# *Cholesterol, Statins and the Truth about Cardiovascular Health and Disease*

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***Learn to do a full risk assessment of cardiovascular health and set up an effective treatment protocol using herbs and nutrition.***

***Introduction***

Cardiovascular disease (CVD), principally heart disease and stroke, is the nation's leading killer for both men and women among all racial and ethnic groups. Almost 1 million Americans die of CVD each year, which adds up to 42% of all deaths.

Heart disease doesn't just kill the elderly -- it is the leading cause of death for ALL Americans age 35 and older. Heart disease is the leading cause of death in women worldwide, killing around 8 million each year - more than 18 times the rate caused by breast cancer.

The death toll alone is a staggering burden, but it is only part of the picture. The rest of the picture is filled with individuals who daily struggle with the complications of CVD. One out of every four Americans has CVD, that converts to about 57 million Americans. Heart disease and stroke account for almost 6 million hospitalizations each year and cause disability for almost 10 million Americans age 65 years and older.

The World Heart Federation, a leading heart health charity is calling for every country to develop a policy for preventing cardiovascular disease, also the leading cause of death in the world, killing nearly 17 million people annually. [1]

CVD costs the nation $274 billion each year, including health expenditures and lost productivity. The 1999 cost is estimated to be $286.5 billion, and the burden continues to grow as the population ages.

Until fiscal year (FY) 1998, NO Federal Funding had been directed to states to target CVD. [2]

The effectiveness of conventional medicine as far as early detection and treatment, in actually preventing heart attacks is questionable according to a recent study that was published in the journal ***Circulation***. In this study, the medical records were of 326 individuals who had received medical examinations within the six month period before they died from a sudden heart attack were analyzed. Eighty-six of the 326 examinations were done within the *seven-day period prior to death from heart attack.* The physicians had not predicted a single one of the 326 heart attacks. [2]

The Allopathic approach is medication and surgery but several published studies indicate that a second and even third opinion should be obtained before proceeding with surgery. "Angiograms, bypass surgery, and angioplasty are a big business. Over one million heart angiograms are performed each year for a total annual cost of over ten billion dollars. But based upon extensive analysis, it appears that most of this money is wasted. The use of expensive surgery is physically invasive and traumatic for the heart patient. Upon evaluation of case histories it has been shown to be five to ten times more deadly than the disease and in many instances unnecessary!" [3]

According to studies conducted by the U.S. Center for Disease Control, where you live geographically might affect your exposure to factors causing heart disease (i.e. environmental pollution, daily stress, lifestyle behaviors). Also, a number of health-related behaviors practiced by people every day contribute markedly to cardiovascular disease. These include:

Stress (elevated stress hormones): "Mental stress" that may not even be noticed, is a stronger indicator of heart attack or other severe heart event than other known risk factors including smoking, having high cholesterol or diabetes or being a man. The Mayo Clinic reported that psychological stress is the strongest risk factor for predictive future cardiac events, including myocardial infarction and cardiac death, among individuals with an existing coronary artery disease. Anger, anxiety and chronic worrying are all associated with coronary heart disease. People whose blood pressure rise during periods of "mental stress" are six times more likely to have a coronary heart disease event within six years than those who remain calm under the stress. Conscious stress and biological stress may be two different things. People's capacity, particularly men, to tell you that they are stressed is worth about nothing. [4]

Research published in an issue of *Circulation,* the journal of the American Heart Association, suggests that mental stress can trigger a potentially deadly slowdown in blood flow to the heart. Moreover, stress was shown to increase the risk of death by as much as three times for people with cardiovascular concerns compared to those without them. Stress in those people causes the walls of blood vessels to thicken, resulting in a narrowed flow of blood, especially to the heart's critical coronary arteries. This increased pressure within the blood vessels forces the heart to work harder and causes certain portions to contract more vigorously or to bulge. Furthermore, the vascular resistance and coronary artery constriction that occur during mental stress increase blood pressure, while at the same time decreasing the amount of blood available to the heart. This results in the heart being deprived of essential nutrients and increases its demand for oxygen. [168]

**Anxiety Characteristics Independently and Prospectively Predict Myocardial Infarction in Men**

Type A go-getters aren't the only ones stressing their hearts. Nervous Nelsons seem to be, too. Recent research reported that chronic anxiety can significantly increase the risk of a heart attack. The findings add another trait to a growing list of psychological profiles linked to heart disease, including anger.

Dr. Nieca Goldberg of the New York University School of Medicine, a spokeswoman for the American Heart Association sated that "This is very important research because we really are focused very much on prescribing medicine for cholesterol and lowering blood pressure and treating diabetes, but we don't look at the psychological aspect of a patient's care," she added. Doctors "need to be aggressive about not only taking care of the traditional risk factors ... but also really getting into their patients' heads." [300]

**Depression, Type D behavior and heart disease**

Many studies have demonstrated the role of psychosocial and behavioral risk factors in the etiology and pathogenesis of cardiovascular disorders. Recently, a new personality construct, the type D or 'distressed' personality, has been proposed. Type D behavior is characterized by the joint tendency to experience negative emotions and to inhibit these emotions while avoiding social contacts with others. The observation that cardiac patients with type D personality are at increased risk for cardiovascular morbidity and mortality underlines the importance of examining both acute (e.g. major depression) and chronic (e.g. certain personality features) factors in patients at risk for coronary events. Both type D dimensions (negative affectivity and social inhibition) are associated with greater cortisol reactivity to stress. Elevated cortisol may be a mediating factor in the association between type D personality and the increased risk for coronary heart disease and, possibly, other medical disorders. [242]

A bidirectional relationship exists between depression and cardiovascular disease. Patients with major depression are more likely to develop cardiac events, and patients with myocardial infarction and heart failure are more likely to develop depression. A feature common to both clinical syndromes is activation of proinflammatory cytokines and stress hormones, including the hypothalamic-pituitary-adrenal axis and the renin-angiotensin-aldosterone system. In the present study we examined the hypothesis that exposure to chronic mild stress (CMS), an experimental model of depression that induces anhedonia in rats, is sufficient to activate the production of proinflammatory cytokines and stress hormones that are detrimental to the heart and vascular system. Four weeks of exposure of male, Sprague-Dawley rats to mild unpredictable environmental stressors resulted in anhedonia which was operationally defined as a reduction in sucrose intake without a concomitant effect on water intake. Humoral assays indicated increased plasma levels of

tumor necrosis factor-alpha (TNF-alpha), interleukin-1 beta (IL-1beta), plasma renin activity, aldosterone, and corticosterone in the CMS exposed rats. Tissue TNF-alpha and IL-1beta were increased in the hypothalamus, and TNF-alpha was increased in the pituitary gland. These humoral responses to CMS, associated with anhedonia as an index of depression in the rat, are likely to be associated with neurohumoral mechanisms that may contribute to adverse cardiac events. The findings provide a basis for examining more directly the interactions among the central, endocrine, and immune systems in depression associated with heart disease. [242]

Diet - Poor Nutrition (elevated glucose and insulin – obesity): Between 30% - 40% of the nation's adults are obese and thus have a higher risk for heart disease, high blood pressure, high cholesterol, and other chronic diseases and conditions such as diabetes. Only 27% of women and 19% of men report eating the recommended five servings of fruits and vegetables each day. I recommend 7-10 serving of vegetables and 4-5 servings of fruit. Just by increasing your vegetable, fruit and 'wholegrain' intake serum lipids can greatly improve. [4] If, as we have been told, heart disease results from the consumption of saturated fats, one would expect to find a corresponding increase in animal fat in the American diet. In actuality, the reverse is true. During the sixty-year period from 1910 to 1970, the proportion of traditional animal fat in the American diet declined from 83% to 62%, and butter consumption plummeted from eighteen pounds per person per year to four. During the past eighty years, dietary cholesterol intake has increased only 1%. During the same period the percentage of dietary vegetable oils in the form of margarine, shortening and refined oils increased about 400% while the consumption of sugar and processed foods increased about 60%. [6]

Lowering cholesterol by dietary means does not improve health. There isn't little support from trials: there is none at all. Two meta-analyses of all controlled, randomized dietary trials, in which the only type of intervention was a lowering of dietary saturated fats, an increase of dietary polyunsaturated fats, or both, found that the total number of deaths was identical in the treatment and the control groups.

Simply lowering the percentage of energy from total fat in the diets is unlikely to improve lipid profile or reduce CHD incidence. The same applies for treating obesity by diet; long-term clinical trials have provided no good evidence that reducing dietary fat per se leads to weight loss. There is much evidence to suggest that omega-3 fatty acids have a beneficial influence on cardiovascular disease. [176-179]

A recent meta-analysis by scientists from France's INSERM in Paris, Lille's Pasteur Institute, and Rouen's Department of Epidemiology and Public Health, pooled nine cohort studies giving an overall study population of 91,379 men, 129,701 women, and 5,007 coronary heart disease events. The analysis found that the risk of coronary heart disease (CHD), conditions that cause of 20 per cent of deaths in the US and 17 per cent of deaths in Europe, was cut by four per cent for each additional fruit and vegetable portion consumed, and by seven per cent for fruit portion intake.

The link between the risk of CHD and vegetable intake however was mixed with a more beneficial relationship observed for general cardiovascular mortality (26 per cent risk reduction) than for the more specific fatal and nonfatal heart attacks (myocardial infarction) (five per cent). *This meta-analysis of cohort studies shows that fruit and vegetable consumption is inversely associated with the risk of CHD.* [270]

A recent animal study conducted determined the effects of a diet rich in green and yellow vegetables on the development of atherosclerosis, the underlying cause of coronary heart disease, in a mouse model of atherosclerosis, the LDL receptor -/-, apolipoprotein B transgenic mouse. The mice were randomized into 2 diet groups: 1) a vegetable-free control diet (n = 53) and 2) the same diet with 30% (w:w) replaced by an equal-parts mixture of freeze-dried peas, green beans, broccoli, corn, and carrots (n = 54). Mice were fed these diets for 16 wk. Aortic atherosclerosis, as estimated by cholesteryl ester content, was reduced 38% ($P < 0.001$) in mice fed the vegetable-rich diet. Plasma total cholesterol (-12%), VLDL + ILDL cholesterol (-32%), serum amyloid A (-37%), and body weight (-7%) (all $P < 0.01$) were also lower in these mice at the end of the treatment period. In a regression model, antiatherogenic effects of the vegetable diet remained largely unexplained by the variation in plasma lipoproteins or body weight. Although the pathway(s) involved remain uncertain, the results indicate that a diet rich in green and yellow vegetables inhibits the

development of atherosclerosis and may therefore lead to a reduction in the risk of coronary heart disease. [271]

Lack of Physical Activity: People who are sedentary have twice the risk of heart disease as those who are physically active. Despite these risks, America remains a predominantly sedentary society. Surveys show that more than half of American adults do not practice the recommended level of physical activity, and more than one-fourth are completely sedentary. After a 17-year study on almost 9,800 Americans, the researchers concluded that expending energy through physical activity might be the key to cutting the risks of heart disease. [7] In another study scientists found that increasing exercise, not reducing calories, may be the best way to ward off heart disease. [8]

Tobacco Use: Smokers have twice the risk of heart attack as nonsmokers. One-fifth of the annual 1,000,000 deaths from CVD are attributable to smoking. Surveillance data indicate that an estimated 1,000,000 young people become "regular" smokers each year.

## Let's dispel some popular myths regarding statin drugs, cholesterol and heart disease:

***MYTH 1***

***"High cholesterol {and LDL} is the number-one cause of heart disease in this country."*** Dead wrong. High cholesterol is among the risk factors for heart disease, but is not the leading risk factor. The most prevalent risk factor is low HDL, along with small LDL particles, which commonly occur together. In fact, of every 100 people with coronary heart disease, 60-70 will have low HDL and small LDL particles, but fewer than 30 will have high LDL. If this is the case, why do we not hear more about low HDL and small LDL particles? The answer is simple: because treating these is not as profitable for drug companies. But just wait—when a profitable drug becomes available to treat this more prevalent risk factor for heart disease, we can expect to hear about an "epidemic" that will justify billions of dollars in new drug expenditures. [182-185]

What qualifies as low HDL? National guidelines say it is a level of less than 40 mg/dL for men and less than 45 mg/dL for women. [186] In fact, a level of less than 60 mg/dL is probably very significant. [187] HDL is already a standard measure in everyday cholesterol panels. Small LDL particles, on the other hand, need to be measured specifically. The medical world focuses on statin therapy for LDL, while the most prevalent risk factor for heart disease goes untreated in the great majority of cases.

***MYTH 2***

***"If I take a statin agent, I won't have a heart attack."*** This is simply untrue. Lowering cholesterol (even to rock-bottom levels) reduces, but does not eliminate, the risk of heart attacks. Many heart attacks still occur in people with low cholesterol levels, whether or not they take cholesterol-lowering drugs. [188] We must consider that there are other risk factors for heart disease besides cholesterol, such as small LDL particles, low HDL, lipoprotein(a), homocysteine, and high insulin levels. Results from the most recent National Health and Nutritional Survey show that 47 million US adults have metabolic syndrome (low HDL, high triglycerides, high blood pressure, excess abdominal fat), which substantially heightens the risk of heart disease even in the presence of low cholesterol levels. [189]

***MYTH 3***

***"I feel fine and my stress test was normal. My doctor says I don't have heart disease."*** This is among the most widely propagated fallacies spread by many primary care physicians and even cardiologists. First, lack of symptoms should not be reassuring, as most heart disease is silent—without symptoms and undetectable by conventional means such as electrocardiograms and cholesterol testing. Second, stress testing is a miserable failure for screening asymptomatic people. Most future deaths and heart attacks, in fact, occur in people with normal stress tests (when symptoms are not present). This is why you will hear about your neighbor passing a stress test on Tuesday, only to drop dead from a heart attack on Thursday. The net result of this misperception is that most future heart-attack victims are walking around now, feeling fine and unaware of their risk. [190] Cholesterol can be high, low, or in between, but all too frequently fails to shed light on this murky situation.

**Cholesterol: the lipid with a bad reputation**

Hyperlipidemia refers to elevated blood levels of lipids (fats), including cholesterol and triglycerides. Most people with hyperlipidemia have no symptoms. However, hyperlipidemia is a contributing factor associated with an increased risk of coronary heart disease (CHD), a thickening or hardening of the arteries that supply blood to the heart muscle. CHD, in turn, can result in angina pectoris (chest pain), a heart attack, or both. Although hyperlipidemia is considered a risk factor to heart disease, it is one of many risk factors and what actually causes hyperlipidemia is a debatable issue. It not as simple as foods that contain cholesterol, elevate lipids.

Another important risk factor, which has been largely overlooked, is the oxidation of low-density lipoprotein (LDL) cholesterol caused from a lack of antioxidant-rich foods, herbs, and nutrients and/or a large intake of foods and chemicals that contains damaging free radicals. Chronic inflammation also contributes to oxidative stress and an increase in CHD. When LDL cholesterol oxidizes, it promotes atherosclerosis by a process referred to as the macrophage-foam cell mechanism, particularly in the presence of stressors, like cortisol and insulin. Cortisol and insulin together act as a dynamic duel causing all kinds of disruptions including an increased oxidative and inflammatory state. These are the real underline causes to chronic disease. Inflammation is also involved in the process of LDL oxidation and contributes to the development of vascular disease. [205-207, 264]

The production of C-reactive protein is an essential part of the inflammatory process, and the measurement of this substance reflects the level of inflammatory activity deep within the body. It appears that certain conditions create a state of excessive inflammation within the circulatory system. High C-reactive protein levels are evidence of this type of inflammation. [9-12]

Multiple risk markers for atherosclerosis and cardiovascular disease act in a synergistic way through inflammatory pathways. There are many key inflammatory biochemical risk markers for cardiovascular disease; in particular, the role of three basic cell types affected by these risk markers (endothelial cells, smooth muscle cells, and immune cells), the crucial role of inflammatory mediators, nitric oxide balance in cardiovascular pathology, and the use of nutrients (flavonoides, carotenoids, sterols, vitamin C and E, n'3 fatty acids etc.) to circumvent several of these inflammatory pathways. Most risk markers for cardiovascular disease have a pro-inflammatory component, which stimulates the release of a number of active molecules such as inflammatory mediators, reactive oxygen species, nitric oxide, and peroxynitrite from endothelial, vascular smooth muscle, and immune cells in response to injury. Nitric oxide plays a pivotal role in preventing the progression of atherosclerosis through its ability to induce vasodilation, suppress vascular smooth muscle proliferation, and reduce vascular lesion formation. Nutrients such as arginine, antioxidants (OPCs, vitamins C and E, lipoic acid, selenium, glutathione), and enzyme cofactors (vitamins B2 and B3, B6, B12, folate, zinc) help to elevate nitric oxide levels and may play an important role in the management of cardiovascular disease. Other dietary components such as DHA/EPA from fish oil, tocotrienols, vitamins B6 and B12, and quercetin contribute further to mitigating the inflammatory process. [13]

Within the broad range of cholesterol levels from 180 to 240 there is little to no evidence that this alone correlates with heart disease. Below 180 there is increased risk of hemorrhagic stroke, depression, and suicide. Above 240 there is increased risk of cardiovascular disease and ischemic stroke. Over age 70, elevated cholesterol and cardiovascular events no longer correlate. All told, total serum cholesterol alone is a poor indicator of cardiovascular disease. Half of all heart attack patients have normal total cholesterol levels.

