(Complementary and) Integrative Medicine: Effective Herbal Therapies and other Approaches to Primary Care Problems

Primary Care Internal Medicine

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Disclosure

I have no financial relationship with a commercial entity producing healthcare-related services

Donald B. Levy, M.D.
Integrative Medicine

A.K.A.

Holistic
Alternative
Complementary
Complementary and Alternative (CAM)
Complementary and Integrative (NCCIH)*

*National Center for Complementary and Integrative Health
What is Modern Integrative Medicine?

......health care with an attitude of mind that seeks preferentially those therapies or therapeutic lifestyle changes (TLC) that enhance one’s innate ability to recover from illness and maintain good health.

(An incremental change in the approach and scope of Primary Care Medicine)
Integrative Medicine

- No single healing paradigm or tradition

- Roots in Western, Asian, naturopathic, manual, functional, nutritional and behavioral medicine.

- Always guided and informed by scientific evidence and research
Today’s *Prepared Agenda*: An Introduction to Integrative Medicine with a focus on the **Rational Use of Dietary Supplements**

1. **A Rational Approach**
   - Long Latency vs. Short Latency deficiency syndromes
   - Determining an Optimal dose —i.e. Vitamin D
   - **Case #1--Daily Multivitamins —helpful or harmful?**
   - Finding high quality supplements
   - The herbal “Entourage Effect”

2. **Useful Supplements for several common conditions**
   - **Case #2--Hyperlipidemia**
   - **Case #3--Hypertension**
   - **Case #4--URI’s/ Influenza: “I always get sick”**
   - **Case #5--URI’s/ Influenza: “What can I take?”**
   - **Case #6—“I am tired, burned-out...stressed and depressed”**
Dietary Supplements:
Prevalence of Use in the United States

2003-2006: > 50% of Adults
> 32% of Children

1988-1994: 40% of Adults


Three Rational Uses of Dietary Supplements

1. Prevent or treat an acute (Short Latency) deficiency condition

2. Prevent or treat a chronic (Long Latency) deficiency condition

3. Treat an acute or chronic disease (“Green Pharmacy”)

For another day:
4. Provide For Optimal Health (very complex)
5. Avoid toxicity or interference with current medical therapy
Preventing or treating an Acute Deficiency or **Short Latency Syndrome**

May 1941—NAS Subcommittee established **RDA’s** to prevent acute deficiency syndromes in the general population. i.e. Take daily to prevent:

- **Scurvy**  
  Vitamin C — 75-90 mg
- **Rickets**  
  Vitamin D — 600 IU
- **Pellagra**  
  Vitamin B3 (Niacin) — 16 mg
- **Berberi**  
  Vitamin B1 (Thiamin) — 1.2 mg

However: What is the optimal life-long dose of these vitamins?
Preventing or treating a Chronic Disease or Long Latency Syndrome

There is suggestive evidence that specific vitamins, minerals or other supplements may prevent, delay or ameliorate:

- Osteoporosis
- Osteoarthritis
- Coronary Heart Disease
- Depression
- Hypertension
- Multiple Sclerosis
- Alzheimer’s Disease
- Prostate Cancer
- Complications of Pregnancy


Holick MF. Vitamin D deficiency. NEJM. 2007;357(3):266-81. Review
Can We Really Prevent or Treat a Chronic Disease with a Micronutrient?

If so, how do we investigate Long Latency Hypotheses Without VERY LARGE, 10-30 Year Studies?
Hypothesis: Osteoporosis is Partially Due to a Long latency Vitamin D Deficiency Syndrome

Osteoporosis and Vitamin D Insufficiency:

• Increased risk of falls
• Increased risk of vertebral and non-vertebral fractures
• Muscle weakness
Look at physiologic feedback loops to determine what levels exist when there is optimal homoeostatic balance
Optimal Daily Dose of Vitamin D for Bone Health is likely When We See:

✔ Maximal Calcium Absorption and Transport
✔ Lowest Parathyroid Hormone (PTH) level
✔ Greatest Muscle Strength
✔ Greatest Bone Density
All of the Above are Achieved When:

Serum 25 (OH) D = Approx. 32 ng/mL* (80nmol/L)

Ballpark optimal dose for bone homeostasis is whatever it takes to achieve that level.

