



**SPECTRACELL LABORATORIES**  
*ADVANCED CLINICAL TESTING*



# Nutritional Considerations of Cardiovascular Disease

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# Cardiovascular Risk Factors



- **Total Cholesterol (elevated)**
- **LDL (elevated)**
- **HDL (decreased)**
- **Triglycerides (elevated)**
- **Homocysteine (elevated)**
- **C - Reactive Protein (elevated)**
- **Lipoprotein (a) (elevated)**
- **Hypertension**



# Vitamin D

Recent evidence suggests that low 25(OH)D concentrations are associated with higher rates of;

- Hypertension
- Myocardial Infarction
- Cardiovascular Disease
- Peripheral Artery Disease

Hypertension 2007

Arch Intern Med 2008

Circulation 2008



# Etiologies of Vitamin D Deficiency



- **Fat malabsorption**
- **Gastric bypass surgery**
- **Medications**
  - Antiseizure
  - Glucocorticoids
- **Obesity**
- **Lactose Intolerance**

# Vitamin D and Cardiovascular Disease



Aging is associated with decreased concentrations of 7-dehydrocholesterol, the precursor of vitamin D<sub>3</sub> in the skin.

A 70 yr old individual has ~ 25% of the dehydrocholesterol that a young adult does and thus has a 75% reduced capacity to make vitamin D<sub>3</sub>.  
**Lancet – 1989**

Winter increases in cardiovascular mortality, by 30-40% compared with summer, have been confirmed in numerous studies. **EJCN - 1995**

# Hypertension and Vitamin D



Hypertensive individuals who were exposed to a tanning bed raised their blood concentrations of 25(OH)D by >180% in 3 months and become normotensive.

**Lancet – 1998**

# Peripheral Artery Disease

- **Black males have been consistently reported to be more likely to have PAD than are white adults.**

J AM Coll Cardiol 2006, Circulation 2004 &2005.

- **Factors that may account for this racial disparity;**
  - Greater cutaneous melanin content, which blocks the initial conversion of 7-dihydrocholesterol to previtamin D3 in the skin.
  - Dietary intake that includes a lower consumption of dairy products.
  - Racial differences in vitamin D metabolism.

AJCN-2004, J Nutr—2005



# Vitamin D Mechanisms and Cardiovascular Disease

Regulates the expression of a number of proteins relevant to the arterial wall, including vascular endothelial growth factor, matrix metalloproteinase type 9, myosin, elastin, and type I collagen.

Arterioscler Thromb Vasc Biol 2005

Regulates the renin-angiotensin system by suppressing renin gene expression and to inhibit cytokine release from lymphocytes.

J Clin Invest 2002

Vitamin D Receptor activators can protect against vascular calcification.

J Am Soc Nephrol 2008.



# Vitamin D and Magnesium



Vitamin D may increase the gastrointestinal absorption of magnesium (Mg) and increase the transport of Mg from extracellular to intracellular space. [AJCN](#)

# Homocysteine and Cardiovascular Disease



**Approximately 100 epidemiologic and clinical studies that included >10,000 case subjects and an equal number of control subjects have shown that elevated plasma total homocysteine (tHcy) is an independent risk factor for occlusive disease in the coronary, cerebrovascular, and peripheral vessels and for arterial and venous thrombosis.**

**JAMA 1995, NEJM 1996, Haematologica 1997, Annu Rev Med 1998 & AJCN 1999**



# Homocysteine



Results from a meta-analysis of 20 prospective studies indicated that, for every 5- $\mu$ mol/L increase in homocysteine, the odds ratio for risk of ischemic heart disease was 1.32 (95% CI: 1.19, 1.45), and the odds ratio for risk of stroke was 1.59 (95% CI: 1.29, 1.96).

