PREVENTING AND REVERSING CARDIOVASCULAR DISEASE WITH EVIDENCE BASED LIFESTYLE CHANGES

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My goal with this presentation is to help prevent devastating events (Heart attacks, Strokes, & Sudden cardiac deaths) and Feel Great Doing It!

Outline

- Clarify mechanism for plaque formation and plaque rupture; 20 minutes
- Review traditional *(cholesterol)* and "advanced" markers *(Lp(a) and carotid IMT)* for CVD;
- Review 10 steps to lifestyle therapy options that improve clinical outcomes
- Discuss a paradigm switch in addressing lifestyle changes: "Getting Paid More to Provide Better Care—Welcome to Group Visits";
- Cases:

"STATE OF THE ART" REVIEW OF CORONARY ARTERY THERAPIES

- Lifestyle changes are better at preventing **events** than are medications and supplements
- Aspirin and cholesterol lowering meds are better at preventing **events** than are cardiac procedures

MAGNITUDE OF CARDIO-VASCULAR DISEASE (CVD)

- ~ 40% of deaths in the US and Canada are from CVD
- 500,000 new cases of coronary artery disease (CAD) are diagnosed yearly in the US
- Care for this 4% of the population consumes 15% of our US healthcare budget
- In 2000, we spent ~ $200 billion on CAD therapy, but only 6% of that on medical treatment and prevention *Am J Cardiol 1998:82:10T-13T
- 27% of men and 44% of women will die within 1 year after having a heart attack

How do most North Americans think to correct CVD?

- We need to shift our paradigm from interventional cardiology towards evidenced-based lifestyle interventions. Our outdated perspective is both public and medical.

WHY DO WE NEED A PARADIGM SHIFT IN TREATING CVD?

- Interventional cardiology doesn't arrest the disease process; and, for only a few does it actually prevent clinical events*
  - –Angioplasty has a 40% failure at 6 months, and prevents death in only 1 out of 30-40
  - –Stents have improved outcomes (preventing death & heart attacks) but only for 1 out of 30-40
  - –By-pass surgery only improves survival in a small subset of people with coronary heart disease* (those with bad pump function)
  - –Angioplasty, stents, and by-pass surgery are effective at treating angina (chest pain)*Am J Cardiol 1998:82:10T-13T

Large stable plaques don't cause events, they are the fire alarm that causes angina
If Plaque Rupture Causes Events, Then Treating Large Obstructions Won't Work

- Thus plaques at greatest risk of causing heart attacks and strokes aren't identified by cath and thus can't be treated by
  - –Angioplasty, Stent placement, CABG
- Studies that compare conservative therapy with cardiac procedures are equally effective

WHAT ARE THE RISKS OF CARDIAC INTERVENTIONS?

- Death and strokes are rare,1%-2%
  - Caused by plaque showering
- 42% of patients may have a 20% loss in cognitive function with CABG (NEnglJMed2001;344:395)
  - 261 subjects with elective CABG were found to have 53% cognitive decline at discharge, and 24% decline at 6 months
  - Cerebral plaque showers have been noted during cardiovascular procedures for some time. This loss is greater than expected.

WHEN WOULD YOU WANT A CVD PROCEDURE?

- If having a heart attack, get to medical attention immediately, time is important
- If you have waited until you have angina despite lifestyle changes, and you can't exercise at your 70-80% of your maximum predicted heart rate, then you LIKELY WILL WORSEN without exercise
  - Procedures are great at treating angina and restoring exercise

If cardiac interventions are great at treating angina (especially angina with pump failure) and heart attacks, but are not a highly effective way to prevent events--

THINK OF ARTERY PLAQUES DIFFERENTLY

Baby plaques

- Pus filled pimples
- Pimples can rupture and stroke or kill you

Big plaques

- Solid fortified artery obstructions
- They block flow and cause you symptoms

Large stable plaques don't cause events, they are the fire alarm that causes angina

ASSESSING THE RISK OF CARDIOVASCULAR EVENTS

- If you wait until your patient is diagnosed because of coronary flow obstruction, potentially 1/3 may be dead and 1/3 may have had a MI from plaque rupture
- Options:
  - Risk factor analyses
  - Cardiac flow assessments
  - Plaque assessments

RISK FACTORS FOR CVD

More Than 50 Factors Identified; >80% of Events Accounted for by TC, FBS, BP, BMI, Tobacco

- Lipid abnormalities: High LDL or low HDL
- High hs-CRP (stronger relationship for women)
- Lipid fractionation (LDL size, Lp(a), and HDL type)
- High homocysteine level
- Hypertension (high blood pressure)
- Diabetes and the Metabolic Syndrome
- Smokers (current)
- Inactivity
- Obesity (BMI > 30)
- Family History

The Top Five Risk Factors Still Predict >80% Events

•Cholesterol, Diabetes, Smoking, Hypertension, Obesity, Family History remains the wild card

Advanced Lipid Testing

•Testing for advanced lipid markers has not been shown to be cost effective and isn't evidenced based

•However, in special cases they are predictive of cardiac risk and change modify treatment plans

–Lp(a)

–VAP or NMR testing (LDL size, HDL typing)

–Apolipoprotein B

Lp(a)

•Lp(a) binds to proinflammatory oxidized phospholipids (Tsimikas S et al. NEJM 2005;353:46-57.)

•Lp(a) appears to be independently associated with the risk of CVD and CVD events

•Lp(a) responds fairly well to therapy with niacin (Niaspan being the best tolerated and safest form of niacin-more later)

•We lack an evidenced-based recommendation for screening for Lp(a); clinical judgment required

–E.g. not for routine medical insurance use, but consider when CVD progression exceeds normal expectation

VAP and NMR LIPID TESTING

•These lack an evidenced-based process to clarify testing and treatment

•Identify LDL size and HDL type

–Low LDL size increases CVD risk substantially

–Low HDL-2 increases CVD risk substantially and corrects for false reassurance related to "good HDL" levels

–Helpful in confirming the Metabolic Syndrome

CORONARY FLOW ASSESSMENTS

•Exercise Treadmill Testing (ETT)

–Cardiac screen and a measure of fitness

–Every increased minute in fitness on a Bruce Protocol is associated with ~ a 10% drop in future CVD event rates

–Has false negative and false positive rates, but any question of a false positive test can generally be resolved with either:

•Stress Thallium ETT

•Stress Echo

The Indications for Exercise Testing with the American Heart Association (Circulation 1997;96:345-54; being updated AHA website October 2005)

•Class I: Evidence for testing is useful and effective

•Class II: Conflicting Evidence

–IIa: Weight of evidence supports testing

–IIb: Weight of evidence is less well established

•Class III: Lack of evidence that testing is useful/effective

Class I Evidence for Stress Testing

•Evaluation of known CVD

•Evaluation of suspected angina

•Testing diabetics starting a vigorous exercise program

- Testing specific to occupation that could impact public wellbeing (a fireman)

Exercise capacity is the most powerful predictor of mortality

•Myers J, et al. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med 2002;346:793-801.

Treadmill Testing

- The best part of treadmill testing is measuring fitness
  - Fitness is the best predictor of future cardiac risk
  - Abnormal treadmill testing indicates advanced arterial blockage, at least 70% obstructed flow
- 1 Minute heart rate recovery is another excellent measure of cardiac fitness
- BP response is a great measure of artery health

VO_2 Max is the Best Measure of Fitness

Hawkins SA et al. A longitudinal assessment of change in V02max and maximal heart rate in master athletes. Med Sci Sports Exerc 2001;33:1744-50.