Holick MF. Vitamin D deficiency. NEJM. 2007;357(3):266-81. Review.

* Notes:
   — I.O.M. Report says data more consistent with level of ~20 ng/mL
   — In sunny countries 25 (OH) D levels = 54-90 ng/mL
PTH levels fall and level off as 25(OH) D levels rise
Rational Use of Vitamin D

Order a 25(OH) D Level
Aim for level > 32 ng/mL (80nmol/L)

For many: every 1,000 IU of D3 daily raises 25(OH) D level approx. 10 ng/mL
Case # 1: *Daily Multivitamin/Multimineral?* (MVMM)

- “I Try to eat well...very busy...not always time to prepare a good meal...”
- “.... *just for insurance?*”
- “but they say on the news there may be danger:

Multivitamins According to the Media

• Vitamins Lack Clear Health Benefits, May Pose Risks — Forbes
• Studies suggest vitamins provide no health benefits — Fox Business News
• How do Americans waste $28 billion a year? On vitamins... — TIME
• Docs Say Stop Taking Multivitamins — Associated Press
• Do vitamins block disease? Some disappointing news — CBS Nightly News
• Vitamins, mineral supplements deemed waste of money — CNN
• Multivitamins don’t hold any health benefit, experts say — Reuters
• Multivitamins not tied to memory or heart benefits — The New York Times
• Dr. Nancy: Forget multi-vitamins, just eat good food — USA Today
• Medical journal: ‘Case closed’ against vitamin pills — Wall Street Journal

• Multivitamins found to have little benefit — WebMD
Multivitamin-Multimineral (MVMM)
Some literature worth reading


Horrobin D. *Why do we not make more medical use of nutrition knowledge? How an inadvertent alliance between reductionist scientists, holistic dietitians and drug-oriented regulators and government has blocked progress.* Brit J of Nutr. 2003;90:233-38


Willett WC and Stampfer MJ. *What vitamins should I be taking, doctor?* NEJM. 2001;345(25): 1819-24
Nutrition experts are almost unanimous in suggesting:

The best path is to eat a fully balanced **diet** of high quality foods to obtain all the essential micronutrients.

Many also admit: In practice this is *nearly impossible to achieve*.
Consensus of an Expert Panel Regarding Taking a MVMM

“Present evidence is insufficient to recommend either for or against ...to prevent chronic disease...”

......the totality of scientific trials show that there is “no evidence of any safety issues or harm” from taking daily MVMMs.
Dissenting Experts:

“Certain vulnerable populations who likely do not get all the essential micronutrients from diet should definitely be advised to take a MVMM.”
Vulnerable Populations

• Elderly
• Poor Urban-dwelling
• Pregnant or might become
• Vegans
• Drinking > 2 alcoholic beverages daily
• Hospitalized
• Mentally ill
One “dissenting expert” worth reading:

Bruce Ames, Ph.D*

“Evidence is accumulating that a multivitamin/mineral supplement is good insurance, and would markedly improve health e.g., heart disease, cancer, immune function and cataracts...particularly for those with inadequate diets such as many of the poor, young, obese and elderly, who need improvement the most.”


* Prof. Emeritus of Biochemistry and Molecular Biology, University of California, Berkeley
One Rational Daily Regimen for Adults

• **Multivitamin/Multimineral:** moderate doses—100%--200% of DRI

• **Vitamin D3:** 1,000 units daily—or titrated to serum 25(OH) Vit D level >32 ng/mL

**(Omega-3 Fish Oil):** 1,000-2,000 mg. —especially if no fish in the diet

**(Micronutrients tailored to Age, Gender, FH):**

Ca+, B12, Probiotic, Lutein, Mg+ etc.
What About **Quality**?

- **Quality**, purity, potency and bioavailability vary tremendously!