**BMJ 2002**

# Homocysteine Mechanisms



**Damages cells and tissues of arteries by inciting the release of cytokines, cyclins, and other mediators of inflammation and cell division.**

**Produces the connective tissue changes of arteriosclerotic plaques, causing fibrosis, calcification, proteoglycan deposition, and damage to elastin tissue layers.**

**Potent procoagulant that promotes the deposition of fibrin and thrombosis in artery walls.**

**Causes oxidation stress by effects on cellular respiration, leading to oxidation of LDL and other constituents of plaques.**

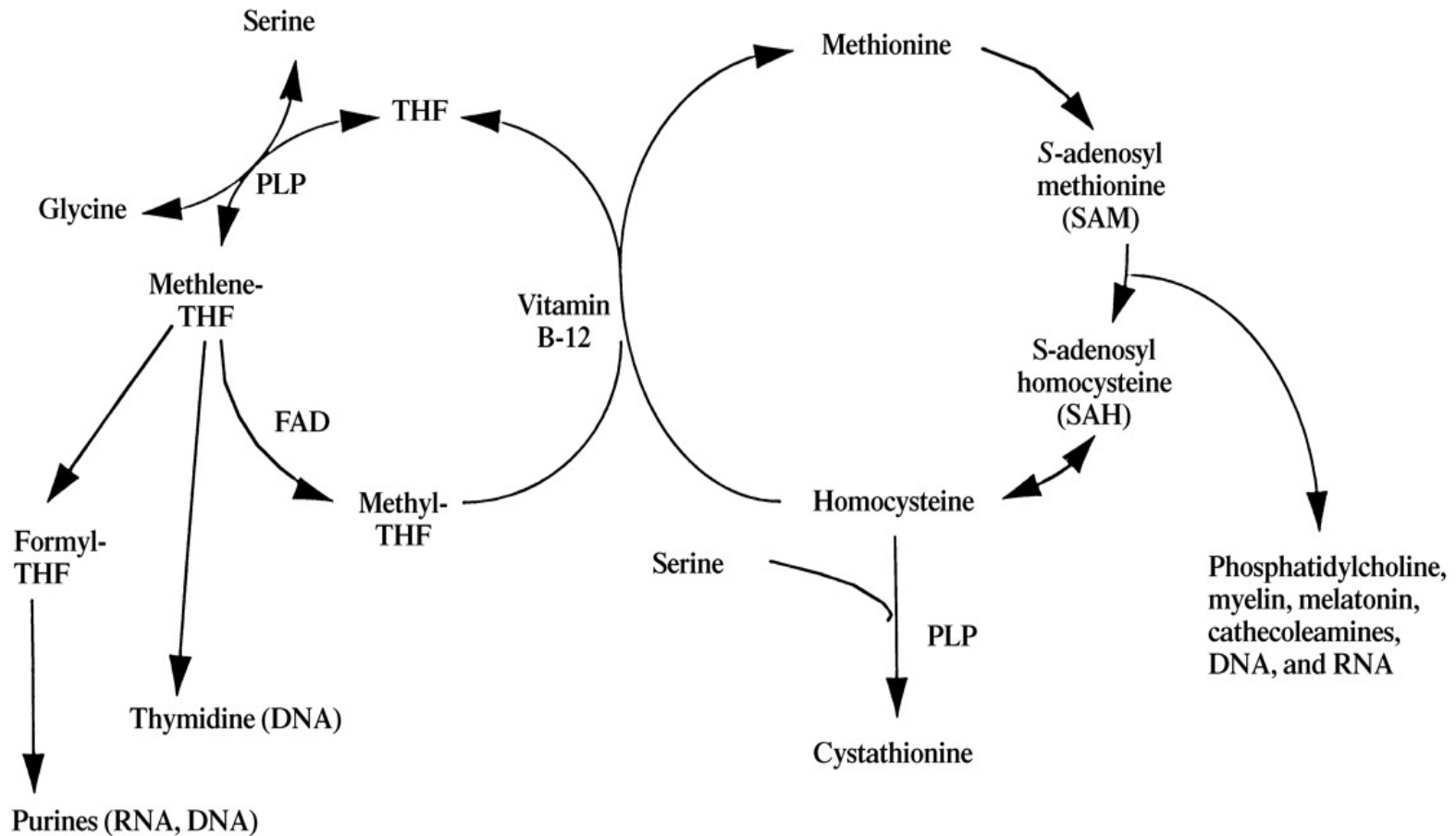
**Antagonizes the vasodilator properties of nitric oxide.**

