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

- Vitamin A
  - Required for helping our blood clot
  - Supports structure and function of bones and teeth

- Vitamin E

- Vitamin K
  - Important for vision
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>
</tr>
<tr>
<td>1-3 years</td>
<td>15 mg</td>
<td>15 mg</td>
<td></td>
<td></td>
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<tr>
<td>4-8 years</td>
<td>25 mg</td>
<td>25 mg</td>
<td></td>
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<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>
</tbody>
</table>

Smokers: Individuals who smoke require 35 mg/day more vitamin C than nonsmokers.

* 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.
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

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<td>0-12 months*</td>
<td>400 IU</td>
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</tr>
<tr>
<td></td>
<td>(10 mcg)</td>
<td>(10 mcg)</td>
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</tr>
<tr>
<td>1-13 years</td>
<td>600 IU</td>
<td>600 IU</td>
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<tr>
<td></td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
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</tr>
<tr>
<td>14-18 years</td>
<td>600 IU</td>
<td>600 IU</td>
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<tr>
<td></td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
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<tr>
<td>19+50 years</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
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<tr>
<td></td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
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<tr>
<td>51-70 years</td>
<td>600 IU</td>
<td>600 IU</td>
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<tr>
<td></td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
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<tr>
<td>&gt;70 years</td>
<td>800 IU</td>
<td>800 IU</td>
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<tr>
<td></td>
<td>(20 mcg)</td>
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<td></td>
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* 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

![Image of vitamin D and food sources]
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

Inconclusive

- Asthma
- Inflammatory bowel disease
- Renal disease
- Lupus
- Bone density
- Diabetes
- Cognitive function

Greater Potential

- Rheumatoid arthritis
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
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
• Federal Drug Administration
• National Center for Complementary and Integrative Health