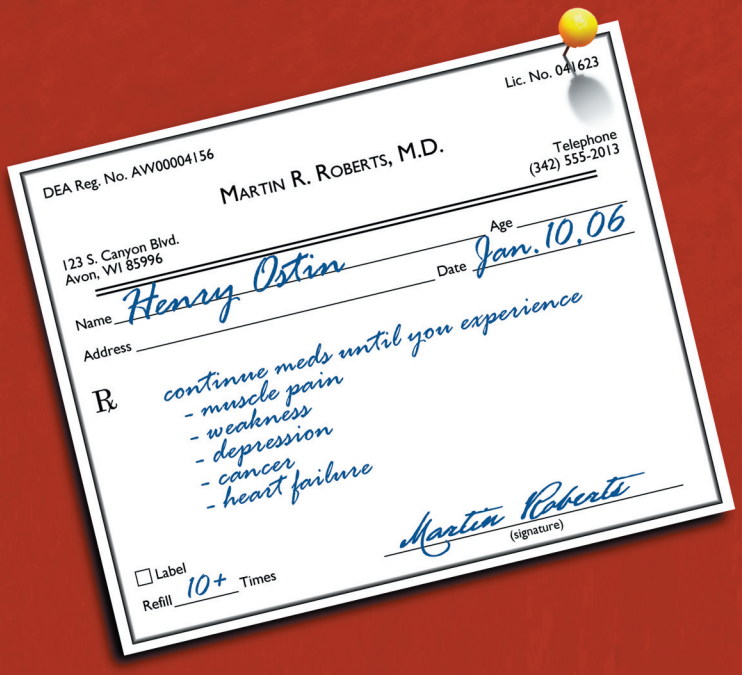
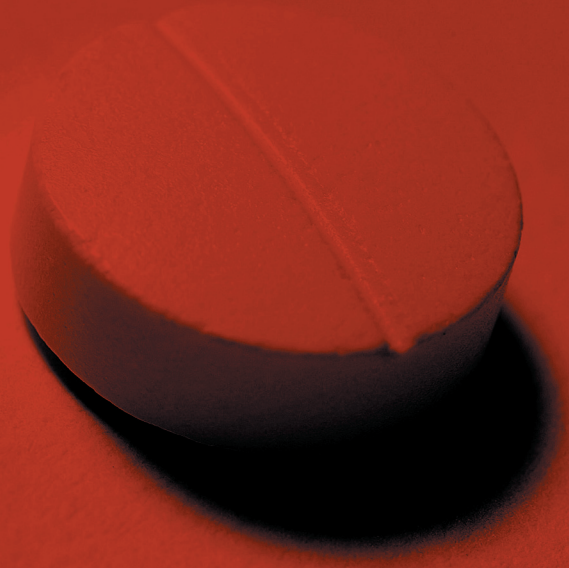
# Dangers of Statin Drugs:

## What You Haven't Been Told About Cholesterol-Lowering Medicines

by Sally Fallon and Mary G. Enig, PhD



**Hypercholesterolemia** is *the* health issue of the 21st century. It is actually an invented disease, a "problem" that emerged when health professionals learned how to measure cholesterol levels in the blood. High cholesterol exhibits no outward signs—unlike other conditions of the blood, such as diabetes or anemia, diseases that manifest telltale symptoms like thirst or weakness—hypercholesterolemia requires the services of a physician to detect its presence. Many people who feel perfectly healthy suffer from high cholesterol—in fact, feeling good is actually a symptom of high cholesterol!

Doctors who treat this new disease must first convince their patients that they are sick and need to take one or more expensive drugs for the rest of their lives, drugs that require regular checkups and blood tests. But such doctors do not work in a vacuum. Their efforts to convert healthy people into patients are bolstered by the full weight of the US government, the media and the medical establishment—agencies that have worked in concert to disseminate the cholesterol dogma and convince the population that high cholesterol is the forerunner of heart disease and possibly other diseases as well.