**In the case of an elevated cholesterol level, normalizing it without drugs is one of the easiest things to do with nutritional and botanical medicine.**

**Diet, Cholesterol and CHD**

Cholesterol has unjustly received most of the blame for cardiovascular disease and has thus become a lipid with a poor reputation. There is much confusion and many misconceptions about what foods are good to eat versus what foods are bad to eat. Foods like eggs and butter are thought to be major contributors to heart disease because of their cholesterol content, but in fact studies have shown, with a balanced diet, eggs do not increase plasma blood cholesterol. Eggs that come from chickens that are free range, and that have eaten natural organic grains contain high amounts of lecithin. Lecithin is a phospholipid that emulsifies other fats and improves the liver's ability to break down and absorb fat properly. A recent study done in Korea found that daily consumption of 3 eggs per day, enriched with docosahexaenoic acid (DHA) reduced platelet aggregation, total cholesterol, LDL cholesterol and triglycerides. Another new study found eating an egg a day does not impact the cholesterol particles in the blood most likely to cause heart disease, debunking myths surrounding the role of eggs in the diet. [14-18]

An extensive study of diet and disease patterns in China found that the region in which the populace consumes large amounts of whole milk had half the rate of heart disease as several districts in which only small amounts of animal products are consumed. Butter, although a saturated fat, does not oxidize in the body nor generate free radical damage as hydrogenated polyunsaturated fats do. [19] A survey of South Carolina adults found that men eating butter ran half the risk of developing heart disease as those using margarine. [20]

Mother's milk provides a higher proportion of cholesterol than almost any other food. It also contains over 50% of its calories as fat, much of it saturated fat. Both cholesterol and saturated fat are essential for growth in babies and children, especially the development of the brain. Yet, the American Heart Association is now recommending a low-cholesterol, lowfat diet for children! Commercial formulas are low in saturated fats and soy formulas are devoid of cholesterol. A recent study linked low-fat diets with failure to thrive in children. [21]

The ingestion of rancid fats, refined sugars, and refined starches, will cause an over-oxidation of lipids, including cholesterol, and elevation of insulin levels. This will lead to serious damage of cardiac function and cause atherosclerosis. It is also damaging to the liver, spleen and other organs. Replacing fat with refined sugar and starch, which is so common today, can cause hyper-insulinism, adrenal exhaustion, and obesity. Eating a diet rich in refined sugars and refined starch has shown to decrease the "good" HDL cholesterol. [22] The fat-free diet that many people believed to be the way to go presented many health problems including low energy, difficulty in concentration, depression, weight gain and mineral deficiencies. [23]

There is a clear association of heart disease with the increased consumption of devitalized, processed food items, including sugar and refined fructose (found in soda), pasteurized milk, fortified white flour, milk, and refined powered foods, excess stimulants, imitation broth products, oxidized heavily refined vegetable oils, and hydrogenated fats. Foods high in the glycemic load (refined carbohydrates and sugars – the white stuff), and commercial polyunsaturated fats are what really contribute to CVD and other related diseases. These two groups of foods make up the majority of the commercial food eaten today. Diet together with a lack of physical exercise and the impact of stress, disrupting hormones and hormone signaling, are really the culprits. We can stop blaming eggs and tofu!

**Are there any risks of having cholesterol levels too low?**

Having too low of cholesterol, as I have stated earlier, can lead to a number of health problems:

<u>Depression and suicide:</u> Epidemiological and clinical studies have described an association between lower serum cholesterol concentrations and increased suicide risk that is not entirely attributable to depression-related malnutrition and weight loss. Recent epidemiological studies with greater samples and longer follow-up periods, however, have even shown a positive correlation between cholesterol concentrations and suicide risk after controlling for potential confounding variables. A meta-analysis of earlier intervention trials suggested that cholesterol lowering could cause or worsen depressive symptoms and increase the risk of suicide. [24] Results of a study conducted by Dutch researchers provide additional evidence for a link between low cholesterol levels and an increased risk of depression in men. [25]

Linked to Violence: Lowering cholesterol could trigger changes in brain chemistry that encourages violent behavior. Dozens of studies support a connection between low or lowered cholesterol levels and adverse violent outcomes in certain populations. Cholesterol levels directly affect the activity of serotonin. It is possible that lowered cholesterol levels may lead to lowered brain serotonin activity; this may, in turn, lead to increased violence. [26]

Low cholesterol in combination with low levels of the protein albumin in the blood may indicate a high risk of decline and death in elderly people. [27]

Many studies have reported an association between a low or lowered blood total cholesterol (TC) level and subsequent nonatherosclerotic disease incidence or death. The question of whether low TC is a true risk factor or alternatively a consequence of occult disease at the time of TC measurement remains unsettled. Falling TC level was accompanied by a subsequent increased risk of death caused by some cancers (hemopoietic, esophageal, and prostate), non-cardiovascular non-cancer causes (particularly liver disease), and all causes. Research shows that a catabolic state can cause TC to decrease which causes a decline in overall health and can even lead to death. [161]

The number one risk factor relating to heart disease is body mass index (BMI). This is far and beyond more important than lipid scores. Maintaining a lower BMI via a reduced fat component is more beneficial in lowering CVD risks than other factors. [254, 255]

**Abdominal obesity, a great risk factor for heart disease**

According to the results of a new study, belly fat is a better measure of the risks than BMI, and abdominal obesity could be a greater risk factor than overall obesity. Researchers looked at data from more than 100,000 men and women to test whether measuring sagittal abdominal diameter, or SAD, would improve the accuracy of predicting heart disease risk.

SAD is the distance from the back to the upper abdomen midway between the top of the pelvis and the bottom of the ribs. SAD is a more standardized measurement than waist circumference, and therefore less subject to error. Men with the largest SAD were 42 percent more likely to develop heart disease, and a large SAD similarly increased heart disease risk by 44 percent for women. Heart disease risk also rose with SAD within BMI categories, even among men of normal weight.

The relationship between SAD and heart disease risk was strongest among the youngest men and women, indicating that people who develop central obesity earlier in life are more likely to have more serious problems. [295]

Obesity is associated with low HDL cholesterol, high triglycerides, and elevated C-reactive protein. [256]

There is some evidence of an association between low serum cholesterol and cancer from several prospective studies. [163, 164]

**What should the diet be?**

Also just as bad is the high fat and protein diet. The diet I preach is rich in organic undenatured vitalizing foods, with an emphasis on vegetables, fruits, whole grains, a balanced intake of organic protein-rich foods as well as a variety of foods providing a balance of Omega 9, 6 and 3 fatty acids. This can include organic free-range meat but doesn't have too. It should take in to account the energetic nature of the person as well as the geographical location and the time of year. For example the diet during the hot summer months should have a larger intake of summer fruits, mono and saturated fat, and in the winter more root vegetables and n'3 and 6-rich foods such as walnuts, and flax seeds. Not only is this typically more convenient, it is what your body wants and needs for optimal health and adaptation. Just by increasing vegetable and fruit intake, in particularly berries, research has concluded that serum levels of lipids normalize to a healthy range. [28]

The Mediterranean diet has been shown in epidemiological trials to be associated with reduced risk of heart disease. A team from Laval University in Québec tested the typical Mediterranean diet on a group of 71 healthy women under free-living conditions. The 12-week intervention involved two courses on nutrition and 7 individual sessions with a dietitian. A score based on the 11 components of the Mediterranean pyramid was established to determine the women's adherence to the Mediterranean food pattern. Among all women, levels of oxidized LDL particles circulating in the blood decreased by 11.3 per cent after 12 weeks of nutritional intervention despite a lack of change in plasma LDL cholesterol. More specifically, increases in servings of fruits and vegetables were associated with decreased in LDL concentrations. [239]

**A new meta-analysis of scientific evidence for nuts' ability to lower cholesterol levels confirms that almonds, peanuts, walnuts and pecans could be useful as part of an overall heart-healthy diet. [253]**

***Walnuts*** - Walnut consumption lowers total cholesterol levels as well as LDL or 'bad' cholesterol. This may be due to the walnuts rich source of alpha-linolenic acid (ALA), which can also improve vascular function, aiding the prevention of heart disease and stroke. [29] Walnuts go great in salads with apples or pears, and some goat cheese.

***Raw almonds -*** A handful (1/4-1/2 cup) of raw almonds daily not only lowers cholesterol, but also lowers the dreaded genetic risk factor for coronary disease, lipoprotein(a). Almonds also blunt abnormal spikes in blood sugar after eating and help prevent diabetes. They are tremendously filling and are great for sugar addicts who need to snack, since almonds take the edge off your sweet tooth. [180, 181]

The flavonoides, as well as the monoterpene, limonene, found in the orange and tangerine peels has the potential to lower cholesterol more effectively than some prescription drugs, and without side effects, according to a study by US and Canadian researchers. [30] I often recommend the use of citrus rind in teas, fish dishes, and salad dressings.

Prolonged stress can suppress activity of anti-oxidant systems, increasing lipid peroxidation, and inflammation. Besides important lifestyle changes that can prevent and even reverse coronary heart disease, foods rich in flavonoids, namely procyanidolic polymers, along with other phenolic compounds, present mostly in berries, possess unique pharmacological properties and unique benefits (anti-oxidant, anti-inflammatory, anti-thrombotic, vascular-tissue-enhancing etc.). They can maintain antioxidant function under normal conditions and can raise our antioxidant abilities when under stressful conditions. Flavonoids in general act as one-electron donors, which eliminate free radicals. The phenolic antioxidants eliminate oxygen, carbon, and nitrogen-centered free radicals by donating to them the single electron they require. The phenolics themselves become free radicals in the process, but do not seek to capture electrons from adjacent molecules because of a special property. They are a conjugated structure (alternating double and single bonds) that permits the remaining orbital electron to "delocalize" and spend time in orbits surrounding other atoms in the molecules. By means of the process of electron delocalization, the phenolic free radical is said to undergo "resonance stabilization" and becomes relatively unreactive. The phenolic antioxidants are known to stop lipid peroxidation of cell membranes, a prominent free radical chain reaction among unsaturated fatty acids that is carcinogenic by virtue of being both mutagenic and mitogenic. [31]

Carotenoids, such as dietary lycopene, found in tomatoes, pink grapefruits, and water melon, may significantly reduce the risk of heart disease, suggests new research, which found that women with the highest levels of the antioxidant in their blood had a 34 per cent reduced risk of the disease compared to those with lower levels of the nutrient. [32]

**Maintain normal body weight and a good muscle to fat ratio**

The relationship of weight at age 65 years and subsequent mortality was examined in a population of 1723 nonsmokers who were followed up from one to 23 years (mean, 9.5 years) during the Framingham Heart Study. In sex-specific proportional hazards analyses, risks of mortality were increased for men and women at the high and low extremes of body mass index, even when accounting for potential effects of excess

weight on serum cholesterol level, blood glucose level, and systolic blood pressure. For those at the lower extreme of body mass index, the relative risk of death was almost twice as high in the years immediately after age 65 years as in later follow-up, suggesting that the increased early death rate was due to disease that was already present. At the upper extreme, risk of death was twofold over the entire follow-up period for persons with body mass indexes at or above the 70th percentile at both 55 and 65 years of age. We conclude that, even when accounting for cardiovascular risk factors, being overweight is a serious health problem for older people, especially for those with long-standing weight problems. [162]

High fasting insulin levels, which can lead to obesity and diabetes, are a strong independent predictor for ischemic heart disease. [33] Rather than not eating any starch at all (the trendy Atkin's diet), I recommend switching from refined starch to whole grains. Whole grain intake verses refined grain intake is inversely associated with body mass index, waist-to-hip ratio, total cholesterol, LDL cholesterol and fasting insulin. These are markers associated with a reduction in the risk of type-2 diabetes, cardiovascular disease and certain cancers. [34, 35] Overweight and obesity are associated with several risk factors for morbidity and mortality, and those who are extremely obese have a several-fold higher risk of related health conditions including CVD. [36]

**Distribution of lifestyle and emerging risk factors by 10-year risk for coronary heart disease.**

The Framingham risk score has been used for coronary heart disease (CHD) risk assessment. Recently, additional risk factors not included in the Framingham algorithm have received much attention and may help improve risk assessment. The distributions of lifestyle and emerging risk factors by 10-year risk of CHD was assessed. They calculated 10-year CHD risk (<10%, 10-20%, and >20%) for 8355 participants in the National Health and Nutrition Examination Survey (NHANES) 1999-2002 using the Framingham risk score as modified by the National Cholesterol Education Program Adult Treatment Panel III guidelines. They examined the prevalence of lifestyle risk factors [body mass index (BMI) and waist circumference] and various emerging risk factors [C-reactive protein (CRP), white blood cell count, fibrinogen, homocysteine, glycosylated hemoglobin, and albuminuria] as well as prevalence of high CHD risk by levels of these risk factors. RESULTS: All examined CHD risk factors were significantly associated with increasing 10-year CHD risk among men and women. Odds of being in the highest CHD risk group were greater at higher levels of examined risk factors. Means for most risk factors were slightly higher for women than the means for men. Sizeable proportions of participants with lower 10-year CHD risk had high levels of lifestyle and emerging risk factors: **60.8% were overweight, 33.8% had high CRP concentrations, 24.1% had serum fibrinogen >400 mg/dl and 6% had an albumin/creatinine ratio >/=30**. [272]

**What's up with those Statin Drugs? The good, the bad and the ugly!**

With half the population anticipated to take these drugs in the future, it is time that we seriously re-evaluated what we are doing with them. Just like our weight, there is an optimum with cholesterol as well. Some people believe that the lower your cholesterol, the healthier you are. Nothing could be further from the truth. If your cholesterol is too low you will have an increased risk of mood disorders, depression, stroke, violence, and even cancer.

The American College of Physicians released a recent report that stated "regardless of cholesterol levels, most people with diabetes should be taking cholesterol-lowering medication to cut their risk of having a heart attack". [37]

An estimated 25 million people world wide are taking drugs known as statins to lower their cholesterol levels and according to 'experts' 200 million could use them. Now, researchers are claiming that doubling the doses that is currently used reduces the risk of heart attack, bypass surgery and chest pains more than 'more gentle' doses.

This advice will most likely put pressure on doctors to use even more aggressive and expensive doses of statin drugs. The United States already spends $12.5 billion more on statins than any other medicine. When you consider that a starting dose for Lipitor will run you $900 per year, while the 80-milligram dose used in

the new study costs approximately $1,400 annually, you get a good idea of how much more expensive this will be.

Experts, whoever they might be, are now reported that using higher doses of drugs to reduce cholesterol decreases the risk of heart attack, bypass surgery and chest pains. In this study it was found that people who took a double dose of the drug Lipitor, had their LDL levels drop to 62 milligrams per deciliter of blood compared to the patients whose LDL level dropped to 95 milligrams per deciliter after taking a standard dose of Pravachol. The study showed that the patients treated with Lipitor lowered their risk of dangerous chest pain, heart attack and bypass surgery by 16 percent compared to those patients that took Pravachol. The finding could place new pressure on doctors to treat their patients more aggressively by using higher doses of statin drugs to reduce cholesterol levels in people with heart disease. This advice could mean a huge increase in health care costs because in the United States, only 11 million of the 36 million people who experts say should be taking cholesterol medication are actually taking them. [38]

Suppose that lowering your "bad" (LDL) cholesterol was not actually the key to lowering your risk of heart attacks and heart disease? Would you still want to risk all of those statin side effects? Not to mention how effective a combination of diet, exercise, stress management and a well developed nutritional and botanical supplement regime can do. With this approach, there is really no need for these drugs. Well, this is just what several research studies have found, raising the basic question of whether statin drugs even work to lower the risk of heart disease.

A better predictor of heart disease, with respect to cholesterol, is the HDL/total cholesterol ratio, than total cholesterol, although there are many other risk factors that are either more important or just as important as the HDL/total cholesterol ratio.

Statin drugs do, in fact, lower bad cholesterol levels. But they do this by compromising the ability of the liver to create all types of cholesterol, including the "good" cholesterol and important hormones that the body manufactures from cholesterol. Statins may have one measurable, positive effect according to the medical charts, but they simultaneously *throw off the body's healthy physiology in a hundred other ways* such as blocking your sex drive.

Clinical trials don't pay much attention to these other effects; they're just looking to prove one particular thing and get FDA approval to market the drug as a miracle cholesterol fighter. What other effects the drug has on the human body are largely ignored. And when clinical trial participants start showing these severe effects, they are typically "dismissed" from the trial in order to ensure that trial results look positive. In this way, extremely toxic drugs are actually approved by the FDA as "safe."

A recent published study found that lowering bad cholesterol with statin drugs might not reduce the rate at which plaque builds up in the arteries surrounding the heart. This finding flies in the face of the widespread belief that lowering LDL cholesterol levels is the best way to reduce arterial plaque. In the study, participants taking varying doses of a statin did generally lower their cholesterol. However, all the groups had an average increase in arterial plaque of 9.2 percent. [39]

Another published study looked at the effect of statin drugs versus usual care (improving diet, exercise, etc.). While the statin group did lower their bad cholesterol levels significantly more than the usual care group, both groups had the SAME rates of death and heart disease. [40] Even another study confirmed that a healthy diet, low in fats, refined fats, starches and sugars, was just as effective as a statin drug in lowering LDL cholesterol. [41]

Statin drugs induce myopathy (muscle weakness) [43, 44, 171, 172, 294] and remember that the heart is really a muscle that never stops working. What does that tell you?

