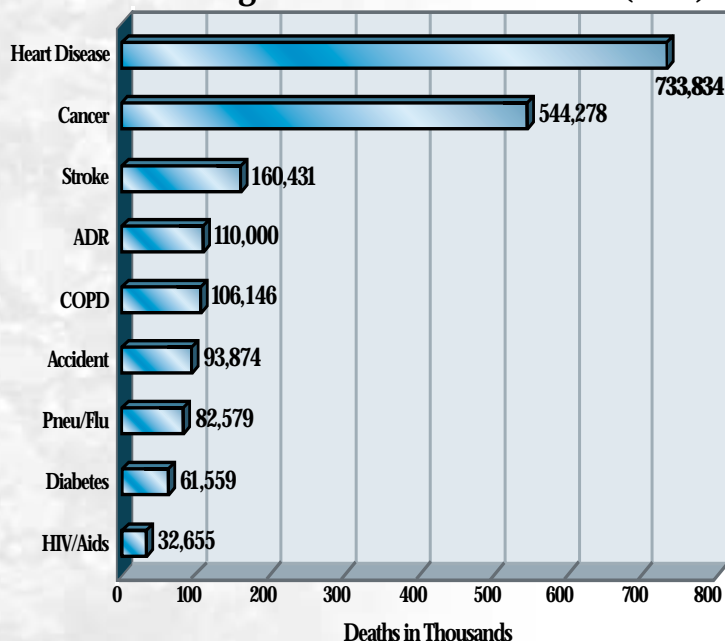


MANAGING CHOLESTEROL: NATURALLY

To say that the concerns about cholesterol are rampant would be quite an understatement. In fact, from much of the news and advertising, one would think that cholesterol is a poison rather than the essential component that it is. Yes, cholesterol is not only necessary for almost every cell in the body, but our bodies produce (not ingest) most of the cholesterol we use. Our main concern is with elevated blood (or serum) cholesterol and the secondary conditions, such as lipid peroxidation and atherosclerosis, caused by chronic increased levels of cholesterol in the blood. Since there are thousands of articles and reviews on cholesterol, this article will only briefly cover the metabolism and pharmaceutical management of cholesterol, focussing primarily on the management of cholesterol using natural ingredients.

Leading Causes of Death in the U.S. (1996)



“Leading causes of death in the United States for 1996 as reported by the Centers for Disease Control, modified by the adverse drug reaction (ADR) statistics reported in JAMA, 1998; 279 (15): 1200-1205. COPD is Chronic Obstructive Pulmonary Disease. Pneu/Flu is Pneumonia/Influenza.”

Cholesterol: The Good, The Bad, and The Ugly

We have all been guilty of reducing the whole of cholesterol metabolism down into “good” (HDL) cholesterol and “bad” (LDL) cholesterol. While this is a drastic over-simplification, it does help underscore that not all cholesterol is hazardous to one’s health.

Since cholesterol is not soluble in the blood, it must be carried to and from the liver (the primary organ for synthesis and removal of the body’s cholesterol) via lipoprotein particles. The difference between lipoprotein particles (LDL, IDL, VLDL, HDL etc) is not only their density, as the names imply, but the composition of the proteins within the particle. Many of the diseases associated with hypercholesterolemia are a result of genetic mutations in these proteins or the cellular receptors that recognize these proteins.

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The cholesterol and fatty acid portion of LDL particles are susceptible to oxidation, which can result in further free-radical damage to associated vessel walls and increased adhesion leading to vessel damage, loss of elasticity (arteriosclerosis) and build up of plaques along vessel walls (atherosclerosis). This has placed increased serum cholesterol (and especially LDL) as one of the leading causes of heart disease, itself the leading cause of death in the Western world.

