

# **Does your Prescription Medication cause Nutritional Deficiency?**

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# Overview



Of almost 900 drugs and fixed-drug combinations used in the U.S.:

- z Almost 400 may deplete specific nutrients.
- z Over 400 may interact with food or food components.
- z Over 300 have been shown to interact with dietary supplements, with adverse and beneficial interactions equally common.

# Types of Interactions

- z **Pharmacodynamic:** two substances exhibit pharmacologic actions that reinforce or interfere with each other's actions.
- z **Pharmacokinetic:** the absorption, distribution, excretion or enzymatic transformation of one substance is altered by another. **Most adverse interactions are of this type.**

# Pharmacokinetic Mechanisms



- z Alteration of gastrointestinal or urinary pH.
- z Stimulation, induction or inhibition of enzymes involved in biotransformation or transport of drugs or nutrients.
- z Displacement of a drug from binding to plasma proteins.
- z Alteration of solubility.

# Effects of Interactions

- z **Nutrient depletion:** Individual nutrients may have their dietary requirement increased by specific drugs (or supplements).
- z **Adverse:** A specific supplement may undesirably decrease or increase the effect of a drug or supplement being taken.
- z **Beneficial:** Drugs (or supplements) may have their actions enhanced or side effects diminished by specific supplements.

# Drug-Induced Nutrient Depletion



- z About 50% of the drugs used in clinical practice have documented nutrient depleting effects.
- z Co-enzyme Q10, folic acid, B2, B6, Mg, Zn are nutrients most likely to be depleted.
- z Mechanisms include impaired absorption or bioactivation, and increased excretion.