Statin-related side effects, including statin cardiomyopathy, are far more common than previously published and are reversible with the combination of statin discontinuation and supplemental CoQ 10 and other mitochondrial-enhancing nutrients and botanicals. [294]

Statins have been shown to cause myotoxicity and rhabdomyolysis. In most cases rhabdomyolysis occurs following the use of these drugs for at least one week. Cases of rhabdomyolysis after just a single dose of simvastatin have been reported. [44]

**Baycol Pulled From Market as Numerous Deaths Linked to It**

The maker of Baycol (cerivastatin), a popular cholesterol-lowering drug used by about 700,000 Americans, voluntarily pulled the medicine off the market August 8 because of numerous deaths associated with its use. Officials at the Food and Drug Administration said 31 people have died of complications of severe muscle breakdown, a rare but well-recognized side effect of many cholesterol-lowering drugs. In about one-third of the cases, the person was on a second cholesterol drug, gemfibrozil, known to especially increase the risk of problems. Baycol is one of six "statins," a popular family of drugs prescribed to about 12 million Americans to treat, and possibly prevent, coronary heart disease. Reports of severe side effects, including death, are at least 10 times more common for Baycol than for other drugs in the class. The FDA is currently not considering any regulatory action with regard to the other approved statins which are lovastatin (Mevacor), pravastatin (Pravachol), Zocor (Zocor), fluvastatin (Lescol) and atorvastatin (Lipitor). Bayer AG, the German company that makes Baycol, introduced the drug under the trade name Baycol in January 1998. The first death was reported in January 2000, with the number of complications rising markedly when a high-dose pill was introduced last August.

Before and after the first death, Bayer officials warned doctors against prescribing Baycol with gemfibrozil and strongly advised that patients be started on a low dose. That advice, and changes in Baycol's official labeling, appeared to change prescribing behavior to some extent, but not enough to eliminate the problem. Drug recalls are rare. From 1981 to 2000, the FDA approved 543 new drugs for use. Fourteen, or 2.6 percent, were subsequently recalled—either voluntarily, or by FDA action—for safety reasons. Baycol is fifth out of the six statins in number of prescriptions written, according to data provided by IMS Health, a pharmaceutical monitoring company in Pennsylvania. But the drug's market share was growing. It was 6.7 percent at the end of June, up from 2.5 percent at the end of 2000.

The drug is the third biggest selling prescription drug in Bayer's portfolio. Worldwide, it accounted for $560 million in sales last year, and was expected to grow to about $880 million this year. Baycol, which is used worldwide by about 6 million people, is also being taken off the market in Europe. It will remain available only in Japan, where gemfibrozil is unavailable. Physicians have known since the first statin was introduced in 1987 that a few patients develop muscle inflammation, experienced as soreness or tenderness, while taking the drug. Occasionally, that progresses to whole-scale muscle breakdown, a condition called rhabdomyolysis. That, in turn, can lead to kidney failure, as the bloodstream is flooded with relatively toxic proteins released by the dissolving tissue. Jenkins said 29 of the 31 people who died had kidney failure.

People at increased risk for the complication are those taking both Baycol and gemfibrozil (sold under the trade name Lopid), and those taking the 0.8 milligram Baycol dose. The FDA advised people in those groups to stop taking Baycol and consult their doctors about alternative medicines. Some deaths have also occurred with use of the 0.4 milligram pill, and when the drug is taken alone. The elderly, and possibly women, also appear to be at higher than usual risk for the complication.

Combination use of statins and fibrates—the family to which gemfibrozil belongs—isn't necessarily a mistake. The two types of drugs alter blood fats in different ways, and are sometimes intentionally prescribed to patients with severe cholesterol problems despite the rare risk of rhabdomyolysis, which generally reverses itself if the drugs are stopped immediately. [251]

**Rhabdomyolysis with HMG-CoA reductase inhibitors and gemfibrozil combination therapy.**

Statin drugs are often combined with another class of drugs, fibric acid derivatives, to lower both cholesterol and triglyceride levels. Rhabdomyolysis is a known, rare serious side effect of statin monotherapy and of statin-fibrate combination therapy. To examine Food and Drug Administration's (FDA's) postmarketing database for cases of rhabdomyolysis in relation to monotherapy and combination use and calculate reporting rates for this event. Domestic cases of statin- and statin/gemfibrozil-associated rhabdomyolysis were culled from FDA's database and reviewed. Rhabdomyolysis was defined by CPK > or = 10,000 IU/L, myopathic signs and symptoms and clinical diagnosis of rhabdomyolysis. Reporting

rates, consisting of number of reported cases/number of prescriptions for each drug, were then calculated to determine whether the reporting of rhabdomyolysis cases was commensurate with extent of use of each statin in the population. Cases were obtained from the FDA adverse event reporting system (AERS) database. PATIENTS: NA. MAIN OUTCOME MEASURES: Number of rhabdomyolysis cases were evaluated, along with outcomes, such as renal failure, dialysis and death. Of 866 total reported cases, 482 (56%) were associated with monotherapy and 384 (44%) related to combination therapy. More than 80% of reported cases for each drug resulted in hospitalization for renal failure and dialysis. 80 patients expired from events related directly to rhabdomyolysis. Rhabdomyolysis is serious side effect of statin monotherapy and of statin-fibrate combination therapy. Clinicians need to remain cognizant of this potential adverse event and discuss signs and symptoms of muscle toxicity with patients in order improve the benefits-to-risks of treating dyslipidemia with statins. [171]

Rhabdomyolysis and the cardio-mypathy associated with statins could easily be prevented and/or treated with a few mitochondrial anabolic enhancing supplements, namely CO Q 10, Magnesium Creatine, Carnitine, Magnesium Gycol Glutamine, and various adaptogens with enhanced anabolic/anti-catabolic actions such as Rhaponticum carthamoides. These can be used even when creatine kinase levels are within normal levels on blood test. [43]

It is down right criminal that CO Q 10 is not recommended for every person taking a statin drug. I think everyone with a risk of cardiovascular disease should be taking CO Q 10.

***Statins have shown to Stimulate the Growth of New Blood Vessels, a possible increase in cancer risk***

Tests in human cell samples and in rabbits show that the cholesterol-lowering drug simvastatin (Zocor) seems to activate a molecule called protein kinase Akt/PKB, which helps regulate blood vessel development properly. Zocor produces effects on the growth of new blood vessels, a process called angiogenesis. Statins might increase the growth of blood vessels in cancerous tumors. [45]

So now it appears that these drugs might also contribute to increased cancer risks. This is not the first time that the cancer-causing potential of cholesterol-lowering medications has been discussed. Several studies provide some excellent information on this. [46] "If statins act on the same pathway as VEGF, as the study states, it further explains the cancer connection. A just-published study shows that VEGF plays an important role in the spread of cancer and found that survival time was diminished in patients whose cancerous tumors tested positive for VEGF." [47] Another study showed that VEGF plays a role in diabetic retinopathy [48] Therefore, if statins act along the same pathway, this is another potential adverse effect of the drugs. Considering the fact that a high percentage of diabetics have heart disease and are probably on these drugs, this is significant.

Some members of the research community have suggested that statin drugs—the drugs of choice for cholesterol reduction—may prevent heart disease not because of their effects on cholesterol, but because they have anti-inflammatory activity. This helps to explain why statins have been found to protect the heart regardless of their effects on cholesterol levels. [173, 174]

This may also explain why they have also shown in some studies to inhibit cancer (breast and prostate cancer). [247-249] Breast and prostate cancer risk increases with poor lipid profiles (low HDLs). [249, 250]

**May causes cognitive decline and even dementia**

Taking statin drugs also has shown to reduce cognitive function. Emerging data associate statins with a decreased risk of Alzheimer's disease; however, we report two women who experienced significant cognitive impairment temporally related to statin therapy. One woman took atorvastatin, and the other first took atorvastatin, then was rechallenged with simvastatin. Clinicians should be aware of cognitive impairment and dementia as potential adverse effects associated with statin therapy. [244]

In another study involving 283 people -- 94 in the placebo group, 96 in the 10-mg simvastatin group, and 93 in the 40-mg simvastatin group was conconducted. Compared with placebo, simvastatin was associated with minor negative changes in performance on several tests assessing attention, memory, and overall

mental efficiency. In the team's earlier trial, 20 mg of lovastatin given every day for six months produced similar changes on these same tests. [204]

A survey by the MedWatch drug surveillance system of the Food and Drug Administration (FDA) from November 1997-February 2002 for reports of statin-associated memory loss was conducted. Of the 60 patients identified who had memory loss associated with statins, 36 received simvastatin, 23 atorvastatin, and 1 pravastatin. About 50% of the patients noted cognitive adverse effects within 2 months of therapy. Fourteen (56%) of 25 patients noted improvement when the statin was discontinued. Memory loss recurred in four patients who were rechallenged with the drug. None of the 60 reported cognitive test results. Two placebo-controlled trials found no benefits for statins on cognition or disability. One randomized controlled trial of simvastatin found no effects on cerebrospinal amyloid levels. In one small, randomized study, patients receiving statins showed a trend toward lower cognitive performance than those receiving placebo. There are no available prospective studies that show cognitive or antiamyloid benefits for any statin, although some people are actually touting statins to be beneficial for the prevention of dementia. In addition, case reports raise the possibility that statins, may be associated with cognitive impairment. [245]

According to a German study, Lipitor, Pfizer's cholesterol-lowering statin drug and the best-selling drug in the world, is no more effective than similar cholesterol drugs, and in some cases may have worse side effects.

**Lipitor No Better and Often Worse**

The study, which involved a survey of previous studies from around the world, found that:

* Lipitor did not prolong the life of people with chronic coronary heart disease
* For acute diseases, Lipitor, Zocor, and Pravastin provided similar results
* Lipitor did not prolong life in people with diabetes mellitus
* Some studies on Lipitor had to be stopped because it had more side effects compared with Zocor

**The San Francisco Chronicle September 4, 2005**

**Lipitor increases the risk of stroke and Doesn't Work any Better Than Placebos**

A study found that not only do cholesterol-lowering statin drugs fail to help patients with severe diabetes, but statins may also double their risk of experiencing a deadly stroke.

The study, led by Dr. Cristoph Wanner at the University of Wurzburg, Germany, was conducted on severely ill diabetics, and tested relatively low doses of the statin drug Lipitor against dummy pills. At the end of the four-year study, the patients who took Lipitor showed virtually no difference from those who took the placebos in terms of the combined risks of heart attacks, strokes and death.

However, when fatal strokes were looked at individually, more than twice as many patients died on Lipitor (27) as died on the placebo (13).

Lipitor is currently the most commonly prescribed drug in the world. [252]

**Recent large-scale study giving statin drug Crestor to patients with CHF found a slight increase in death in that group compared to a placebo**

A randomized, double-blind, placebo-controlled trial in 326 cardiology and 31 internal medicine centers in Italy. We enrolled patients aged 18 years or older with chronic heart failure of New York Heart Association class II–IV, irrespective of cause and left ventricular ejection fraction, and randomly assigned them to rosuvastatin (Crestor) 10 mg daily (n=2285) or placebo (n=2289) by a concealed, computerized telephone randomization system. Patients were followed up for a median of 3·9 years (IQR 3·0–4·4). Primary endpoints were time to death, and time to death or admission to hospital for cardiovascular reasons. Analysis was by intention to treat. 657 (29%) patients died from any cause in the rosuvastatin

group and 644 (28%) in the placebo group (adjusted hazard ratio [HR] 1·00 [95·5% CI 0·898–1·122], p=0·943). 1305 (57%) patients in the rosuvastatin group and 1283 (56%) in the placebo group died or were admitted to hospital for cardiovascular reasons (adjusted HR 1·01 [99% CI 0·908–1·112], p=0·903). [306]

An earlier study conducted using Crestor in CHF patients found no benefit. [307]

Metoprolol, a selective $\beta_1$ receptor blocker used in treatment of several diseases of the cardiovascular system, especially hypertension, used shortly prior to non-cardiac surgery increases the risk of hypotension, stroke and death, despite reducing the risk of myocardial infarction. [308]

## To Stain or not to statin

Statins are not the only anti-atherosclerosis treatments available. Years 2–4 of the Lyon trial showed that a Mediterranean diet produced Absolute risk reduction (ARR) of CAD values greater than 4 statin trials, to date. [273, 274] Many other studies have demonstrated that the Mediterranean diet over significant protection from heart disease, and cancer, and increases substantially lifespan. [275-278]

Another recent study again confirms the cardiovascular benefits, as well as over all health enhancing attributes of the Mediterranean diet. [279] This cohort study was conducted between 1988 and 2000. Ten-year mortality from all causes, coronary heart disease, cardiovascular diseases, and cancer was assessed. The results demonstrated that during follow-up, 935 participants died: 371 from cardiovascular diseases, 233 from cancer, and 145 from other causes; for 186, the cause of death was unknown. Adhering to a Mediterranean diet (hazard ratio [HR], 0.77; 95% confidence interval [CI], 0.68-0.88), moderate alcohol use (HR, 0.78; 95% CI, 0.67-0.91), physical activity (HR, 0.63; 95% CI, 0.55-0.72), and nonsmoking (HR, 0.65; 95% CI, 0.57-0.75) were associated with a lower risk of all-cause mortality (HRs controlled for age, sex, years of education, body mass index, study, and other factors). Similar results were observed for mortality from coronary heart disease, cardiovascular diseases, and cancer. The combination of 4 low risk factors lowered the all-cause mortality rate to 0.35 (95% CI, 0.28-0.44). In total, lack of adherence to this low-risk pattern was associated with a population attributable risk of 60% of all deaths, 64% of deaths from coronary heart disease, 61% from cardiovascular diseases, and 60% from cancer. A recent meta-analysis of cohort studies shows that fruit and vegetable consumption is inversely associated with the risk of Cardiovascular disease. [292] <u>The bottom line was that among individuals aged 70 to 90 years, adherence to a Mediterranean diet and healthful lifestyle is associated with a more than 50% lower rate of all-causes and cause-specific mortality</u>. [280]

While there are likely to be some people who benefit from taking statins, it is perhaps far less than five percent of the people who currently take them. Some people (about one in 500) with impaired LDL receptors (familial hypercholesterolemia) do require these drugs and they should be on Coenzyme Q10, as this important nutrient is blocked by many cholesterol-lowering drugs. However, one in 500 people is sure a bit different than the one in 2 that are being predicted to take these drugs. **The Mediterranean diet with a basic supplemental protocol is what I recommend.** Compared to statins this diet alone is more effective, offers the most important stat, a healthy and long life, and has no side effects.

## *Assessment of Lipids:*

Total serum cholesterol doesn't correlate with cardiovascular disease in the range of 180 to 240 but certain fractions of that total cholesterol do correlate. These fractions are HDL and LDL cholesterol. HDL cholesterol carries cholesterol to the liver where it used by the body in many beneficial ways. Low HDL cholesterol is strongly associated with an increase in CHD. [160] This is why you need a Lipid Profile (also called a Lipid Panel) and not just a total cholesterol when you get your blood drawn.

1) **Lipid panel**

   1 (a) HDL/Cholesterol ratio – Optimum goal is to be under 4%

   1 (b) Total Cholesterol – Although most authorities state that the optimum goal is to be less than 200, if even 180, it is far less relevant compared to all the other risk factors.

1 (c) Triglycerides – Optimum goal is to be under 140

1 (d) Lipoprotein A - Lp (a)

1 (d) Apolipoprotein (a & b)

1 (e) LDL particle number

**Lp(a)** consists of a particle of low-density lipoprotein cholesterol (LDL-C) linked by a disulfide bond to a large hepatically derived glycoprotein, apolipoprotein(a), which is structurally similar to plasminogen. In theory, then Lp(a) could promote cardiovascular disease in two ways: it could promote thrombogenesis and atherogenesis. Levels above 30 mg/dL are generally considered elevated. [49, 50]

**Apolipoprotein A1** is the major protein component of HDL cholesterol. Reduced lipoprotein A below 140 is associated with ischemic heart disease. The goal is to be above 140.

**Apolipoprotein B** (b) is the major component of LDL cholesterol. Elevation of lipoprotein B, above 135, is an independent risk factor for the development of atherosclerosis and cardiovascular disease. Lipoprotein (b) Lp(b) is a plasma lipoprotein whose structure and composition closely resemble that of low-density lipoprotein, but with an additional molecule of apoprotein attached to apolipoprotein B by a disulfide bond. Several studies have indicated that elevated plasma levels of Lp(b) is an independent risk factor for heart disease. Lp(b) is thought to promote atherosclerosis by interfering with plasminogen. One of the mechanisms of plasminogen is to break down fibrin. The goal is to be below 135.

The ratio between Apolipoprotein A1 and Apolipoprotein B should be in the range of .66-1.91. Decreased Apo A1/Apo B ratio has been associated with increased risk for CHD.

Apolipoprotein A, consists of a large, “fluffy” protein called apoprotein A that is cardioprotective when bound to LDL. The second, apolipoprotein B, consists of a small, dense protein called apoprotein B that plays a major role in cardiovascular disease when bound to LDL. Apolipoprotein-B particles enable cholesterol to penetrate and lodge in vascular walls, an important step in initiating the formation of atherosclerotic plaque. Apo-lipoprotein B is the predominant form of apolipoprotein, and over 90% of all LDL cholesterol particles in the blood carry apolipoprotein B, making it an especially accurate (and convenient) marker for measuring the cholesterol-depositing capacity of blood.[197-200]

A recent study comparing various cardiovascular risk factors measured apolipoprotein-B levels in 1,522 individuals and compared them with an array of standard lipid markers, as well as C-reactive protein, fibrinogen, and carotid artery intima-media thickness, to assess cardiovascular disease risks. They found that elevated apolipoprotein-B levels were strongly associated with cardiovascular disease, and concluded that apolipoprotein-B levels are a better predictor of vascular risk than are LDL levels. [201]

**LDL Particle Number, Not Size, a Significant Predictor of CVD Risk**

The number, not the size, of low-density lipoprotein (LDL) cholesterol particles predicts heart disease risk, according to an analysis of blood samples from more than 3,200 participants in the Framingham Heart Offspring Study. "It's the total particle number rather than size or anything else that is important," lead investigator Ernst J. Schaefer, MD. The study analyzed frozen blood samples from 1,529 men and 1,708 women who were followed for an average of eight years to monitor the development of fatal or nonfatal myocardial infarction, stroke, claudication, and angina. During the follow-up period, 220 men and 116 women developed one or more of those conditions. The LDL particle numbers and size were analyzed using nuclear magnetic resonance spectroscopy, Dr. Schaefer explained at a press conference.