- Some formulations may be more **physiologic** than others (Folate vs. methyltetrahydrofolate)

- **Cost** does not always reflect quality
A *Start:* Look for these Product Seals

- Confirm the identity and quantity of *some* of the ingredients declared on the label
- Confirm product is free of *selected* contaminants and undeclared ingredients
- Demonstrate conformance to *industry* GMPs
- On-going *monitoring*
One Independent Distributor’s Quality Program

www.emersonecologics.com
Some of the Quality Supplement Brands That are Available Through Retail Outlets*

Enzymatic Therapy
Gaia Herbs
Nature’s Way
NOW Vitamins
Nordic Naturals  (for fish oils, Omega-3 fatty acids)

Cost: Look on-line; i.e. www.vitacost.com

*Some of the highest quality brands of dietary supplements are available only through health care professionals.
Rational Use of Dietary Supplements for some Common Conditions in Primary Care

Case #2: Hyperlipidemia
Case #3: Hypertension
Case #4-5: Upper Respiratory Infections
Case #6: “Burned-out/ Stressed-out”
Case # 2a: Hyperlipidemia—Statin intolerant
but patient really needs this medication and willing to try

Consider:

☑️ Vitamin D—if deficient
☑️ Red Yeast Rice (see 1b)

☒ Coenzyme Q10? —Current evidence suggests no benefit for statin-induced myalgias
2a. Hyperlipidemia—Statin intolerant: Vitamin D Supplementation

- Check 25(OH) D level
- Supplement if level below 32 ng/mL (80 nMol)


Waqas A et. al. Low serum 25(OH) vitamin D levels (<32 ng/mL) are associated with reversible myositis-myalgia in statin-treated patients. Translational Res 2009;153:11-16.

2a. Hyperlipidemia—Statin intolerant

Co-Enzyme Q10?

Safe, nutritionally reasonable, but latest trials speak against significant benefit for statin-induced myalgias


Case # 2b: **Hyperlipidemia— “No statin please!”**
The individual who *cannot* or *will not* take a statin

- **Therapeutic Lifestyle Changes--especially Diet**—Classic Mediterranean (Lyon Diet Heart Study) + **Soluble Fiber** (Psyllium, oat, flaxseed) + nuts

- **Plant Stanols and sterols**

- **Red Yeast Rice**

- **Nuts**

- **Niacin** --still benefit if *not already on a statin* *(Coronary Drug Project—1980’s)*

- **Theaflavin-enriched Green Tea Extract** (1 RCT)

- **Policosanol**

- **Guggulipid**  (Both unlikely to be helpful based on good studies)
Hyperlipidemia: Plant Stanols and Sterols
(Present in Western diet in small amounts--250-500 mg/d)

• Can lower LDL cholesterol by 10-14% in doses of 2,000-3,000 mg /daily

• Well tolerated; does not affect serum levels of fat-soluble vitamins


Hyperlipidemia: Plant Stanols and Sterols

Note: 450 mg. per cap. *(Need 5 daily not 4)*
Hyperlipidemia: Red Yeast Rice

Dietary staple in some countries and used for 13 centuries in China--contains plant sterols, isoflavones and naturally occurring statins (monacolins)

- Trials using a **dose of 2.4 --3.6 grams daily** lasting at least 6 months have shown it to be well tolerated **even in patients who had previously been statin- intolerant**

- **20-25% reductions in LDL cholesterol**

- Study of almost 5,000 patients in China with previous MI; 4.5 years; **Decreased Cardiac events and CVD mortality**

- Must be high quality product to avoid contaminant (citrinin)
Red Yeast Rice: Literature


Hyperlipidemia: Nuts!

- Substituting a handful of almonds, walnuts, hazelnuts, pistachios and other nuts for isocaloric foods lowers cholesterol in a dose-related manner.
- May Reduce the risk of CHD to a degree beyond that expected from cholesterol-lowering alone.
- May exert beneficial effects by improving endothelial function, lowering oxidative stress, lowering the risk of type 2 diabetes or by ?

