Fats & Oils News

Reducing serum cholesterol cuts heart disease

The National Institutes of Health announced in mid-January that its 7-year Lipid Research Clinic Coronary Primary Prevention Trial study had demonstrated "conclusively that the risk of coronary heart disease can be reduced by lowering blood cholesterol."

Although other studies have linked cholesterol and heart disease, NIH officials said this study was important as it was the first to show that reducing low-density lipoprotein cholesterol (LDL-cholesterol) and overall cholesterol can reduce incidence of coronary heart disease death and myocardial infarction.

The NIH study involved 3,806 men age 35 to 59 with high blood-cholesterol levels (at least 265 mg/dL) who showed no previous evidence of heart disease when selected for the study. Those selected had maintained high serum-cholesterol levels after being placed on a moderate cholesterol-lowering diet.

After being selected for the trial, all were continued on a moderate cholesterol-lowering diet. In a double-blind study, half were assigned randomly to a group that received daily dosages of 24 grams of cholestyramine, a bile-sequestrant drug. The other half received a similarly packaged placebo.

At the end of the 7-year trial, participants who received cholestyramine showed a reduction of 13.4% in total cholesterol and 20.3% in LDL cholesterol; those in the placebo group showed an 8.5% reduction in total cholesterol, 12.6% in LDL cholesterol. The difference was somewhat less than expected, but still statistically significant. Researchers noted some participants had to be given a reduced dosage because of side effects or other reasons.

A 19% difference in coronary heart disease death or non-fatal heart attacks was found between the cholestyramine group and the placebo group. The difference in development of angina was 20%; in coronary bypass surgery, 21%; and in a new positive exercise test, 25%. "As a rough rule of thumb, each 1% fall in cholesterol was associated with a 2% reduction in the rate of heart attack," said Dr. Basil Rifkind of the National Heart, Lung and Blood Institute.

The effect of lowering cholesterol solely by diet was not examined by the study. Researchers said they would not recommend patients use drugs to reduce cholesterol unless diet therapy did not lower serum cholesterol levels significantly. There is no "threshold" level of serum cholesterol below which persons can assume themselves safe from coronary heart disease, the researchers said, but stressed drug usage was considered only for persons with high serum cholesterol. One researcher estimated cholestyramine for a dosage level comparable to that in the study might cost $150 a month.

Dr. Rifkind said scientists and doctors would examine and discuss the results of the study over a period of time before considering whether to make any specific dietary recommendations for the general population.

Dr. John LaRosa, director of the Lipid Research Clinic at George Washington University, said he hoped the announcement of the results of the study would cause patients to be more aware of the importance of their cholesterol levels and would encourage doctors to be more vigorous in emphasizing cholesterol-lowering regimens to their patients.

Results of the study were announced in 2 articles in the January 20 issue of the Journal of the American Medical Association (JAMA) and included descriptions of the methodology and statistical analysis used. Multivariant analysis confirmed that the lower cholesterol levels were what led to reduced coronary heart disease, the researcher said.

Because some participants did not take the full dosage of medicine each day, researchers were able to determine that the reduction in risk was related to the total drug dosage.

The study focused on middle-aged men, but researchers said younger men with high serum cholesterol could benefit by the findings, as drug intervention could begin at an earlier stage in the development of the underlying atherosclerotic process. Similarly, the researchers said women with high serum cholesterol should benefit from serum-cholesterol reduction.

The study also suggests that persons with a more modest cholesterol elevation, say in the top 15% to 20% of distribution, "are also at increased risk for coronary heart disease and are also candidates for cholesterol reduction."

The question of dietary guidelines, meanwhile, was still being reviewed by a federal advisory committee. The committee is scheduled to meet again in May and the NIH study probably will be discussed, said advisory committee member Dave Kritchevsky. The current guideline—"Avoid too much fat, saturated fat and cholesterol"—has been criticized by different groups for different reasons. Kritchevsky believes the guidelines should promote reducing caloric intake, which would mean cutting dietary fat.

During December, Fred H. Mattson, director of the

Lipid Research Clinic at the University of California at San Diego, presented a paper saying monounsaturated fats have the same potential for lowering serum cholesterol and LDL-cholesterol as do polyunsaturated fats. The December 21, 1983, Food Chemical News said Mattson noted some researchers have questioned the safety of a diet high in polyunsaturates and said monosaturates may be safer. Dietary sources of monosaturated fats include olive oil, some nut oils, safflower and sunflower oil (from warmer growing regions).

