• Prescription product (Lovaza)
  – Higher amounts of EPA/DHA
• Multiple dietary supplements
  – Check label for content of EPA and DHA as well as source
  – Algal oils provide a vegetarian source of DHA
Fish Oil and Chemotherapy

• Question of whether a specific fatty acid found in fish oil (supplemental and natural) can cause resistance to chemotherapy
  – Seen in mouse models with cisplatin
  – Ingestion of recommended daily amount of fish oil by health volunteers raised levels of this fatty acid

• Not concrete, but given potential detriment, we recommend to hold fish oil (and not to eat fatty fish) the day before, during and day after chemotherapy
Black Cohosh

- Potential use in postmenopausal women for hot flashes
  - Binds estrogen receptors
- Most well studied product – Remifemin
- While majority of studies (small and short duration) showed benefit, there is difficulty in evaluating the effect
  - Short duration (6 months or less) of study
  - Varying amounts used from different sources
- New study being conducted by NIH: 12 months long
  - Will also try to better determine mechanism of action
Melatonin

• Use has more than doubled from 2007 to 2012
  – 0.6% up to 1.3%

• Significant evidence (in children too!) to show improvement in sleep duration and quality
  – This is generally the only sleep aid we recommend in pediatric patients
  – Often used in patients with underlying neurological disorders and cancer
Noteworthy Interactions

• Vitamin K
  – What are some good sources of Vitamin K?
  – Who has ever heard of COUMADIN?

• St. John’s Wort
  – Potential for benefit in mild depression?
  – No benefit over placebo in moderate depression
  – Many drug interactions: additive side effects with other antidepressants
  – Should never be used with certain medications for HIV, anti-rejection, chemotherapy
What To Look For

• The guys on TV are good, but do not always present the most robust information
• Large, randomized trials are the best!
• While studies may find a “statistically significant” difference within the numbers and confines of their design, the CLINICAL SIGNIFICANCE is very important to note
  – So while supplementation may increase blood levels of a vitamin/mineral, the actual effect in benefiting the patient may not be evident/clear
What To Look For

• If it claims to “cure” a disease or has a “money-back guarantee” BEWARE!

• Check the label for all ingredients listed (THEY HAVE TO DO THIS!)
  – Look for wheat, soy, dairy, nuts, other allergens

• These are ideal to see on a label:
  – NSF International (nsf.org)
  – US Pharmacopeia
    • (www.usp.org/usp-consumers/dietary-supplements-consumers)
  – Consumer Lab seal
Conclusions

• Vitamins (and fish!) are beneficial to support many bodily processes that we need to maintain healthy lifestyles
• Ensure you always discuss addition of new vitamins and herbal supplements with your healthcare providers
  – Doctors, pharmacists and complementary medicine professionals should play nicely in the sandbox together
Sources For Information

• National Institute of Health (NIH)
• National Center for Complementary and Integrative Health (part of NIH)
• Federal Drug Administration
• Call the manufacturer
  – Ask for published reports/studies