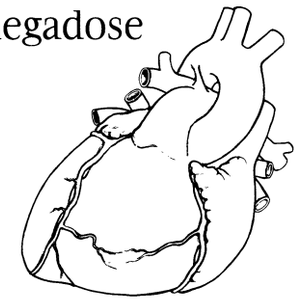
'Hearty' Vitamins

Sparing arteries with megadose supplements



By JANET RALOFF

The same chemical reaction that turns meat and butter rancid appears to play a pivotal role in atherosclerosis — the development of artery-clogging plaque. But a new study now suggests that megadoses of certain vitamins may help limit plaque buildup, a leading contributor to heart attacks and stroke.

Low-density lipoproteins (LDLs) — the so-called "bad" lipoproteins — carry 60 to 80 percent of the cholesterol in blood. Over the past decade, studies have strongly suggested that the accumulation of fatty deposits along artery walls may trace to the chemical modification of LDLs through the process of oxidation.

For instance, macrophages are cells that usually scavenge foreign debris. But they voraciously consume LDLs — if those LDLs are oxidized. Indeed, macrophages will pig out on oxidized LDLs until they swell into unrecognizable "foam" cells. Congregating along arterial walls, these foam cells constitute the beginnings of an atherosclerotic plaque. To a growing number of researchers, observes Ishwarlal Jialal of the University of Texas Southwestern Medical Center in Dallas, "oxidative modification of LDL is now the most plausible explanation of how cholesterol promotes atherosclerosis."

Though LDLs naturally carry a number of antioxidants, the rampant coronary artery disease in most Western societies would seem to indicate that our diets do not contain enough antioxidants to meet the challenge LDLs face. Jialal and co-worker Scott Grundy decided to see if they couldn't offer LDLs more help.

The two recruited 24 men, age 25 to 70, and divided them into two age- and weight-matched cohorts. Ranging from lean to obese, these men included both healthy individuals and persons receiving treatment for coronary artery disease. One group received a three-month supply of soybean-oil capsules. The other group got identical capsules containing 800 international units (I.U.s) of vitamin E (tocopherol) — 80 to 100 times the recommended daily allowance of this, the body's premier antioxidant.

Before the study and at six and 12 weeks into it, Jialal's team withdrew blood from each volunteer and prepared extracts of their LDLs, which they then subjected to conditions that foster oxidation.

Initially, there was little difference between the groups. By 12 weeks, however, concentrations of tocopherol in the blood were 4.4 times higher in the vitamin-supplemented group, according to a report in the June JOURNAL OF LIPID RESEARCH. More important, by six weeks, LDLs from the vitamin-E-supplemented men sustained less than half the oxidative damage of LDLs from unsupplemented men — and remained less susceptible to oxidation throughout the rest of the study, Jialal notes.

"This is the first study to clearly show in a large number of patients that vitamin E has something to do with LDL oxidation," Jialal told SCIENCE NEWS.

Hermann Esterbauer and his colleagues at the University of Graz, Austria, observed a similar trend in a pilot trial they reported in the August 1991 JOURNAL OF LIPID RESEARCH. Just three weeks long, that study compared the oxidation vulnerability of LDLs from eight men receiving tocopherol supplements (two each receiving 140, 225, 800, and 1,200 I.U.s daily) to that of four men receiving placebo capsules of oil.

Like the Dallas study, this one found that as the LDLs' vitamin E content increased, they were able to resist oxidation longer. But in the Graz study — which also assayed another class of antioxidants called carotenoids — that lag was tied more closely to the LDLs' total antioxidants than to tocopherol alone.

The Dallas study "clearly shows the protective effect [of antioxidant vitamins on LDLs]," says Daniel Steinberg of the University of California, San Diego. "What we don't know is the degree of protection needed to have an impact on the atherogenic process."

Last September, Steinberg headed a National Heart, Lung, and Blood Institute workshop on antioxidants and atherosclerosis. Its participants concluded that experiments by Steinberg and others offer "reasonably strong" evidence that oxidation can foster atherosclerosis and that antioxidants can slow plaque deposition — at least in animals.

Studies published since then suggest that oxidation also plays a central role in human heart disease. For instance, a study of 60 men reported in the April 11 LANCET found that blood concentrations of antibodies to oxidized LDLs correlated with the amount of plaque clogging the carotid artery. Jukka T. Salonen of the University of Kuopio, Finland, and his coworkers conclude that their finding provides "the first prospective evidence in humans for an *in vivo* role of lipid [oxidation] in atherogenesis."

A Swedish team has also linked the severity of coronary atherosclerosis in 35 men who survived heart attacks with the susceptibility of each man's LDLs to oxidation. These researchers also found a "strong correlation" between the triglyceride content of a man's LDLs and their vulnerability to oxidation.

If these findings are substantiated, write Jan Regnström of the King Gustaf Vth Research Institute in Stockholm and his colleagues in the May 16 LANCET, "LDL susceptibility to oxidation would need to be taken into account as an important risk factor for coronary heart disease."

If nontoxic doses of antioxidants offer the health benefits Steinberg, Jialal, and others now anticipate, physicians may soon begin prescribing one or more of these vitamins to slow the inexorable deposition of potentially lethal plaque.

Steinberg says several researchers have begun planning or implementing trials to tease out the human health benefits of boosting LDL oxidant defenses — usually with some combination of vitamin E, vitamin C, and beta carotene. Because smokers inhale many powerful oxidants, he noted, "we're probably going to include cigarette smokers in our study rather than exclude them, because we think they may get more benefit."

How soon until the results are in? It depends on the trial. "If you wait to clock heart attacks, it will probably take about five years," Steinberg says. "If you just do angiographic studies [to map the progressive deposition of arterial plaque], it might take only two years."

That's exciting, he says, when you consider that "we're dealing with an aspect of atherosclerosis that had not even been suspected until about eight years ago." □