The relative danger of elevated total cholesterol (TC) should be assessed with concurrent secondary risks such as smoking, obesity, family history, homocysteine levels and others. According to the Adult Treatment Panel II of the National Cholesterol Education Program (1), those with no heart disease and relatively few secondary risks should be assessed as follows: TC <200 mg/dl are classified as desirable, TC from 200 to 239 mg/dl are classified as border-line high, and those over 240 mg/dl are classified as high blood cholesterol. As secondary risk factors are added, the relative risk of cholesterol increases and should be treated more aggressively. HDL levels below 35 mg/dl have also been associated with high risk of CHD.

According to a recent publication, the guidelines set forth for cholesterol management by this panel are being neglected by a majority of physicians caring for heart patients (2). While this was primarily a survey of Midwestern States, it likely reflects the treatment throughout the rest of the United States. In fact, unless patients ask specifically for cholesterol screening, they are unlikely to be tested on a consistent basis, even when they have previously been classified as having high cholesterol.

Managing Cholesterol

There are essentially 5 ways to reduce elevated serum cholesterol.

1. Decrease the dietary intake of cholesterol, saturated fats, and trans fatty acids: While increased levels of cholesterol in the diet have only a small direct effect on total

serum cholesterol levels, chronic ingestion of cholesterol will decrease liver LDL receptors and keep serum levels high. This will be discussed further in the "Diet" section of Natural Approaches.

- 2. Increase bile production and secretion while providing a mechanism to bind and remove bile:** Probably one of the most under-utilized ways to decrease serum cholesterol. Bile salts are synthesized primarily from cholesterol, and when secreted from the liver to the gall bladder, bile includes more cholesterol. Using choloretics to stimulate bile production and secretion along with bile acid sequestering fibers is an extremely helpful way to reduce serum cholesterol levels.
- 3. Decrease the production of cholesterol:** Although every cell in the body can synthesize cholesterol, the cells in the liver provide most of the cholesterol to the rest of the body. While feedback loops exist linking cholesterol synthesis with LDL receptor function and overall fatty acid metabolism, limiting precursors or reducing the amount (or activity) of enzymes that produce cholesterol is an effective approach to reducing cholesterol.
- 4. Increase the liver's ability to bring in excess LDL particles from the blood, while reducing it's ability to secrete LDL particles into the blood stream:** This can be done by increasing the amount of LDL receptors on liver cells, which decreases de novo synthesis in the liver and gives the opportunity to remove the cholesterol via the bile or catabolic processes. Various processes also regulate the amount of cholesterol (LDL particles) secreted into the blood. These pathways can be modified to reduce the amount of LDL particles secreted.
- 5. Increase the cellular use and catabolism of cholesterol:** This speaks for itself. Through exercise and proper fatty acid metabolism, the body will

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utilize its available cholesterol for cell membranes and steroid hormones. Proper carbohydrate metabolism and blood sugar levels will keep fatty acid metabolism (β -oxidation for energy) in balance and help keep cholesterol levels down.

The best way to maintain healthy cholesterol levels or reduce already elevated cholesterol levels is to use as many of the above mechanisms as possible, simultaneously. The potency of many pharmaceutical drugs makes this difficult, if not dangerous. The natural approach, on the other hand, would combine several ingredients, each having an independent mechanism for reducing cholesterol levels at synergistic levels (sometimes sub-therapeutic if considered alone). Let us compare these approaches.

The Drugs: How They Work

Bile acid sequestrants:

Essentially this is a pharmaceutically synthesized fiber. Using a basic anion exchange resin (cholestyramine), and artificial colors, sweeteners and flavors; Bristol Laboratories produced Questran®. Cholestyramine adsorbs and combines with bile, limiting its reabsorption via the enterohepatic circulation. Side effects (constipation, gas, and intestinal pain) have lead to very low compliance.

Nicotinic acid: The use of nicotinic acid (niacin) is considered one of the first steps in the treatment of hypercholesterolemia. Usually 1-2 grams per day are given to patients with low HDL, high LDL or high triglycerides. Nicotinic acid reduces the amount of VLDL and LDL particle

production and excretion by the liver. Significant side effects (flushing, gastrointestinal, and liver toxicity) have kept this treatment from being used in a large number of patients.