**JAMA 1999, J Nutr 1996**



# Folic acid, Vitamin B12 & Pyridoxine

## Homocysteine Regulation



# Riboflavin and Homocysteine



**Riboflavin has been largely ignored, despite the fact that FAD is a cofactor for methylenetetrahydrofolate reductase, which metabolizes folate to the form used in homocysteine methylation.**

**AJCN – 6/2003**

# Homocysteine and Smoking



Several studies showed that smoking is associated with elevated Homocysteine (tHcy) concentrations and that there is a strong dose-response relation between the number of cigarettes smoked and tHcy concentrations.

JAMA 1995 , Am J Clin Nutr 2001,

Am J Epidemiol 2001

Eur J Vasc Surg 1993

# Homocysteine and Coffee Consumption



**Subjects who stopped drinking coffee had a decrease in tHcy concentration of 0.3  $\mu\text{mol/L}$ , whereas much larger decreases in tHcy concentration of 1.1–1.5  $\mu\text{mol/L}$  were detected in intervention studies.**

Am J Clin Nutr 1997

Am J Epidemiol 2001

# Magnesium



**Calcium channel blocker**

**Enhances NO release from coronary endothelium.**

**Modulates lipid metabolism.**

**Stress depletes this nutrient**

**Caffeine depletes this nutrient**

**Diuretics deplete this nutrient (non potassium sparing).**

**Anti-platelet aggregation effect.**

**Low levels have been associated with Metabolic Syndrome.**

# Magnesium & Stress



## Adrenalin

- Depletes heart and blood vessel magnesium.
- 72% of magnesium deprived animals developed large heart necroses after administering adrenalin.



# L-Carnitine

## Synthesis

- Tissues
  - Liver
  - Kidney
  - Brain
- Storage
  - Skeletal mm
  - Cardiac mm



# L- Carnitine



**Previous studies reported that 2 g of L-carnitine reduced plasma lipoprotein(a) without clinically relevant adverse events or negative impact on plasma glucose control.**

*Clin Ther 2003 & Atherosclerosis 2006*

**L-Carnitine may provide protective effects on cardiovascular disease by:**

- Increasing HDL cholesterol
- Inhibiting the oxidation of LDL cholesterol
- Neutralizing the atherogenic effects of Ox-LDL cholesterol.

*AJCN – 1/2009*



# Acetyl-L-Carnitine

- 
- Ester of L – Carnitine
  - Functions:
    - Antioxidant
    - Improve cardiolipin levels in the aged heart.
    - Maintains crucial membrane factors in cardiac mitochondria.
  - Dosage: 500 mg/b.i.d.



# Niacin (Nicotinic acid)

## Mechanisms

- Decreases FFA mobilization
- Decreases LDL & TG by decreasing VLDL synthesis.
- Increases HDL by decreased catabolism
- Inhibitory effect on lipolysis

## Adverse reactions

- Flushing
- Pruritus
- GI complaints
- Hepatotoxicity
- Hyperuricemia
- Impaired glucose tolerance



# Coenzyme Q10



**Levels have been found to be significantly lower in ischemic heart disease.**

**Concentrations of CoQ10 decline progressively in blood and myocardial tissue with increasing severity of heart disease.**