Somewhat expensive to measure as it requires gas measurements during stress testing

- You can multiply the met level achieved by 3.5 to give a rough estimate of VO_2Max
- Class I indication for testing only noted for CHF (assessing for heart transplant)

PLAQUE ASSESSMENTS

- Chest Computerized Tomography (Fast CT)
  - Measures hard plaque (old plaque)
- Electron Beam Tomography (EBT)
  - Measures hard plaque more effectively than fast CT, but newer CT may match EBT
- Carotid Intimal Media Thickness measurements (IMT)
  - Measures soft (new) and hard (old) plaque very well

Coronary CT Limitations

- Screening and treatment with coronary CT results is NOT evidenced-based
- Calcium score is dependent upon equipment; need a 10 to 64 slice CT scanner to properly identify artery plaque
- Limited by pulse rate (preferably less than 80 beats per minute)
- A 0 score does NOT mean no plaque
- Doesn't measure plaque rupture risk (sees old plaque, not new soft plaque)

Coronary CT Results

- A score less than 0 implies less than a 35-40% artery obstruction
  - CVD events can occur prior to a score of 1
- A score of 0-100 notes minimal plaque, but is in itself very significant
  - Indicates current or prior plaque growth
- What you want to see in someone with an abnormal score is stability over time
  - Keep the score from increasing

IMT in Clinical Practice

- Is not recognized by evidenced-based medicine
- Carotid IMT is an excellent predictor of future MI risk (Circulation 2004;109:1089-94)
- Carotid IMT useful for assessing CVD with the metabolic syndrome (J Am Coll Cardiol 2004;43:1388-95)

•Several studies have noted plaque regression with lipid therapy and Carotid IMT testing appears to be the "gold standard" in non-invasive testing for assessing plaque regression (Am J Med 2004;22:31S-36S)

The 1980's were the time of bypass surgery
The 1990's were the time of lipid reduction
The 2000's should be focusing on plaque and platelet stability

NEW THERAPY PARADIGM
"Lifestyle as Therapy to Prevent Plaque Formation
and for Plaque Stabilization"

Lifestyle Impacts:

❖LDL oxidation into plaque, Antioxidants block the conversion of LDL cholesterol into plaque

❖LDL levels, LDL normally transports antioxidants to cells, LDL size

•Size is strongly related to food and activity choices

Dietary Choices Impact Artery Function (Masley, AFP 1998)

THERAPY GOALS

1. Lower LDL
2. Reduce Total Cholesterol/HDL ratios and TG/HDL levels (Reversing the Metabolic Syndrome)
3. Add special, beneficial foods
4. Change Type of Fat Intake
5. Decrease LDL oxidation
6. Decrease clotting
7. Improve artery function and blood pressure
8. Supplement
9. Stress management
10. Succeed in making lifestyle changes

THERAPY GOAL #1:

LOWER LDL LEVELS; LDL REDUCTIONS

•Medications (They work and they decrease events for 1 out of 20 taking them)

•Increase soy and bean intake

•Encourage garlic intake

•Drastically cut saturated and hydrogenated fat intake. Foster a switch from these fats to unsaturated fats –I prefer monounsaturated fats over polyunsaturated fats

•Plant sources of n-3 fatty acids (omega-3 fats) decrease LDL levels

•Encourage monounsaturated nut intake

LOWERING LDL LEVELS ALONE IS NOT ENOUGH

•In patients with known CAD, statin medications lower death rates by 30%; yet, 70% of deaths persist in patients treated with "statin" medications

•Eliminating tobacco use, changing diet patterns, and promoting activity will further reduce CAD death rates.

•Lifestyle choices account for 70% of the total illnesses seen in the USA

THERAPY GOAL #2: Improve TC/HDL and TG/HDL Ratios; aka "Reversing the Metabolic Syndrome Epidemic"

INCREASE HDL LEVELS

- Prolonged, regular aerobic exercise helps to raise HDL levels in many patients
  - Over 30-45 minutes, 6 days per week
  - Not shown with 20-30 minutes, 3 days per week
- Moderate Alcohol Intake Raises HDL levels (1-2 drinks per day maximum)
- Garlic and Onion Intake Raises HDL levels slightly (3-5%)
- Soy intake increases HDL levels 2-3%
- Choose carbs that don't raise blood sugar or insulin levels, which decrease HDL

Type of Carbohydrate Intake Impacts Insulin levels and TC/HDL & TG/HDL Ratios Frost., The Lancet 1999;353:1045

- Choose dense, unprocessed grain and vegetable sources of carbohydrates (low-glycemic "load" carbs)
  - Leafy veggies, fruits, beans, and whole-grain such as bulgur wheat, quinoa, wild rice
- Picking "whole grains" isn't enough
  - Fluffy whole wheat breads and potatoes can raise blood sugar levels and lower TC / HDL ratios just like table sugar (glycemic load)
- Glycemic load is more important than glycemic index (You should eat carrots!)

The Metabolic Syndrome

- You don't need 3 signs to take action; 1 sign should do:
  - Waist: > 35" in women, and > 40" in men
  - TG >150
  - HDL: <50 in women, and <40 in men
  - BP >130/85
  - FBS >100
  - (Low HDL-2, high hs-CRP are also important signs)
- The Metabolic Syndrome isn't a disease; but rather, a lifestyle that doesn't match genetic make-up

The Metabolic Syndrome is Overtaking Hypercholesterolemia as the #1 Cause of CVD

To Treat the Metabolic Syndrome

- Build a beautiful frame
  - Get more active
  - Build muscle mass (The Metabolic Syndrome starts with muscle cell insulin resistance!)
  - Decrease fat mass
- Enhance your diet
  - Watch your glycemic load (refined carbs!)
  - Especially if you are overweight, inactive, and have low fiber intake
  - Avoid saturated and trans fats
  - Consider supplements (fish oil, ginseng, minerals)

Glycemic Index Vs Load

<u>Glycemic Index</u>

- Measure of blood sugar rise after a specific amount of carbohydrate (not related to a serving of food)
- Modified by fiber, protein, & fat with meal
- Density, fiber, length of cooking and swelling, plus type of carbohydrate bonding

<u>Glycemic Load</u>

- Reflection of glycemic index multiplied by the amount of carb in a serving of food
- Reflects blood sugar rise with a meal, not the lab
- Glycemic index of carrots = 47 (high), but the load is only 3 (quite low)
  - You can and should eat carrots!

Adding "Healthy" Fat Appears to Improve the TC/HDL Ratio

- Pritikin Diet and Exercise Program (<15% fat calories) lowered TC/HDL by 11%. (Barnard RJ. Arch Intern Med 1991;151:1389-94)
- Adolescents at Pritikin with 20% of calories from fat noted a 25% TC/HDL reduction (Abstract AHA Epidemiology Mtg, San Francisco, 1994)

THERAPY GOAL #3: Choose Beneficial Foods Lifestyles Determine Cardiac Risk, More than Does Cholesterol Levels

NCEP STEP I-II (The AHA Diet)

- Sets specific limits
  - –cholesterol (300mg/200mg qd),
  - –total fat intake (30% fat cal)
  - –saturated fat intake (8-10% fat cal/<7% fat cal)
  - –encourages the moderate use of polyunsaturated and monounsaturated fats
- Is an improvement over the typical American diet; however,
  - –FOLLOWING THE NCEP STEP II-III RESULTS IN PROGRESSION OF CVD
  - –Hence, it is NOT the optimal diet for CVD treatment or prevention

The Ornish Program (Diet, Exercise, Meditation)

- Program with <10% calories from fat, 1 hour exercise and 45 min meditation daily
- After 24 days, patients noted a 91% reduction in frequency of angina, LDL decreased 37%
- At one year, plaque reduction was limited -1.75%, but dietary adherence was excellent
- At 5 years, the 20% lifestyle induced LDL reduction decreased cardiac events 50% more than the 20% lipid medication induced LDL reduction (28 events in the exp. group vs 45 events in control)
- But, will people follow it? Only about 5-10% will