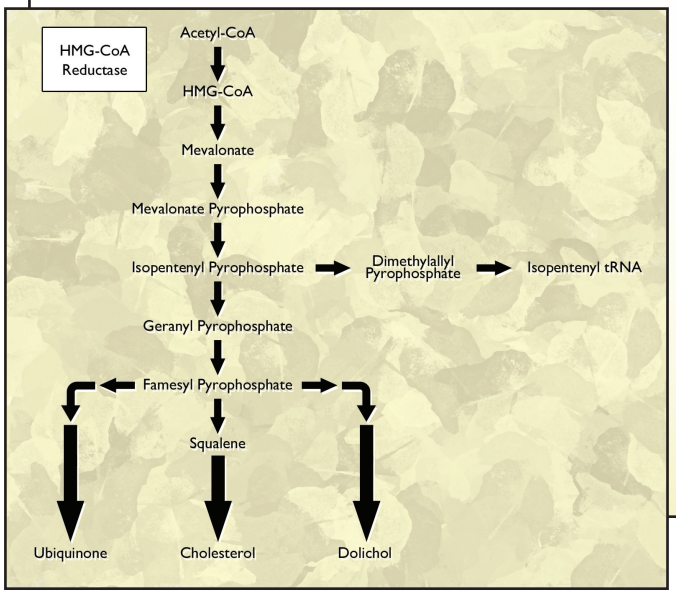
Who suffers the most from hypercholesterolemia? Peruse the medical literature of 25 or 30 years ago and you'll get the following answer: any middle-aged man whose cholesterol is over 240 with other risk factors, such as smoking or overweight. After the Cholesterol Consensus Conference in 1984, the parameters changed; anyone (male or female) with cholesterol over 200 could receive the dreaded diagnosis and a prescription for pills. Recently that number has been moved down to 180. If you have had a heart attack, you get to take cholesterol-lowering medicines even if your cholesterol is already very low—after all, you have committed the sin of having a heart attack so your cholesterol must therefore be too

high. The penance is a lifetime of cholesterol-lowering medications along with a boring, low fat diet. But why wait until you have a heart attack? Since we all labor under the stigma of original sin, we are all candidates for treatment. Current edicts stipulate cholesterol testing and treatment for young adults and even children.

The drugs that doctors use to treat the new disease are called statins—sold under a variety of names including Lipitor (atorvastatin), Zocor (simvastatin), Mevacor (lovastatin) and Pravachol (pravastatin).

## How Statins Work

The diagram below illustrates the pathways involved in cholesterol production. The process begins with acetyl-CoA, a two-carbon molecule sometimes referred to as the "building block of life." Three acetyl-CoA molecules combine to form six-carbon hydroxymethyl glutaric acid (HMG). The step from HMG to mevalonate requires an enzyme, HMG-CoA reductase. Statin drugs work by inhibiting this enzyme—hence the formal name of HMG-CoA reductase inhibitors. Herein lies the potential for numerous side effects, because statin drugs inhibit not just the production of cholesterol, but a whole family of intermediary substances, many if not all of which have important biochemical functions in their own right.




Consider the findings of pediatricians at the University of California, San Diego who published a description of a child with an hereditary defect of mevalonic kinase, the enzyme that facilitates the next step beyond HMG-CoA reductase.[1] The child was mentally retarded, microcephalic (very small head), small for his age, profoundly anemic, acidotic and febrile. He also had cataracts. Predictably, his cholesterol was consistently low—70-79 mg/dl. He died at the age of 24 months. The child represents an extreme example of cholesterol inhibition, but his case illuminates the possible consequences of taking statins in strong doses or for a lengthy period of time—depression of mental acuity, anemia, acidosis, frequent fevers and cataracts.

Cholesterol is one of three end products in the mevalonate chain. The two others are ubiquinone and dilochol. Ubiquinone or Co-Enzyme $Q_{10}$ is a critical cellular nutrient biosynthesized in the mitochondria. It plays a role in ATP production in the cells and functions as an electron carrier to cytochrome oxidase, our main respiratory enzyme. The heart requires high levels of Co-$Q_{10}$. A form of Co-$Q_{10}$ called ubiquinone is found in all cell membranes where it plays a role in maintaining membrane integrity so critical to nerve conduction and muscle integrity. Co-$Q_{10}$ is also vital to the formation of elastin and collagen. Side effects of Co-$Q_{10}$ deficiency include muscle wasting leading to weakness and severe back pain, heart failure (the heart is a muscle!), neuropathy, and inflammation of the tendons and ligaments, often leading to rupture.