HMG-CoA reductase inhibitors (Statins):

The most popular and well known of these has been lovastatin (Mevacor®), and now Lipitor®. These drugs work by inhibiting the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, an enzyme that converts HMG-CoA to mevalonate (one of the rate limiting steps

in cholesterol synthesis). These should be avoided in patients with liver conditions and has been shown to reduce levels of CoQ-10 (36), a necessary electron transport component of all tissues (especially the heart). Long-term effect on steroid hormone synthesis is still being researched.

Others: Other drugs exist, such as Clofibrate and

Gemfibrozil, which are used primarily for increased serum triglycerides although they have some effects on both LDL and HDL levels. Some of these have quite serious side effects and are being used only on difficult and high-risk patients.

In most cases, pharmaceutical drugs are unnecessary for the treatment of hypercholesterolemia, (one obvious exception would be a patient with homozygous familial hypercholesterolemia). The NCEP cholesterol recommendation was to delay the use of pharmaceuticals in all patients with high LDL and without other high CHD risk factors (1). The pharmaceutical companies have another approach. Kohn and Roth say, "Many experts have expressed concern that because of

“Many experts have expressed concern that because of vigorous promotion by pharmaceutical companies, these drugs are being urged on patients who might have benefited from a less aggressive approach. Worse yet, there seems to be an increase in noncardiac related deaths in patents who have been placed on lipid-lowering drugs. Although the reason for this has not been discovered, it does suggest that use of these drugs is not entirely innocuous and should not be undertaken without adequate justification.”(3)



NEWS PERSPECTIVES

IRON Adds To Heart Disease Risk.

In the past several years, conflicting reports have been published as to whether dietary iron has an influence on the risk of heart disease. Recent publications seem to link high blood levels of iron to the risk of heart attacks (1) and dietary iron to coronary heart disease (2). The first study investigated the amount of body iron stores (using Transferrin receptor to serum ferritin ratios) in relation to the occurrence of acute myocardial infarctions in men. After adjusting for other risk factors, men in the highest third body iron stores were 2.9 times more likely to have an acute myocardial infarction than those in the lowest third. This report confirmed previous studies by this group and others.

The second study investigated the association between dietary iron intake and risk of coronary heart disease. Again, adjusting for other variables that adversely effect heart disease, these researchers found a positive correlation between increased iron intake and coronary disease in the elderly. Women over the age of 60 seemed to be particularly at risk (odds ratio 3.5) with increased iron levels.

Increased iron levels have been implicated in two mechanisms that increase risk of coronary disease, increased red blood cell adhesion and increased lipid peroxidation. Whether these are the only mechanisms effecting vascular conditions is still undetermined. We anticipate that more studies will be conducted to investigate the extent to which iron plays a role in heart disease. What does this mean for patients?

Iron deficiency is one of the most widely spread deficiencies in the world and requires serious attention and intervention. Fortunately, the same can not be said of most of the U.S. population. With the advent of iron fortification and the amount of red meat in the diet of most Americans, iron deficiency is not a common condition in the U.S. The population we are most concerned about is women within their child-bearing years. A recent study found that only 10% of such women were iron deficient (3). While this number is still quite high (over 7 million women), these results show that 90% of these women, considered the most at risk, are not iron deficient. In men, iron deficiency is extremely rare in the U.S.

With these data in hand, it is strongly recommended that individuals should not add iron to a supplemental regimen unless they indeed have an iron deficiency. This is especially true if the individual is at any increased risk to cardiovascular disease. Unfortunately, many of the most common multi-vitamin products have 10-20 mg of iron per tablet. Physicians should become familiar with multivitamin/mineral products that are available without iron for the majority of their patient body. This will ensure that what is meant to help them, does not end up harming them.