# Even OTC Pharmaceuticals can induce nutritional deficiencies which are often treated with additional pharmaceuticals



# Top 10 Drug-induced Nutrient Deficiencies

## Lipid- Lowering agents- CoQ10 deficiency

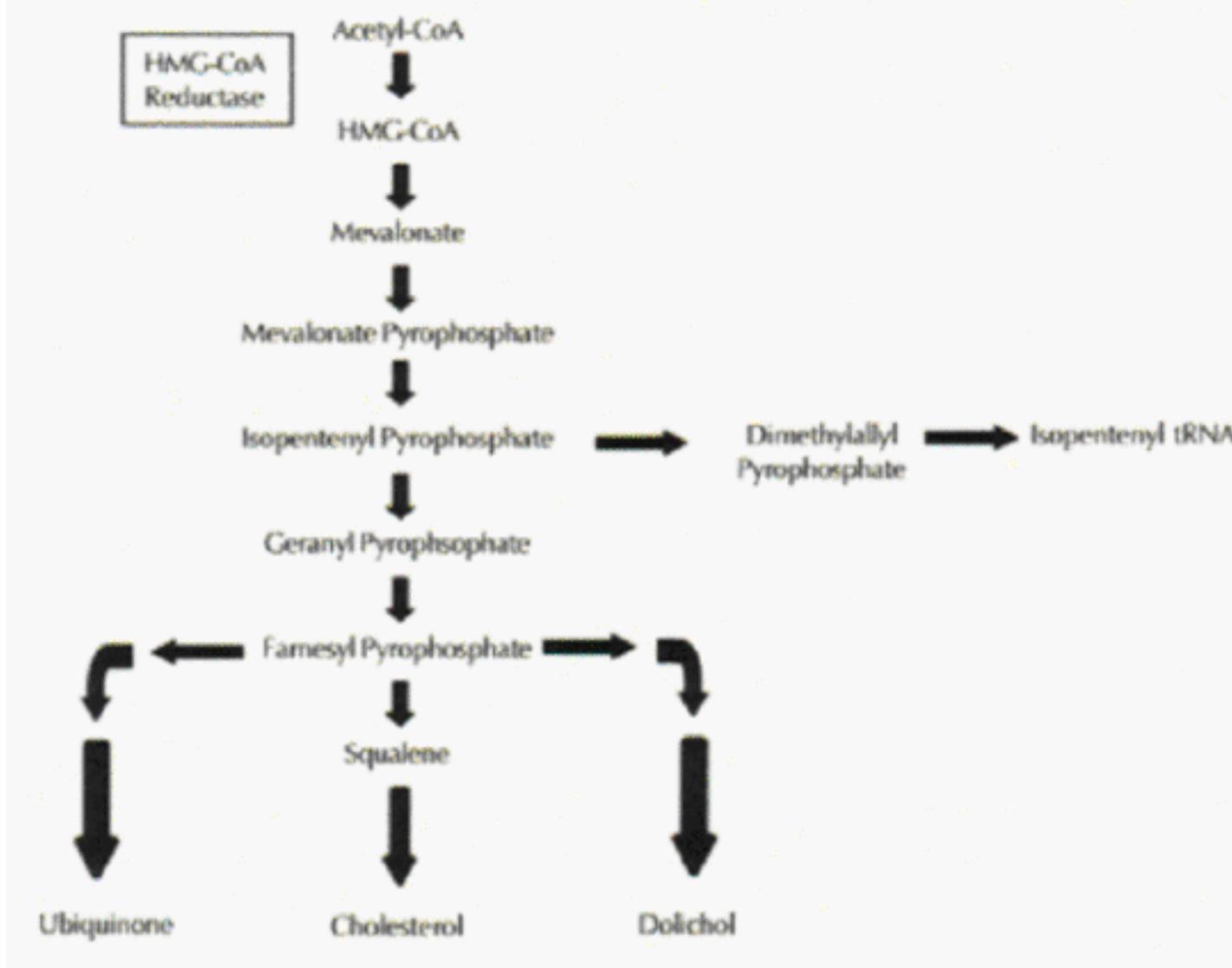


- z **Cholesterol lowering medications** (HMG-coA reductase inhibitors), aka statins.
- z Medications: Atorvastatin (Lipitor), Fluvastatin (Lescol), Pravastatin (Pravachol), etc.

### **Depletion:**

- z HMG-CoA reductase inhibitors (e.g. lovastatin) lead to a decreased concentration of CoQ10.
- z The major symptoms of CoQ10 depletion due to statin drugs include muscle aches and weakness.

# Biosynthetic Pathway for Coenzyme Q10



# Co-enzyme Q10 (CoQ10) (Ubiquinone) Depletion



- z Statin-induced co-Q depletion impairs mitochondrial function, raising the serum lactate/pyruvate ratio.
- z In a study done by Mabuchi, et al, all patients treated with Liptitor (Atorvastatin) showed definite reductions of serum ubiquinone-10 levels
- z As atorvastatin reduces serum CoQ10 levels as well as serum cholesterol levels in all patients, **it is imperative that physicians are forewarned about the risks associated with ubiquinol-10 depletion.**

