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A CLOSER LOOK AT THE CHOLESTEROL ISSUE

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Cholesterol levels have become the source of much national anxiety, even though cholesterol is one of the most valuable substances in the human body. Over the past few years the amount of cholesterol information bombarding the public has grown exponentially. New receptor proteins have been identified and research is opening doors to help us understand why "good" cholesterol is *good* and "bad" cholesterol is *bad*.

Cholesterol is a fat-like alcohol that travels through the bloodstream transported by the lipoproteins, LDL (Low-Density Lipoproteins) and HDL (High-Density Lipoproteins). Research suggests that high cholesterol levels interact with oxygen in the body to produce an excess of oxygen-free radicals. These free radicals interfere with the production of nitric oxide, a gas produced in the body which causes widening of the blood vessels. Less nitric oxide production results in less flexible blood vessels, or "hardening of the arteries." The majority of information regarding cholesterol focuses on lowering serum cholesterol to "acceptable" levels by increasing HDL, the so-called "good" cholesterol, and diminishing the LDL, the so-called "bad" cholesterol, fraction. Oxidative modifications of LDLs are also recognized as one of the major processes in atherogenesis. The concept of "good" and "bad" cholesterol arises from the way HDL removes LDL cholesterol from the tissues and transports it back to the liver for excretion as bile, thus eliminating the free radicals that inhibit nitric oxide production. In addition, some scientists theorize that HDL may actually prevent fatty deposits from clogging the blood vessels.

The standard definition of high blood cholesterol is anything in excess of 200 mg/dL, although many doctors are now citing 180 mg/dL as the maximum. An estimated 97.2 million, or 52.1%, of American adults have cholesterol levels over 200 mg/dL.

There appears to be a connection in certain populations to high or low cholesterol. Norwegians with high cholesterol levels[1] also report cardiovascular disease as the leading cause of death. Asians, in contrast, overall have inherently low cholesterol levels.[2]

Longevity: Conflicting Reports

In a more recent study in LANCET there was a surprise finding: the higher an individual's cholesterol, the longer the person may survive. Starting in 1986, an ongoing study of 724 males and females aged 85 and older in the city of Leiden, Netherlands were monitored for ten years. By 1996, 88 percent of the participants in the study had died. However, the overall conclusion of this study shows that the lower cholesterol group experienced a higher death rate from cancer and infections. In a correlating and more recent study also done by another group in Netherlands, mice were injected with large quantities of pneumonia-causing bacteria and actually survived due to higher concentrations of low-density lipoprotein cholesterol. It appears that the so-called "bad" cholesterol bound up the poison produced by the bacteria, thus facilitating its "detoxification." This raises the question of whether increasing HDL and lowering LDL is perhaps too simplistic of an approach. Indeed, as Udo Erasmus states in the title of his book, there are "Fats that Kill and Fats that Heal." All fats are not bad. People who restrict their fat intake to 10 to 12 percent often deprive themselves of essential fatty acids, which are crucial to proper cellular metabolism and hormone synthesis. Obtaining the proper balance of HDL and LDL fats may be a more healthful approach than simple reduction of fat intake.

There are two sources of cholesterol in the body, food and synthesis by the liver. The average American ingests between 300-500 mg of cholesterol per day from dietary eggs, dairy products, organ meats, beef, and pork. Even without the dietary intake of cholesterol containing foods, our bodies are sufficiently balancing the cholesterol ratios at the level of the liver. In fact, most of the cholesterol the body needs (2000 mg per day) is synthesized by the liver, which is used (in part) by the body for hormone production and lipid metabolism.

For many years, epidemiological studies provided

strong evidence that lowering elevated cholesterol levels reduced the risk of heart disease. However, recent evidence suggests other important factors are involved.