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vigorous promotion by pharmaceutical companies, these drugs are being urged on patients who might have benefited from a less aggressive approach. Worse yet, there seems to be an increase in noncardiac related deaths in patents who have been placed on lipid-lowering drugs. Although the reason for this has not been discovered, it does suggest that use of these drugs is not entirely innocuous and should not be undertaken without adequate justification" (3). We could hardly agree more. The use of dietary changes and proper use of natural ingredients can have a dramatic effect on cholesterol levels as well as provide other effects that benefit the patients

overall health. The use of these ingredients will make the need for pharmaceuticals unnecessary, except in rare, high-risk patients.

The Natural Approach

Diet and Exercise: While this topic has been covered over and over by thousands of sources, it cannot be overemphasized. When a patient ingests large quantities of fat, cholesterol and refined sugars; their cholesterol levels will increase. Perhaps the greatest offender to cholesterol management has come in like the Trojan Horse ... trans fatty acids. Trans fatty acids are formed by taking a

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“healthy” polyunsaturated oil (liquid) and partially saturating it with hydrogen atoms (partially hydrogenated) to make it more solid (margarine, vegetable shortening). This process forms *trans* double bonds rather than the naturally occurring *cis* double bonds. Heating polyunsaturated oils (as with most deep frying) will not only produce *trans* fatty acids, but will produce oxidized oils. These unnatural fats effect the entire metabolism of lipids by slowing down enzymatic turnover rates and producing secondary metabolites that require further conversion prior to their use or removal. The irony is that these products have been considered healthier because they are cholesterol-free and made from polyunsaturated oils.

We recommend using poly-unsaturated oils in their unheated, liquid form, and using butter, coconut or palm kernel oil (we know this is against current orthodoxy) in moderation when cooking with oils. These oils are already saturated and will not be altered dramatically by heating and the body should have ample enzymatic machinery to handle these fats in **small doses**. Olive oil is a slight exception, as it is only singly unsaturated. When using olive oil, add it with the food items (not to the hot pan alone) and do not reuse oil for deep-frying.

The benefits of exercise are obvious. Not only will regular activity increase carbohydrate and lipid metabolism, it will stimulate hormonal and enzymatic activities which benefit fat metabolism. Since the work force is moving increasingly away from strenuous labor and toward automated and sedentary activities, exercise has become a recreational activity. [Our nation's youth are now moving to sedentary recreation (Nintendo etc.) making exercise labor once again.]

Oxidized Cholesterol and Antioxidants: When cholesterol loses electrons to oxygen, it becomes oxidized and changes properties. This reaction can occur as cholesterol-rich food is being processed or cooked, as well as in LDL particles floating around in the blood. Researchers at the University of California at San Francisco have now confirmed that oxidized

cholesterol is much more likely to form plaques on arterial wall (atherosclerosis) (4). Oxidized cholesterol is not only more adhesive, but can cause further damage to other lipid membranes by oxidative damage.

Significant ingestion of antioxidants is becoming more popular to combat the damage induced by cholesterol in its oxidized form (5). One of the most beneficial antioxidant in this regard is Vitamin E. The natural form of vitamin E (d- α -tocopherol) is added directly to LDL particles by the body to prevent and even reverse (reduce) the oxidized state of cholesterol. It is best to use the natural form of Vitamin E, because while the artificial form (dl- α -tocopherol) is a useful antioxidant *in vitro*, only approximately half of this is added to membranes and LDL particles.

Other antioxidants have been shown to benefit oxidized cholesterol levels directly or by “recharging” Vitamin E. One such antioxidant would be α -Lipoic acid (formerly known as Thiocetic acid). Having both fat-soluble and water-soluble components, Lipoic Acid is able to bridge the recharging of Vitamin E from Ascorbic Acid (a strictly water-soluble antioxidant). Other excellent antioxidants include grape seed extracts, other flavonoid components, selenium, glutathione, N-acetyl cysteine, natural β -carotene, and zinc to name a few. We will have expanded coverage of antioxidants and their use in subsequent newsletters.