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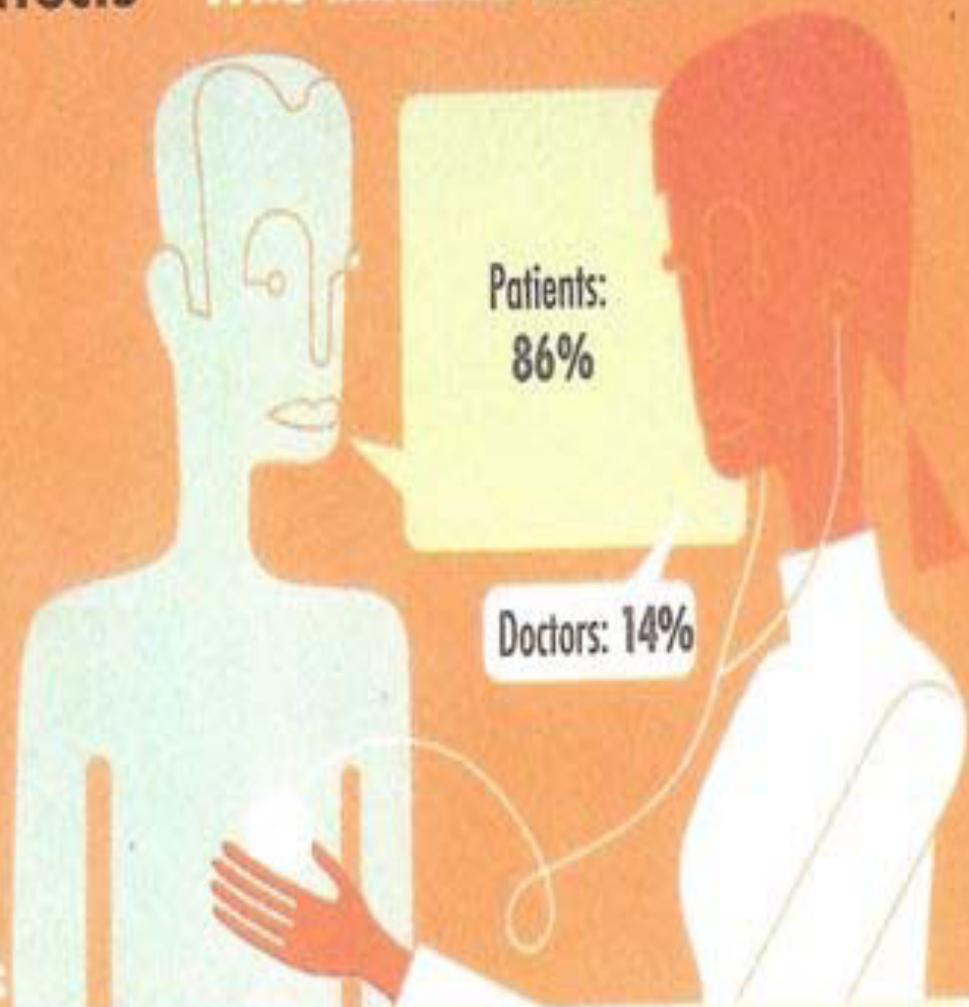
# CoQ10 depletion (cont.)

- z Based on human studies, CoQ10 concentrations decreased in patients treated with pravastatin and lovastatin, or pravastatin and simvastatin.
- z References: [Mol Aspects Med.](#) 1997;18 Suppl:S137-44. **Dose-related decrease of serum coenzyme Q10 during treatment with HMG-CoA reductase inhibitors.**
- z [J Clin Pharmacol.](#) 1993 Mar;33(3):226-9. **Evidence of plasma CoQ10-lowering effect by HMG-CoA reductase inhibitors: a double-blind, placebo-controlled study.**

## Talking about drug side effects

### Who initiated discussion:

One recent study found that doctors often dismissed patients' concerns about muscle pain after taking cholesterol-lowering "statin" drugs. That may be because doctors tended to focus on the drugs' benefits. But even minor side effects can stop you from taking the drugs you need. So if you suspect a symptom is a side effect of a drug, talk with your doctor about trying a lower dose or a different medication. But don't stop on your own.