Case # 3. **Hypertension:**
Non-Pharmacologic Management always begins with:

*Therapeutic Lifestyle Changes*

- Exercise/physical activity
- Diet: “DASH”
- ETOH
DASH Diet: Literature


• Elmer PJ et. al. PREMIER Collaborative Research Group. Effects of comprehensive lifestyle modification on diet, weight, physical fitness, and blood pressure control: 18-month results of a randomized trial. Ann Intern Med. 2006;144(7):485-95

Sample (partial) handout:

Good Food Sources of Potassium

Cantaloupe  Avocado
Dates       Acorn/winter squash
Honeydew melon Artichoke
Dried Apricots Baked beans
Raisins     Broccoli
Banana      Chick peas
Oranges     Potato
Tomato paste/sauce
Hypertension
Beyond Medications and Diet

Mind-Body Therapies as Adjuvants:
- Mindfulness Meditation, Biofeedback, Tai Chi; Yoga; Resperate device
- Acupuncture trial

Rational Supplements:
- Magnesium citrate
- Tomato/Tomato extract
- (Coenzyme Q10)
- (Quercetin)
Mind-Body Techniques as *Adjuvants*

*Varying styles/approaches = Heterogeneity of Literature; Some great responders with multiple benefits*

- Mindfulness Meditation; Yoga
- Biofeedback; *RESPeRATE™*
- Tai Chi / Qi Gong


de fatima Rosas Marchiori. *Decrease in blood pressure and improved psychological aspects through meditation training in hypertensive older adults: a randomized control study.* Geriatr Gerontol Int. **2014**


Cernes R. *RESPeRATE: the role of paced breathing in hypertension treatment.* J Am Soc Hypertens. **2014**

Two Popular Types of Mindfulness Training

Jon Kabat-Zinn
Herbert Benson
Common Aspects of Mindful Awareness Practice (i.e. Meditation)

- **Intention**
- **Focusing the attention via repetition** or return to focus
- **Nonjudgmental attitude** toward everything experienced
Mindfulness Practice (Meditation) Alters Brain *Function*

May strengthen the ability to choose where to put attention and then to keep it there

(“Protecting your mind from hijacking”)
Regular Meditation also Alters Brain Structure

(A Likely result of Neuroplasticity)
Mindfulness, Tai Chi, Yoga Literature

de fatima Rosas Marchiori. Decrease in blood pressure and improved psychological aspects through meditation training in hypertensive older adults: a randomized control study. Geriatr Gerontol Int. 2014

Mindfulness and Breathing

RESPeRATE™ Device
RESPeRATE in Use

Guided paced breathing: (1) monitoring breathing movements, (2) composing breathing–guiding tones, and (3) synchronizing breathing

From: Cernes. J Am Soc Hypertens 2014;S1933-1711(14) 00834-1
Magnesium

• Magnesium Citrate or glycinate well absorbed
• Often a good *adjunct* to ongoing care
• Dose: **400-600 mg**; May take 6 weeks to show effect


Magnesium: “Side effects”
Depends on dose and formulation

Magnesium Citrate
2 caps = 500 mg

Magnesium Citrate Laxative
1 bottle = 17,450 mg
Tomato Extract

• **Lycopene** content : 15-20 mg daily

• Is it the **Lycopene** or the **whole extract**?


Engelhard YN et al. *Natural antioxidants from tomato extract reduce blood pressure in patients with grade-1 hypertension: a double-blind, placebo-controlled pilot study.* Am Heart J. 2006;151(1):100
Tomato Extract: **Lyc-O-Mato™**

Is it the Lycopene or the whole extract? ("Entourage effect")
Pharmaceutical vs. Herbal remedies

Are herbal remedies simply “messy” drugs?

Pharmaceuticals

• Usually have 1 or 2 chemical compounds: isolated, identified, measured
• Impurities or less active ingredients removed

Herbal extracts

• Contain numerous chemical compounds
• Not all identified, isolated, measured
For example: A current scientific/social dilemma:
Medical *Marijuana* (Cannabis *sativa*

**Plant composition:**

1. THC—Tetrahydrocanabinol
2. CBD—Cannabidiol
3. CBG—Cannabigerol
4. CBN—Cannabinol
5. CBC—Cannabichromene
6. THCV—Tetrahydrocannabivarin

+ 66 other Cannabinoids

+ **Terpenoids**, Amino acids, Proteins, Sugars, Enzymes, Fatty acids, Esters, Flavonoids.....
The “Entourage Effect”
The synergistic interaction of numerous chemical constituents