Dolichols also play a role of immense importance. In the cells they direct various proteins manufactured in response to DNA directives to their proper targets, ensuring that the cells respond correctly to genetically programmed instruction. Thus statin drugs can lead to unpredictable chaos on the cellular level, much like a computer virus that wipes out certain pathways or files.

Squalene, the immediate precursor to cholesterol, has anti-cancer effects, according to research.

The fact that some studies have shown that statins can prevent heart disease, at least in the short term, is most likely explained not by the inhibition of cholesterol production but because they block the creation of mevalonate. Reduced amounts of mevalonate seem to make smooth muscle cells less active, and platelets less able to produce thromboxane.

Atherosclerosis begins with the growth of smooth muscle cells in side artery walls and thromboxane is necessary for blood clotting.

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## Cholesterol

Of course, statins inhibit the production of cholesterol—they do this very well. Nowhere is the failing of our medical system more evident than in the wholesale acceptance of cholesterol reduction as a way to prevent disease. Have all these doctors forgotten what they learned in biochemistry 101 about the many roles of cholesterol in the human biochemistry? Every cell membrane in our body contains cholesterol because cholesterol is what makes our cells waterproof—without cholesterol we could not have a different biochemistry on the inside and the outside of the cell. When cholesterol levels are not adequate, the cell membrane becomes leaky or porous—a situation the body interprets as an emergency, releasing a flood of corticoid hormones that work by sequestering cholesterol from one part of the body and transporting it to areas where it is lacking. 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, necessary for numerous biochemical processes including mineral metabolism. The bile salts, required for the digestion of fat, are made of cholesterol. 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, the body's feel-good chemical. When cholesterol levels drop too low, the serotonin receptors cannot work. Cholesterol is the main organic molecule in the brain, constituting over half of the dry weight of the cerebral cortex.

Finally, cholesterol is the precursor to all the hormones produced in the adrenal cortex including glucocorticoids (which regulate blood sugar levels) and mineralocorticoids (which regulate mineral balance). Corticoids are the cholesterol-based adrenal hormones that the body uses in response to stress of various types. It promotes healing and balances the tendency to inflammation. The adrenal cortex also produces sex hormones out of cholesterol including testosterone, estrogen and progesterone. Thus, low cholesterol—whether due to an innate error of metabolism or induced by cholesterol-lowering diets and drugs—can be expected to disrupt the production of adrenal hormones and lead to blood sugar problems, edema, mineral deficiencies, chronic inflammation, difficulty in healing, allergies, asthma, reduced libido, infertility and various reproductive problems.

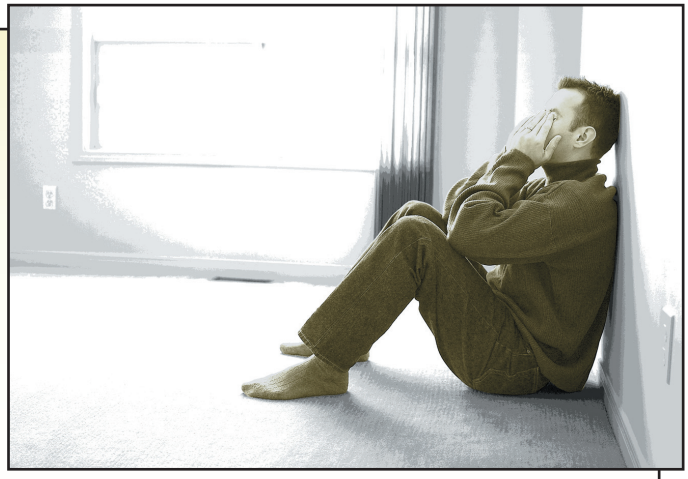
## Enter The Statins

Statin drugs entered the market with great promise. They replaced a class of pharmaceuticals that lowered cholesterol by preventing its absorption from the gut. These drugs often had immediate and unpleasant side effects, including nausea, indigestion and constipation, and in the typical patient they lowered cholesterol levels only slightly. Patient compliance was low: the benefit did not seem worth the side effects and the potential for use very limited. By contrast, statin drugs had no immediate side effects: they did not cause nausea or indigestion and they were consistently effective, often lowering cholesterol levels by 50 points or more. During the last 20 years, the industry has mounted an incredible promotional campaign—enlisting scientists, advertising agencies, the media and the medical profession in a blitz that turned the statins

into one of the bestselling pharmaceuticals of all time. Sixteen million Americans now take Lipitor, the most popular statin, and drug company officials claim that 36 million Americans are candidates for statin drug therapy. What bedevils the industry is growing reports of side effects that manifest many months after the commencement of therapy. The November 2003 issue of *Smart Money* magazine reports on a 1999 study at St. Thomas' Hospital in London (apparently unpublished), which found that 36 percent of patients on Lipitor's highest dose reported side effects; even at the lowest dose, 10 percent reported side effects.[2]