Is there another alternative that is equally effective and more palatable?
Mediterranean and Japanese Diets for CVD
The most effective treatment studied to date for preventing CVD events when compared with the AHA diet

- Can work without reduction in fat intake or cholesterol levels
- Relies on selecting type of fat intake and "ADDING" other beneficial foods

BALANCED DIET; BALANCED HEALTH

- "ADDING" healthful foods is the centerpiece of my program
- Limiting fat intake is only a small part of a healthy diet
- Choosing the best types of fat and carbohydrate are more important than cutting fat

My approach is to give you easy-to-make, delicious, recipes that make you feel great!
My Sweet 16 Foods to Eat Daily

• Green leafy (1-2 cups)	Lean Not Mean Protein	Seafood (2-3 serv/wk)
• Beans (½-1 cup)	Soy products (1 serv)	Whole grains (2-3 ¾-cup servings)
• Cruciferous veggies (1 cup)	Berries (1/2-1 cup daily)	Nuts (1 handful; ~1 oz)
• Flax seed, ground (1 Tbsp)	Fresh garlic (1 clove)	Herbs and Spices (1 tbsp)
• Nonfat yogurt (½-1 cup)	Green tea (1-2 cups)	Red wine (4-5 ounces)
• Cocoa (real chocolate) (1 cup)		

ADD SPECIFIC FOODS

- Garlic, Beans, Low glycemic load carbohydrates, Omega-3 rich foods
- Antioxidant-rich foods

GARLIC: Herb or Wonder Spice?

- Decreases LDL levels, 9% with a clove/day (not seen with steam distilled extract)
- Slightly increases HDL levels
- Decreases clotting (platelet aggregation)
- Lowers systolic BP, 5-6 mm Hg
- Improves immune function
- Decreases oxidation
- Kills cancer cells in the lab

GARLIC USE

- Garlic should be crushed

–Allowing alliinase (an enzyme in garlic) to convert alliin to allicin, which is the active agent

- Allicin is then converted to polysulfides which provides the aroma and plausible therapeutic benefits
- Don't overcook or deodorize
- Commercial products quantitate alliin content (which is not the active agent)

LEGUMES (Beans):
A wonder food!

- Lower LDL levels *
- Raise HDL levels
- Control blood sugar and insulin levels
- Suppress appetite
- Associated with decreased cancer risk (especially soy products)

SOY PRODUCTS

- Soy protein

–lowers total cholesterol and LDL cholesterol with a small increase in HDL cholesterol

- Soy isoflavones (genistein, etc.)

–improve endothelial function

–decrease clot formation

–are associated with reduced cancer risk, especially breast and prostate cancer

CHOCOLATE AND COCOA

<u>CHOCOLATE</u>

- Hi source of calories
- Make sure it has cocoa butter, not palm oil, milk, or butter
- Rich source of magnesium, stress-relieving compounds
- Biochemically cocoa butter acts more like olive oil than butter

<u>COCOA</u>

- Usually non-fat, low calorie

- Rich source of magnesium, and stress relieving compounds
- Decreases clotting (Am J Clin Nutr 2000;72:30-5)
- Potent anti-oxidant (anti-aging) agent
- Suppress LDL oxidation, lowering plaque formation

THERAPY GOAL #4; CHANGE TYPE OF FAT INTAKE FATS
Rule #1: *"The type of fat we choose is more important than how much fat we eat"*
Rule #2: *"Moderate even healthy fats if you need to control your weight"*

FAT CALORIE SOURCES

- Nuts (walnuts, hazelnuts, almonds, pecans)
  - 2 tsp has ~30 calories and 0.2 grams of saturated fat
  - 1/3 cup (1 hand-full) has 280 calories and ~2.0 grams of saturated fat (Good satiety)
  - 4 handfuls of nuts has > 1,000 calories
- Extra Virgin Olive Oil
  - 1/6 tsp (1 second spray) has 5 calories with 0.1 grams of saturated fat
  - ½ tsp has 19 calories with 0.3 grams of saturated fat
  - 2 Tbsp has 228 calories with 3.6 grams saturated fat
- 200 extra calories per day could cause a 20-pound weight gain over one year

CLINICAL STUDIES SUPPORT HEALTHY FAT INTAKE:

- <u>Olive and Canola Oil in Moderation:</u> (20-30% calories)
- Decrease LDL oxidation
- Improve Total Cholesterol / HDL lipid levels
- Improve cardiac outcomes compared to the AHA diet
- <u>Nut Intake:</u>
- Associated with decreased cardio-vascular mortality and morbidity
- Improves Total Cholesterol / HDL lipid levels

CANOLA OIL

- Use of canola oil is NOT without controversies, and it may not be equal to olive oil in the long run
  - But face it, it is hard to bake a cake or make cookies with olive oil
- Choose organic, expeller-pressed products
- Observational studies that look at how canola oil is used in the restaurant industry could show it to be harmful
- Randomized studies show lower mortality and heart attack rates with selected canola oil use

<u>Saturated Fats:</u> (animal meats, fatty dairy products, and some oils)

- Increase blood clot formation
- Increase bad LDL cholesterol levels
- Promote weight gain
- Increase insulin levels (more so than some carbohydrates)

Trans Fats Are Worse Than Saturated Fats <u>TRANS FATS</u> or <u>Hydrogenated Fats</u> (Margarines and processed foods)

- Make your intracellular fats stiff

- Act like saturated fats
  - Raise LDL levels
  - Lower HDL levels
- Their intake is associated with increased cancer rates, especially breast cancer
- They are hidden in the food supply, and their intake in Americans is rising rapidly

The Bottom Line: Chose Lean Rather Than Mean Protein

- Look for protein sources that are low in saturated fat
  - Seafood
  - Nonfat Dairy (in contrast to "high fat" 2% dairy products with 35% of their calories from fat
  - Chicken and Turkey breast are excellent choices

THERAPY GOAL #5: REDUCE LDL OXIDATION OXIDATION IMPACTS CAD IN SEVERAL WAYS

- LDL is oxidized into plaque
- Oxidation fosters vasoconstriction and poor artery function
- Clot formation increases during oxidative stress

REDUCE LDL OXIDATION

- **Add** fruits and vegetables
  - Five-a-day is the minimum
  - 5 cups daily is better
- Add garlic and spices daily
- Choose healthy fats when you eat fat
- Vitamin E and D intake reduces LDL oxidation
- If you drink alcohol, choose red wine, 1serving/day
  - The type of alcohol intake has not been shown to decrease event rates, but does decrease oxidation

LIFESTYLE INTERVENTIONS HAVE BEEN SHOWN TO DECREASE LDL OXIDATION

- 21% Reduction in LDL oxidation with the Pritikin Program over three weeks

Plant Pigments Have Greater Antioxidant Activity than Vitamin E

FOODS THAT BLOCK LDL OXIDATION

- Red and black beans, Blueberries, Pomegranates, Green leafy veggies, Most colorful produce

THERAPY GOAL #6; DECREASE CLOTING AND EVENTS DECREASE CLOT FORMATION

- Avoid saturated and trans fat
- Garlic and mild alcohol intake decreases clot formation (High alcohol intake increases your risk of a hemorrhagic stoke)
- Vitamin E decreases clot formation
- Omega-3 fats decrease clot formation

- IF YOU ARE AT ELEVATED RISK FOR CAD OR STROKE, TAKE AN ASPIRIN DAILY ! *(Unless you take coumadin)*