Considering just LDL factors, indicated that LDL particle size and number were significantly ($P < .001$) associated with cardiovascular event risk in both men and women, but on multivariate analysis, particle size becomes nonsignificant, Dr. Schaefer said, and only particle number was a significant predictor.

Other known risk factors such as age, smoking history, diabetes, blood pressure, and high-density lipoprotein cholesterol level were significant for both men and women in the univariate model. But in the multivariate analysis, the best risk predictor model for men was age, systolic blood pressure, diabetes, smoking, and LDL particle number. For women, multivariate analysis identified age, systolic blood pressure, smoking, and LDL particle size, but not diabetes. [296]

**Apolipoprotein E4 (Apo E4)**

Apolipoprotein E4 (Apo E4) is a new diagnostic marker used to assess one's risk for Alzheimer's disease. A positive ApoE4 increases the risk of developing Alzheimer's disease by 50 to 64%. The presence of two copies of ApoE4 may increase the probability of Alzheimer's disease to over 90%. The regulation of ApoE4 gene expression plays an important role in the development of Alzheimer's disease. The interaction of different transcription factors with the regulatory region of the ApoE gene is important to understand the neuroinflammatory process seen in Alzheimer's disease. The pathology of Alzheimer's disease is linked to tangles and plaques in the brain, and these structures are associated with beta-amyloid protein. Alzheimer's disease brain tissue contains higher levels of free radicals and oxidative damage. The ApoE was also found to be associated with oxidative damage to the brain. [51-57]

Those with a tendency for having a higher risk of ApoE include those with African or American Indian ethnic backgrounds. Those with genetic roots in northern Europe have a somewhat lower probability than the first two ethnic groups, and the probability is lower among southern Europeans. [58]

ApoE is associated with regulating the metabolic process of food regarding the storage of excess energy as fat, which is an important survival trait among certain ancestral people. ApoE acts as a cholesterol transporter in the brain and may also be a risk factor for increased transition metal (iron, mercury, zinc, etc.) and aluminum ion concentrations in the body and brain. [59, 60]

Also, individuals who carry the Apo E4 allele are more susceptible to oxidative stress and LDL oxidation. This marker helps to identify individuals at high risk for smoking-related heart disease and to focus resources in smoking cessation and potential ways of reducing the adverse effects of smoking on this group. [61]

The September 2004 issue of the American Heart Association journal *Stroke* (published the findings of Japanese researchers that higher levels of plasma glutathione (GSH) are associated with a lower incidence of cardiovascular disease, particularly cerebral small vessel disease. [175]

Another recent study found that abnormalities in intracellular GSH cycling are associated to increased lipid peroxidation in congestive heart failure. [298] Also, reduced cysteine has been found in the progression of chronic Ischemic Heart Disease to heart failure status, as an additional pro-oxidant stimulus for worsening oxidative stress. [299]

Glutathione is formed in the body from three amino acids (cysteine, glycine, and glutamic acid), and forms a part of the antioxidant enzyme glutathione peroxidase. Undenatured Whey Protein Concentrate, rich in Cysteine, raises glutathione levels. Many of the companion adaptogens such as turmeric, green tea, grape skin and seed, rosemary etc. spare glutathione and reduce oxidative damage.

There are far safer ways to decrease cardiac deaths and treat abnormal cholesterol levels without risking drug side effects. Despite this, you would be astounded how many patients would rather take a pill with potential severe side effects than consider changing their lifestyle.

Other important CVD risk markers include C reactive Protein, Homocysteine, Fibrinogen, Hemoglobin A1C, fasting insulin, DHEA sulfate, Testosterone (total & free) and Thyroid, including a total thyroid panel.

## CVD and stress

There now substantial evidence connecting stress as the number one risk factor for heart disease.

Stress causes hormones (cortisol and insulin) to be released, which further cause a prothrombotic and proatherogenic state. This increases the susceptibility for abnormal blood clotting. [65] Stress increases the likelihood of smoking and using caffeinated foods and beverages. Smoking cigarettes raises a person's heart rate an average of 14 beats per minute. This effect, when combined with stress, can cause the heart rate to increase as much as 38 beats a minute. Elevated cortisol and insulin, both of which trigger a low-grade inflammatory state, are the two main culprits causing elevated lipids and blood pressure. This is what then leads to heart disease, as well as diabetes, cancer, obesity, dementia and a host of other chronic diseases.

Cardiovascular disease can often begin with an elevation of blood pressure. Once a physician makes the diagnosis they typically proceed by prescribing a drug, or drugs, to lower the high blood pressure (HBP). These drugs, being functional, will work, either by forcing the arteries to dilate, or by causing the kidneys to urinate, or by blocking calcium, or by inhibiting vascular constriction. We should first look at the possibilities of why a condition like HBP is manifesting. Could it be insulin resistance, stress, elevated aldosterone, which causes a salt sensitivity, or peripheral atherosclerosis, whereby the narrowing of peripheral blood vessels causes pressure to be higher. Our blood pressure rises and falls during the day as physical and emotional demands change, providing adequate blood flow as needed. [62] Yet repeatedly elevated blood pressure resulting from additional allostatic load promotes the generation of atherosclerotic plaques, particularly when combined with a supply of cholesterol, lipids, and oxygen-free radicals that damage the coronary artery walls. Beta-adrenergic receptor blockers are known to inhibit this cascade of events and to slow down the atherosclerosis that is accelerated in dominant male cynomologus monkeys exposed to an unstable dominance hierarchy. [63] Thus catecholamines and the combination of glucocorticosteroids and insulin can have dangerous effects on the body besides their important short-term adaptive roles. [64]

When we determine what may be the root cause or causes of the condition, we can then work towards bringing about balance to this person in a rational, harmonious way. This approach will in turn enable a partnership to occur, that involves one's own self-healing to occur. A plan should then be developed to remove the causative factors through diet and life style modifications and the use of herbs and nutrients. When the causative factors are removed and the organ systems are enhanced, blood pressure slowly drops, as it should. Combining primary adaptogens with companion adaptogens, such as hawthorn leaf, flower and berry, will enhance and strengthen the endocrine system along with the cardiovascular system thus aiding in the prevention of cardiovascular disease. Then if BP is still elevated to move to additional herbs such as relaxing diaphoretics such as linden or yarrow, or a nervine relaxant like celery seed. If still the blood pressure is elevated you can combine stronger hypotensive herbs such as mistletoe (Viscum album) or even rauwolfia. What I typically do is compound a formulation made up of 50% primary adaptogens and companion adaptogens, along with the specific indicated herbs. I then recommend certain nutritional agents including special forms of magnesium, potassium, vitamin C, arginine, carnitine and CO Q 10. When you do integrative protocols using herbs, nutritional agents, diet and life style modifications it is amazing how effective it can be for people. The best thing of all is that they lower the blood pressure, lower their biological age and feel great. Rather than the sex life going south because of using blood pressure meds, it actually improves. This result is a byproduct of getting healthy with adaptogenic remedies and other natural healing modalities. Many adaptogens, such as Rhodiola rosea, Eleuthero, or Reishi could easily be classified as cardiovascular tonics, but the cardiovascular effects and actions are secondary to their overall adaptogenic-neuroendocrine enhancing/normalizing abilities.

In the chronically stressed individual the repair and healing systems of the body are compromised and this leads to increased damage and slower repair of injuries to the heart and body.

Along with cardiovascular problems, stress can also cause muscular, respiratory, and skin problems, sexual problems, depression, gastrointestinal and eating disorders, and chemical dependence, we refer to these conditions as Stress-Related Disorders. Stress-related Disorders can lead to illness, disease, chronic disease and even death.

It is often very difficult for the average individual to identify how much stress he or she has and to what degree it is affecting their body. If you believe that you are stress free yet you have unexplained illnesses or vague symptoms you may have hidden stress.

**Control inflammation and oxidative damage, and enhance mitochondrial energy: important keys to heart disease, cancer, and other chronic degenerative disease**

Although primary adaptogens are effective modulators of inflammation and oxidative damage it is the companion adaptogens that really excel in this area and this is one of many reasons why I believe in combining them together. The production of C-reactive protein is an essential part of the inflammatory process, and the measurement of this substance reflects the level of inflammatory activity deep within the body. It appears that certain conditions create a state of excessive inflammation within the circulatory system. High C-reactive protein levels are evidence of this type of inflammation. Elevated CRP is a critical risk factor for heart disease and maybe cancer as well. [205-207, 264]

In concert with other pro-inflammatory cytokines, interferon-gamma is the most important trigger for the formation and release of reactive oxygen species (ROS). Chronic ROS-production leads to the depletion of antioxidants like vitamin C and E and glutathione, with a consequence that oxidative stress develop. Oxidative stress plays a major role in the atherogenesis and progression of cardiovascular disease, and it may also account for the irreversible oxidation of other oxidation-sensitive substances like B-vitamins (e.g. folic acid and B12). They are essential cofactors in homocysteine-methionine metabolism. Associations between moderate hyperhomocysteinaemia and cellular immune activation are found in several diseases including coronary heart disease, and data indicate that hyperhomocysteinaemia may develop as a consequence of immune activation. Homocysteine accumulation in the blood is established as an independent risk factor for cardiovascular disease. Homocysteine itself has the capacity to further enhance oxidative stress. Interferon-gamma appears to be a central player in atherogenesis and in the development and progression of cardiovascular disease. [264]

A report published in the September 13, 2004 issue of the *Archives of Internal Medicine* described the finding of Mayo Clinic researchers that high-sensitivity C-reactive protein (hs -CRP) can be a marker for heart disease in people with no disease symptoms. [208-209]

Research on C-reactive protein indicates that cholesterol-filled plaques in blood vessels may not pose any real danger unless they are affected by inflammation. Inflammation weakens plaques, making them more vulnerable to bursting or pinching off a clot that can then block coronary vessels. [210-213]

Some members of the research community have suggested that statin drugs—the drugs of choice for cholesterol reduction—may prevent heart disease not because of their effects on cholesterol, but because they have anti-inflammatory activity. This helps to explain why statins have been found to protect the heart regardless of their effects on cholesterol levels. [214,215]

Although statin drugs do appear to lower CRP, there are many better and safer choices that are more effective and possess multiple other beneficial actions in our body in regards to cardiovascular disease and other age-related diseases as well. For example to lower CRP in people, I combine primary endocrine enhancing adaptogens with companion adaptogens such as turmeric, ginger, Indian Gooseberry, grape seed and skin extracts together with enzyme such as bromelain, nattokinase, and/or lumbrokinase and be taken between meals 2 or 3 x daily. I combine this with a multiple redox/antioxidant supplement that contains vitamin E succinate, vitamin C, as a mineral ascorbate, selenium, etc. and a Fatty acid supplement rich EPA/DHA fish oil, Sea Buckthorn oil, and Pine seed oil supplement taken with meals. Lastly, if cholesterol is also elevated I will use a small dosage of red yeast extract too. I have found supplement regime this to be extremely effective. Remember lower CRP is just important for CVD it also applies to cerebral related circulatory diseases and possible even some cancers.

The effects of extracts of Rhodiola rosea radix on blood levels of inflammatory C-reactive protein and creatinine kinase were studied in healthy untrained volunteers before and after exhausting exercise.

Rhodiola rosea extract exhibited an antiinflammatory effect and protected muscle tissue during exercise. [238]

Vitamin E's ability to protect against heart disease has also been attributed to the blood-thinning effects, but recent research has shown that it lowers C-reactive protein levels considerably. [216-210]

One of the best ways to control inflammation is to take fish oil supplements daily. Fish oil supplements should contain both DHA and EPA.

Omega-3 fatty acids incorporated into the diet have a wide spectrum of favorable effects on cardiovascular risk factors. [258] They demonstrate a reduction in platelet clumping by up to 11% and also significantly decrease triglycerides. [259]

In a study of 38 subjects with lipid disorders (between 40 and 69 years of age) who received either 3 g/day of EPA, 3 g/day of DHA or placebo in 12, 12 and 14 subjects, respectively, EPA and DHA compared with placebo increased the systemic arterial compliance and reduced pulse pressure and total vascular resistance, which may help reduce the risk of cardiovascular events. [260]

A recent study by researchers at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University and their colleagues showed that postmenopausal women who had previously been diagnosed with coronary artery disease (CAD) and who consumed more fish in their diet had a slower progression of plaque buildup in their arteries than those women who consumed little fish in their diet. This association was particularly strong for women with diabetes. [261]

**EPA and DHA from fish has profound beneficial effects on the heart and lifespan**

A recent review was conducted from Tufts-New England Medical Center that only considered studies that lasted for more than one year, and that reported or estimated omega-3 intakes and CVD outcomes. Care was taken to separate interventions using alpha-linolenic acid (ALA) from interventions using eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), or EPA plus DHA. Primary prevention of CVD was reported in one randomized clinical trial (RCT), 25 prospective studies and seven case-control studies. *Most of the large cohort studies reviewed, which involved more than 340,000 participants in total, reported significant reductions after multivariate adjustment in one or more CVD outcomes of interest.* For secondary prevention of CVD 11 clinical trials were identified, along with one prospective cohort study. These included six RCTs with supplements, and five diet and dietary advice trials. The supplement trials considered by the researchers included EPA or EPA plus DHA in doses ranging from 0.27 to 4.8 grams per day. Five of the trials were consider to be of high standard, receiving grades A or B for their methodological quality. <u>The largest reported that a 850 mg. per day supplement of EPA plus DHA was reported to reduce the risk of all-cause mortality by 21 per cent, cardiac death by 35 per cent, and sudden death by 45 per cent.</u> [262]

**Omega-3-rich fish has a beneficial effects on heart rhythms, and is protective against fatal arrhythmias**

And the new cross-sectional cohort study, lead by Darius Mozaffarian from Harvard Medical School, extends previous research on fish oil and heart health by reporting that fish consumption is linked to improved electrical properties of heart cells (electrophysiology).

The Cardiovascular Health Study (CHS) recruited 5,096 men and women between 1989-1990 (average age 73, average BMI 26 kg per sq. m) in four US communities. Dietary intake was assessed using a picture-sort version of the National Cancer Institute food frequency questionnaire (FFQ). Average consumption over one year was assessed by asking participants about intake of tuna, other fish (broiled or baked), and fried fish or fish burgers. Responses ranged from less than four portions per year to more than five portions per week. The participants also underwent heart rhythm measurements using a standardized electrocardiograph (ECG). A subset of 56 participants was selected to measure blood levels of omega-3s, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

People who ate five or more servings of tuna and/or other broiled or baked fish every week were found to have lower heart rates, averaging 3.2 beats per minute less than those who ate less than one portion per month. A higher resting heart rate, said the researchers, has been linked by other studies to an increased risk of sudden death, and so lowering the heart rate is a significant health benefit.

High intake of Omega-3 rich fish was also associated with a lower likelihood of extended ventricular repolarisation – an electrical property of the ventricle part of the heart that needs to revert back to its original electrical state before the heart beats again. Abnormalities, such as prolonged time needed to repolarise the ventricle are important factors in developing arrythmias (abnormal beating of the heart).

The researchers also report that similar findings were observed when they took into account the omega-3 blood concentrations from the subset of 56 participants.

*A one gram per day higher intake [of EPA and DHA] was associated with 2.3 beats per minute lower heart rate and 46 per cent lower likelihood of prolonged ventricular repolarisation, Thus although other mechanisms may also contribute to reductions in clinical risk, the observed differences in HR and ventricular repolarisation may, in part, account for the lower incidence of arrhythmic events seen with fish and fish oil intake.*

The mechanism behind the lower risk of prolonged repolarisation seen in this study may be the effects of the omega-3 fatty acids on the flow of sodium and calcium in the ion channels associated with electrical signals in cells. *"In experimental studies, marine omega-3 fatty acids inhibit the fast voltage-dependent sodium ion current and the L-type calcium ion current."* [263]

Antioxidant supplements help to control free radicals produced by inflammation. [221]

Low levels of DHEA have been correlated with increased C-reactive protein levels in rheumatoid arthritis (RA) patients. A low-glycemic load diet lowered C-reactive protein levels, raised DHEA levels, and improved symptom states in people with RA. Primary and many secondary Adaptogens, such as Tribulus terrestris, (15-20% Protodioscin), and Eurycoma longifolia jack, are potent endocrine enhancers that have shown to raise depressed levels of DHEA up to normal level.

Optimal **testosterone** levels are of great importance in both men and woman for every aspect of health however, I am not in any way suggesting testosterone replacement therapy, as I am not recommending any hormone replacement therapy. You can achieve healthy testosterone levels in a gentle, harmonious way with herbal and nutritional supplementation.