## Muscle Pain And Weakness

The most common side effect is muscle pain and weakness, a condition called rhabdomyolysis, most likely due to the depletion of Co-$Q_{10}$, a nutrient that supports muscle function. Dr. Beatrice Golomb of San Diego, California is currently conducting a series of studies on statin side effects. The industry insists that only 2-3 percent of patients get muscle aches and cramps but in one study, Golomb found that 98 percent of patients taking Lipitor and one-third of the patients taking Mevacor (a lower-dose statin) suffered from muscle problems.[3] A message board devoted to Lipitor at forum.ditonline.com contains more than 800 posts, many detailing severe side effects. The Lipitor board at www.rxlist.com contains more than 2,600 posts.



The test for muscle wasting or rhabdomyolysis is elevated levels of a chemical called creatine kinase (CK). But many people experience pain and fatigue even though they have normal CK levels.[4]

Tahoe City resident Doug Peterson developed slurred speech, balance problems and severe fatigue after three years on Lipitor—for two and a half years, he had no side effects at all.[5] It began with restless sleep patterns—twitching and flailing his arms. Loss of balance followed and the beginning of what Doug calls the "statin shuffle"—a slow, wobbly walk across the room. Fine motor skills suffered next. It took him five minutes to write four words, much of which was illegible. Cognitive function also declined. It was hard to convince his doctors that Lipitor could be the culprit, but when he finally stopped taking it, his coordination and memory improved.

John Altrocchi took Mevacor for three years without side effects; then he developed calf pain so severe he could hardly walk. He also experienced episodes of temporary memory loss.

For some, however, muscle problems show up shortly after treatment begins. Ed Ontiveros began having muscle problems within 30 days of taking Lipitor. He fell in the bathroom and had trouble getting up. The weakness subsided when he went off Lipitor. In another case, reported in the medical journal *Heart*, a patient developed rhabdomyolysis after a single dose of a statin.[6] Heel pain from plantar fascitis (heel spurs) is another common complaint among those taking statin drugs. One correspondent reported the onset of pain in the feet shortly after beginning statin treatment. She had visited an evangelist, requesting that he pray for her sore feet. He enquired whether she was taking Lipitor. When she said yes, he told her that his feet had also hurt when he took Lipitor.[7]

Active people are much more likely to develop problems from statin use than those who are sedentary. In a study carried out in Austria, only six out of 22 athletes with familial hypercholesterolemia were able to endure statin treatment.[8] The others discontinued treatment because of muscle pain.

By the way, other cholesterol-lowering agents besides statin drugs can cause joint pain and muscle weakness. A report in *Southern Medical Journal* described muscle pains and weakness in a man who took Chinese red rice, an herbal preparation that lowers cholesterol.[9] Anyone suffering from myopathy, fibromyalgia,

coordination problems and fatigue needs to look at low cholesterol plus Co-$Q_{10}$ deficiency as a possible cause.

## Neuropathy

Polyneuropathy, also known as peripheral neuropathy, is characterized by weakness, tingling and pain in the hands and feet as well as difficulty walking. Researchers who studied 500,000 residents of Denmark, about 9 percent of that country's population, found that people who took statins were more likely to develop polyneuropathy.[10] Taking statins for one year raised the risk of nerve damage by about 15 percent—about one case for every 2,200 patients. For those who took statins for two or more years, the additional risk rose to 26 percent.

According to the research of Dr. Golomb, nerve problems are a common side effect from statin use; patients who use statins for two or more years are at a four to 14-fold increased risk of developing idiopathic polyneuropathy compared to controls.[11] She reports that in many cases, patients told her they had complained to their doctors about neurological problems, only to be assured that their symptoms could not be related to cholesterol-lowering medications. The damage is often irreversible. People who take large doses for a long time may be left with permanent nerve damage, even after they stop taking the drug.

