Are the most commonly prescribed drugs of our time safe?

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Do you find yourself talking with your physician about why your cholesterol is too high. Is your physicians telling you that you should take a cholesterol-lowering pill, or you will probably have a heart attack or even worse a stroke that might leave you horribly disabled? Unfortunately, this is a common scenario, but the threatening way information is forced upon these unknowing patients is unconscionable. The reason is that there is no data that supports the use of a statin agent in patients based solely on cholesterol levels. There is no data that supports any protective effect of statin agents against stroke And there is no data to support that a women should ever receive statins or cholesterol-lowering medications. Absolutely no data. So why is your physician recommended those therapies. Please don't blame your doctor, as he is be duped like yourself. Unfortunately in the busy clinical practice of medicine, physicians are dependent on accurate and sound recommendations or guidelines for using medications. The guidelines created for the use of statins came from the National Cholesterol Education Program(NCEP) are thoroughly inaccurate and tainted by the fact that eight out of the nine members of the NCEP panel had financial ties to the over 15 billion dollar a year cholesterol lowering drug makers. It's difficult to maintain objectivity when faced with those kind of financial gains. Are lipid lowering guidelines really accurate as we are led to believe?
Guidelines for recommended statin use were revised in 2001, and increased its anticipated use from 13 million to 36 million patients . You can be sure that the stocks went up with this announcement. They recommended primary prevention of disease by lowering cholesterol in women and men over 65 years, yet not one of the trials cited actually provided evidence for that recommendation? Look for yourself :

Third report of the National Cholesterol Education Program(NCEP) expert panel on detection, evaluation, and treatment of high blood pressure in adults(adult treatment panel III) final report table 11. September 2002: http//www.nhlbi.nih.gov/guidelines/cholesterol

Third report of the National Cholesterol Education Program(NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults(adult treatment panel III) final report . September 2002: http//www.nhlbi.nih.gov/guidelines/cholesterol/atp3full.pdf.

Or listen to what an unbiased Harvard University physician says. Dr. Abramson at Harvard Medical School carefully examined all of the trials used to establish guidelines for statin therapy. He determined that lipid-lowering statins should not be prescribed for primary prevention in **women of any age** or for men older than 69 years of age. Also the men 30-69 years who were at high risk need to know that the it would take over 50 patients to be treated for 5 years to prevent one event. I believe it is the obligation of the prescribing physician to clearly identify the potential risks and benefits of this therapy and to not adopt the philosophy that “if you don’t take this pill you will have a heart attack”.

Unfortunately that is what the physicians are being told and thus telling their patients.

There is more convincing data to support statin use in adults 30 to eighty years of age who already have vascular disease associated with blockages in the arteries. The big question is should we be offering this to patients without vascular disease? The data does not support it, but the author's establishing guidelines still recommended it. Needless to say there are immense financial considerations driving the use of these drugs and unfortunately it is the patient that suffers the untoward consequences of unneeded therapy.

The ASCOT trial was one of the largest randomized trials studying the effectiveness of statins in women. This study found that women who took Lipitor, developed **more heart attacks** than women in the placebo group. Though not statistically significant it clearly doesn't support any cardiovascular benefits for women. So why do physicians continue to prescribe statin agents to women when numerous clinical trials fail to support their benefit? Despite the aggressive television promotions for statin use in women, the FDA repeatedly stresses the relationship between heart disease and cholesterol lowering effects of statin agents are not known.

Rosenberg in a comprehensive review published in Scandinavian Cardiovascular Journal in 2008, summarized that in the reports of statin use in women they have found a consistent pattern of "overestimation of benefit and under estimation of harm." Again, just like previous careful scrutinization of the trials, they found insufficient evidence in any of the studies to determine whether lowering lipid levels by any method reduced the risk of heart attack or stroke because women were under-represented in trials. Dr. Rosenberg et al determined that the after exhaustive literature search found that high cholesterol in women was not a predictor of cardiovascular events or stroke after age 50. Scand Cardiovasc J. I also find it interesting that to truly clarify the benefits of statin use, or lack of benefits the literature is primarily outside of the primary academic and peer reviewed journals in the United States Patients and physicians are unaware of the true risks of the lucrative statin therapies. Dr.Jay Cohen, has been in the forefront of trying to show the life-threatening qualities of cholesterol lowering therapy with Statin agents(Lipitor, Crestor, Pravachol etc). Dr. Ravnskov wrote a careful review of how two (EXCEL and AFCAPS/TexCAPS) of the three clinical trials examining healthy patients on statin therapy actually demonstrated that patients had a better chance of survival if you **didn't take the statins**, then if you did. In the infinite wisdom of the peer reviewed Archive of Internal Medicine, this simple but accurate and probing letter was rejected for publication.(34). The bottom line is that physicians in the United States are told that only the US peer-reviewed journals are accurate, and simultaneously the pharmaceutical companies and the paid-consultants/reviewers dictate what is actually being published. Something doesn't sound right with this but when you realize that it is a 15 billion dollar industry then all objectivity is escorted out the back door.