Supplemental Oils: One of the best ways to improve the body's use of fatty acids is to give it fresh oils high in essential fatty acids. Fresh flax seed, evening primrose, borage, black current seed and fish oils taken in bulk or capsule form is an excellent way to increase the proper balance of lipid metabolism and protect against the damage caused by oxidized cholesterol and *trans* fatty acids. The oils should be as fresh as possible and processed without chemicals or heat, as these polyunsaturated oils can go rancid (oxidized) and possibly add to the problem.

Inositol Hexaniacinate: While the use of niacin is considered to be an excellent and conservative approach to cholesterol management, the side effects have kept it from its frequent use. Inositol Hexaniacinate (IH) is

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the only form of niacin not linked to significant side effects in clinical trials. IH is a central inositol molecule with 6 niacin esters attached to its six-membered ring. It is unknown why this form works just like niacin (6), but without the side effects. Most of the research has used high doses (up to 4 grams per day) of IH for the condition of intermittent claudication (7, 8). Most have found that 1000 to 1500 mg per day in divided doses is quite adequate for lowering cholesterol, especially when added to other cholesterol reducing natural ingredients.

Choloretics and natural fibers:

One of the most underutilized natural approaches to reducing cholesterol is the combined use of natural, bile sequestering fibers such as psyllium or guar gum with potent natural choloretics. There are many natural products that will stimulate bile production and secretion like dandelion root, black radish root, beet leaf tops, silymarin etc. One of the best and most consistent would be Globe artichoke (*Cynara scolymus* L.) extract containing 1-2% cynarin. A daily dose of 100-200 mg/day of a standardized artichoke extract will force the liver to produce and dump bile into the gall bladder and then into the small intestines. The liver will then take more cholesterol from the blood via its LDL receptors and produce more bile. When this is combined with a bile-sequestering fiber, the bile is unable to reabsorb and is removed with the stool. This should be a natural part of any regimen dealing with liver conditions, especially when fat or cholesterol is involved.

Garlic: Much has been written about garlic's (*Allium sativum* L.) ability to lower cholesterol, inhibit platelet aggregation and increase fibrinolysis (18, 19, 20, 21). Garlic contains an odorless compound called alliin. When crushed or chewed the alliin contacts an enzyme called allinase, which converts alliin to allicin, the active and strong smelling component of garlic. Allicin and ajoene seem to be able to interfere with the liver's ability to synthesize cholesterol. Garlic helps prevent the oxidation of cholesterol and even inhibits platelet aggregation. If your

patients can stand the smell, the best way to take garlic is fresh. Several cloves a day ought to do it. Enteric coated tablets and capsules are available which contain high amounts of alliin and allinase, which produces allicin once ingested and mixed in the small intestines. 5-10 mg of allicin/day is sufficient for most of the cardiovascular benefits derived from garlic.

Gugulipids: Gugulipids come from the resin of the mukul myrrh tree (*Commiphora mukul*). Used in India for centuries, gugulipids were researched significantly since the 1960's for obesity and lipid disorders (23). The active ingredients are the guggulsterones, which can be extracted with ethyl acetate and standardized. Gugulipid has been shown to lower serum cholesterol and triglycerides, lower LDL and raise HDL

levels. It's primary mode of action seems to be the ability to increase the number of hepatic LDL receptors (22). It has also

been implicated to increase bile secretion and decrease cholesterol synthesis, possibly due to the increased LDL receptors on liver cells. As a single ingredient, patients should try to get 50-75 mg of guggulsterones per day in divided doses (24, 29). Much less (10-25 mg/day) can be used when added with synergistic ingredients for long-term cholesterol management.

Tocotrienols: Tocotrienols are very closely related to Vitamine E (tocopherols). Found abundantly in rice bran oil and palm oil, tocotrienols may play a significant role in the natural approach to cholesterol management. A significant body of research is available which shows direct reduction of serum cholesterol (25, 26, 27, 28) with the ingestion of gamma-tocotrienols as well as closely related compounds. The mechanism is thought to be a suppression of the enzyme HMG-CoA reductase, but rather than inhibiting the enzyme (leading to build up of the enzyme as well as other precursors), tocotrienols increase the breakdown of the enzyme. Available in soft gel capsules, tocotrienols should be an adjunct therapy with capsule and tablet form

“Tocotrienols are sure to be one of the leading natural products in the next decade.”