OMEGA-3 FATS (N-3 FATTY ACIDS)

- Sources include many nuts, seafood, flax seed, canola oil, green leafy veggies
- Only long-chain n-3 fatty acids decrease clotting
  - Fish oil used in Europe to treat rheumatoid arthritis and inflammatory bowel disease
  - NFL orthopedic surgeons now use fish oil to treat herniated disc disease

SOURCES OF OMEGA-3 FATS

LONG CHAIN

- Seafood (fish oil)

MEDIUM CHAIN

- Flax (Ground flax seed better than oil), Soy products, Nuts, Green leafy veggies, Canola oil (organic, expeller-pressed)

Increase Omega-3 fat Intake

- Increasing omega-3 fat intake is more important than cutting saturated fat intake Ascherio, BMJ 1996;313:84
- The Mediterranean Diet Study and DART showed lower death rates with greater omega-3 fat intake
- The Italian, GISSI-Prevenzione Trial showed that with known CAD, omega-3 fat intake appears more important than Vitamin E intake Lancet 1999;354:471

SEAFOOD

- Seafood includes fish, shellfish, and seaweed products
- Provides a rich source of omega-3 fats which decrease inflammation, clot formation, and are associated with decreased rates of sudden death

PEOPLE WITH KNOWN CVD BENEFIT BY EATING "SEAFOOD" 1-2 TIMES/WK

Seafood intake:

- **is associated with decreased sudden death, arrhythmic events, and MI's.**
- **decreases platelet aggregation**
- raises LDL levels (garlic can offset LDL rise)
- increases LDL oxidation (Vitamin E can offset this)
- contains mercury

Balancing High Omega-3 Sources with Low Mercury Content

- BEST CATCH (Cold water small mouth fish, and omega-3 filter feeders from "pristine waters")
  - Salmon, trout, sardines, muscles, oysters
- GOOD CATCH (lower fat fish with smaller mouths)
  - Other shellfish such as shrimp, crab, and clams, sole, cod, small mahi mahi, halibut (mercury < 2ppm)
- OCCASIONAL CATCH (large mouth fish) Limit to 1-2 servings/month; (mercury > 2ppm)
  - Blue-fin tuna, grouper, snapper, bass
- THROW IT BACK (huge mouth fish)
  - Swordfish, King fish, Shark

Fish Oil Supplements; Should everyone take one???

Lower triglycerides, Decrease inflammation, Enhance brain function (↓ depression risk and ↑ memory), Improve insulin sensitivity, Decrease arrhythmias, Although less of an evidenced-based indication, also used for macular degeneration and depression

Omega-3 Fat Dosing

- For routine health, aim for 1 gram daily in a supplement (~300 mg of both EPA and DHA)
  - Or, eat 2-3 servings of cold water fatty fish weekly (avoiding large-mouth high mercury choices)

- For high triglycerides: 2-4 grams daily
- For inflammatory problems: 2-4 grams daily
- For disc herniations: 2-4 grams daily
- For arrhythmias: 1-2 grams daily
- Associated with lower Alzheimer's risk: 1-2 grams daily

Choosing Fish Oil Supplements

- Mercury and heavy metal free

–Should be distilled or independently testing for heavy metals (usually not an issue)

- Use anti-coagulant caution >2 gram/day
- Lipid peroxides should be low

–It shouldn't taste or smell highly fishy

–Nordic Naturals have been 3rd party tested to have the lowest levels of lipid peroxides

Food Versus Supplements

- 2-3 servings of cold water fish servings equals about 1 gram per day of omega-3 fats
- Daily supplements can be used for non-fish eating people

THERAPY GOAL #7; Enhance Endothelial Function and Improve Your Blood Pressure

- Exercise tunes your endothelium
- Ace-inhibitors (and maybe Angiotension Receptor Blockers) improve arterial function

–Ace-inhibitors include lisinopril, accupril, monopril, -pril etc.
–The benefits are worth tolerating a mild cough

- Dietary and vitamin sources of antioxidants and potassium improve arterial function

–garlic, fruits and veggies, soy products, Vitamin E

- **Avoid unhealthy fats and passive tobacco use**

EXERCISE TUNES YOUR ARTERIES

- Exercise tunes not only your muscles, but also the muscular lining of your arteries
- Regular exercise teaches your arteries to dilate when stressed

EXERCISE--THE FAST TRACK TO SUCCESS

- Aerobic exercise

–45-60 minutes of moderate activity, and 6 days per week

- Burning at least 2,000 calories per week
- Increases energy, efficiency, and metabolism
- Required for long-term weight control and to prevent weight regain

STRENGTH TRAINING
(Resistance Exercise)

- Strength train 2-3 times per week, working at least 8-12 body parts

–Increases bone strength and protects joints from arthritis

–Increases your capacity to burn calories during exercise; hence, increases baseline metabolism and improves weight control

–Muscle mass stores a large reserve of amino acids and produces glutamine, which regenerates your antioxidant system

IT IS NEVER TO LATE TO BE MORE FIT

- Inactive people can reverse the aging process
- Seniors over age 63 can increase aerobic power and conditioning with regular exercise

- 80 year olds can still build muscle mass

ENCOURAGE REGULAR ACTIVITY

- A regular (daily) walking program is associated with 40% fewer cardiac events
- The greatest benefit is shifting from sedentary to regular moderate activity (20 minutes 3 times per week)
- Next benefit comes from reaching moderate activity for 30-60 minutes, 5-6 days per week

Blood Pressure Targets

- Optimal is ~ 110/70
- Acceptable is < 120/80
- > 120/80 is pre-hypertensive and a sign of sick arteries

BLOOD PRESSURE THERAPY

- Eat more fruits and vegetables
- Limit salt
- Reverse the metabolic syndrome
- Stress management
- Regular exercise to "tune" your arteries

THERAPY GOAL #8; SUPPLEMENT

NUTRIENT SUPPLEMENTS

- **Supplements are SUPPLEMENTAL to a healthy diet!**
- Study after study shows that nutrient rich foods are superior to supplements
- Folic acid, B-vitamins, and mineral intake is critical; most Americans need to take a One-A-Day supplements with folic acid, selenium, calcium/magnesium & minerals!

First Do No Harm

Quality Issues

- **USP** (Labs assessed and samples in stores tested for active agents and contaminants)
- **GMP** (Good Manufacturing Practices--Lab)
- **Pharmaceutical laboratory production**
- **A**re they approved in the **European Community** (they have higher drug company level standards)
- **Consumerlab.com**

– Independent testing for dosing and contaminants

- **Brands** worth considering include Pfeizer, Merck, Metagenics, and ProThera

Quality Concerns Regarding Supplemental Vitamins

- Most vitamins are made by one pharmaceutical company

– Hence, Vit D, A, C, etc are good quality and exact dosing

MINERALS

- Dosing is usually very precise
- Contaminants do occur, especially with calcium

- Excess mineral dosing can be toxic!!!

HERB QUALITY CONCERNS

- Quality issues occur more often with herbs than with vitamins
  - Contaminants (heavy metals) occur rarely
  - Inadequate active agents occurs more often
- There is no guaranteed way to avoid these problems; yet
  - Brands produced by major pharmaceutical companies are likely better
  - Independent quality controls done by ConsumerLab (www.consumerlab.com)
- $5 / topic search,or $15.95/12 months of access
  - Doses should be listed in mg or grams

HERB EFFICACY DEPENDS UPON:

- Quality of herbal product
- What part of plant used: whole plant, leaves, roots, vs flowers: (e.g., echinacea)
- Plant maturity (e.g., ginseng)
- Shelf life
- Deodorized (garlic, St John's Wort)

Customize who receives Vitamin E (alpha-tocopherol) for CVD

- Alpha-tocopherol lowers HDL_2 levels
- Associated with elevated risk of plaque formation and CVD events in subjects with low HDL taking a statin-med + niacin
- Vitamin E in natural (mixed tocopherol) form might be warranted for Alzheimer's, macular degeneration, immune augmentation post cancer therapy, fibrocystic breast pain

GET YOUR FOLIC ACID!