The question is, does widespread statin-induced neuropathy make our elderly drivers (and even not-so-elderly drivers) more accident prone? In July of 2003, an 86-year-old driver with an excellent driving record plowed into a farmers' market in Santa Monica, California, killing 10 people. Several days later, a most interesting letter from a Lake Oswego, Oregon woman appeared in the *Washington Post*:[12]

> "My husband, at age 68, backed into the garage and stepped on the gas, wrecking a lot of stuff. He said his foot slipped off the brake. He had health problems and is on medication, including a cholesterol drug, which is now known to cause problems with feeling in one's legs.
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> "In my little community, older drivers have missed a turn and taken out the end of a music store, the double doors of the post office and the front of a bakery. In Portland, a bank had to do without its drive-up window for some time.
>
> "It is easy to say that one's foot slipped, but the problem could be lack of sensation. My husband's sister-in-law thought her car was malfunctioning when it refused to go when a light turned green, until she looked down and saw that her food was on the brake. I have another friend who mentioned having no feeling in her lower extremities. She thought about having her car retrofitted with hand controls but opted for the handicapped bus instead."

## Heart Failure

We are currently in the midst of a congestive heart failure epidemic in the United States—while the incidence of heart attack has declined slightly, an increase in the number heart failure cases has outpaced these gains. Deaths attributed to heart failure more than doubled from 1989 to 1997.[13] (Statins were first given pre-market approval in 1987.) Interference with production of Co-$Q_{10}$ by statin drugs is the most likely explanation. The heart is a muscle and it cannot work when deprived of Co-$Q_{10}$.

Cardiologist Peter Langsjoen studied 20 patients with completely normal heart function. After six months on a low dose of 20 mg of Lipitor a day, two-thirds of the patients had abnormalities in the heart's filling phase, when the muscle fills with blood. According to Langsjoen, this malfunction is due to Co-$Q_{10}$ depletion. Without Co-$Q_{10}$, the cell's mitochondria are inhibited from producing energy, leading to muscle pain and weakness. The heart is especially susceptible

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because it uses so much energy.[14]

Co-$Q_{10}$ depletion becomes more and more of a problem as the pharmaceutical industry encourages doctors to lower cholesterol levels in their patients by greater and greater amounts. Fifteen animal studies in six different animal species have documented statin-induced Co-$Q_{10}$ depletion leading to decreased ATP production, increased injury from heart failure, skeletal muscle injury and increased mortality. Of the nine controlled trials on statin-induced Co-$Q_{10}$ depletion in humans, eight showed significant Co-$Q_{10}$ depletion leading to decline in left ventricular function and biochemical imbalances.[15]

Yet virtually all patients with heart failure are put on statin drugs, even if their cholesterol is already low. Of interest is a recent study indicating that patients with chronic heart failure benefit from having high levels of cholesterol rather than low. Researchers in Hull, UK followed 114 heart failure patients for at least 12 months.[16] Survival was 78 percent at 12 months and 56 percent at 36 months. They found that for every point of decrease in serum cholesterol, there was a 36 percent increase in the risk of death within 3 years.

## Dizziness

Dizziness is commonly associated with statin use, possibly due to pressure-lowering effects. One woman reported dizziness one half hour after taking Pravachol.[17] When she stopped taking it, the dizziness cleared up. Blood pressure lowering has been reported with several statins in published studies. According to Dr. Golumb, who notes that dizziness is a common adverse effect, the elderly may be particularly sensitive to drops in blood pressure.[18]

## Cognitive Impairment

The November 2003 issue of *Smart Money*[19] describes the case of Mike Hope, owner of a successful ophthalmologic supply company: "There's an awkward silence when you ask Mike Hope his age. He doesn't change the subject or stammer, or make a silly joke about how he stopped counting at 21. He simply doesn't remember. Ten seconds pass. Then 20. Finally an answer comes to him. 'I'm 56,' he says. Close, but not quite. 'I will be 56 this year.' Later, if you happen to ask him about the book he's reading, you'll hit another roadblock. He can't recall the title, the author or the plot." Statin use since 1998 has caused his speech and memory to fade. He was forced to close his business and went on Social Security 10 years early. Things improved when he discontinued Lipitor in 2002, but he is far from complete recovery—he still cannot sustain a conversation. What Lipitor did was turn Mike Hope into an old man when he was in the prime of life.