**In one study, CoQ10 levels were low in ~ 75% of patients undergoing cardiac surgery.**



# Cardiac Benefits of CoQ10



- **Congestive Heart Failure**
- **Angina**
- **Arrhythmias**
- **Adriamycin Toxicity**
- **Mitral Valve Prolapse**
- **Hypertension**



# Drug – Nutrient Interactions



## Statins

- Coenzyme Q10
  - Myalgia

## Bile acid Sequestrants

- Questran
  - Vitamin A, B12, D, E, K, Beta-carotene, Folic acid and Iron



# HYPERTENSION



# DASH Trial

## Dietary Approaches to Stop Hypertension



# DASH Diet

(Dietary Approaches to Stop Hypertension)

## High

- Fruits, vegetables, nuts, whole grains, fish, poultry, and low-fat dairy products.

## Low

- Red meat, sugar, fat and cholesterol.

**DASH Diet - lowers blood pressure more than sodium restriction alone.**



# New Sodium Guideline



## Less than 1500 mg/day

- ~ 2/3 tsp of salt

## Previous recommendation

- Less than 2400 mg/day
- 1 tsp/day

## Potassium recommendation

- 4,700 mg/day (offset sodium)

National Academies of Science, 2/11/04



# Potassium



**Research states that the ratio of Na:K may be more important in causing HTN than the level of sodium alone.**

## **High Potassium Containing Foods**

- Spinach, dark leafy vegetables, cantaloupes, bananas, oranges, tomatoes, almonds, winter squash, potatoes, and beans. Some dairy products.



# Coenzyme Q10 (CoQ10) Deficiency



- **Cardiovascular disease**
- **Diabetes**
- **Cancer**
- **Muscular diseases**



# PROPERTIES



**CoQ is a powerful antioxidant**

**Bioenergetic agent and enhances the availability of adenosine triphosphatase (ATP) in the cells.**

# Coenzyme Q10



**Ubiquinone deficiency may be present in essential hypertension.**

- 59 patients
  - 39% deficient
  - 6% controls

**Effects both systolic and diastolic blood pressure.**

# L - Carnitine



**Synergistic relationship with Coenzyme Q10.**

**Primary function is in the oxidation of long-chain fatty acids.**

**Shown to reduce blood pressure and attenuate the inflammatory process associated with arterial hypertension.**

**Might produce a partial inactivation of the renin-angiotensin system resulting in a reduction in the production and effects of angiotensin II.**

**Dosage: 2 g/d for adults and 100mg/kg/d for children**



# Free Radicals



**Promote platelet aggregation.**

**Injure endothelium.**


**Promote monocyte-macrophage chemotaxis.**

**Enhance intravascular thrombosis**

**J Lab Clin Med - 1990**



# Ascorbic Acid



Subjects in the highest quintile of vitamin C intake (median intake of 756 mg/d) had a 24% lower risk of CHD than did those in the lowest quintile. [AJCN- 12/2004](#)

Some hypertensives tend to have a reduced dietary intake of ascorbic acid.

May reduce blood pressure in the borderline and normotensives (1000 mg/d).

Influences prostaglandin production, such as prostacyclin (PGI-2) which is a vasodilator.

May decrease norepinephrine release from nerve endings and adrenal medulla to produce a hypotensive effect.

May lower BP by altering leukotriene metabolism.



# Vitamin C and Glutathione



**Each 1-mol change in ascorbate is associated with a change of 0.5 mol in glutathione.** *AJCN – 1/2003*

**Vitamin C at daily dosages of 500mg has been shown to increase red cell glutathione by 50%.**

# Vitamin E



**Inhibition of protein kinase C activity in a variety of cells. Protein kinase C is necessary for platelet activation process. Blood - 1991**

**Chronic vitamin E administration (600mg/day) improves oxidative stress in patients with type 2 diabetes and that this effect seems to be associated with a decrease in plasma catecholamine concentrations and cardiac Sympathetic Nervous System (SNS) activity.**

AJCN – 6/2001

# Selenium



**Has been shown to cause vascular smooth muscle relaxation.**      **Drugs - 1998**



# Magnesium and Hypertension



**Low magnesium intake has been associated with elevated levels of;**

- C-Reactive Protein
- E-selectin
  - Endothelial adhesion molecule.
  - Expressed exclusively by endothelial cells.