- Folic acid is a B vitamin
- Folic acid usually lowers homocysteine
- Homocysteine is toxic to your arteries and brain cells
- High doses of folic acid are inexpensive and very safe
- Most multi-vitamins contain 400 mcg

REDUCE HOMOCYSTEINE

- I recommend at least 400-800 mcg of folic acid for everyone (diet plus multi-vitamin)
- You also need B_6 (10-25mg) and B_{12} (10-1000 mcg)

Policosanol

- Bee wax or sugar cane product that blocks cholesterol absorption (Efficacy is questionable
- May lower LDL and TC by 10-15%
- No change in HDL
- No worrisome side effects seen in studies to date, but not clearly effective

Phyto-Sterols (i.e. Smart Balance®)

- Commonly seen as food additives (spreads)
- Lowers LDL cholesterol by 10-15%
- Endorsed by the American Heart Association

- Lowers carotenoid blood levels (concerning)
- No data available regarding long-term outcome studies
- Better to get them from food than from margarines to maintain carotenoid levels (Jenkins et al)

CoEnzyme-Q-10

- We don't have an evidenced based cardiac indication for Co-Q-10
- A dosage of 100 mg daily will lower blood pressure similar to other HTN medications
- Theoretical indications are fascinating !

CO-ENZYME Q-10

- The membranes within your mitochondria create a HUGE energy field, nearly 3 football fields in size
- Oxidative stress impacts the function of your mitochondria

Many Supplements Appear To Enhance Mitochondrial Function

- Co-Q-10, Alpha Lipoic Acid, N-Acetyl-L-Cysteine, Acetyl-L-Carnitine, Resveratrol

CO-ENZYME Q-10 Needed for Statin Therapy?

- Co-enzyme Q-10 is recommended for theoretical reasons; e.g. if you are taking a statin (cholesterol lowering) medication

–Co-enzyme Q-10 works as an electron transporter in your cells and also acts as a potent anti-oxidant, removing aging exhaust after energy production

–Statin meds lower co-enzyme Q-10 levels about 20%

–Taking 100 mg of Q-10 daily restores normal levels, but we have no evidence from clinical trials that you benefit from Co-Q-10 yet

- It is expensive!

CoEnzyme-Q-10 (The evidence)

- Improves symptoms of people with CHF but no objective measures of improved cardiac function (echo treadmill testing) have been shown
- Modestly increases INR; caution with warfarin (Coumadin)
- Does lower BP significantly, ~10 mm reduction with 100+ mg daily (cost is about $35/month)

Hawthorn

- Lowers blood pressure, modest benefit (5mm reduction)
- Commonly used in many products
- Not clearly defined

Calcium-Magnesium Intake

- Calcium intake is helpful for overall health
- Calcium supplements can worsen magnesium deficiency, which is common in the US
- Magnesium deficiency is associated with CVD events
- Aim for a 2:1 or 3:1 calcium-magnesium ratio in supplements

Magnesium Supplements

- Magnesium oxide is the most common but often causes GI distress
- Goal should be for 400-500 mg daily (common in nuts, greens, and legumes)

•I prefer magnesium citrate, glycinate, or other chelated forms of magnesium for tolerability (Calcium alone also causes constipation)

•Aim for a 2:1 or 3:1 calcium-magnesium ratio with calcium supplementation

Therapy Goal #9; Stress Management

•Excess cortisol production worsens lipid profiles and glucose regulation

•While Type A personalities likely don't predict CVD; Hostility and Depression are strongly related to CVD events

•Meditation is effective in decreasing future CVD events. Any form of stress reduction should be helpful

•If you don't manage your stress, diet and exercise compliance fall rapidly

THERAPY GOAL #10; SUCCEED IN MAKING LIFESTYLE CHANGES
ENHANCE YOUR SUCCESS AT CHANGING LIFESTYLES

•Involve partners and family members

•Add "Group Visits" to your clinical practice

•ADD FOODS to your menu plans!

•ADD MENTAL WELLNESS

•ADD ACTIVITY to your life

–walk, bicycle, dance, swim

Getting Paid More for Better Outcomes; Welcome to Group Visits for Dyslipidemia
Cardiovascular Disease Targets
•Reach and follow lipid, blood pressure, and Glycemic targets
•Improve diet and activity levels
•Add anti-coagulation
•Improve endothelial function
•Encourage tobacco cessation
•Address new angina or new CHF

How Much Time Do You Need To Provide a Group Visit?
(one tested example used commonly in large clinics)
Allow 4 hours total time for a group visit with 20-30 patients/session. This allows:

•1 hour to prepare materials

•1 hour for chart reviews prior to visit

•1/2 hour for 2-3 nurses to collect data, and for the provider to document specific plans

•1 hour to share information with the group

•1/2 hour for wrap-up (planning for the next group visit session, and seeing a rare individual patient--i.e. a pt for an earache)

How Do I Organize My Time During the 2-Hour Group Visit Session?

•30 minutes to collect patient data, meet individually, and write notes

•15 minutes for the group to address their concerns to me and each other

•45 minutes to introduce didactic material and information

•30 minutes to answer questions and plan for the next group visit together, and on occasion, to see a couple patients alone for brief evaluations

•Actual physician time can vary

You Can Vary The Time

- Choose a group visit size that reflects your style, patient population, and group visit room *(conference center with electronics versus patient waiting room)*
- You could see 10 patients during a 1 hour group visit session

– Allow two hours to chart review, prepare materials, and complete the appointment

Chart Review

- Addresses key targets for the specific diagnosis
- If you have a registry of your high risk cohort patients, this is very easy
- If your charts lack cohort specific targets, the first review can be lengthy, but critically important
- Once a template is built for the chart review, a nurse/MA can add the data for the physicians review

Registration

- First visit, during registration forms must be signed *(we strongly recommend confidentiality and HIPAA forms)*, patients should be registered and fees collected
- Thereafter, register, collect co-payment or normal appointment fee, and begin data collection

Agreement to Participate

- I agree to meet with a group of patients and my doctor. I have the choice to be seen by my physician in this group, or individually.
- Like any doctor's appointment, I agree to be responsible for the bill or co-payment associated with this doctor's visit.

Confidentiality Form

- I agree to keep all information regarding other patients at these visits private, and agree not to disclose any information regarding other patients in these group visits.
- Respect each others' privacy - ok to discuss what you have learned in these sessions, <u>but don't mention anyone's names outside this group</u>!

HIPAA

- Receptionist should mention this when they register for the appoint

– See handout

- Signed HIPAA Disclosure Form Essential !!!

– During a Group Medical Appointment, it is possible that some of my personal health information will be disclosed. For example, at a Group Visit for Diabetes, it might be assumed that everyone attending has diabetes. Discussions may occur regarding personal health information during a group visit. I have been notified of this potential disclosure and I wish to participate in a group medical visit. I realize that I have the option of being seen individually.