1. THC considered the “Psychoactive ingredient” but...

2. CBD (cannabidiol) modifies the effects of THC
   • Blocks anxiety caused by THC
   • High CBD = less psychotic experiences
   • Attenuates memory impairment
   • (Potent anti-inflammatory)
“Attempts to isolate the active principles from plant extracts may be ultimately self-defeating”

- “The presence of several psychoactive compounds in one plant may have a ‘synergistic’ effect…

- The ‘silver bullet’ concept adopted by orthodox Western medicine for the drug discovery over the past 100 years, is now increasingly viewed as inadequate in many clinical situations…”

Update: Hypertension and Vitamin D

LATEST LITERATURE: No benefit in supplementing Vitamin D deficiency in Hypertension


Still reasonable to Check a 25(OH) D level
☑ Supplement only if low (<32 ng/mL)-- for other health benefits
Acupuncture

Some people respond especially as an **adjunctive therapy**: worth a defined therapeutic trial


"More rigorous trials are warranted........."
Hypertension: Supplements to watch for additional literature

- **Coenzyme Q10 (C0Q10):** A naturally occurring, fat soluble enzyme found in every cell in the body—an antioxidant involved in multiple cellular processes
  

- **Quercetin:** An antioxidant flavanol found in apples berries and onions
  

- **Pycnogenol (French maritime pine bark)** Herb with antioxidant, anti-inflammatory and vasodilator properties; May augment the effect of a medication: 100 mg. daily for 12 weeks helped reduce the dose of nifedipine
  

- **Potassium supplementation**... Judicious, monitored (?)
Rational Use of Therapeutic Lifestyle Changes

Is it too late….
by the time a middle-aged patient with hypertension arrives in the office?
Turning Back the Clock: Adopting a Healthy Lifestyle in Middle Age

1. Fruits/Vegetables—5 servings/day
2. Exercise—2.5 hours/week (at least walking)
3. Weight Control—(BMI=18.5—30.0)
4. No Smoking

Next 4 years:
Decreased mortality (2.5% vs. 4.2%)
Decreased cardiovascular Disease (11.7% vs. 16.5%)

Dana et. al. Am J Med. 2007; 120: 598-603
3. Upper Respiratory Infections

Offering a Patient Something Rationale For Prevention or Treatment Rather Than the often unnecessary, inappropriate, but requested antibiotic
Case #4:  “I always get sick”

Reasonable Evidence for Preventing a URI

✓ Exercise-- Moderate daily
✓ Handwashing—also outside the hospital*
• Diet +/- multivitamin
• Green Tea Extract formulations
• Probiotics— growing literature
• Quercetin
• Vitamin D (if deficient)
  o Vitamin C (special cases; doses)
  o Zinc (oral, dissolving, may be effective)

Highest Hotel room microflora:  TV Remote, Telephone, Alarm clock, Bathroom faucet, Thermostat, Ice bucket, Door handles, Bible
URI—Prevention: Quercetin

Dietary flavonol found in apples, onions, berries, black tea, leafy green vegetables and red grapes.
Antioxidant, anti-inflammatory, antihistamine and antiviral properties.

- Physically stressed cyclists were given 500 mg. bid, they had significantly fewer upper respiratory tract infections despite no changes in several measures of immune function.

- A reduction in URI related sick days and severity noted in middle-aged and older subjects taking 1000 mg/day who rated themselves as physically fit

(Much of the literature = animal models or tissue culture)
URI—**Prevention**: Green Tea Extract

**Randomized, controlled trial** of a proprietary formulation

**Two capsules daily**—equivalent to drinking about 10 cups daily—for 3 months.

Significant decrease in the incidence of cold and flu illnesses and for those who became ill, a significant decrease in the number of days that subjects had symptoms. *Interestingly, there was not a prolonged increase in certain T cell subsets or interferon levels, but there was a vigorously enhanced response of T cell function when there was an antigenic challenge.*


(There is an additional literature base on green tea and infection/inflammation, i.e:)
- Matsumoto K. *Effects of green tea catechins and theanine on preventing influenza Infection among healthcare workers.* BMC Complement Altern Med. 2011; Feb21
- Park M. *Green tea consumption is inversely associated with the incidence of influenza Infection among school children in a tea plantation area of Japan.* J Nutr. 2011; 141(10)
Case # 5: “I am coming down with a cold; I need an antibiotic or something...now!”