The newest finding about testosterone and heart disease is very exciting. It turns out that testosterone actually dilates the coronary arteries, improving blood flow to the heart. This alone could explain the earlier finding that testosterone diminishes or eliminates angina. Angina happens when the heart muscle is not getting enough oxygen from the blood. Maintaining healthy testosterone levels may in fact be an important treatment for heart disease. Testosterone also helps prevent diabetes, and may help treat diabetes.[224]

According to several recent studies, low androgen levels in men correlated with increased risk of atherosclerosis.[225, 281-290] Normalizing free testosterone levels in men improves strength and increases protein synthesis as well as muscle mass. It also has been shown to decrease body fat, and particularly visceral body fat, and increases libido. Mood is also improved with testosterone, particularly in the older population. Higher endogenous testosterone has been correlated in many studies with a reduction in a number of cardiovascular risk factors, among them; lower - blood pressure, total cholesterol (TC), LDL-cholesterol (LDL), triglycerides (TG), visceral body fat, waist-hip ratio (WHR), serum insulin, fasting and post-prandial glucose, higher HDL-cholesterol (HDL) and greater insulin sensitivity.[226]

A consistent finding in the scientific literature is that obese men have low testosterone and very high estrogen levels. Central or visceral obesity (pot belly) is recognized as a risk factor for cardiovascular disease and type II diabetes. Boosting testosterone levels decreases the abdominal fat mass, reverses glucose intolerance, and reduces lipoprotein abnormalities in the serum. Further analysis has also disclosed

a regulatory role for testosterone in counteracting visceral fat accumulation. Longitudinal epidemiological data demonstrate that relatively low testosterone levels are a risk factor for development of visceral obesity. [227, 228, 281-290]

In woman low plasma levels of SHBG are associated with CHD in women independently of insulin, obesity markers, and dyslipidemia. [291]

Because low testosterone increases one's risk of heart disease as well as obesity, diabetics and other age-related diseases supplementation with primary and many secondary adaptogens to assist naturally in enhancing testosterone levels, bringing them up to a healthy normal range. Rhaponticum carthamoides, Pantocrin, Epimedium, Tribulus terrestris and Eurycoma longifolia jack are particularly effective for helping to raise testosterone levels.

It seems the world of conventional medicine is in a predicament: The very same anti-inflammatory drugs, known as COX-2 inhibitors (proven to increase cardiovascular risks) have been found to lower lethal C-reactive protein (CRP) levels.

CRP has been discovered to be as powerful an indicator of heart disease as high cholesterol. Linked to inflammation, it is noted that the higher the level of this protein, the greater the risk of heart attacks. In fact, some researchers have suggested CRP itself might be the culprit behind heart disease.

**COX-2 inhibition - The Dilemma**

Vioxx, the COX-2 inhibitor pulled from the market due to its cardiovascular-related side effects, was found (only a month prior to its removal) to cut CRP levels in half. The drug was shown to reverse CRP levels from that of a danger zone to an exceptional level. Similarly, Celebrex, also linked to heart attacks yet still on the market, has been found to lower high levels of CRP. [223, 224]

Such contradictory properties of these drugs are merely one of the medical and ethical quandaries discovered. Although these drugs may lower dangerous CRP levels, we cannot assume that just because something lowers CRP it's a good thing, and we are constantly reminding of this the latest being Vioxx.. Thus, the standard advice for the public to achieve normal, healthy CRP levels is to:

* maintain a health weight, low fasting insulin, and anabolic to catabolic ratio,
* Eat healthy and don't smoke,
* Take botanical cardio-tonics agents that help control inflammation, reduce oxidative damage, and strengthen the vascular system,
* Maintain a healthy DHEA to Cortisol ratio - reduce stress and take adaptogenic formulas on a regular basis. Rhodiola extract has demonstrated an ability to reduce CRP.

**Homocysteine and Cardiovascular Disease**

Homocysteine is created when the body uses the amino acid, methionine, for methylation. Methylation is an important reaction in the body, which leaves homocysteine as a by-product. Normally homocysteine is converted back to methionine, or used to create cysteine and other useful substances. If these conversions are blocked, however, homocysteine accumulates which can lead to a host of negative reactions. Abnormal metabolism and elevated blood levels of homocysteine is a condition that is highly toxic to both cellular and fibroelastic components of the vascular wall. [229] Homocysteine can damage blood vessels and nerves, and has been linked to heart attacks, strokes, cancer (particular colon, breast, and prostate), Alzheimer's disease and other neurological diseases, depression, birth defects, gout, cervical dysplasia, erectile dysfunction, and rheumatoid arthritis.

Homocysteine damages mitochondrial, which causes cellular damage. [230] Homocysteine interferes with nitric oxide, a substance that relaxes blood vessels. However, this phenomenon may only happen in older people. Research has recently shown that while homocysteine impairs blood flow in people who are 50-70 years old, it doesn't typically in people 21-40 years old. [231]

Efficient conversion of homocysteine requires certain nutrients. These nutrients neutralize homocysteine's toxicity by transforming it into useful substances. The most well-studied of the nutrients are folic acid, vitamin B12 and vitamin B6. Choline, betaine (TMG), creatine, riboflavin, zinc, magnesium and other nutrients also help detoxify homocysteine. Folate deficiency is one of the most common deficiencies associated with homocysteine in Western populations. Studies show that folate supplements (1-5 mg/day) have a significant impact on reducing homocysteine levels. Increasing your intake of fruits and vegetables, which has numerous other benefits, and/or supplementing the B vitamins can help convert homocysteine to other amino acids that are not harmful. Homocysteine levels can rise when people eat a diet heavy in animal protein and/or few fruits or leafy vegetables. Folate is found mostly in vegetables and legumes. This would suggest that people on vegetarian diets would have higher folate and lower homocysteine. This is in fact the case. One recent study shows that a supervised vegan diet (no animal products whatsoever, and excluding tobacco, alcohol and caffeine) lowers homocysteine 13% in one week without supplements. [232]

I have had tremendous success in reducing homocysteine levels to the optimal range of under 9 by implementing these nutrients into client protocols.

In a study of 30 men and 27 women (mean age 61.2 years) with elevated homocysteine of at least 20 umol/l and atherosclerotic disease, 2 months of folic acid treatment at 10 mg/day resulted in a significant decrease in total homocysteine, fibrinogen and malonyldialdehyde, with an increase in parameters suggesting an improvement of hypercoagulation, oxidative stress and endothelial dysfunction. [233]

A study conducted in India demonstrated that low intakes of folic acid and vitamin B12, and hyperhomocysteinemia, in both the healthy population living in urban slums and adjacent urban non-slum areas, are important observations for the prevention of nutritional and cardiovascular diseases. [234]

When cholesterol is elevated, usually so is homocysteine. And homocysteine promotes the oxidation of low density lipoprotein (LDL) cholesterol—a phenomenon associated with heart disease. Iron enhances this oxidation, which can be prevented by vitamin E. It apparently takes a fair amount, however. In one study, vitamin E had to be increased three times normal to prevent homocysteine from oxidizing LDL in the presence of iron. [235]

For quite some time an association between homocysteine and cardiovascular disease has been recognized To investigate the causal role of homocysteine in cardiovascular disease, Dr. Wald from Southampton General Hospital, UK, and colleagues performed a meta-analysis of 72 studies in which the prevalence of a mutation in the methylenetetrahydrofolate reductase (MTHFR) gene was determined in 16,849 cases and controls. They also analyzed 20 prospective studies, which included 3820 subjects and measured the relationship between homocysteine and disease risk. Dr. Wald's team found a significant association between homocysteine and the risk for ischemic heart disease, deep vein thrombosis and stroke. A 5-mol/L increase in homocysteine was associated with an increased risk of ischemic heart disease in both the genetic studies (odds ratio 1.42) and in the prospective studies (odds ratio 1.32). The same association was seen for deep vein thrombosis with and without pulmonary embolism (odds ratio in genetic studies 1.60; there were no prospective studies), and for stroke (odds ratio 1.65 in the genetic studies and 1.59 in the prospective studies), the researchers report. The results of this study strengthen the evidence that a raised serum homocysteine concentration is a cause of cardiovascular disease. By lowering homocysteine concentrations by 3 mol/L from current levels (achievable by increasing folic acid intake) you would reduce the risk of ischemic heart disease by [an average of] 16%, deep vein thrombosis by 25% and stroke by 24%." [236]

Stroke is the third most common cause of death in developed countries. There are 125,000 cases of stroke in the UK each year and 60,000 deaths.

Observational studies measuring homocysteine concentrations in healthy individuals have found that, on average, those with high levels of homocysteine in their blood are more likely to have a stroke. But other factors that increase homocysteine concentration and stroke risk— such as smoking and socioeconomic class—may be responsible for the relationship observed in these studies, confounding the result.

Writing in the 15 January issue of *The Lancet* (365: 217-23), Aroon Hingorani from the University College London and colleagues describe an approach known as Mendelian randomisation used to overcome some of the problems of confounding factors seen in observational studies.

The investigators analyzed published data on the association between stroke and common variation in a gene called MTHFR, which is known to influence homocysteine concentration. People randomly inherit variant (TT) of the gene, which gives them a higher concentration of blood homocysteine, or variant (CC), which results in lower levels of the amino acid in their blood.

The authors compared risk estimates from observational studies of homocysteine and stroke with those obtained from genetic studies of MTHFR and stroke. They found individuals who carried the TT genotype of MTHFR had, on average, both a higher concentration of homocysteine, and a small increase in the risk of stroke. The effect of the variant on stroke risk was close to that expected from its effect on homocysteine concentration.

*"Because of the random allocation of the gene variant in advance of disease development this concordance of risk estimates implies that the relation between homocysteine and stroke seen in observational studies is not substantially confounded by other factors,"* said Dr Hingorani.

*"Our study therefore provides evidence for a role of homocysteine in the development of stroke, though it must be emphasized that a systematic review of published studies such as this might be affected to some degree by reporting bias,"* he added. [237]

## ADMA (Asymmetric Dimethylarginine)

### Description

Asymmetric dimethylarginine (ADMA) is the principal endo-genous inhibitor of nitric oxide synthetase. Thus it regulates rates of nitric oxide (NO) formation. Nitric oxide acts as a signal molecule in the nervous system, as a weapon against infections, as a regulator of blood pressure, and as a gate keeper of blood flow to the organs. Elevated ADMA is a risk factor for hypertension, cardiovascular disease, renal failure, and erectile dysfunction. Two factors that contribute to elevated ADMA are increased oxidative challenge and folic acid insufficiency. ADMA activates homocysteine which induces endothelial dysfunction. IN a recent study high-dose antioxidant treatment prevented methionine-induced elevation of oxidized LDL and interleukin 6 but failed to prevent the increase in ADMA or endothelial dysfunction. [293]

### L-Arginine lowers ADMA

There is abundant evidence that the endothelium plays a crucial role in the maintenance of vascular tone and structure. One of the major endothelium-derived vasoactive mediators is nitric oxide (NO), an endogenous messenger molecule formed in healthy vascular endothelium from the amino acid precursor L-arginine. Endothelial dysfunction is caused by various cardiovascular risk factors, metabolic diseases, and systemic or local inflammation. One mechanism that explains the occurrence of endothelial dysfunction is the presence of elevated blood levels of asymmetric dimethylarginine (ADMA) - an L-arginine analogue that inhibits NO formation and thereby can impair vascular function. Supplementation with L-arginine has been shown to restore vascular function and to improve the clinical symptoms of various diseases associated with vascular dysfunction. [240]

### Testosterone: important to nitric oxide production/regulation

Our aim was to investigate whether plasma l-arginine and asymmetric dimethylarginine (ADMA) concentrations and nitric oxide (NO) production are altered in male idiopathic hypogonadotropic hypogonadism (IHH) patients in the hypogonadal state and after single dose testosterone administration compared with those in control subjects. Eighteen newly diagnosed male patients with IHH and 20 healthy volunteer controls matched by age and body mass index were enrolled in the study. Single dose

testosterone was administrated im. Initially, pretreatment blood samples were collected after overnight fasting. Posttreatment blood samples were drawn 10 d after the injection. ADMA, l-arginine, and NO were measured in pre- and posttreatment blood samples. The pretreatment ADMA and l-arginine levels were significantly higher, and plasma nitrite plus nitrate (NOx) levels were lower than those in the control group. After 10 d of treatment, ADMA and l-arginine levels were significantly reduced, and NOx levels were significantly increased. There was a significant positive correlation (P < 0.01) between ADMA and l-arginine and a negative correlation between ADMA and NOx levels in patients and controls. In conclusion, the patients with IHH showed elevated plasma ADMA levels associated with a reduction in NO production. Single dose parenteral T administration lowered ADMA concentrations and increased NO production to the control group values. [241]

**Low testosterone and high estrogen associated with progressive heart disease in men**

Estrogen treatment of men with prostate cancer is associated with increased cardiovascular morbidity and mortality; however, the role of endogenous estrogen levels for atherosclerotic disease in men is unknown. Objective: To determine whether endogenous serum estradiol levels predict the progression of carotid artery intima-media thickness in men. Design, Setting and Participants: Population-based, prospective cohort study (the Atherosclerosis and Insulin Resistance (AIR) study) conducted in Goteborg, Sweden among 313 Caucasian men without cardiovascular or other clinically overt diseases. Carotid artery intima-media thickness, an index of preclinical atherosclerosis, was measured by ultrasound at baseline (58 yr of age) and after 3 yr of follow-up. Serum sex hormone levels and cardiovascular risk factors (body-mass index, waist-to-hip ratio, systolic blood pressure, serum triglycerides, plasma c-peptide and smoking status) were assessed at study entry. Intervention: -- Main Outcome Measures: Association between baseline total and free estradiol levels and progression of carotid intima-media thickness over 3 yr with adjustments for cardiovascular risk factors. Results: In univariate analyses, both total and free estradiol levels at baseline were positively associated with the annual change in intima-media thickness. In linear regression models including estradiol and cardiovascular risk factors, LDL and HDL cholesterol and estradiol were identified as independent predictors of progression of carotid artery intima-media thickness (total estradiol beta=0.187, P = 0.001 and free estradiol beta=0.183, P = 0.003). Conclusions: Circulating estradiol is a predictor of progression of carotid artery intima-media thickness in middle-aged men. Further studies are needed to investigate the role of endogenous estradiol for incident cardiovascular disease events. [266]

The burden of atherosclerosis especially afflicts the increasing older segment of the population. Recent evidence has emphasized a protective role of endogenous sex hormones in the development of atherosclerosis in aging men. METHODS AND RESULTS: We studied the association between endogenous sex hormones and progression of atherosclerosis in 195 independently living elderly men. Participants underwent measurements of carotid intima-media thickness (IMT) at baseline in 1996 and again in 2000. At baseline, serum concentrations of testosterone (total and free) and estradiol (total and free E2) were measured. Serum free testosterone concentrations were inversely related to the mean progression of IMT of the common carotid artery after adjustment for age (beta=-3.57; 95% CI, -6.34 to -0.80). Higher serum total and free E2 levels were related to progression of IMT of the common carotid artery after adjustment for age (beta=0.38; 95% CI, -0.11 to 0.86; and beta=0.018; 95% CI, -0.002 to 0.038, respectively). These associations were independent of body mass index, waist-to-hip ratio, presence of hypertension and diabetes, smoking, and serum cholesterol levels CONCLUSIONS: Low free testosterone levels were related to IMT of the common carotid artery in elderly men independently of cardiovascular risk factors. [267]

Circulating testosterone levels (T) decrease with age in men. Low T has been associated with coronary disease and with risk factors for atherosclerosis. This study examines the relationship in men between androgenic hormones and arterial stiffness, a major risk factor for cardiovascular events. T, sex hormone-binding globulin (SHBG), and dehydroepiandrosterone sulfate (DHEAS) were measured longitudinally over 33 yr (follow-up 11.8 +/- 8.3 yr) in 901 men from the Baltimore Longitudinal Study of Aging, of whom 206 (68.1 +/- 13.7 yr) underwent carotid duplex ultrasonography. The 901 men were used to characterize age-associated hormone levels by means of mixed-effects models. Hormone values were estimated for the 206 men at the time of ultrasonography. Free T index (FTI) was calculated by dividing T by SHBG. The arterial stiffness index was calculated from peak systolic and end diastolic diameters of the

common carotid artery and simultaneous brachial artery blood pressure. T, FTI, and DHEAS were correlated negatively with age, pulse pressure (PP), and stiffness index (each P < 0.01), whereas SHBG was correlated positively with age and stiffness index (P < 0.01). However, T was the only hormone that predicted the stiffness index after adjustment for age, PP, fasting plasma glucose, body mass index, and total cholesterol. T values 5-10 yr before the carotid study also predicted the stiffness index (P < 0.05). Thus the adverse influence of low T on the cardiovascular system in men may be mediated in part via the effects of T on vascular structure and function. [268]