– Share with your HIPAA compliance officer to confirm clinic consistency

Patient Role

- Arrive on time, Register, Find a chair and complete subjective aspect of the SOAP note, Then meet with the nurse, Next meet with the doctor, Return to chair

Nurse Exam Stations (2-3)

- Maximum 3-4 minutes/ pt (sees 10 pts/30 min)
- Medical Record (EMR or paper)
- New progress note completed. MD has already made comments from chart review
- Scale, BP cuff, monofilament for foot exam, peak flow meter, etc, etc

- Subjective and Objective part of the note completed at this station
- Physician will complete the note and sign the progress note

MD Role (Station Optional)

- Not more than 45-90 seconds 1-on-1 per person

–Signed HIPAA disclosure essential; comments may be overheard

- Clarify assessment with the patient, face-to-face
- Get permission to share questions and answers with the group

–Might include starting a new medication and the risks, benefits with that Rx

–Put issues to address on the clip board

- Can be done to the side of the room, or at the center table

–Moving to another room could be limited to 1-2 patients maximum after the visit is completed

Sample CVD Progress Note

- HPI: Subjective

Any <u>new</u> angina. Any <u>new</u> signs CHF (SOB, edema, wt increase?)
ROS: Recent Activity Level

–no activity/ moderate 2-3 times / wk/ **moderate 4-6 times / wk *** vigorous <4 times / wk vigorous 4 or more x / wk

Produce serving intake

–less than 2 cups daily

–2-3 cups daily

–**4 or more cups daily**

Past Med Hx: (See chart) Meds: (See med chart) Tobacco Use:

- Objective

–Wt, BP, Recent lipid profile, FBS or HbgA1C

- Assessment

–CAD; At target? Yes/No

- Plan

–Treat and follow lipids, ASA daily (or other Rx), Encourage activity and healthy diet, Review med options: risks, benefits, effects, Mange HTN & glycemia

Billing for a CVD Group Visit

- **<u>99213,</u>** with 4 parts to the history, a brief exam, and decision making regarding a complex problem, with a stable patient and no therapy changes for a diagnosis of CAD
- **<u>99214,</u>** with 4 parts to the history, 2 past med parts, and 2 ROS parts, a brief exam, and a CAD patient requiring a change in therapy with documentation of a risk benefit discussion related to that therapy change

Treatment Summary
Choosing an evidenced based cardio-protective lifestyle means

–<u>ADDING</u> more antioxidant-rich foods, especially colorful fruits and veggies, legumes (soy), garlic, and spices <u>daily</u>

–<u>MODERATING</u> FAT INTAKE

–<u>CHOOSING</u> healthy fats!

–<u>ENSURING</u> adequate B vitamins and omega-3 fat intake

–<u>ADDING</u> a regular exercise (activity) program

–<u>ADDING</u> mental wellness

Cases

Case #1: 45-Year-Old Male, In Your Office For A Physical Exam

- Lipid profile
  - TC= 220, LDL= 150, HDL= 35, TG= 175
- Blood pressure = 135/85
- FBS = 105; BMI = 30; waist = 41 inches
- Activity: works out 20 min 2-3 x per week
- Diet: Lots refined carbs, saturated fat, and hydrogenated fat

What Else Do You Want to Know?

- Diagnosis
  - Metabolic syndrome, Elevated blood pressure
- Limitations to exercise?
- Treadmill testing?
- Omega-3 intake, CRP, Homocysteine?
- Plaque testing?

Treatment Plan?

- Activity/Diet Change/Supplements/Medications/Further Testing

Case #2: 55-Year-Old Female, In Your Office For A Physical Exam

- Lipid profile
  - TC = 260, LDL = 180, HDL = 55, TG = 125
- BMI = 28 Waist = 33 inches
- Blood pressure 128/78
- FBS = 95
- Activity: Active 30 minutes 3-4 x per week
- Diet: Low saturated fat, high fiber

What Else Do You Want to Know? (55 yr-old woman)

- Diagnosis
  - Hypercholesterolemia (Lipid goals ???)
- Willingness to change?
- Treadmill testing?
- Omega-3 intake, Homocysteine level, CRP assessment
- Plaque testing?

Treatment Plan?

- Activity/Diet Change/Supplements/Medications/Further Testing

Case #3: 75-Year-Old Female, In Your Office for Shortness of Breath with Exercise

- Lipid profile
  - TC= 242, LDL= 160, HDL=50, TG= 160
  - Intolerant of statin/fibrate medications (muscle aches)
- BMI = 28 Waist = 37 inches

- Blood pressure = 140/90
- FBS = 105
- Activity: walks, no strength training
- Diet: AHA diet

What Else Do You Want to Know? (75 yr-old woman)

- Diagnosis
  - Hypercholesterolemia, HTN, ? Angina
  - (Lipid goals and BP therapy goals ???)
- Treadmill testing? What kind? What to do with the results?
- Willingness to change? (med intolerant !)
  - What can she achieve with lifestyle?
- Omega-3 intake, Homocysteine level, CRP, Plaque testing?

Treatment Plan?

- Activity/Diet Change/Supplements/Policosanol, Red Yeast Rice Extract?, Phytosterols, Nuts, Fiber at > 30 grams daily/Medications (Could try Niacin)/Further Testing

Case #4: 75-Year-Old Male in Your Office for HTN

- Lipid profile
  - TC = 170, LDL = 110, HDL = 30, TG = 150
- BMI = 26
- Blood pressure 150/100
- FBS = 100
- Activity: walks 20 min 7 days per week, no strength training
- Diet: Ultra-low fat saturated fat

What Else Do You Want to Know? (75 yr-old man)

- Diagnosis
  - Hypercholesterolemia, Metabolic Syndrome
  - (Lipid goals and BP therapy goals ???)
- Willingness to change?
- Treadmill testing? What kind?
- Omega-3 intake, CRP, Homocysteine level
- Plaque testing?

Treatment Plan?

- Activity/ Diet Change/ Supplements/ Medications/ Further Testing

References

ALCOHOL

- Berger K, et al. Light to moderate alcohol consumption and the risk of stroke among US male physicians. N Engl J Med 1999;341:1557-64.
- Cho E, et al. Alcohol intake and colorectal cancer. Ann Intern Med 2004;140:603-13.
- Fuhrman B, et al. Consumption of red wine with meals reduces the susceptibility of human plasma and low-density lipoprotein to lipid perioxidation. Am J Clin Nutr 1995;61:549-54.
- Gronbaek M, et al. Type of alcohol consumed and mortality from all causes, coronary heart disease, and cancer. Ann Intern Med 2000;133:411-419.
- Klatsky AL et al. Alcohol and mortality. Ann Intern Med. 1992;117:646-54.
- Levitan EB, et al. Association between consumption of beer, wine, and liquor and plasma concentration of high sensitivity-C-reactive protein in women aged 39-89 years. Am J Cardiol 2005;96:83-88.
- Meyer KA, et al. Alcohol consumption patterns and HbA1c, C-peptide, and insulin concentrations in men. J Am Coll Nutr 2003;22:185-94.
- Renaud S, DeLorgeril M. Wine, alcohol, platelets, and the French paradox for coronary heart disease. The Lancet;1992;339.1523-26.
- Reynolds K, et al. Alcohol consumption and risk of stroke. JAMA 2003;289:579-88.
- Saitz R. Unhealthy Alcohol Use. New England Journal Medicine 2005;352:596-07.
- Solomon CG, et al. Moderate alcohol consumption and risk of coronary heart disease among women with type 2 diabetes mellitus. Circulation 2000;102:494-9.
- Thun MJ, et al. Alcohol consumption and mortality among middle-aged and elderly US adults. 1997;337:1705-14.
- Parisi AF et al. A comparison of angioplasty with medical therapy in the treatment of single-vessel coronary artery disease. N Engl J Med 1992;326:10-16.

Interventional Procedures versus Conservative Therapy

- Pitt B et al. Aggressive lipid-lowering therapy compared with angioplasty in stable coronary artery disease. N Engl J Med 1999;341:70-76
- RITA-2 trial participants. Lancet 1997;350:461-68.
- Myers J, et al. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med 2002;346:793-801.