- Herbal preparations: many claims
- Some have actually been tested and are especially effective when just becoming ill with a viral-type URI....rather than the often unnecessary, inappropriate, but requested antibiotic
Black Elderberry Extract (Sambucus nigra)

- Clinically: reduces symptoms when administered to patients with influenza
- Anthocyanins readily detected in bloodstream following ingestion
- May inhibit neuraminidase to roughly same degree as prescription meds
- Studied by mass spectrometry and molecular docking in cell culture and in clinical trials
Black Elderberry: Literature

- Swaminathan K. Binding of a natural anthocyanin inhibitor to influenza neuraminidase by mass spectrometry. Anal Bioanal Chem. 2013;405(20) 6563-72

- Krawitz C. Inhibitory activity of a standardized elderberry liquid extract against clinically-relevant human respiratory bacterial pathogens and Influenza A and B viruses. 2011;25(11):16

Anthocyanin Binding and Inhibition of Influenza Neuraminidase

Swaminathan 2013
Black Elderberry (Sambucus nigra)

One High Quality Extract

Directions

• Herbal dosing can be confusing based on whether crude herb, extract, standardization, etc.

• Can take equivalent of 3-5 grams of crude herb 4x daily

• Follow Label for minimal effective dosing
Sambucol™ contains 3.8 g Black Elderberry Extract per 10 ml. Buy the “Original Formula” (center) and take Q.I.D.
Questionable Vitamin/Herbal products

- **No study** (or single study often by the manufacturer)
- Minimal or no **scientific plausibility**
- **Pseudo-scientific** extrapolations
- Minimal **meaningful clinical result**
Airborne™

- Mixture of many vitamins, amino acids (lysine and glutamine) and 7 herbs (in very low doses)
- No clear evidence of efficacy
- Perhaps helps those very deficient in the vitamins provided (C, Zn, Se)
Oscillococcinum™

- Homeopathic remedy tested against influenza-like illness
- 17.1% vs. 10.3% recovery w/in 48 hours*

Case # 6: “I am tired, burned-out, stressed and depressed....”

“I do not want, or tolerate or need an antidepressant.....”

☑ Lifestyle changes
☑ Exercise
☑ Therapist

What else?
Rhodiola rosea

Adaptogen (non-medical term)

...A substance that can act to increase an organism's resistance to physical, chemical and biological stressors

Long history of use in Eastern Europe and Asia for:

• Combating stress-induced fatigue and depression ("burnout")
• Improvement of mental performance
Rhodiola rosea

- Studies in humans and animals: Some support for the claims made at doses of 340 or 680 mg. of an extract known as SHR-5
- Effects can be seen after single dose
- May reach maximal benefit in two weeks.
- No significant adverse effects reported (theoretical risk of interaction with SSRI's)


Rhodiola rosea
High Quality Manufacturers

NOW Foods
Gaia Herbs
For More Information: Look for these databases (often linked to Electronic Medical Records)

1. **Natural Standard**/ Natural Medicines Comprehensive Database

2. Micromedex/PDR (becomes *AltMedDex®* when you type in a nutraceutical)
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   - Case #1--Daily Multivitamins —helpful or harmful?
   - Finding high quality supplements
   - The herbal “Entourage Effect”

2. **Useful Supplements for several common conditions**
   - Case #2--Hyperlipidemia (Vit. D, Red Yeast Rice, Stanols/sterols, Nuts, DASH)
   - Case #3--Hypertension (Mg+, Tomato extract, Mind-Body, Acupuncture)
   - Case #4--URI’s/ Influenza: “I always get sick” (Exercise, Quercetin, Green Tea)
   - Case #5--URI’s/ Influenza: “What can I take?” (Black Elderberry)
   - Case #6—“I am tired, burned-out...stressed and depressed” (Rhodiola rosea)
Thank You for Listening!

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