Cases like Mike's have shown up in the medical literature as well. An article in *Pharmacotherapy*, December 2003, for example, reports two cases of cognitive impairment associated with Lipitor and Zocor.[20] Both patients suffered progressive cognitive decline that reversed completely within a month after discontinuation of the statins. A study conducted at the University of Pittsburgh showed that patients treated with statins for six months compared poorly with patients on a placebo in solving complex mazes, psychomotor skills and memory tests.[21]

Dr. Golomb has found that 15 percent of statin patients develop some cognitive side effects.[22] The most harrowing involve global transient amnesia—complete

memory loss for a brief or lengthy period—described by former astronaut Duane Graveline in his book *Lipitor: Thief of Memory*.[23] Sufferers report baffling incidents involving complete loss of memory—arriving at a store and not remembering why they are there, unable to remember their name or the names of their loved


ones, unable to find their way home in the car. These episodes occur suddenly and disappear just as suddenly. 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?

While the pharmaceutical industry denies that statins can cause amnesia, memory loss has shown up in several statin trials. In a trial involving 2502 subjects, amnesia occurred in 7 receiving Lipitor; amnesia also occurred in 2 of 742 subjects during comparative trials with other statins. In addition, "abnormal thinking" was reported in 4 of the 2502 clinical trial subjects.[24] The total recorded side effects was therefore 0.5 percent; a figure that likely under-represents the true frequency since memory loss was not specifically studied in these trials.

## Cancer

In every study with rodents to date, statins have caused cancer.[25] Why have we not seen such a dramatic correlation in human studies? Because cancer takes a long time to develop and most of the statin trials do not go on longer than two or three years. Still, in one trial, the CARE trial, breast cancer rates of those taking a statin went up 1500 percent.[26] In the Heart Protection Study, non-melanoma skin cancer occurred in 243 patients treated with simvastatin compared with 202 cases in the control group.[27]

Manufacturers of statin drugs have recognized the fact that statins depress the immune system, an effect that can lead to cancer and infectious disease, recommending statin use for inflammatory arthritis and as an immune suppressor for transplant patients.[28]

## Pancreatic Rot

The medical literature contains several reports of pancreatitis in patients taking statins. One paper describes the case of a 49-year-old woman who was admitted to the hospital with diarrhea and septic shock one month after beginning treatment with lovastatin.[29] She died after prolonged hospitalization; the cause of death was necrotizing pancreatitis. Her doctors noted that the patient had no evidence of common risk factors for acute pancreatitis, such as biliary tract disease or alcohol use. "Prescribers of statins (particularly simvastatin and lovastatin) should take into account the possibility of acute pancreatitis in patients who develop abdominal pain within the first weeks of treatment with these drugs," they warned.

## Depression

Numerous studies have linked low cholesterol with depression. One of the most recent found that women with low cholesterol are twice as likely to suffer from depression and anxiety. Researchers from Duke University Medical Center carried out personality trait measurements on 121 young women aged 18 to 27.[30] They found that 39 percent of the women with low cholesterol levels scored high on personality traits that signalled proneness to depression, compared to 19 percent of women with normal or high levels of cholesterol. In addition, one in three of the women with low cholesterol levels scored high on anxiety indicators, compared to 21 percent with normal levels. Yet the author of the study, Dr. Edward Suarez, cautioned women with low cholesterol against eating "foods such as cream cakes" to raise cholesterol, warning that these types of food "can cause heart disease." In previous studies on men, Dr. Suarez found that men who lower their cholesterol levels with medication have increased rates of suicide and violent death, leading the researchers to theorize "that low cholesterol levels were causing mood disturbances."

How many elderly statin-takers eke through their golden years feeling miserable and depressed, when they should be enjoying

their grandchildren and looking back with pride on their accomplishments? But that is the new dogma—you may have a long life as long as it is experienced as a vale of tears.

## Any Benefits?

Most doctors are convinced—and seek to convince their patients—that the benefits of statin drugs far outweigh the side effects. However, the results of major studies generally showed only small differences, and these differences were often statistically insignificant and independent of the amount of cholesterol lowering achieved. In the next issue of *HealthKeepers Magazine*, we will discuss many of these recently published studies. Additional uses for statin drugs and the financial repercussion of these drugs will also be investigated. HK


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