Dietary Modifications Are Key

Specific dietary changes can reduce blood total cholesterol concentrations. Dietary interventions are generally less expensive than drug therapy and appear to be more cost-effective for primary prevention of coronary artery disease in high-risk individuals. Foods contain a mixture of saturated, polysaturated and monosaturated fats. The "bad" fats, those that contribute to LDL production, which dietary changes can reduce are the *saturated* fats, are found in animal products such as beef and pork. Some vegetable products such as coconut oil, palm oil, and palm kernal oil also contain saturated fats. Some liquid oils, such as shortening, are "hydrogenated" by a chemical process to make them harder at room temperature and become saturated fat. The fats in chicken and turkey are mostly saturated, too.

The "good" fats are the *unsaturated* fats. Fish is an example of animal protein that contains almost entirely unsaturated fats. Salmon, halibut, marlin, swordfish, mahi mahi, and nearly any fish but cod will supply good fats. The average egg has 300 milligrams of cholesterol, but the 1500 milligrams of phospholipids more than offset any possible adverse effects of egg cholesterol.

Therapeutic foods such as garlic, artichoke, wheat germ, alfalfa sprouts, buckwheat, watercress, rice polishings, apple, celery, cherries are also important. Fresh juices such as carrot and pineapple with honey, liquid chlorophyll, parsley, alfalfa and spinach, beet and celery are also beneficial. A low sugar, low fat diet of unsaturated fats and soluble fiber, combined with increasing omega 3 and omega 6 fatty acids and avoiding hydrogenated oils, refined carbohydrates such as white flour, and processed foods all contribute to a healthful way to reduce the risk of cardiovascular disease.

Cholesterol Lowering Foods: Garlic and Artichoke

In cases where dietary therapy may not be sufficient to control lipid levels, natural compounds can lower cholesterol levels and, in general, are less expensive than drugs. The composition and method of preparation of **garlic** supplements may contribute to lowering cholesterol levels, although there are conflicting studies on its effectiveness. Since the 1980s, four out of five studies have shown that garlic lowers cholesterol. According to Michael Murray, N.D., the majority of studies do show a positive effect when preparations deliver a sufficient dosage of allicin, the component which imparts the characteristic garlic odor. The commercially prepared alliin or **odorless garlic** is converted to allicin in the body. Garlic reduces atherosclerosis by inhibiting platelet aggregation, increasing fibrinolysis, enhancing antioxidant activity, and reducing serum lipids in general to lower cholesterol levels and other significant risk factors for coronary artery disease.

Another beneficial food is *Cynara scolymus*, also known as your common **artichoke**. The German Kommission E has published one monograph on the preparations of artichokes for use as a choleretic drug. Animal experiments and clinical trials indicate that both the drug and its major active ingredient cynarine reduce raised blood fat values. Three clinical trials were carried out on a total of 84 patients, most of whom had very high lipid values. These recent cynarine extract studies produced an 11.5% reduction in the average serum cholesterol and triglycerides were reduced up to 12.5%. An in vitro study determined that artichokes inhibit cholesterol biosynthesis by indirectly modulating and inhibiting HMG CoA reductase, the key enzyme in the biosynthetic pathway for cholesterol synthesis. The cynaroside and particularly aglycone luteolin were mainly responsible for HMG CoA inhibition. Luteolin also efficiently blocked the insulin effect on cholesterol bio synthesis. It is important to note that the highly concentrated juice from the fresh artichoke plant may be the most effective method of dosage administration.

Vitamins

Inositol and choline (in a sustained release form) as well as high levels of **vitamin C** have been found to influence cholesterol and tryglyceride levels. **Phosphatidyl choline** is a good cholesterol antagonist; however, monitor therapy closely since it is also a calcium antagonist. Mixed tocopherol (vitamin E), L-carnitine, beta-sitosterol (a plant sterol), and minerals chromium and magnesium have all been shown to raise HDL cholesterol. For years, doctors have known that large doses of the B vitamin-**niacin** lowers blood cholesterol levels. However, niacin's popularity in mainstream medicine suffered because of research linking large doses (5 grams daily and above) of time-released niacin to liver damage. Newer studies have reported reduced side effects with long-term niacin use. The current dose is now far lower than what was previously thought to be effective. Natural sources of niacin include nuts, whole grains, and brewer's yeast. **Inositol hexaniacinate** (a safer form of niacin) is beneficial in lowering cholesterol levels and removing fatty deposits from blood vessels. Concomitant use of chromium may also lower dosages.