Historically, high androgen levels have been linked with an increased risk for coronary artery disease (CAD). However, more recent data suggest that low androgen levels are associated with adverse cardiovascular risk factors, including an atherogenic lipid profile, obesity and insulin resistance. The aim of the present study was to evaluate the relationship between plasma sex hormone levels and presence and degree of CAD in patients undergoing coronary angiography and in matched controls. We evaluated 129 consecutive male patients (mean age 58+/-4 years, range 43-72 years) referred for diagnostic coronary angiography because of symptoms suggestive of CAD, but without acute coronary syndromes or prior diagnosis of hypogonadism. Patients were matched with healthy volunteers. Out of 129 patients, 119 had proven CAD; in particular, 32 of them had one, 63 had two and 24 had three vessel disease, respectively. Patients had significantly lower levels of testosterone than controls (9.8+/-6.5 and 13.5+/-5.4 nmol/l, P<0.01) and higher levels of gonadotrophin (12.0+/-1.5 vs 6.6+/-1.9 IU/l and 7.9+/-2.1 vs 4.4+/-1.4, P<0.01 for follicle-stimulating hormone and luteinizing hormone, respectively). Also, both bioavailable testosterone and plasma oestradiol levels were lower in patients as compared to controls (0.84+/-0.45 vs 1.19+/-0.74 nmol/l, P<0.01 and 10.7+/-1.4 vs 13.3+/-3.5 pg/ml, P<0.05). Hormone levels were compared in cases with one, two or three vessel disease showing significant differences associated with increasing severity of coronary disease. An inverse relationship between the degree of CAD and plasma testosterone levels was found (r=-0.52, P<0.01). In conclusion, patients with CAD have lower testosterone and oestradiol levels than healthy controls. These changes are inversely correlated to the degree of CAD, suggesting that low plasma testosterone may be involved with the increased risk of CAD in men.International Journal of Impotence Research advance online publication, 31 August 2006; doi:10.1038/sj.ijir.3901504. [269]

**Primary Markers:**

| II. MAINTAIN OR ENHANCE CELLULAR HEALTH | |
|---|---|
| 1) **Mitochondrial efficiency:**<br>**Oxygen**<br>**Carbohydrate**<br>**Lipid** | Energy transfer (ATP, cellular respiration)- CO Q 10, magnesium creatine, magnesium glycol glutamine, carnitine, alpha lipoic acid, PAK, and primary adaptogens. (also check endocrine status) |
| 2) **Redox / antioxidant balance** | Reduce the production of free radical damage and even more importantly improve free radical scavenging capability – glutathione enhancement etc. Adaptogens, companion adaptogens, carotenoids, lipoic acid, carnosine, vitamin C, E, tocotrinols, and A, selenium etc. |
| 3) **Methylation** | Homocysteine – Folic acid, B-12, B-6, Choline (as AGPC), Betaine etc. |
| 4) **Control inflammation** (inflammation is involved in all degenerative diseases including cancer, heart disease, and dementia) | C-reactive Protein (CRP) – Companion adaptogens, enzymes such as bromelian, red yeast rice etc. |
| 5) **Maintain healthy lipid metabolism** | HDL / LDL ratio, triglycerides, lipoprotein A, apolipids a & b, and E[4] |
| 6) **Normalize blood viscosity** | Fibrinogen, D-Dimer – Adaptogens, companion adaptogens, vitamin E, enzymes (lumbrokinase, nattokinase, and bromelian) |
| 7) **Normalize blood flow** | Asymmetric dimethylarginine (ADMA) – folic acid, L-Arginine, normalize testosterone |
| 8) **Immune status** | T-Helper Cell 1 (TH1) & T-Helper Cell 2 (TH2) |
| **I. MAINTAIN OR ENHANCE ENDOCRINE/HORMONE BALANCE** | |
| (1) **Anabolic vs. Catabolic activity** | HPAA status: DHEA – cortisol balance, creatine kinase, creatine clearance - urine |
| (2) **Insulin/Glucose Metabolism** | Hemoglobin A1C, fasting glucose & insulin levels; *Reduce glycation, inhibit advanced glycation end products (AGE), Leptin (a related hormone of significance) |
| (3) **Thyroid** | TSH, T-4 (free & total), T-3 (free, total & reverse), Basal Metabolic Rate |
| (4) **Testosterone** | Free and total Testosterone, SHBG, DHT, Prolactin, estrogen. |
| (5) **Human Growth Hormone** | Insulin like growth factor – I (IGF-I) |
| (6) **Body Composition** | Body Mass Index (BMI) |
| (7) **Pineal Gland** | Melatonin |

**Three basic objectives from the Physiomedical System for treatment of Vascular Disease:**

1. To treat the cause or causes of the disease and remove – elevated insulin/cortisol, inflammation, hyperlipidemia, elevated homocysteine etc.
2. To equalize blood flow, regulate peripheral capillary blood flow and regulate the arterial-venus system.
3. To revitalize the exhausted organs (adrenal/kidney-liver-heart etc) and tissues using vitalizing-tonic herbs and adaptogens. For 'deficient-types' bringing up the persons vitality; or to assist in reduce over active organ; and for the sympathetic dominate 'excess-types' toning done organs and tissues through nervine-tonic herbs. In TCM adrenal function is referred to as kidney function. Deficiency-types are yin-dominate, yang deficient, and excessive types are yin-deficient, yang-dominant. Remember the whole idea is to gently balance and restore normal function.

   Because stress is the # 1 cause of CHD building up the neuroendocrine system (the HPAA) and adaptive energy should be the foundation of any long-term wholistic protocol.

**A wholistic approach to elevated lipids and heart disease prevention**

**1) Fatty acids shown to improve lipids and lower the risk of heart disease: EPA/DHA & GLA from Omega-3 Fish/Marine Oils, Pine seed oil, carotenoids-rich Siberian Sea Buckthorn oil, and olive oil.**

Omega-3 fatty acids have been associated with numerous health benefits, from brain development and preventing memory loss to suppressing tumors and cutting heart disease. EPA/DHA: Decrease triglycerides, VLDL cholesterol, and raise HDL modestly. Has additive effect with statins — no interference. Researchers found that omega-3 oils stop the build up of fatty deposits in the arteries, which is why oily fish and fish oils protect against heart disease and stroke.

The overall cardiovascular beneficial effects of EPA/DHA omega-3 fatty acids include anti-inflammatory, anti-thrombotic, lipid-modulatory and immunomodulatory actions due somewhat to its role in eicosanoid physiology and biochemistry. EPA and DHA have both similar and dissimilar physiologic roles. EPA appears to be more important in those roles where the eicosanoids are involved, whereas DHA seems to play its most important roles in the membranes of CNS cells. EPA is the precursor to series-3 prostaglandins (PG), the series-5 leukotrienes (LT) and the series-3 thromboxanes (TX). Specifically, EPA is the precursor of TXA3, and LTB5, eicosanoids, which reduce platelet aggregation and increase vasodilation. This could account in part for those fish oil effects that may lead to a reduced clotting activity and decreased blood pressure.

The lack of Omega-3 in our diets may be one of the primary reasons behind many of the diseases Americans face, and our shorter lifespan in relation to many other "first world" countries such as Japan or Greece. Overall, fish consumption seems to be beneficial, and a systematic review of 11 prospective cohort studies concluded that fish intake notably reduced mortality due to coronary heart disease in populations at increased risk. [66]

The outcome of a trial, conducted by researchers in Italy on 11,323 patients, showed that one gram daily of EPA as a fish oil supplement taken for three months reduced the risk of sudden cardiac death from arrhythmia by one half compared to those who received a placebo. [67]

Women with diabetes, who are at an especially high risk of cardiovascular disease, can benefit from a diet rich in fish, according to research. The study found that the more fish these women ate, the less likely they were to develop heart disease over a 16-year period. In the study, women who ate fish at least five times per week showed the largest reduction in risk; they were 64 percent less likely to develop heart disease compared to women who rarely ate fish. [68]

When adjustments are insufficient to achieve desirable results, the combined treatment with statins and Omega-3 fatty acids is an efficient treatment alternative for the prevention of heart disease. The mechanisms involved are only partly explained, however, the synergistic effects of statins and omega-3 fatty acids significantly reduce the risk for coronary heart disease (CHD) in patients with dyslipidemia. [69]

EPA-DHA rich fish oil also has mood-stabilizing properties when used in the treatment of bipolar disorder could potentially help control seizures. [70]

**Siberian Sea Buckthorn (Hippohae rhamnoides)**
Sea Buckthorn oil is used to promote the healing of skin problems, such as burns, sunburns, eczema, psoriasis and conditions of mucous membranes of the gastro-intestinal tract - anti-ulcer. It possess radiation protective and cardiovascular enhancing actions: Antioxidative - inhibition of oxidation of LDL; Lipid modulation - inhibition of HMG CO-enzyme A reductase. Siberian Sea Buckthorn Concentrate to fish oil acts to protect against the oxidative stress that can be potentially induced by taking fish oil. The carotenoid mixture also enhanced the plasma triglyceride-lowering effect of the fish oil. Siberian Sea Buckthorn oil Concentrate is the richest source of fat-soluble carotenoids, including β-carotene 997 mg/L, Lycopene 689 mg/L, Astaxanthin 56 mg/L, Lutein 56 mg/L, α-carotene 344 mg/L, and many other

carotenoids 2111 mg/L. Sea Buckthorn possesses adaptogenic actions normalizing the neuroendocrine hormonal system when under stress. [71-75]

**Siberian Pine Oil (Oleum Pini sibiricae)**
Siberian Pine Seed oil is rich in gamma linolenic acid (GLA) 20% (approximately 2 1/2 times that of Evening Primrose oil), and alpha linolenic 20%; monounsaturated fatty acids as oleic acid 20%, saturated fat 6-7 percent make up respectively of total fat in cedar seeds. Other lipid fractions contain phospholipids,1.3-1.7%. Omega 3 essential fatty acids contained in Siberian Pine oil have a very unique chemical structure including two Delta5 unsaturated polymethylene interrupted fatty acids (all cis-5, 9, 12-18:3 and all cis-5, 11,14-20:3 acids) one of which resembles eicosapentaenoic acid (EPA) found in fish oil. [76]

Siberian Pine seed oil vitamin E content is about five times higher than that of olive and peanut oils, three times higher than almonds and one and half times higher than walnut oil. Siberian Pine oil is also a good source of iodine, which is important for the health of the thyroid gland (production of T-4). [77, 78]

A recent animal study demonstrated that Siberian pine-seed oil consumption lowers overall cholesterol, while increasing HDL and apolipoprotein (Apo) A-I levels, the beneficial forms of cholesterol. [79] In another study Siberian Pine seed oil was found to lower VLDL and LDL cholesterol. [80] Siberian Pine seed oil also has a triglyceride-lowering effect in rats, an effect that is due to a reduction in circulating VLDL. [81]

**Olive oil**
The high intake of olive oil in the Mediterranean diet is associated with a low incidence of coronary heart disease. Replacing saturated fat with olive oil (rich in oleic acid) leads to a reduction in LDL cholesterol without decreasing the concentration of HDL cholesterol. [82]

Extra virgin olive oil is also rich in a number of phenolic compounds, which together have excellent oxidative stabilizing ability. Hydroxytyrosol, found in olive oil, is the newest phenolic compound to be gaining popularity as an antioxidant. Hydroxytyrsol can donate to free radicals repeatedly, thereby neutralizing their potential harmful effects. Another factor is that hydroxytrosol is able to chelate metal ions, which are themself pro-oxidant agents. Hydroytrosol has been shown to be a highly effective scavenger of free radicals. Both hydroxytrosol and oleuropein protect not only against LDL oxidation but also are capable of sparing vitamin E from over oxidation. [83]

**Effective Herbal Alternatives to Statin drugs:**

Twenty-five randomized clinical trials involving 11 herbal medicinal products were identified. Guggul (Commiphora mukul), red yeast rice, artichoke (Cynara scolymus) and fenugreek (Trigonella foenum-graecum), have been most extensively studied and have demonstrated reductions in total serum cholesterol levels of between10% and 33%. [84]

A recent study was conducted that compared the lipid-lowering effects of an alternative regimen (lifestyle changes, red yeast rice, and fish oil) with a standard dose of a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (statin). This randomized trial enrolled 74 patients with hypercholesterolemia who met Adult Treatment Panel III criteria for primary prevention using statin therapy. All participants were randomized to an alternative treatment group (AG) or to receive simvastatin (40 mg/d) in this open-label trial conducted between April 1, 2006, and June 30, 2006. The alternative treatment included therapeutic lifestyle changes, ingestion of red yeast rice, and fish oil supplements for 12 weeks. The simvastatin group received medication and traditional counseling. The primary outcome measure was the percentage change in low-density lipoprotein cholesterol (LDL-C). Secondary measures were changes in other lipoproteins and weight loss. There was a statistically significant reduction in LDL-C levels in both the AG (-42.4%+/-15%) (P<.001) and the simvastatin group (-39.6%+/-20%) (P<.001). No significant differences were noted between groups. The AG also demonstrated significant reductions in triglycerides (-29% vs -9.3%; 95% confidence interval, -61 to -11.7; P=.003) and weight (-5.5% vs -0.4%; 95% confidence interval, -5.5 to -3.4; P<.001) compared with the simvastatin group. Lifestyle changes combined with ingestion of red yeast rice and fish oil reduced LDL-C in proportions similar to standard therapy with simvastatin. Pending

confirmation in larger trials, this multifactorial, alternative approach to lipid lowering has promise for a subset of patients unwilling or unable to take statins. [310]

**Guggul (*Commiphora mukul*)**
Guggul extract is derived from the mukul myrrh tree that grows in India. Guggul exerts effective lipid-lowering activity, lowering both cholesterol and triglyceride levels. Guggul lowers VLDL and LDL cholesterol while at the same time elevating HDL cholesterol, protection against heart disease due to atherosclerosis. Guggul contains a group of compounds known as *guggulsterones* that account for the lipid-lowering action of the extracts. Z-guggulsterone and E-guggulsterone are believed to be the most active guggulsterone-components in guggul responsible for lipid-lowering effects. It is believed Guggul, works by two distinctive mechanisms: 1) improving the liver's ability to process, metabolize and excrete cholesterol, in particular LDL cholesterol; 2) by improving thyroid function by increasing T-4 to T-3 conversion. Guggul is traditionally used for arthritis and its anti-inflammatory activity has been confirmed. It also aids in weight loss because of this effect and may also be effective in cystic acne. Guggul extract decreases LDL and triglycerides by about 12%. Guggul works much better in combination with niacin, plant sterols, red yeast and other lipid lowering agents. Guggul has also shown to decrease platelet adhesiveness, and increase fibrinolytic activity. It has shown not only an ability to prevent atherosclerosis, but also has helped regress pre-existing atheroscleric plague in animal studies. [85,86]

**Red Yeast Rice extract**
Red yeast rice is a fermented rice product that has been used in Chinese cuisine as a medicinal food to promote "blood circulation" for centuries. Chinese medicine, red yeast rice is used to promote blood circulation, soothe upset stomach, and invigorate the function of the spleen, a body organ that destroys old blood cells and filters foreign substances. In addition, this dietary supplement has been used traditionally for bruised muscles, hangovers, indigestion, and colic in infants. Red yeast rice lowers lipids by acting as an HMG-Co A reductase inhibitor. The HMG-CoA reducatse activity of the food comes from a family of naturally occurring substances called monacolins. Monacolin K is also known as mevinolin or lovastatin, which is a common statin drug used to lower cholesterol. Red yeast contains at least nine monacolins as well as many other important substances that contribute to its lipid lowering effects, including sterols (beta-sitosterol, campesterol, stigmasterol, sapogenin), isoflavones, and mono-unsaturated fats. The amount of lovastatin found in red yeast rice is approximately .2-3% percent of the total product. Initial phase II clinical trials are highly encouraging. This herb is likely to be able to directly impact the process of atherosclerosis. New evidence shows that red yeast rice lowers cholesterol levels (2-3 grams per day dosage) compared to statin drugs, but with the added advantage of causing adverse effects. [87,88] Red yeast rice extract, similar to guggul, works better in combination with other natural agents such as artichoke extract, turmeric, ginger, chromium, and fenugreek.

**Artichoke (*Cynara scolymus*)**
Traditional medicine has long used artichoke extracts as a heptoprotectant, and several bioactives in artichoke extract have been identified, including chlorogenic acid, cynarin, caffeic acid, and luteolin. Consumption of encapsulated artichoke extract has been shown to result in absorption of these bioactives in humans, resulting in the production of beneficial metabolites such as ferulic acid. Ferulic acid, chlorogenic acid and cynarin provide strong antioxidant protection, which may account for some of their health-promoting activities. Moreover, in cultured liver cells, artichoke extract not only provided antioxidant protection from a toxic chemically induced insult, but also showed diminished loss of cellular glutathione reserves. [89] A recent German clinical trial found that artichoke leaf extract (ALE) significantly reduced levels of 'bad' cholesterol in people with high cholesterol. [90]

Researchers at the University of Reading have found that an over-the-counter Artichoke Leaf Extract (ALE) from the globe artichoke plant can lower cholesterol in otherwise healthy individuals with moderately raised levels. Cardiovascular diseases are the chief causes of death in the UK, and are associated with raised circulating levels of total cholesterol in the plasma. Once plasma cholesterol reaches a certain level, drugs such as statins are often prescribed to help reduce it. Intervention before concentrations reaches these levels may help reduce the risk of developing cardiovascular diseases without the need for drugs. This new piece of research has shown that otherwise healthy people with moderately raised plasma cholesterol may be able to lower their levels by taking this herbal supplement.