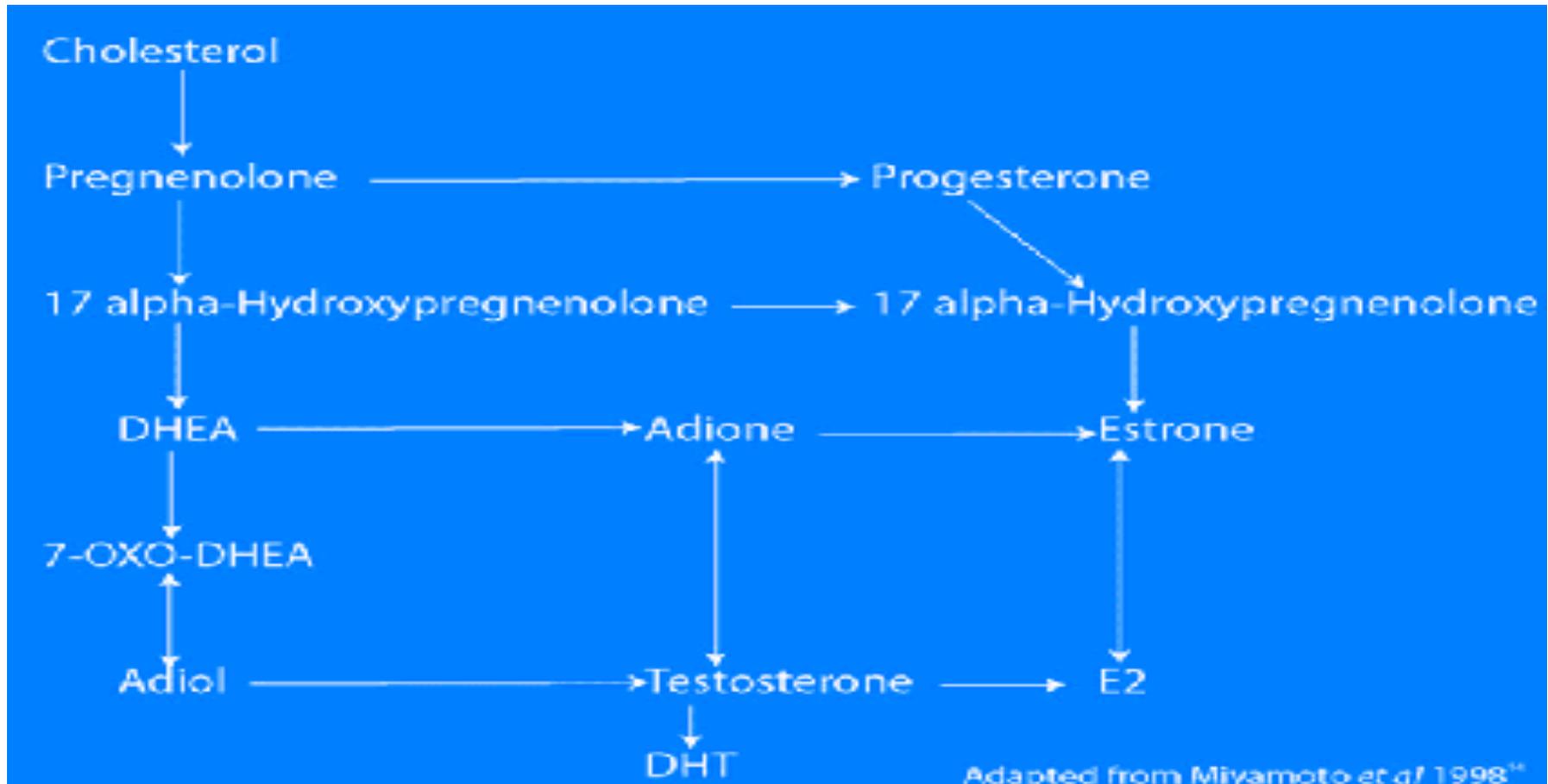
### How doctors responded:

Dismissed side effects as unrelated to drugs 47%

No opinion 24%

Said they might be related 29%

# Potential Effects of DHEA depletion



# **Anti- Inflammatory** **( Indomethacin, colchicine)**



- z** Nutrients depleted:
- z** Amino Acids- ( Increased rate of gastric emptying, decrease absorption of proteins)
- z** Vitamins: Ascorbic Acid, Niacin, Iron, beta- carotene (key anti-oxidant necessary for free radicals scavenging), Vitamin B12.

# Antacids (Gaviscon, Maalox, Mylanta)

- z Popular over-the-counter remedies for heartburn, antacids are weak bases that neutralize stomach acid.