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hypercholesterolemia products.

Pantethine: As a precursor to Coenzyme A, a necessary component of the lipid catabolic process, pantethine would be a logical addition to lipid lowering regimens. Interestingly, pantethine has been shown to lower triglycerides and LDL while increasing HDL by a mechanism other than the coenzyme A portion of the molecule (9). Pantethine is thought to inhibit cholesterol synthesis (35) as well as accelerate fatty acid break down in the mitochondria. When using pantethine as a single product, doses of 900 mg are indicated. Sub-therapeutic doses can work synergistically with other ingredients to reduce cholesterol and triglyceride levels.

Chromium: As we mentioned previously, proper carbohydrate metabolism is tied to lipid metabolism. Chromium has been used for a long time to increase insulin's effect. Known as GTF (Glucose Tolerance Factor), a niacin derivative of chromium has been used to help reduce serum glucose levels and move the body into a state of lipid catabolism. This primarily helps reduce triglycerides and to some extent cholesterol. Chromium supplementation has been shown to increase HDL and decrease total cholesterol and triglycerides (34, 35). 100-200 mcg of

chromium is more than sufficient to improve glucose tolerance and work synergistically with the other natural ingredients mentioned.

Conclusion

Since heart disease is the number one cause of death in the western world, and increased serum cholesterol one of the major risk factors, we cannot overlook natural approaches to treating this condition. Decreasing dietary intake of cholesterol, trans fatty acids and refined sugars is a foundation for any natural approach. Using a wide variety of natural ingredients to synergistically take advantage of their different cholesterol lowering properties is the best natural approach to managing cholesterol. Since the treatment will last for years, safety is a major concern. Using these natural ingredients, in sub-therapeutic, but synergistic doses will ensure good results, low side effects, and increased patient compliance. Becoming familiar with these ingredients and how they work for different metabolic types will make your approach to cholesterol management quit dynamic and will soon become the standard.

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IN MY OPINION

As many of you are aware, the approach to using natural medicines is quite different than current standard medical approaches. It's not just what's in the capsule that is different, it can be everything from the patient interview, diagnosing techniques, treatment modalities, and medications given. Those who think that "natural medicine" is simply replacing the pharmaceutical magic bullets with herbal or natural magic bullets are missing the point. Human beings are complex. When the body begins to show symptoms of disease, rarely are those symptoms directly linked with a single primary cause. Usually the symptoms will appear within the system of the body that is weakest in that individual, but your diagnosis and treatment may start elsewhere. Your goal is health, not merely lack of symptoms.

Preventative medicine is no longer truly preventative, but a management of sub-clinical conditions. We are told that atherosclerosis begins at a very young age in the United States (this was confirmed by the 18-25 year old men, autopsied after being killed in the Korean War). Taking flavonoid antioxidants, vitamin E and other lipid protecting natural ingredients may prevent an eventual cardiac event, but is truly beginning to reverse a sub-clinical blockage of the arteries. This is why natural medicine needs to be consider all aspects of the individual when diagnosing and treating.

For instance... if bowel elimination is poor, the liver will be adversely affected. If the liver is performing sub-optimally, all sorts of "unrelated" functions in the body can be affected (hormone imbalances, serum glucose levels, heartburn to name a few). One could spend a lot of time treating each symptom until it was alleviated and another manifest, while the more simple increase of bowel transit times may help alleviate a host of symptoms.

Remember that natural medicine is no more "wholistic" (sic) than other systems of medicine unless the one administering it makes it so. You need to understand a whole range of diagnosing, treatment, and natural ingredient options to become the best resource for your patients. It would be a tragedy to limit natural medicine to just herbal alternatives to prescription drugs.