New research is revealing some alarming concerns over the safety of Statin agents and questioning its effectiveness in a high percentage of patients taking these drugs.

How do Statins Work?

Statins were initially developed by identifying a poison that is emitted from a fungus known as red yeast as a defense against attack. The original form of this discovery is known by the name Lovastatin. So statins are essentially a poison that has been patented and marketed as the miracle drug of the century.

The diagram below illustrates the means by which cholesterol is produced. The process begins with a two carbon molecule, acetyl-CoA, known as the "building block of life." Acetyl-CoA molecules combine to form hydroxymethyl glutaric acid (HMG). The enzyme HMG-CoA reductase is required for this reaction to occur. Statin drugs block this enzyme and that is why they are known as HMG-CoA reductase inhibitors. This is the reason for the reported numerous side effects. Statin drugs don't just inhibit the production of cholesterol, they inhibit the production of an entire group of intermediary enzymes and molecules that have essential biochemical functions.

Normally there are three main after the reaction where statin agents work. That means statins will block the formation of all three of these life preserving products. One of those is Cholesterol, and the other two Ubiquinone and dilochol. You probably never heard of those, but neither had I until five years ago. Medical school never emphasized these compounds, and my eight years of General surgical and Cardiothoracic surgical training never focused on these compounds and so they must not be that important. Wrong, they are extremely critical for life, but in our infinite wisdom as physicians who follow the recommendations of cholesterol experts we stop them from ever being produced. Ubiquinone also known as Co-Enzyme Q10 is an essential cellular nutrient formed in the mitochondria is necessary for ATP production and functions as the primary respiratory enzyme. Sounds rather important doesn't it? High levels of Co-Q10 are required by the heart to function. in all cell membranes where it plays a vital role in maintaining proper cell membrane structure for nerves and muscles to function. Reduction in Co-enzyme Q-10 levels have been described after statin therapy.(Mabuchi H, et al, J Atherosclero Thromb. 2005; 12(2) : 111-9) Co-Q10 deficiency can cause muscle wasting, pain and weakness and heart failure (the heart is a muscle!) as well as weakness and other tendon and ligament damage. Interestingly replenishment of Co-enzyme Q-10 will result in improved congestive heart failure in patients with dilated cardiomyopathy,(Eishershari H.,Ozer S.,et al. Potential usefulness of Coenzyme Q-10 in the treatment of idiopathic dilated cardiomyopathy in children. Int J Cardiol 2003;88: 101-2.) and improvement in Ejection fraction and NYHA classification.

Proteins are synthesized within the membranes of the endoplasmic reticulum. This complex creation of peptides is directed by dolichol phosphate. The Dolichols are also critical in the assembly of glycoproteins, which allow complex protein structures to fold and interact with receptors and membranes. Dolichol-mediated processes create complex neuropeptides, and mechanisms critical in cellular communication, identification, and immune function. It is difficult to understand how these complex functions can occur in the face of a severe statin induced Dolichol deficiency. The reality of Dolichol inhibition by statin agents is evident and the resultant turmoil in cellular function is not unexpected. It is also not unexpected that altered cognition and abnormal behavior can result from statin induced neuropeptide formation. Increased incidence of malignancies have also been described in Dolichol deficiencies relating to erroneous signals in genetically programmed directives. Statin drugs can interfere with these directives causing problems at all cellular levels with unpredictable results.

Cholesterol

Another common side effect associated with statin agents when used to dramatically reduce cholesterol levels are the neurodegenerative type diseases, almost like Lou Gehrig's disease or Multiple sclerosis, and this is because there is damage to the cellular membranes that make up the insulation around the nerves. It is like electrical wiring in an old house where the insulation around the wire has broken down leaving exposed wiring. It just doesn't work as well, and inadequate electrical supply and short circuiting becomes more common. These poorly functioning nerves and membranes result in muscle aches/pains as well as decrease strength and decreased nerve function. Memory and thought process may also be severely affected.

Dr. Graveline points out that we are all at risk when the general public is taking statins--do you want to be in an airplane when your pilot develops statin-induced amnesia?

It seems that a lot of these problems begin when cholesterol levels become elevated and aggressive reduction occurs with the use of statin agents.

Therefore elevated cholesterol levels have been described as the initiating phase in the development of atherosclerosis. Lipitor also blocks the important production of coenzyme q-10, which is necessary to maintain heart muscle health and energy. In women with low coenzyme q-10 levels the incidence of breast cancer is markedly increased. The importance of coenzyme Q-10 is derived from its ability to provide energy to the body. It helps process ATP, and transports it into the cells. Coenzyme q-10 is very beneficial in patients with cardiomyopathies from heart damage, because they are chronically starved for energy. By introducing coenzyme q-10, the energy producing ATP is express delivered into the energy starved heart muscle cells.

Co-enzyme Q-10, is a vitamin like substance and is found in all cells, and it is critical for the production of energy. In fact, 95 % of all energy made by our cells is produced with the assistance of Co-enzyme Q-10. Organs that need an incredible amount of energy to function, such as the heart, lungs, and liver will have the highest concentration of Q-10.