Depletions caused by antacids:

- z **Protein indigestion** (acidic environment is needed for protein metabolism)
- z **Vitamin B12** mal-absorption
- z **Vitamins A,D, and Zinc**
- z **Antibiotic** (Fluoroquinolones) mal-absorption (formation on inactive complexes in the presence of aluminum, calcium, magnesium, and zinc)

# Proton Pump Inhibitors (PPI)

## (Omeprazole and Lansoprazole)

- z **Decrease the absorption of vitamin B12** - The reduced secretion of gastric acid and pepsin produced by proton pump inhibitors (PPIs) may reduce absorption of protein-bound (dietary) vitamin B12, but not supplemental vitamin B12.
- z Reduced vitamin B12 levels may be more common with PPIs than with H2-blockers, due to pronounced achlorhydria (complete absence of gastric acid secretion).
- z **Note:** PPI taken with cranberry juice or any other acidic liquid increases the uptake of vitamin B12 from food sources.
- z Vit. B12 deficiency have be seen with prolonged PPI therapy (two years or more).
- z Based on results of recent studies, vitamin B12 levels should be monitored in people taking high doses of PPIs for prolonged periods.

# Nutrient depletions by PPIs (cont.)



- z PPIs neutralize the acidic environment of upper GI--> prevent proper digestion and absorption of **proteins**.
- z **Depletion of Vitamin C and Zinc** - PPI therapy lowers the concentration of vitamin C in gastric juice and the proportion of the vitamin in its active antioxidant form i.e., ascorbic acid.
- z There is also evidence that PPIs may reduce the bioavailability of ingested **vitamin C**.
- z PPI therapy reduces the absorption of **iron**.

# Analgesics

## (Aspirin and NSAIDs)

- z Analgesics are used widely for pain control. Most frequently utilized pain killers are: Aspirin and NSAIDs, like ibuprofen, Naproxen, Celecoxib (Celebrex).

### Depletions:

- z Folic Acid- Decrease absorption.
- z Depletion of Iron stores - Increase the risk of GI bleeding, leading to anemia.
- z Decrease absorption of vitamin C
- z Interaction of vitamin E and ASA/NSAID may increase the risk of bleeding.
- z Vitamin K: Based on animal evidence, high doses of salicylates may act as vitamin K-antagonists.
- z Zinc: Based on human evidence, aspirin and/or indomethacin may decrease blood levels of zinc.

## Hydrocodone and Acetaminophen (APAP) products: Hydrogesic, Lortab, Vicodin

- z APAP overdose can lead to liver failure.
- z High doses of APAP may deplete **glutathione** levels (major detoxifier of APAP metabolites).
- z Both Hydrocodone and APAP cause **selenium** depletion.
- z Alcohol consumption potentiates liver damage.

# Restoring the Nutrient Balance



- z N-acetyl-cysteine 600-1200 mg (precursor to glutathione) can prevent liver damage.
- z Vitamin C > 3 g/day extends protective effects of N-acetyl-cysteine.
- z Selenium 200 mcg/day.
- z Pre-treatment with standardized Milk Thistle extract, Silymarin or Schisandra extract can mitigate and prevent liver damage.

# Antibiotics



- z **Calcium**- Based on *in vitro* evidence, fluoroquinolones and tetracyclines may form complexes with calcium in the gastrointestinal tract that may lead to reduced absorption of both if taken at the same time.
- z **Carnitine**- Based on human studies, cephalosporins (cephalexin, etc.) may reduce carnitine due to an increase in urinary carnitine excretion and a decrease in free carnitine concentration.
- z **Folic Acid**- Antibiotic therapy, such as chloramphenicol and cycloserine, may disrupt the normal gastrointestinal (GI) flora, interfering with the absorption of folic acid.
- z **Bifidobacteria bifidum and Lactobacillus acidophilus**- Based on human studies, antibiotics taken internally may destroy beneficial bacteria that normally assist in digestive and immune functions.

# Restoring Nutritional Balance



- z Probiotic (preferably, broad-spectrum), containing various (multiple) strains of beneficial bacteria.
- z Well-balanced Multivitamin/Mineral containing key nutrients lost during ABX therapy.
- z Healthy diet rich in antioxidants and pro/prebiotics.