CARDIOVASCULAR DISEASE

- Barnard et al. Circulation 2002 ;106 :2530-32
- Boden WE et al. Outcomes in patients with acute non-Q-wave myocardial infarction randomly assigned to an invasive as compared with conservative management strategy. N Engl J Med 1998;338:1785-92.
- Falk E. Why do plaques rupture? Circulation 1992;86:30-42.
- Forrester JS. Role of plaque rupture in acute coronary syndromes. Am J Cardiol 2000;86:15-23
- Fuentes F et al. Mediterranean and low-fat diets improve endothelial function in hypercholesterolemic men. Ann Intern Med 2001;134:1115-19.
- Fujii K et al. Intravascular ultrasound assessment of ulcerated ruptured plaques. Circulation 2003;108:2473-78.
- Hu FB, Willett WC. Optimal diets for prevention of coronary heart disease. JAMA 2002;288:2569-2578. (Editorial response to authors by: Masley SC, et al. JAMA 2002:289.)
- Jenkins DJ et al. JAMA 2003
- Joshipura KJ et al. The effect of fruit and vegetable intake on risk for coronary heart disease. Ann Intern Med. 2001;134:1106-1114.
- Lopez-Miranda J et al. J Lipid Res 1994;35:1965-75.
- Masley SC. Dietary Therapy for Preventing and Treating Coronary Artery Disease. American Family Physician 1998;57:1299-1301.
- Masley SC. Group office visits change dietary habits of patients with coronary artery disease. JFP 2001;50.
- Morgan SA et al. A low-fat diet supplemented with monounsaturated fat results in less HDL-C lowering than a very-low-fat diet. J Am Diet Assoc 1997;97:151-156.
- Ordovas JM; Biochem Soc Trans 2001;30:68-73
- Ridker PM et al. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Eng J Med 2000;342:836-43.
- Rimm EB et al. Alcohol in the Mediterranean diet. Am J Clin Nutr 1995;61:1378S-82S
- Shephard RJ et al. Exercise as cardiovascular therapy. Circulation. 1999;99;963-72.
- Spiller GA et al. Effects of plant-based diets high in almonds on serum lipoproteins in humans. American College Nutrition 2003;22:195-200.
- Thun MJ et al. Alcohol consumption and mortality among middle-aged and elderly US adults. N Eng J Med 1997;337:1705-14.
- Vélez-Carrasco W et al. Dietary restriction of saturated fat and cholesterol decrease HDL ApoA-1 Secretion. Arterioscler Thromb Vascu Biol. 1999;19:918-24.
- Wan Y et al. Effects of cocoa powder and dark chocolate on LDL oxidative susceptibility and prostaglandin concentrations in humans. Am J Clin Nutr 2001;74596-602.
- Trappe SW et al. Aging among elite distance runners : a 22-year longitudinal study. J. Appl. Physiol. 1996;314:605-13.
- LaCroix AZ et al. Does walking decrease the risk of cardiovascular disease hospitalizations and death in older adults? JAGS 1996;44:113-20.
- Manson JE et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. N Eng J Med 1999;341:650-8.
- Wessel TR et al. Relationship of physical fitness versus body mass index with coronary artery disease and cardiovascular events in women. JAMA 2004;292:1179-87.
- Williams RB. Psychosocial risk factors for cardiovascular disease: More than one culprit at work.. JAMA 2003;290:1190-92.
- Willett WC, et al. Coffee consumption and coronary heart disease in women. JAMA 1996;275:458-62.

•Kris-Etherton PM, et al. High-monounsaturated fatty acid diets lower both plasma cholesterol and triacylglycerol concentrations. Am J Clin Nutr 1999;70:1009-15.
•Kris-Etherton PM, et al. Trans fatty acids and coronary heart disease risk. Am J Clin Nutr 1995;62 S
•Larsen LF et al. Are olive oil diets antithrombotic? Diets enriched with olive, rapeseed, or sunflower oil affect postprandial factor Vii differently. Am J Clin Nutr 1999;70:976-82.
•Lopez-Garcia E, et al. Consumption trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. J Nutr 2005;135:662-6.
•Renaud S, et al. Cretan Mediterranean diet for prevention of coronary heart disease. Am J Clin Nutr 1995;61:1360S-7.
•Yaqoob P, et al. Effect of olive oil on immune function in meddle-aged men. Am J Clin Nutr 1998;67:129-35.

FIBER

•Anderson JW. Whole grains and coronary heart disease: the whole kernel of truth. Am J Clin Nutr 2004;80:1459-60.
•Anderson JW, et al. Cholesterol-lowering effects of psyllium intake adjunctive to diet therapy in men and women with hypercholesterolemia. Am J Clin Nutr 2000;71:472-9.
•Chandalia M, et al. Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. N Eng J Med 2000;342:1392.
•Jenkins DJ et al. Viscous and nonviscous fibres, nonabsorbable and low glycaemic index carbohydrates, blood lipids and coronary heart disease. Curr Opin Lipidol 2000;11:49-56
•Joshipura KJ, et al. Fruit and vegetable intake in relation to risk of ischemic stroke. JAMA 1999;282:1233-1239.
•Joshipura KJ, et al. The effect of fruit and vegetable intake on risk for coronary heart disease. Ann Intern Med 2001;134:1106-14.
•Liu S, et al. Whole grain consumption and risk of ischemic stroke in women. JAMA 2000;284;1534-40.
•Meyer KA, et al. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. Am J Clin Nutr 2000;71:921-30.
•Mozaffarian D, et al. Cereal, fruit, and vegetable fiber intake and the risk of cardiovascular disease in elderly individuals. JAMA 2003;289:1659-1666.
•Salmeron J, et al. Dietary fiber, Glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. JAMA 1997;277:472-77.
•Vuksan V et al. Konjac-mannan improves glycemia and associated risk factors for coronary heart disease in type 2 diabetes. Diabetes Care 1999;22:913-919.
•Vuksan V et al. Beneficial effects of viscous dietary fiber from Konjac-mannan in subjects with the insulin resistance syndrome: results of a controlled metabolic trial. Diabetes Care. 2000;23:9-14.
•Vuksan V et al. Konjac-mannan and American ginseng: emerging alternative therapies for type 2 diabetes mellitus. J Am Coll Nutr 2001;20(5):370S-383S.
•Wu H, et al. Dietary fiber and progression of atherosclerosis: the Los Angeles Atherosclerosis Study. Am J Clin Nutr 2003;78:1085-91.
•GARLIC
•Berthold HK, et al. Effect of a garlic oil preparation on serum lipoproteins and cholesterol metabolism (Deodorized Garlic) JAMA 1998;279:1900-02.
•Srivastava KC, et al. Effects of a garlic-derived principle on aggregation and arachidonic acid metabolism in human blood platelets. Prostaglandins, Leukotrienes and Essential Fatty Acids 1993;49:587-595.
•Steiner M, et al. A double-blind crossover study in moderately hypercholesterolemic men that compared the effect of aged garlic extract and placebo administration on blood lipids. Am J Clin Nutr 1996;64:866-70.
•GLYCEMIC LOAD (GLYCEMIC INDEX)
•Brand-Miller J et al. The New Glucose Revolution. Marlowe & Company, New York. 2003
•Frost. The Lancet 1999;353:1045
•Salmeron J et al. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes in women. JAMA 1997;277:472-77.