Antioxidants Inhibit Atherosclerotic Damage

Vitamins E and **C** are antioxidants that may play a role in countering the release of triglycerides, the blood fats that hinder the

release of nitric oxide. Nitric oxide helps keep the blood vessels open, thus enabling healthy blood flow to the heart. In one study, plasma blood lipids and vitamin C levels were evaluated in 316 women and 511 men, ranging between 19 to 95 years of age. In a 7-day dietary record of 485 individuals, total fat, saturated fatty acids, and energy from fat and cholesterol intakes were not associated with plasma vitamin C levels. These results suggest a high plasma concentration of vitamin C may lower atherogenic risk. The relationship was even stronger in older men where the mean intakes of vitamin C were well above the recommended daily allowance.

The well-known plant *Vaccinium myrtillus* (Bilberry or European blueberry) is rich in **flavonoids**, the polyphenolic compounds that promote antioxidant activity. A study conducted on the antioxidative potential of *Vaccinium myrtillus* showed potent protective action on LDL particles during in vitro copper-mediated oxidation. The study concluded that this extract may be more potent than either ascorbic acid or butylated hydroxytoluene in the protection of LDL particles from oxidative stress.

A recent study on another well known antioxidant, **green tea** epicatechins, in the People's Republic of China demonstrated a reduction in serum triglycerides and cholesterol. This was most likely mediated by inhibition of absorption of dietary fat, cholesterol and reabsorption of bile acids, rather than inhibition of cholesterol synthesis.

Soy Protein

Research indicates that serum cholesterol is lowered by soy protein. Although results have been contradictory, it appears that substitution of isolated soy protein for animal protein in a regular diet reduces the risk of cardiovascular disease by lowering circulating LDL cholesterol concentrations. The jury is still out on which particular component of soy lowers the cholesterol, although many investigations have focused on the isoflavone components of soy, including genistein and daidzein, which are also referred to as plant sterols because of their estrogenic activities. A recent study reports that consumption of intact soy protein resulted in a significant decrease in VLDL cholesterol in female rheusus macaques when compared to a diet containing soy protein with isoflavones removed. In another study, the hypocholesterolemic effect of soy protein was found to decrease the plasma concentrations of LDL cholesterol as well as the ratio of plasma LDL cholesterol to HDL cholesterol in a randomized two part crossover study that included 13 normocholesterolemic and 13 hypercholesterolemic men aged 20-50 years old.

Soy and Lactobacillus

Fermented dairy products (yogurt, tofu, miso) can also serve as functional foods to lower elevated cholesterol concentrations in the prevention of cardiovascular disease. Beliefs about the health benefits of fermented milk products can be traced back to the early 1900's. In 1908, Metchnikov wrote that milks fermented by lactic bacteria "prevented intestinal putrefication" and "helped maintain the forces of the body." Human studies in the area of fermented dairy products and cholesterolemia have been conducted since the 1970's. In light of these findings, several fermented dairy products available on the market today have the potential of being classified as useful cholesterol-lowering agents. **Bifidus** and **acidophilus**-containing yogurt milk beverages, and kefir, a fermented diary product containing several types of bacteria in symbiosis with yeasts are good examples. Since these products contain live bacteria strains that do not normally colonize the intestine and are quickly eliminated in the feces, daily consumption of probiotic products is necessary for long-term effects of lowering cholesterol metabolism.