# Laxatives



- z **Mineral Oil**- Based on human evidence, mineral oil may reduce absorption of fat-soluble vitamins, including beta-carotene. (*Am J Dis Child*. 1987 Nov;141(11):1210-2. Serum beta-carotene, retinol, and alpha-tocopherol levels during mineral oil therapy for constipation.
- z **Other Fat-soluble vitamins affected: Vit-s: E and K.**
  - z (*Clin Pediatr (Phila)*. 2006 Nov;45(9):856-8. The safety of mineral oil in the treatment of constipation--a lesson from prolonged overdose. Gal-Ezer S, Shaoul R.
- z **Mineral Oil and Stimulant Laxatives**- (Cascara, Senna, and Bisacodyl) when used for prolonged periods, may reduce dietary calcium and vitamin D absorption, often causing osteomalacia (bone softening).

# Antidepressants

## (Prozac, Zoloft, and other SSRIs)

- z SSRIs -Selective Serotonin Reuptake Inhibitors- work by increasing the levels of serotonin in the brain to treat depression.
- z **Melatonin**- based on human studies, melatonin changes after antidepressant use may be due to pharmacological action of SSRIs on melatonin secretion.
- z After treatment with (SSRIs), levels of 6-sulphatoxymelatonin (aMT6s), the main melatonin urinary metabolite, increased, indicating increased metabolism of melatonin.
- z Reference: J Psychopharmacol. 2009 May;23(3):315-21. Epub 2008 Jun 18. Effect of antidepressants on melatonin metabolite in depressed patients.
- z **Sodium** - According to a review, hyponatraemia may be a possible reaction to treatment with SSRIs. Measurement of serum electrolytes is recommended, particularly in patients over the age of 65.

# Beta-Blockers

- z **Melatonin:** According to human studies, beta-blocker blood pressure medications such as atenolol (Tenormin®) or metoprolol (Lopressor®, Toprol®) may decrease melatonin release via specific inhibition of adrenergic beta1-receptors.
- z **Calcium:** May form complexes with beta-blockers, specifically sotalol, reducing its absorption.
- z **Coenzyme Q10 (CoQ10):** Based on human data, beta-blockers reduce serum concentrations of CoQ10.
- z References: Res Commun Chem Pathol Pharmacol. 1977 May;17(1):157-64. Bioenergetics in clinical medicine XV. Inhibition of coenzyme Q10-enzymes by clinically used adrenergic blockers of beta-receptors.
- z Acta Pharmacol Toxicol (Copenh). 1979 Jan;44(1):7-12. Effect of food, food constituents and fluid volume on the bioavailability of sotalol.

# Chelation and Drug Absorption



- z Chelation by minerals impairs absorption of quinolone or tetracycline antibiotics, thyroid, bisphosphonates, L-DOPA, some ACE inhibitors.
- z Even some herbs like dandelion and fennel can be so rich in minerals that they inhibit absorption of these same drugs.

# Beneficial Drug-Supplement Interactions



- z Reflect additive/complementary effects of supplements and drugs, or amelioration of toxic drug effects by supplements.
- z Fish oils enhance anti-inflammatory, antiarrhythmic, anti-lipemic, antidepressant, and neuroleptic drugs, beta-blockers, lithium and insulin.

# **Fish oils, NSAIDs, ASA**

- z 2600 mg of EPA + DHA for 3 months allow NSAID reduction in rheumatoid arthritis. Plasma phospholipid EPA must reach 5%.
- z Fish oil 30 ml/day reversed ASA's increase of LTB4 synthesis; no hemorrhage.
- z ASA increases synthesis of anti-inflammatory resolvins and protectins from DHA in vitro by acetylating COX-2.

# Conclusion



- z Almost half the drugs commonly used in the US may deplete specific nutrients, creating a need for nutritional supplementation.
- z Adverse interactions have received extensive press coverage.
- z Beneficial drug-supplement interactions are at least as important and permit creative nutritional therapies.