CHOCOLATE AND COCOA

•Denke, MA. Effects of cocoa butter on serum lipids in humans. Am J Clin Nutr 1994;60(suppl):1014S-6S.
•Fraga CG. Cocoa, diabetes, and hypertension: should we eat more chocolate? Am J Clin Nutr 2005;81:541-2.
•Grassi D et al. Short term administration of dark chocolate is followed by a significant increase in insulin sensitivity and a decrease in blood pressure in healthy persons. Am J Clin Nutr 2005;81:611-4.
•Hu FB, et al. Dietary saturated fats and their food sources in relation to the risk of coronary heart disease in women. Am J Clin Nutr 1999;70:1001-8.
•Rein D et al. Cocoa inhibits platelet activation and function. Am J Clin Nutr 2000;72:30-5.
•Sarafini M et al. Plasma antioxidants from chocolate. Nature 2003;424:28.
•Wan Y, et al. Effects of cocoa powder and dark chocolate on LDL oxidative susceptibility and prostaglandin concentrations in humans. Am J Clin Nutr 2001;74:596-02.

CHOLESTEROL AND LIPIDS

•Barnard RJ. Effects of Life-style Modification on Serum Lipids. Arch Intern Med 1991;151:1389-94.
•Frost. (Type of Glycemic Intake Impacts HDL levels) The Lancet 1999;353:1045
•Most MM, et al. Rice bran oil, not fiber, lowers cholesterol in humans. Am J Clin Nutr 2005;81:64-8.
•Shai I et al. Multivariate Assessment of lipid parameters as predictors of coronary heart disease among postmenopausal women. Circulation 2004;110:2824-2830.
•Visich PS, et al. Effects of exercise with varying energy expenditure on HDL cholesterol. Eur J Appl Physiol 1996;72:242-8.
•Williams PT. HDL cholesterol and other risk factors for coronary heart disease in female runners. N Engl J Med 1996;334:1298-303.

ENDOTHELIAL FUNCTION (BLOOD VESSEL FUNCTION)

•Fuentes F, et al. Mediterranean and low-fat diets improve endothelial function in hypercholesterolemic men. Ann Intern Med 2001;134:1115-1119.

•Hambrecht R et al. Effect of exercise on coronary endothelial function in patients with coronary artery disease. N Engl J Med 2000;342:454-60.
•Tomaino RM et al. High-fat meals and endothelial function. Nutrition Reviews 1998;56:182-85.
•Ziccardi P, et al. Reduction of inflammatory cytokine concentrations and improvement of endothelial functions in obese women after weight loss over one year. Circulation 2002;105:804-09.
•FATS (DIETARY)
•Abbasi F, et al. High carbohydrate diets, triglyceride-rich lipoproteins, and coronary heart disease risk. Am J Cardiol 2000;85:45-8.
•Byers T. Hardened fats, hardened arteries? N Engl J Med; 1997;337:1544-45.
•Hu FB, et al. Dietary fat intake and the risk of coronary heart disease in women. N Engl J Med 1997;337:1491-9.
•Judd JT, et al. Effects of margarine compared with those of butter on blood lipid profiles related to cardiovascular disease risk factors in normolipemic adults fed controlled diets. Am J Clin Nutr 1998;68:768-77.
•King IB, et al. Serum trans-fatty acids are associated with risk of prostate cancer in beta-carotene and retinol efficacy trial. Cancer Epidemiol Biomarkers Prev. 2005;14:988-92.

HOMOCYSTEINE
•Chait A, et al. Increased dietary micronutrients decrease serum homocysteine concentrations inpatients at high risk of cardiovascular disease.
•Nurk E, et al. Plasma total homocysteine and hospitalizations for cardiovascular disease. Arch Inter Med 2002;162:1374-81.
•Sato Y, et al. Effect of folate and mecobalamin on hip fractures; inpatients with stroke. JAMA 2005;293:1082-88.
•Schnyder G, et al. Effect of homocysteine-lowering therapy with folic acid, vitamin B12, and vitamin B6 on clinical outcome after percutaneous coronary intervention. JAMA 2002;288:973-79.
•Seshadri S, et al. Plasma homocysteine as a risk factor for dementia and Alzheimer's disease. N Engl J Med 2002;346:476-83.

INFLAMMATION
•Belluzzi A, et al. Effect of an enteric coated fish oil preparation on relapses in Crohn's disease. N Engl J Med 1996;334:1557-60.
•Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Eng J Med 2005; 352:1685-95.
•Ridker PM et al. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Eng J Med 2000;342:836-43.
•Ridker PM. High-sensitivity C-reactive protein, inflammation, and cardiovascular risk. Am Heart J 2004;148:S19-26.
•Wallace JM. Nutritional and botanical

MERCURY
•Guallar E et al. Mercury, fish oils, and the risk of myocardial infarction. N Engl J Med 2002;347:1747-54.
•Hyman MH. The impact of mercury on human health and the environment. Alternative Therapies;2004;10:70-74.
•METABOLIC SYNDROME AND DIABETES
•Weinstein AR et al. Relationship of physical activity versus body mass index with type 2 diabetes in women. JAMA 2004;292:1188-94.

NUTS
•Fraser GE et al. A possible protective Effect of nut consumption on risk of coronary heart disease. Arch Intern Med 1992;152:1416-1424.
•Hu FB et al. Frequent nut consumption and risk of coronary heart disease in women. BMJ 1998;317:1341-5.
•Jenkins DFA et al. Dose response of almonds on coronary heart disease risk factors. Circulation 2002;106:1327-32.
•Kris-Etherton PM et al. The effects of nuts on coronary heart disease risk. Nutrition Reviews 2001;59:103-111.
•Sabaté J et al. Effects of walnuts on serum lipid level and blood pressure in normal men. N Engl J Med 1993;328:603-7.
•Spiller GA et al. Effects of plant-based diets high in raw or roasted almonds, or roasted almond butter on serum lipoproteins in humans. J Am Coll Nutr 2003;22:195-200.

References

OMEGA-3 FATS (FISH OIL)
•Ascherio A et al. Dietary intake of marine n-3 fatty acids, fish intake, and the risk of coronary disease among men. N Engl J Med 1995;332:977-82.
•Covington MB. Omegao-3 Fatty acids. AFP 2004;70:133-40.
•Darlington LG et al. Review of dietary therapy for rheumatoid arthritis. British J Rheum. 1993;32:507-14
•GISSI-Prevenzione Investigators. (Vitamin E and fish oil for cardiovascular disease.) Lancet 1999;354:471
•Mori TA et al. Effect of omega-3 fatty acids on oxidative stress in humans. Redox Report 2000;5:45-6
•Sanders TAB et al. Triglyceride-lowering effect of marine polyunsaturates in patients with hypertriglyceridemia. Arteriosclerosis 1985;5:459-65.
•Vessby B it al. Effect of dietary fat on insulin sensitivity and insulin secretion. Diabetologia 1999;42:A46

TREADMILL TESTING
•Aktas MK. Global risk scores and exercise testing for predicting all-cause mortality in a preventive medicine program. JAMA. 2004 Sep 22;292(12):1462-8.
•Cole CR, et al. Heart rate recovery after submaximal exercise testing as a predictor of mortality in a cardiovascularly healthy cohort. An Inter Med 2000;132:552-555.
•Jouven X et al. Heart-rate profile during exercise as a predictor of sudden death. N Engl J Med 2005;352:1951—8.
•Hawkins SA, et al. A longitudinal assessment of change in V02max and maximal heart rate in master athletes. Med Sci Sports Exerc 2001;33:1744-50.
•Mora S et al. Ability of exercise testing to predict cardiovascular and all cause death in asymptomatic women. JAMA 2003;290:1600-07.
•Vivekananthan DP et al. Heart rate recovery after exercise is a predictor of mortality, independent of the angiographic severity of coronary disease. J Am Coll Cardiol. 2003 Sep 3;42(5):831-8.