The Documented Benefits of Fiber[3]

Fiber comes in many forms, including oats (*Avena sativa*), **guar gum**, and **pectin**. Nearly a dozen studies over the past decade have proven that oat bran lowers cholesterol levels. Recently, the FDA made history by ruling in the first federally sanctioned health claim for manufactured foods that oat-rich cereals and other foods are permitted to advertise their products as "cholesterol lowering." **Beta glucan**, a viscous gel in the soluable fiber of oats, surrounds cholesterol-rich bile acids and limits their reabsorption by the blood, shuttling them off into fecal excretion. Less bile is consequently returned to the liver which causes the liver to make more bile acids, the production of which uses up more cholesterol floating around in your blood.

However, studies from the University of Toronto have shown that not all beta-glucans are created equal. During the milling of oats into flour, cooking, pressure extrusion and other food processing techniques, the beta-glucan chain may be shortened, thereby limiting its effectiveness.

Guar gum, similar to pectin, is well documented regarding its ability to lower cholesterol levels. However, its principal drawback is its extreme viscosity, making foods containing guar gum very unpalatable. Nonviscous forms have been created via PHCC (partial enzymatic hydrolysis) of the gum's polysaccharide component, but there is some controversy regarding whether these processing techniques actually inhibit the guar gum's lipid lowering effects by reducing its digestibility rather than inhibiting bile reabsorption.

Chitosan is a form of fiber that absorbs dietary fat in the gut and can also inhibit LDL cholesterol while boosting desirable HDL

cholesterol levels. The mechanism behind its action may be explained by Chitosan's ability to bind both bile acids and phospholipids, reducing their absorption from the intestines and increasing fecal excretion of cholesterol. Chitosan has been shown to significantly lower plasma cholesterol and reduce the development of atherosclerotic plaques.

As an adjunctive to diet therapy, **psyllium** (*Plantago psyllium*) should be an important component of any cholesterol-lowering campaign. A study was conducted this year on 125 patients, average age 57 years, with Type II diabetes. Patients were evaluated for the effects of psyllium on glucose, cholesterol, triglycerides and HDL/LDL serum values. Patients were randomly assigned 5 grams of psyllium seed powder. In addition to showing a reduction in mean plasma glucose levels from 175 mg/dL to 140 mg/dL, there was a reduction in total cholesterol, triglyceride and LDL values. In addition, HDL values increased. The side effects of psyllium were negligible, with only one report of discomfort, gas and colic pain.

In another randomized, double blind controlled study conducted in 1998, no significant differences were observed in HDL cholesterol or triglycerols in 450 subjects. However, there was a modest LDL cholesterol response, 5% difference in the control group versus the high dose psyllium group. In the high dose psyllium group, the LDL levels remained lower throughout the 14-week treatment period, indicating the potential for long-term benefit. The results of the study suggest that consumption of foods containing psyllium in conjunction with other dietary changes results in the maintenance of reduced LDL cholesterol concentrations.

East Indian Herbal Contributions: Guggulipid, Myrrh, Tumeric , Curcumin and Fenugreek

Gugulipid (*Commiphora mukul*) or myrrh gum is a highly valued and well-known plant. Throughout history it has been used as an invaluable antimicrobial disinfectant herb. It is used extensively in Ayurvedic medicine and actually comes from a tree in India. It has long been used for mouth infections such as mouth ulcers and gingivitis as well as respiratory catarrhal problems in pharyngitis and sinusitis. Numerous studies in humans and animals have shown that the medicinal oleoresin or gum guggul has lipid-lowering activity as well. The active guggulsterones in the plant increase the uptake of LDL cholesterol from the blood by the liver. The effect of gugulipids on cholesterol and triglyceride levels is comparable to lipid lowering drugs, but does not have the toxicity and side effects of drugs. Dosage should be based on the guggulsterone content.

Turmeric (*Curcuma longa*), synonymous with curcumin, is a native East Indian and Southeast Asian herb and one of the medicinal plants listed in an Assyrian herbal text dating from about 600 B.C.

In addition to outstanding clinical activities in HIV and cancer, the anti-platelet activity is equal to that of aspirin, but unlike aspirin did not increase prostacyclin synthesis. An interesting side note is that Tumeric is comparable in potency to the drug phenylbutazone and is nearly as potent as cortisone.