If you are still wondering why it is so important, let's look at these facts. Studies have shown that the use of statin agents for cholesterol control will reduce the level of co-enzyme q-10 by up to 40%, and that by replacing the coenzyme, the muscle aches that are so prevalent with statin therapy disappear. It appears that these statin agents, by altering membrane function actually also impair energy transport to these muscles to keep them functioning properly. Co-enzyme q-10 has also been used in patients with congestive heart failure and this is related to providing energy through ATP to damaged, poorly functioning, energy starved cells. It has also been used in patients on the list for heart transplant, and allows them to safely wait until a heart is available without going into heart failure. Recent reports have also shown improvement in ejection fraction, stroke volume, cardiac index and exercise tolerance. Other studies have been performed to evaluate the benefit of coenzyme Q-10 in patients undergoing heart surgery. It has been shown to improve cardiac function after coronary artery bypass or valve replacement. I like use Coenzyme Q-10 in conjunction with D-ribose on my off-pump coronary bypass patients. When operating on a heart that is still beating, one needs to cause localized ischemia or lack of blood flow to the area that you are operating on. This repeated ischemia causes the heart to not function as well after repeated bypasses, as it leaks all its ATP out of the muscle cells. Adding Co-Q10 and ribose stabilizes this loss and allows coronary artery bypass to be performed safely without ever stopping the heart.

Why does the serum cholesterol levels seem to increase as patients reach their 40's and 50's? Is it because when we were in our 20's we ate so carefully, and now that we approach our 50's we are ambivalent about our diet? I would suspect that is quite the opposite, but then why do the levels increase? The classic stressed type A business man seems to be the poster child for elevated cholesterol and the increased development of heart disease. Why is that? Diet and exercise or lack of certainly play critical roles in this process but how does our body deal with stress? Cortisol and DHEA levels sky-rocket in the face of stress, and in some patients, remain constantly elevated throughout the entire day. Our body has to produce these stress hormones and how does it do it. The precursor, or beginning compound for all of the stress and sex hormones is cholesterol(figure 1). Steroid hormones reduced by statin therapy include Pregnenolone,Progesterone,Estrogen,Testosterone, Aldosteroen, Cortisol and DHEA. Therefore, to compensate for the tremendous need for managing stress, the body and all its very complicated synthetic processes signal the need to appropriately produce more cholesterol. Unfortunately, as physicians, our response is to block that appropriate response mechanism in an attempt to protect the patient from presumed heart disease.

When women develop menopause, and men develop andropause, the body appropriately compensates by signaling the increased production of cholesterol(figure 1), as well as the increased absorption through the gastrointestinal system. The subsequent increase in cholesterol provides precursor molecules for the body to try and produce the needed sex hormones. In men, studies have shown that testosterone replacement therapy will reduce cholesterol levels, and in fact have been shown to reduce insulin resistance and the metabolic syndrome. Proper hormone replacement in women with progesterone and estrogen also results in the reduction of LDL cholesterol. The meticulous feedback mechanisms demonstrated throughout our body are manifested by responsive cholesterol levels. So why do we try and disrupt these mechanisms? The aggressive lowering of total cholesterol below 140 mg/dl will result in the dramatic reduction of testosterone production in males with a resultant drug induced andropause and its associated depression and fatigue.

Of course, statins inhibit the production of cholesterol--they do this very well. Cholesterol is the body's repair substance: scar tissue contains high levels of cholesterol, including scar tissue in the arteries.

Cholesterol is the precursor to vitamin D(see figure 1), necessary for numerous biochemical processes including mineral metabolism. The use of statin agents will reduce the synthesis of Vitamin D. Studies have identified the increased incidence of musculoskeletal pain in patients who are vitamin D deficient, and that replacement results in dramatic improvement.(Al Faraj S.,et al. Vitamin D Deficiency and chronic low back pain in Saudi Arabia," Spine 2003; 28(2): 177-9). Vitamin D has also been shown to dramatic reduce the incidence of cancer in postmenopausal women.(Lappe, American Journal of Clinical Nutrition 2007).

A number of patients describe gastrointestinal symptoms and diarrhea associated with statin therapy. Unfortunately after an extensive gastrointestinal workup, the stain therapy is not discontinued. Statin agents reduce bile salts production, which is required for the digestion of fat.(Figure 1). Those who suffer from low cholesterol often have trouble digesting fats. Cholesterol also functions as a powerful antioxidant, thus protecting us against cancer and aging.

Cholesterol is vital to proper neurological function. It plays a key role in the formation of memory and the uptake of hormones in the brain, including serotonin. When cholesterol levels drop too low, the serotonin receptors cannot function properly. Cholesterol is the main organic molecule in the brain, constituting over half the dry weight of the cerebral cortex, and critical in maintaining cell membranes and the integrity of the nervous system by producing myelin.

It is no surprise that the aggressive control of cholesterol in an attempt to reduce cardiovascular disease, in itself produces it's own disease process.