AJCN – 4/2007



# Thiamin



Up to 50% of elderly persons have been found to be deficient in thiamin.

AJCN - 1987

Aging is associated with different alterations in thiamin metabolism, such as low intake and decreased capacity to activate the vitamin.

Many diuretics utilized to control blood pressure deplete the body of this nutrient.

– Thiazides

It has been reported that furosemide and digoxin inhibit thiamin uptake by cardiac cells.

Thiamin deficiency has been associated with cardiomyopathies.

Thiamin has been shown to improve left ventricular ejection fraction by 22%.

AJM - 1995

Magnesium is required to produce the active form of thiamin (Thiamin pyrophosphate – TPP).



# Omega-3 Fatty Acids



**Evidence suggests that increased consumption of n–3 Fatty Acids from fish or fish-oil supplements, reduces the rates of cardiac disease and possibly stroke.** *AJCN – 6/2006*

**Has been shown to blunt the vasopressor effects of angiotensin II and norepinephrine and may reduce BP and the risk of arrhythmia.**

**Stimulates the production of prostaglandin I<sub>3</sub>, an antithrombotic and antiplatelet-aggregating agent similar to prostacyclin.**

**Vitamin E deficiency may develop with Omega – 3 fatty acid supplementation.**

# Uric Acid



**Hyperuricemia (serum > 7 mg/dL) is an independent risk factor for cardiovascular mortality.**

**There is approximately 8-13% increased risk with every 1 mg/dL increase for CVDs, ischemic stroke, CHF and HTN.**

**Uric acid is a pro-oxidant that can increase oxygen free radicals.**

- Promote lipid oxidation which can lead to;
  - Vascular endothelial dysfunction.
  - Inflammation
  - NO production impairment.
  - Atherosclerosis
  - Thrombogenesis

Hypertension - 2003



# Fructose



**Sugars (particularly sucrose and fructose) tend to increase serum triacylglycerol concentrations by 60%.**

AJCN – 10/2003

**Uric acid elevations can occur with high fructose intake.**

AAFP – 2/1999

- Elevated uric acid levels have been associated with increased cardiovascular events.



# Copper Deficiency



**Hypercholesterolemia**

**Hypertension**

Minerals and trace elements. In: Kohlmeier M, ed. Nutrient metabolism. New York: Academic Press, 2003.

# Case Study #1



**62 year old male**

**CC:** Hypercholesterolemia and Muscle cramps

**Medications:** Exforge, Catapres and Aspirin

**SpectraCell results:**

- Deficiencies: **B2, B12, Pantothenate, Biotin, Choline and Inositol**

**LPP:** Cholesterol: 168, TG: 127, Lp(a): 93.8, CRP: 0.47 and  
Homocysteine: 16.9

# Case Study #2



**15 year old female**

**cc: Asthma, Constipation, Headaches, and PCOS**

**Medications: Singulair and Albuterol**

**SpectraCell: (1/2010)**

- Deficiencies: Magnesium and Selenium**
- Spectrox: 61.0%**

**LPP: Cholesterol: 129, TG: 80, CRP: 0.04, Lp(a): 140.4**

# Case Study #3



**58 year old male**

**cc:** Hypercholesterolemia, hypertriglyceridemia and muscle cramps.

**Medications:** Lipitor and Levoxyl

**SpectraCell:** (12/2009)

- Deficiencies: **Cysteine (Calcium and CoQ10)**
- Spectrox: **55.0%**

**LPP:** Cholesterol: 168, TG: 173, CRP: 0.20 and Homocysteine: 12.9 (13.11)