The cholesterol-lowering effects of curcumin span all levels of lipid lowering mechanisms, including lowering total and LDL cholesterol (by 11% normally), increasing HDL cholesterol (by 29% normally), and reducing lipid peroxidation, thereby limiting the oxidation of LDL cholesterol.

The seeds of fenugreek (*Trigonella foenum-graecum*), a condiment in India, are high in fiber and are reported to have antidiabetic and hypocholesterolemic properties in both animal models and humans. A long-term study was undertaken to determine the hypolipidemic effect of fenugreek seeds. Sixty non-insulin dependent diabetes mellitus patients underwent a metabolic period of one week as a control, and then an experimental period lasting 24 weeks. During the experimental period, each subject consumed 25 g of powdered fenugreek seed divided into two meal servings. There was a steady decrease of serum cholesterol, triglycerides and LDL during the 24-week study and Fenugreek demonstrated the potential to prevent atherosclerosis by selectively reducing LDL and VLDL levels.

Red Yeast Rice

Hypercholesterolemia is treated aggressively with statin drugs, very potent inhibitors of HMG-CoA reductase, and the rate-limiting enzyme in cholesterol biosynthesis at the mevalonate level. Lovostatin's action is its conversion to mevinolin in the body. Mevinolin is the active principle found in **red yeast rice**, which enzymatically inhibits mevalonate, thus lowering cholesterol. It also has antioxidant properties. Numerous clinical trials suggest that red yeast rice (*Monascus purpureus*) has comparable therapeutic effects without the side effects of the statin drugs.[4] It is a yeast grown on rice so that the crimson organism permeates the rice; then it is ground to a powder. It has been used traditionally in China as a food and medicine since at least 800 A.D. One of the most significant aspects of red yeast rice is its nine HMG-CoA Reductase inhibitors, as well as the isoflavones, unsaturated fatty acids, and trace elements such as selenium. Over two dozen clinical studies demonstrate its effectiveness. For example, a total cholesterol decrease of 17% and a 22.4% decrease in LDLs was demonstrated in a clinical trial conducted at UCLA.

More Cholesterol-Lowering Herbs

Milk thistle (*Silybum marianum*) is well known for its high hepatoprotective capabilities in xenobiotic injury (in amanita mushroom poisoning and carbon tetrachloride toxicity). It exerts antioxidant and membrane stabilizing activities, attributes important for liver secretion and uptake of plasma lipoproteins. Inhibition of HMG CoA reductase in vitro has been demonstrated with therapeutic application of milk thistle, implying its possible direct influence on liver cholesterol metabolism. Milk thistle can be compared to probucol, an antioxidant hypocholesterolemic drug. In contrast to probucol, milk thistle caused an increase in high density lipoproteins and a decrease in liver cholesterol content, both additional benefits. In addition to its anticholesterolemic effect, milk thistle partially prevented the HCD-induced decrease in liver-reduced glutathione, an endogenous antioxidant.

The inhibition of ACAT (Acyl-CoA, cholesterol acyltransferase) has become important for the prevention and treatment of hypercholesterolemia and atherosclerosis. ACAT plays a role in the metabolism of cholesterol, including intestinal absorption of cholesterol, hepatic production of lipoproteins, and the deposition of cholesterol esters which accumulate as lipid droplets in macrophages and eventually form "foam cells" in atherosclerotic lesions. Although a large number of synthetic and microbial ACAT inhibitors have been reported, certain inhibitors have not yet been used clinically because of various side effects including hepatic toxicity. Safe and effective ACAT inhibitors have been isolated from the hairy roots of Panax ginseng and a Chinese herb known as *Magnolia obovata*. In one study, the extract leaves of *Magnolia obovata* inhibited rat liver ACAT by 62% ug/mL.

Highlight on Essential Fatty Acids (EFAs)

Fish oil is one of the few substances known to lower concentrations of triglycerides or fatty substances that pose a cardiovascular risk. Many physicians have been reluctant to advocate consuming fish oil in large quantities because it increases the proportion of cholesterol shuttled through the blood in LDLs, which contributes to heart disease.