Prostaglandins

Practical uses emerging from early research

Basic research on prostaglandins began in the early 1960s, but already some practical applications have been developed for these potent biological regulators. Maureen Duffy prepared this article for JAOCS *to provide, in layman's terms, some of the uses being made of what researchers have discovered. Prostaglandins have become a regular session topic at AOCS meetings, with a session on regulation of prostaglandins and other eicosanoids scheduled for the national meeting in Dallas this spring. When scientists determined the structural pathway of the prostaglandins in the early 1960s, they found a key that unlocked the door to one of the most exciting areas of biological research in recent years.*

The work done by these scientists, notably Sune Bergström and David van Dorp, allowed prostaglandin research to take off. Subsequent research has linked prostaglandins to virtually every biological function. Knowledge of their actions has led to new discoveries in medicine as well as to new means of increasing agricultural efficiency.

The prostaglandins are a group of lipid compounds produced in virtually every tissue if the proper stimulus is present. Produced from arachidonic acid, prostaglandins have been credited with a wide variety of effects.

One of these is the effect of prostaglandins on blood pressure. In 1934, Swedish scientist Ulf S. von Euler noted that certain substances found in semen caused a lowering of blood pressure. Other scientists had observed this effect, but von Euler was the first to attribute it specifically to a previously unknown group of substances that he named prostaglandins, in the erroneous belief that they were products of the prostate gland. Subsequent research has shown that the prostaglandins found in semen are actually products of the seminal vesicles, but the name given by von Euler has continued to be used.

Since von Euler's work, much has been learned about the role of the prostaglandins in blood pressure. One prostaglandin, prostacyclin, is now known to be responsible for lowering blood pressure, as well as inhibiting platelet aggregation. Another substance, thromboxane, which is similar in structure to the prostaglandins, has the opposite effect—raising blood pressure and supporting platelet aggregation.

Thromboxane's actions are blamed for high blood pressure problems. Dr. Josef Fried of the University of Chicago describes thromboxane as having "some devastating effects." Fried is interested in developing an antagonist to thromboxane, in the hope of being able to counteract its harmful effects.

Though prostacyclin, a naturally occurring substance, has the opposite effects of thromboxane, it is not clinically useful as an antagonist to thromboxane, according to Fried, because prostacyclin is too unstable, usually disintegrating within a minute of its formation. Also, prostacyclin's effects on blood pressure could be too drastic—it can lower blood pressure to zero.

What Fried would like to develop is an antagonist with properties similar to prostacyclin, but with greater stability and less severity in its effects. If he is successful, this antagonist could be used to treat high blood pressure.

Prostaglandin effects on blood pressure are not their only cardiovascular effects. Prostacyclin's antiaggregatory effects on platelets has led to its use to prevent platelet aggregation during heart bypass surgery, when blood is circulated outside of the body.

For some infants, born with congenital heart defects, prostaglandins can be used to delay the natural closure of the ductus arteriosus. This delay allows oxygen to circulate throughout the body until the infant is strong enough to survive surgery to correct the defect. In the case of so-called "blue babies," this technique has more than doubled the survival rate.

The long mystery of why aspirin works has been traced to prostaglandins. In 1971, English pharmacological researcher John Vane found that aspirin inhibits the production of certain prostaglandins. This discovery served as a spur to more prostaglandin research. Once researchers established that aspirin's main effect was to block prostaglandin production, the systems that aspirin affected could be linked to prostaglandin activity. Prostaglandins are now known to cause rises in body temperature, as well as the pain and inflammation that often accompany a fever. Even the stomach problems that may be a side effect of aspirin have been explained in terms of prostaglandins. Aspirin inhibits production of a prostaglandin that protects the stomach lining. Thus, excessive aspirin may lead to stomach irritation. This knowledge opened the way for research into the role of prostaglandins in ulcers and other gastrointestinal problems.

The connection between prostaglandins and inflammation has led to new discoveries in asthma research. Leukotrienes, another set of prostaglandinlike substances, are known to be instrumental in bringing about bronchial asthma attacks. The leukotrienes stimulate contractions and inflammation in breathing passages, which contribute to the asthma attack. Some prostaglandins already have been used to treat asthma, but work is being done to develop products that can inhibit the production of leukotrienes, which, scientists believe, will be a more effective treatment.

Knowledge of the prostaglandins' inflammatory effect has led to new discoveries in arthritis research. Prostaglandins are known to cause the joint inflammation that is associated with rheumatoid arthritis. Several prostaglandin inhibitors are on the market to treat arthritis while work continues to develop more.