During the trial, 75 volunteers were given 1280mg (4 capsules) of an ALE, or matched placebo, each day for 12 weeks. ALE consumption resulted in a modest but favorable statistically significant reduction in total plasma cholesterol after the intervention period. For over 10 years, the relationship between dietary intakes of antioxidant nutrients and a reduced risk of cardiovascular diseases has been recognized and investigated. Antioxidant nutrients include 'non-essential' phytochemicals (e.g. flavonoids) as well as 'essential' nutrients (e.g. vitamins C, E). Several plant-rich sources of flavonoids, such as fruits and vegetables, tea, red wine, cocoa and olive oil, have been associated with lower risk of cardiovascular diseases, although the exact mechanisms for their protective effects is still not clear. Research has shown that ALEs are rich in various flavonoids. Globe artichokes have been used traditionally in Europe to improve digestive and urinary tract health. Artichoke leaf extracts (ALEs) are currently used in Germany and Switzerland as a remedy for indigestion, and are available in the UK as over-the-counter food supplements. Various studies have provided an evidence base for their use in conditions such as dyspepsia and irritable bowel syndrome. Dr Rafe Bundy said "Reducing cholesterol levels can reduce the risk of developing cardiovascular disease. Our research investigated whether ALE could be beneficial to otherwise healthy people who had raised levels of cholesterol but were not yet at a stage where they needed standard medical intervention. ALE may provide another option which people could try over and above a healthy diet in order to help lower plasma cholesterol." [305]

**Fenugreek seed (*Trigonella foenum graecum*)**
Fenugreek is used in Traditional Chinese Medicine to warm the Kidney energy and disperse dampness and cold, and to alleviate pain. In India, fenugreek has traditionally been used for diabetes. Modern research has confirmed an anti-diabetic effect from its use. Fenugreek has a long history as a galactigauge, increasing lactation in nursing mothers, and also been used to sooth the mucous membranes of the sinuses, lungs, and digestive tract. Externally, fenugreek is used as a soothing drawing agent.

Fenugreek seed has shown to reduce fasting and post-prandiols of glucose, glucagon, somatostatin, insulin, total cholesterol, and triglycerides, and increase HDL-cholesterol. Use of fenugreek seeds, or seed extracts improves glycemic control and decreases insulin resistance in type-2 diabetics. There is also favorable effect on hypertriglyceridemia. Fenugreek contains a compound, *Protodioscin,* that possess anabolic, anti-cancer actions. [91-93]

**Green tea (*Camellia sinensis*)**
In a Japanese study green tea consumption was significantly associated with lower levels of serum total cholesterol in both men and women while its associations with serum triglycerides and HDL cholesterol were not statistically significant. Based upon results of recent research, it is proposed that Green tea polyphenols have the inherent capacity to inhibit the development of atherosclerotic lesions.

The inverse association of serum total cholesterol with green tea consumption appeared to level off at the consumption of more than 10 cups/day. After adjustment for selected dietary factors, one cup of green tea per day was associated with a reduction in serum total cholesterol by 0.010 mmol/L (0.001 to 0.019, $p = 0.03$) in men and 0.012 mmol/L (0.001 to 0.022, $p = 0.03$) in women.

The oxidative alterations of LDL were prevented by green tea catechins. Research demonstrates that green tea guards against cardiovascular disease in many ways. Green tea lowers total cholesterol levels and improves the cholesterol profile (the ratio of LDL cholesterol to HDL cholesterol), reduces platelet aggregation, and lowers blood pressure. [94-99]

**Green tea lowers cholesterol**
Green tea extracts enriched in catechins decrease plasma cholesterol in hamsters, mice and rats. In this study four groups of six New Zealand White rabbits were initially made hypercholesterolaemic by feeding a 0.25% (w/w) cholesterol diet for 2 weeks before the diet was supplemented with a catechin extract from green tea at 0, 0.5, 1 or 2% (w/w) for 4 weeks. Administration of the crude catechin extract from green tea significantly ($p<0.05$) lowered cholesterol in plasma (-60%), VLDL+IDL (-70%), LDL (-80%), liver (total by -25% and unesterified by -15%) and aorta (-25%) compared to control. There was a significant reduction in the cholesterol synthesis index (-60%) and a significant increase in hepatic LDL receptor activity (+80%) and protein (+70%) but there was no change in the intrinsic capacity to absorb cholesterol

from the intestines. These results suggest that green tea catechins lowered plasma, liver and aortic cholesterol in the cholesterol-fed rabbit by lowering cholesterol synthesis and upregulating the hepatic LDL receptor. [265]

**Policosanol**
Policosanol is a natural occurring component found in the wax of the common honeybee and found in whole sugar cane with unique cholesterol lowering ability with a different mechanism other than the inhibition of HMG Co enzyme A reductase. Policosanol is composed of combination of aliphatic long chain fatty alcohols including octacosanol, which seemingly appears to make it much more effective than octacosanol alone. Octacosanol has shown to increase endurance and oxygen utilization during exercise.

Policosanol derived from whole sugar cane contains substantially more octacosanol (about 60%) than from honeybee wax, and it is the form of policosanol used in all the clinical trials so I would recommend it over other forms.

Policosanol has undergone many clinical trials, confirming its cholesterol lowering effects. It has shown equal benefits to statin drugs. It also has shown little to no side effects. Policosanol significantly lowers total cholesterol and LDL, appears to act through the liver, and different from other cholesterol lowering agent, having shown libido enhancing effects.

Policosanol not only significantly lowers cholesterol levels but has many other beneficial effects on other parameters of cardiovascular functions, such as reducing platelet aggregation and inhibiting the development of atherosclerotic lesions. Policosanol has shown in clinical trial to improve peripheral blood flow adding to a list of other beneficial agents to be useful for intermittent claudication. Policosanol reduces the pro-inflammatory thromboxane A2 and B2, significantly reduce platelet aggregation and increases prostacyclin levels. Thromboxanes (TXAs), produced from fatty acid metabolites, form in, and are released by the platelets effecting aggregation. Excessive platelet aggregation is undesirable unless you need to stop bleeding. Furthermore, policosanol has shown to reduce blood pressure. [100,101]

**Plant Sterols**
Decrease LDL by 10-15%. Prevent cholesterol absorption in the gut. Has additive effect with statins — no interference. It is believed that plant sterols displace cholesterol from bile salt micelles. Another proposed mechanism is the possible inhibition of the rate of cholesterol esterificiation in the intestinal mucosa. [102]

**Grape seed & skin**
Grape seed flavonoids are responsible for giving many fruits, in particular berries, their dark purple and blue color. Their free radical scavenging effects are 20-50 times greater than vitamin C or E. They also reinforce the natural cross linking of collagen that forms the matrix of connective tissue, a very important function during any post-surgical healing, and they are anti-inflammatory in that they prevent the release and synthesis of compounds that promote inflammation such as histamines, serine proteases and prostaglandins. [103, 104]

A recent study confirmed that wine, and wine phenolics in particular, could have a more significant inhibitory effect on platelet aggregation and could explain, in part, the hypothesis that red wine is more protective against atherosclerosis and coronary heart disease. [202]

Drinking Concord grape juice significantly increased good cholesterol and significantly lowered two markers of inflammation in people with stable coronary artery disease. In addition to an increase in HDL (good cholesterol) levels, they saw a significant decrease in the production of superoxide, a free radical, and soluble CD40 ligand, an inflammatory marker that is provoking growing interest *"Platelet release of soluble CD40 ligand is thought to contribute to the development of atherosclerosis and vascular inflammation,"* noting that previous studies of healthy subjects have shown that drinking grape juice decreases superoxide production and inhibits platelet aggregation. However, its impact on the inflammatory properties of platelets had not been previously studied. *The soluble CD40 ligand information is new and particularly interesting, given the growing interest in the link between this inflammatory marker and cardiovascular disease.* [203]

Resveratrol phytoalexin, a naturally occurring plant cytokine, is found in grapes, wine, and other plant products. Its job in nature is to fight fungus during the rainy season, and it is especially prevalent in grapes used in making red wine. It has been shown to have anti-inflammatory, anti-oxidant, cell-repair, phyto-estrogen and anti-tumor activities. The discovery of resveratrol has important implications for increasing the effectiveness of cancer therapy, with some clinical trials using resveratrol already showing encouraging results. Resveratrol also helps to control atherosclerosis, heart disease, arthritis, and autoimmune disorders.

Saponins present in Grapes could be just as important as resveratrol, thought to be responsible for the so-called French Paradox — the association between red wine and decreased heart disease. While resveratrol is thought to block cholesterol oxidation (LDL oxidation) by its antioxidant action, saponins also present in the grape skin are believed to work by binding to and preventing the absorption of cholesterol. The biologically active components of seeds and skins of grapes have a significant synergistic effect with regards to inhibition of platelet aggregation, endothelial inflammation, and LDL oxidation. [104-106]

**Red Grape juice concentrate improves lipids, lowers inflammatory biomarkers, and reduces CVD**

Patients treated with hemodialysis frequently experience cardiovascular complications attributed, among other causes, to dyslipidemia, increased oxidative stress, and inflammation. Twenty-six patients receiving hemodialysis and 15 healthy subjects were instructed to drink 100 mL RGJ/d for 14 d. Blood was drawn at baseline, twice during red grape juice (RGJ) supplementation, and twice during the 6-mo follow-up period. As a control, 12 other randomly recruited hemodialysis patients not receiving RGJ were studied. Lipids, apolipoproteins, oxidized LDL, and antioxidant vitamins were measured in plasma. The bioavailability of RGJ polyphenols was assessed in healthy subjects. RESULTS: The maximum plasma concentration of quercetin was achieved 3 h after RGJ ingestion, which indicates that supplement-derived polyphenols are rapidly absorbed. In both healthy subjects and hemodialysis patients, RGJ consumption increased the antioxidant capacity of plasma without affecting concentrations of uric acid or ascorbic acid; reduced the concentration of oxidized LDL; and increased the concentration of cholesterol-standardized alpha-tocopherol. RGJ supplementation also caused a significant decrease in LDL-cholesterol and apolipoprotein B-100 concentrations, while increasing the concentrations of HDL cholesterol and apolipoprotein A-I. In a further study in hemodialysis patients, RGJ supplementation for 3 wk significantly reduced plasma monocyte chemoattractant protein 1, an inflammatory biomarker associated with cardiovascular disease risk. CONCLUSION: Dietary supplementation with concentrated RGJ improves the lipoprotein profile, reduces plasma concentrations of inflammatory biomarkers and oxidized LDL. [297]

**Ginger (*Zingiber officinalis*)**
Ginger's effects on circulation would be classified as a gentle diffusive stimulant, along with having a mild relaxing effect. It is used extensively in Ayurveda to inhibit abnormal clotting, reduce cholesterol and fight arthritis. It significantly reduces serum and hepatic cholesterol levels and possesses potent cardiotonic activity, Ginger extracts (5% gingerol) inhibited platelet cyclo-oxygenase production, thromboxane generation and platelet aggregation in a dose-dependent fashion; gingerol also inhibites thromboxane-mediated platelet aggregation. Ginger is a well-known synergistic herb that potentiates, harmonizes, and improves the deep circulation of other herbs. [107-111]

**Turmeric (*Curcuma longa*) Curcumin**
Curcumin, the natural pigment that gives the spice turmeric its yellow color, has come under the scientific spotlight in recent years, with studies investigating its potential benefits for reducing cholesterol levels, improving cardiovascular health, and fighting cancer. Lead researcher Norbert Nass and colleagues from the Martin Luther University in Germany investigated the effect of different doses of curcumin, ranging from two to 50 micromoles, at the genetic of human liver cells. The specific targets studies were LDL-receptor mRNA, which affects uptake of LDL-cholesterol from the plasma; liver X receptor (LXR), a receptor that binds various oxidized cholesterol derivatives; and retinoic acid receptor (RXR) which forms dimers with LXR as well as activating several genes reportedly involved in cholesterol metabolism.
The researchers report that addition of curcumin results in *"an up to sevenfold, concentration-dependent increase in LDL-receptor mRNA"*, an observation which *"should result in a higher net uptake of LDL-cholesterol from plasma."* The effect was reported to be significant at concentrations higher than 10

micromoles and the curcumin was not toxic to the liver cells. Expression of the LXR and RXR was also increased, and activation occurred even at the low doses (two to 10 micromoles). *"The observed activation of LXR and RXR that occurred at concentrations that can be reached by oral consumption of curcumin holds for a contribution of nuclear receptors to the hypocholesterolemic effect of curcumin,"* concluded the researchers. [256]

**Cut heart failure risk**

When the pigment was given to mice with enlarged hearts (hypertrophy), heart function was restored and scar formation reduced, report the researchers in the February edition of the *Journal of Clinical Investigation*. Lead researcher Peter Liu, scientific director at the Canadian Institutes of Health Research - Institute of Circulatory and Respiratory Health said that curcumin might be a safe and effective means of preventing heart failure in the future, given that it is naturally occurring and readily available at a low cost.

The Canadian researchers found that curcumin appeared to work by preventing abnormal unravelling of the chromosome under stress, in addition to preventing excessive abnormal protein production. The pigment was administered as a curcumin suspension using 0.5 per cent carboxy-methylcellulose solution, "*Curcumin's ability to shut off one of the major switches right at the chromosome source where the enlargement and scarring genes are being turned on is impressive,*" said Liu. However he cautioned that moderation is important, "*the beneficial effects of curcumin are not strengthened by eating more of it.*" Specifically, the pigment was found to act on p300-histone acetyltransferase (HAT), reportedly the most important HAT in muscle that "*modifies chromatin and associated transcription factors and promotes gene activation,*" wrote the researchers.

"*This study is relevant to the understanding of the inhibitory effect of curcumin on cardiac hypertrophy and related molecular mechanisms,*" wrote the researchers. "*It also serves to elucidate the dominant signaling pathways leading to cardiac hypertrophy, inflammation, and fibrosis in response to hypertrophic stimuli.* [301]

**Supporting data**

In a related article in the same journal, Tatsuya Morimoto and co-workers from the National Hospital Organization in Kyoto report similar findings from a study with rats. The Japanese researchers tested curcumin in two models of heart failure - heart disease associated with high blood pressure in salt-sensitive rats, and surgically-induced myocardial infarction in rats. They report that, in both cases, the pigment prevented increases in heart muscle wall thickness after heart failure.

"*We believe that the use of curcumin, which targets nuclear signaling pathways in cardiomyocytes, will provide a novel therapeutic strategy against heart failure,*" wrote Morimoto and co-workers. "*Future application of this nontoxic dietary natural compound as a therapeutic agent for heart failure in humans would be particularly interesting.*" [302]

**Berberine**

The plant compound Berberine, a compound isolated from several herbs including goldenseal, Oregon grape, and Chinese Coptis, can act as a cholesterol-lowering drug. berberine works in a way that doesn't depend on how much cholesterol is in the cell. Like statins, the herb increases the number of cholesterol receptors on the cell surface, but it does this by stabilizing and improving the process by which the receptors are formed. The researchers screened 700 Chinese remedies in lab tests and found that berberine had the greatest effect in increasing cholesterol receptors. Further testing showed that receptor levels were increased further when the herb was used together with a statin. The researchers then assessed cholesterol levels in 91 patients with high cholesterol who were treated with berberine or inactive "placebo" for 3 months. The herb was well-tolerated, and lowered total cholesterol by 18 percent and LDL cholesterol by 20 percent. No effect on levels of HDL ("good") cholesterol was seen. The researchers then analyzed berberine's effect in a subset of patients who were not taking any other medications or herbs before or during the study. Among these individuals, berberine lowered total cholesterol by 29 percent and LDL cholesterol by 25 percent. [191]

**Herbal Adaptogens**
The term adaptogens originated in Russia in late 1950 to early 1960's. It was a term given to describe the actions of certain well researched herbs with regards to their normalizing ability on all major systems of the body. Adaptogens combat the effects of stress, making stress less damaging, prevent disease (acute and chronic), including CVD, slow down the aging process, enhance health and well being, and increase adaptive energy. Adaptogens are therefore defined as any agent that increases the nonspecific resistance of an organism to stress and other environmental influences. Herbal adaptogens are nontoxic, and normalize bodily processes irrespective of the direction of the pathological changes (regulating blood glucose and blood pressure, blood lipids, etc.).