According to Edward Siguel, M.D., PhD, the principal author of EFA research applied to cholesterol, EFA abnormalities are a cause of acquired (not genetic) atherosclerotic disease through their effects on membrane function. He recommends "bringing the fatty acid profiles of patients with high cholesterol closer to those of healthy people preceding any decisions for drug therapy." Dr. Siguel's research leads to a new treatment for abnormal cholesterol ratios, a treatment that is substantially different from the one proposed by the AHA and NIH. The NIH recommends decreasing intake of saturated fat and increasing intake of both carbohydrates and monounsaturated fat. Dr. Siguel recommends that people achieve ideal weight, if necessary by reducing caloric intake from all sources. He has stated that very low-fat diets may be counterproductive for many patients who have no EFA reserves stores in their bodies. EFAs are essential. Eating a diet that tends to correct fatty acid abnormalities may lead to substantial revisions in the way abnormal cholesterol ratios are treated today and may improve quality of life and life expectancy, as well as lowering health care costs. Increasing the rate at which cholesterol is degraded (converted into bile acids and steroid hormones) is key in understanding what represses cholesterol and LDL receptor synthesis when blood cholesterol levels are elevated. Consequently, a good blend of fish oil, evening primrose, flaxseed oil, and/or **GLA** is ideal.

Stress and High Cholesterol

Scientific research suggests that hormones created by stress impair cholesterol metabolism. Exercise, controlled breathing, meditation and other disciplines such as yoga can be of tremendous value in helping to lower stress levels. Lifestyle changes that reduce stress in the home, workplace and family life are therefore important considerations to lowering blood cholesterol counts.

A Multi-faceted Approach To Treat Multi-faceted Causes

Most recent findings indicate a multi-faceted cause to the problem of cardiovascular disease, including excessive intake of saturated fats, carbohydrate metabolism dysfunction, nutritional deficiencies, hormonal imbalance, and a high stress type lifestyle. Different people seem to oxidize cholesterol differently. In addition, certain mechanisms in the body may have gone awry, such as impaired liver LDL receptor uptake in Familial Hypercholesterolemia[5] , requiring more information and monitoring. Lowering the intake of saturated fats is advisable-but not eliminating them. Nature has provided specific compounds capable of augmenting dietary and lifestyle changes for improved cardiovascular health and may afford a way to lower cholesterol without resorting to synthetic drug preparations and their potential side effects.

[1] In 1988, a national cholesterol screening program and nutrition education campaign, was initiated by the National Norwegian Public Health Association. Participants received the results of their cholesterol screenings and were given nutritional information and dietary recommendations by trained health personnel. In summary, it was found that the mean cholesterol levels averaged 259 mg/kL with one of the participants having a cholesterol level of 310 mg/dL or higher. The conclusion was that subjects with the highest cholesterol levels were highly motivated to change dietary habits and an educational program greatly contributed to help the participants achieve this.

[2] A cross-sectional study conducted in a Japanese community in 1987 examined the relationship between intake of soy products and serum cholesterol concentration. The Takayama study involving 1,242 men and 3,596 women concluded there was a decreasing total cholesterol concentration with an increasing intake of soy products, determining a role for soy products in human cholesterol homeostasis.

[3] Avoid taking fiber supplements at the same time you take your other nutrient supplements to avoid potential interference of absorption with fat-soluble vitamins.

[4] Statin drug usage results in CoQ10 deficiency. CoQ10 functions as a fat-soluble electron carrier in oxidative phosphorylation in the mitochondria, a stabilizer of cell membranes, and a potent scavenger of free radicals, thus preventing lipid peroxidation. Treatment with statin drugs should include supplementation with CoQ10.

[5] Familial Hypercholesterolemia and Diabetes complicated by Renal Disease are diseases where the LDL receptors are not taking up cholesterol.

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