**Adaptogenic formulation protects heart from damage during ischemia and reperfusion**

A course administration of the complex plant adaptogenic drug tonizid, containing dry extracts of ***Aralia mandshurica, Panax ginseng, Rhodiola rosea, and Eleutherococcus senticosus,*** was ascertained to increase murine exercise tolerance. In addition, the drug increased murine survival during hypobaric hypoxia (at an altitude of 10,500 m upon 20-min exposure). A model of total 35-min ischemia and that of 30-min reperfusion of the rat isolated heart were used by the Langendorff technique. The course administration of tonizid attenuated a reperfusion decrease in the left ventricular pressure and in the rate of contraction. However, tonizid did not prevent a reperfusion reduction in heart rate, a decrease in the rate of relaxation and an elevation of end diastolic pressure. Tonizid lowered the level of creatine kinase in the venous effluent from the isolated rat heart during reperfusion. At the same time, the plant adaptogen exerted no effect on the incidence of ventricular arrhythmias and coronary flow. <u>It has been suggested that tonizid is an adaptogenic drug that attenuates contractile dysfunction and prevents irreversible cardiomyocytic damage during ischemia and reperfusion of the isolated heart</u>. [304]

A second study on **tonizid** was done. The course administration (5 days) of tonizid led to a decrease in the ratio of necrotic zone size/risk area during a 45-min local ischemia and a 2-hr reperfusion in artificially ventilated chloralose anaesthetized rats. This compound decreased the necrotic zone but did not change the size of the risk area. Tonizid also prevented an appearance of ventricular fibrillation during a 45-min coronary artery occlusion, but did not affect the incidence of ventricular arrhythmias during a brief ischemia and reperfusion. In a separate series of experiments, tonizid was administered during 5 days to rats with postinfarction cardiac sclerosis, which was formed 45 days after coronary artery occlusion. In this case, tonizid dose-dependently elevated the ventricular fibrillation threshold. The experiments in vitro were performed on a model of 35-min total ischemia and 30-min reperfusion of isolated rat heart using the Langendorff technique. The course administration of tonizid attenuated the reperfusion-induced decrease in the left ventricular pressure and the rate of contraction. However, tonizid did not prevent a reperfusion-induced reduction in the heart rate, a decrease in the rate of relaxation, and an increase in the final diastolic pressure. Tonizid decreased the creatine kinase levels in the venous effluent from isolated rat heart during reperfusion. At the same time, the plant adaptogen did not affect the incidence of ventricular arrhythmias and coronary flow. It is suggested that tonizid can be used as an adaptogen drug attenuating the contractility dysfunction and preventing an appearance of irreversible cardiomyocyte damage during ischemia and reperfusion. Tonizid exhibits cardioprotective and antifibrillatory properties during acute cardiac ischemia/reperfusion and postinfarction cardiac fibrosis. [304]

**<u>A short review of the adaptive effects of adaptogens in regards to high cholesterol and cardiovascular disease (cardioprotective)</u>**

***Eleutherococcus senticosus:*** inhibited stress induced hypertension, reducing cardiovascular responses to stress in healthy. [112]
***Rhodiola rosea:*** cardioprotective - prevents stress-induced catecholamine activity in cardiac tissue and reduce adrenaline induced arrhythmias in animals; regulates blood pressure and heart rate. [113, 114]
***Aralia mandschurica*:** Prevents disorders on the lipid metabolism, decreases total cholesterol and triglycerides. [115]
***Panax ginseng*:** protects against the endothelial damage of thrombosis and atherosclerosis, stimulates release of nitric oxide. [116-118] **Also Panax ginseng lowers serum lipids.** [192-196]

***Panax quinquefolius:*** antimyocardial ischemic effects, improves oxygen uptake and utilization. [119]
***Rhaponticum carthamoides:*** cardio-protective and cardio-anabolic (strengthens heart useful in cardiomyopathy), decreases platelet aggregation and pronounced anti-arrhythmic. [120-123]
***Schisandra chinensis****:* cardio-protective. [124]
***Ganoderma lucidum****:* hypolipidemic (cholesterol lowering – HMG co-enzyme A reductase), antiatherosclerotic - inhibits platelet aggregation, cardiovascular-tonic, hypotensive – ACE inhibition. [124-126]
***Royal jelly (Apis mellifica):*** significant reduction in total serum lipids and cholesterol levels. [125]
***Ocimum sanctum*:** cardiotonic, hypolipidemic and insulin-trophic. [126-130]
***Glycyrrhiza glabra*:** antiatherosclerotic, antihyperlipidemic. [131]

**Other commonly used herbs with lipid-modulating/cardiovascular effects**

**Yarrow (*Achillea wilhelmsii*)** is a common, prolific and humble herb that possess immense and diverse healing value. Like so many common therapeutic herbs are seen by many as lowly weeds and their value is overlooked and not given attention they deserve.

Yarrow is rich in flavonoids and sesquiterpene lactone constituents, which have been found to be effective in lowering blood pressure and blood lipids. A double-blind, placebo-controlled trial examined the antihyperlipidemic and antihypertensive effects of Achillea. The researchers randomly selected 120 men and women, aged 40-60 years, and divided them into two groups: (1) moderate hyperlipidemic and (2) hypertensive subjects. Each study group was treated either with an alcohol extract of Achillea or placebo at a dose of 15-20 drops twice daily for six months. Blood pressure and serum lipids (total cholesterol, triglycerides, LDL-cholesterol), were significantly lower in the group treated with the yarrow extract. [132]

**Notoginseng**
Notoginseng, also called Tienchi ginseng, is a relative of Panax Ginseng. It is a superb blood tonic and blood cleanser when cooked. It is a powerful blood-vitalizing agent, and is believed by the Chinese to protect the heart and vascular system. It can be used externally to stop bleeding (so is yarrow). Notoginseng inhibit activation of platelet through multiple components and multiple pathways, which is different from that of Aspirin, only through inhibition on arachidonic acid metabolism to suppress platelet aggregation. Notoginseng has effects of decreasing platelet superficial activation, inhibiting platelet adhesion and aggregation, preventing thrombosis and improving microcirculation, and its therapeutic effect on clinical syndrome is better than that of Aspirin. [133]

**Specific Nutrients for Lipid Modulation**

**Pantethine**
Pantethine is the disulfide dimer of panethine, and is the active form of pantethenic acid. Pantethine converts into coenzyme (Co) A. Co A is involved in the transport of fatty acids to and from the cells, and to the mitochondria. Pantethine has significant lipid-lowering activity. Pantethine has been shown in several clinical trials to reduce serum triglycerides and cholesterol levels while increasing HDL cholesterol. Pantethine also assists in modulating glucose and insulin; while improving gut flora and liver detoxification. There is also some evidence that pantethine protects against cataract formation, and has overall beneficial effects on the central nervous system and adrenal –stress system. Pantethine's liver protective effects have been demonstrated in a number of clinical trials. It has shown to protect against carbon tetrachloride, halocarbon, acetaldehyde, ethanol, and other hepatotoxins. [134]

For the past few decades, pantethine has been used in Japan to help elevate high-density lipoprotein ("good") cholesterol. The medical journal *Atherosclerosis* reported on the effectiveness of pantethine during an eight-week, double-blind trial involving 57 participants with cholesterol difficulties. Before the trial, all the subjects adhered to a low-fat diet for three months, which they maintained during the trial. The researchers found that pantethine positively influenced total cholesterol and low-density lipoprotein ("bad") cholesterol by an average of 13.5%, while increasing good cholesterol 10%. When these people were then switched to a placebo, the results were less striking. The scientists also found that triglyceride levels were positively affected by approximately 30% in participants when given pantethine. [165]

In a long-term clinical trial, pantethine supplementation was similarly shown to significantly impact cholesterol levels in 24 men and women who averaged 51 years of age and were approximately 15% overweight. Some of the participants had blood sugar problems, and others had unhealthy cholesterol levels. After starting the people on pantethine, the scientists checked blood cholesterol levels every three months. They found that at each testing, the participants had better total cholesterol levels, including an increase in good cholesterol. The benefits of pantethine were seen equally in those with blood sugar difficulties as well as those with elevated cholesterol. [166]

The administration of pantethine to mice lowered food intake and mean body weight, insulin and glucose levels and decreased the content of triglycerides, total cholesterol and cholesterol esters in serum and adipose tissue as well as raised the activity of lipoprotein lipase in adipose tissue and serum lipolytic activity in obese mice. Among the compounds studied the reverse effect of panthenol was especially pronounced. The mechanism of hypolipidemic effects of pantothenic acid derivatives can be related to the reduced resistance to insulin and activation of lipolysis in serum and adipose tissue. [167]

**Niacin**

Niacin is one of the best-known vitamins for lowering blood cholesterol levels. And protects against cardiovascular disease. Until recently, niacin's general usage and widespread acceptance have been blunted by the need to take it 4 times a day and by the high incidence of flushing. A sustained-release formulation that is easier to take and has fewer side effects. Based on several studies niacin decreases LDL by about 10%, triglycerides by about 25%. Also, raises HDL by about 35%. [135-138]

**Exercise May Be Particularly Beneficial in Persons Taking Niacin**

Aerobic exercise is more effective than extended-release niacin in reducing postprandial triglyceride concentrations. Although niacin reduces fasting triglyceride concentrations, it appears to attenuate the postprandial triglyceride-lowering effect of exercise. Conversely, aerobic exercise may attenuate the rise in postprandial insulin concentrations after niacin administration, which suggests that the combination of exercise and niacin may be especially beneficial for people with insulin resistance. Further research will be needed to elucidate the mechanisms by which exercise and niacin exert their effects on lipid and glucose metabolism when used in combination. [309]

**L-Arginine**

L-arginine may also have anti-atherogenic activity independent of its role in the enzymatic formation of Nitric Oxide (NO). L-arginine may itself have antioxidant activity. L-arginine has been found to inhibit the oxidation of low-density lipoproteins (LDL) to oxidized LDL (oxLDL). The oxidation of LDL to oxLDL is believed to be a pivotal early step in atherogenesis. L-arginine may also scavenge superoxide anions and hydrogen peroxide (see above), as well as inhibit lipid peroxidation. L-arginine shows promise in the treatment and prevention of cardio- vascular disease (including atherosclerosis, hypertension, hyperlipidemia and angina pectoris), in the treatment of some forms of male infertility and some kidney disorders and it is helpful in accelerating wound healing in some circumstances. It has demonstrated some positive immune-modulating and anticancer effects. [139-141]

**Creatine Magnesium Chelate**

Creatine is a nonessential dietary component that, when supplemented in the diet, has shown physiological benefits in athletes, and recently in patients with various muscle, neurological and neuromuscular disease(s) including heart disease, dementia, chronic fatigue, Cachexia and sarcopenia. Creatine has been called the ultimate ergogenic aid and its use as a supplement for muscle growth has become very popular in the field of sports nutrition over the years. Creatine exerts its influence by increasing muscle creatine and phosphocreatine concentrations, creating a higher rate of ATP resynthesis. This results in a delay in the onset of muscle fatigue and facilitates more rapid recovery during repeated rounds of high intensity exercise. In a study of older men (ranging from 43 to 70 years) suffering from chronic heart failure, researchers noted improvements in exercise performance and increased muscle creatine and phosphocreatine levels after ten days.

Creatine administered to 13 patients hospitalized with congestive heart failure showed after four days a reduction in heart size, reduced vascular resistance, and increased ejection fraction - all indicators of improved heart function. Creatine supplementation displays neuroprotective effects in several animal models of neurological disease, such as Huntington's disease, Parkinson's disease, or amyotrophic lateral sclerosis. Creatine supplementation has been found to reduce atherosclerosis and lower homocysteine levels as well. Elevated homocysteine is associated with an increase CVD.

Creatine MagnaPower" (MP), a patented magnesium creatine chelate that provides the body with a readily available source of magnesium while also making the creatine more active by protecting it from cyclization. This patented mineral amino acid chelate, contributes to an overall positive impact on many functions including, cardiovascular health. [142-146]

**Glutamine Magnesium Chelate**
Glutamine may be suitable as a cardioprotective agent, Glutamine enhances myocardial tissue metabolism, glutathione content, and improves myocardial function. These effects may be mediated by maintenance of myocardial glutamate, ATP and phosphocreatine: and prevention of lactate accumulation. [147-150]

**Carnitine**
Carnitine is essential in the transport of long chain fatty acids into the mitochondrial matrix and plays a key role in the oxidation of lipids. This means that carnitine improves fatty acid utilization and energy production. Several studies have demonstrated that carnitine improves angina and ischemic heart disease. Carnitine lowers triglyceride and cholesterol levels while increasing HDL levels. Carnitine also significantly lowers plasma lipoprotein(a) levels in hypercholesterolemic individuals. [151]

**Chromium**
Chromium is an essential micronutrient for humans. Chromium is a trace element involved in the regulation of carbohydrate and lipid metabolism. Chromium acts primarily by potentiating insulin activity and facilitating insulin sensitivity, as it functions as a cofactor in all insulin-related activities. Chromium promotes better insulin utilization, which leads to an overall decrease in serum triglycerides and total cholesterol, while increasing HDL levels and improving glucose tolerance. [152]

*Chromium nicotinate glycinate chelate* (Albion lab) is a fully reactive amino acid chelate that is far superior in bioavailability to other forms of chromium including chromium picolinate. Vanadium, another trace mineral, also possesses insulin-like anabolic-enhancing actions and works well in combination with chromium. *Vandium Chelavite* (Albion Lab) demonstrates superior assimilation to other forms of vanadium. [153]

**Tocotrienols**
Tocotrienols are a group of minor dietary constituents that are naturally occurring analogues of vitamin E. Tocotrienols are constituents of high fiber cereals and grains (barley, oats, rice, and wheat) and oils extracted from olive, pine and palm fruit. Tocotrienols appear to possess equal to, or greater therapeutic effects than vitamin E. Tocotrienols inhibit cancer and reduce overall LDL cholesterol, and more importantly reduce LDL oxidation. Siberian Sea Buckthorn oil is a rich source of tocotrienols. [154,155]

**Coenzyme (Co) Q10**
Co Q 10 is a crucial component of the oxidative phosphorylation process within the mitochondria, where it converts the energy in carbohydrates and fatty acids into ATP to drive cellular function and synthesis. About 95% of cellular energy is produced from structures in the cells called mitochondria. Co Q 10 can undergo oxidation/reduction reactions within the mitochondria, as well as in other cell membranes such as lysosomers. Within the mitochondria and lysosomers Co Q 10 undergoes reduction/oxidation cycles during which transfers protons across cell membranes. Co Q is involved in redox control of cell signaling and gene expression and can act as a direct antioxidant, or like lipoic acid, can regenerate tocopherol (vitamin E) and ascorbate (vitamin C). [156]

Vitamins C and E working together also support heart health. For instance, in the Established Populations for Epidemiological Studies of the Elderly in 1984–1993 published in the American Journal of Clinical Nutrition, researchers examined the use of vitamins E and C in relation to the risk of death from heart

concerns. The findings showed that the strongest positive effects were associated with the use of vitamin E. However, those people who took both vitamins E and C showed an even lower risk from all causes of mortality. [169]

**Foods rich in antioxidant Compounds**
A study on antioxidants consisted of assessing the amount of antioxidants in over 100 types of foods including fruits, vegetables, spices and nuts.

Highest Ranking Antioxidant Food Sources:

* Fruits: Cranberries, blueberries, raspberries and blackberries
* Vegetables: Beans, artichokes and Russet potatoes
* Nuts: Pecans, walnuts and hazelnuts
* Spices & Culinary herbs: turmeric, ginger, rosemary, cloves, ground cinnamon and oregano

Maybe these findings will motivate doctors to advise people to increase their intake of fruits and vegetables. [157]

Coconut, which many people feel they need to avoid because of the fear (myth) that is caused serum cholesterol to increase, actually has shown to have a beneficial effects with regards to cholesterol. Coconut flakes, added to a breakfast cereal on serum cholesterol levels of humans with moderately raised serum cholesterol lowered their cholesterol in 21 subjects.

The serum total cholesterol of subjects differed and ranged from 259 to 283 mg/dL. The study was conducted in a double-blind randomized crossover design on a 14-week period, consisting of four 2-week experimental periods, with each experimental period separated by a 2-week washout period. The test foods were as follows: corn flakes as the control food, oat bran flakes as the reference food, and corn flakes with 15% and 25% dietary fiber from coconut flakes (made from coconut flour production). Results showed a significant percent reduction in serum total and low-density lipoprotein (LDL) cholesterol (in mg/dL) for all test foods, except for corn flakes, as follows: oat bran flakes, 8.4 +/- 1.4 and 8.8 +/- 6.0, respectively; 15% coconut flakes, 6.9 +/- 1.1 and 11.0 +/- 4.0, respectively; and 25% coconut flakes, 10.8 +/- 1.3 and 9.2 +/- 5.4, respectively. Serum triglycerides were significantly reduced for all test foods: corn flakes, 14.5 +/- 6.3%; oat bran flakes, 22.7 +/- 2.9%; 15% coconut flakes, 19.3 +/- 5.7%; and 25% coconut flakes, 21.8 +/- 6.0%. Only 60% of the subjects were considered for serum triglycerides reduction (serum triglycerides >170 mg/dL). In conclusion, both 15% and 25% coconut flakes reduced serum total and LDL cholesterol and serum triglycerides of humans with moderately raised serum cholesterol levels. Coconut flour is a good source of both soluble and insoluble dietary fiber, and both types of fiber may have significant role in the reduction of the above lipid biomarker. [170]

**The Power Foods of the Mediterranean Diet**

The countries around the Mediterranean basin have different diets, religions and cultures. The diet of Crete represents the traditional diet of Greece prior to 1960. Analyses of the dietary pattern of the diet of Crete shows a number of protective substances, such as selenium, glutathione, a balanced ratio of n-6/n-3 essential fatty acids (EFA), high amounts of fiber, antioxidants (especially resveratrol from wine and polyphenols from olive oil), vitamins E and C, which have been shown to be associated with lower risk of cancer. [158]

The keys to maintaining a healthy heart are to 1st deal with stress by not letting stress take a toll on your health and by taking adaptogens on a regular basis, and 2nd to support your health with herbs, phyto-nutrients, and vitamins that can work to your benefit. For me to determine which herbs and nutrients by be most specific for you I apply what I refer to as my Trinitarian Model which reviews the bioenergetics of the person, the risk factor assessment based mostly on various blood test, and the external environment assessment. A treatment plan will take all three of the areas into consideration.

There are numerous tension and stress relievers you can explore, and with a little practice they can become

second nature. You can also start protecting your heart with these potent heart-friendly herbs and nutrients plus a balanced diet of nutritious food along with daily exercise. You now have the tools to help "mend" your heart before it "breaks."

**Final thoughts: Prayer improves the Heart**

Various researchers have found that religious/spiritual people are less likely to have heart disease and less likely to die from heart disease, and are more likely to have lower blood pressure, less depression, less anxiety, and less substance use and abuse than non-religious/spiritual people. Dr. Paul S. Mueller and his colleagues, from the Mayo Clinic, reviewed 1,200 studies of mental and physical health and found that in most cases, the study participants' spirituality and religious involvement seemed to be associated with better health outcomes. Discerning, acknowledging, and supporting the spiritual needs of patients can be done in a straightforward, ethical and non-controversial manner and may relieve suffering and facilitate recovery from illness. [159]

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