can absorb laser light only when its frequency matches the energy between appropriate Zeeman substates and when it has the correct polarization, the net effect of all these factors is that an atom on the left side of the trap, for example, absorbs light preferentially from the beam coming from the left and therefore pushing it toward the center, whereas an atom on the right absorbs more light from the opposite beam. The net force on the atoms is toward the center and is provided by the same lasers that cool the atoms to about 0.5 mK.

A different approach that also makes use of circularly polarized light is being tried on cesium atoms at JILA by Wieman, David Sesko, and Carol Tanner. In preliminary experiments, trapping has been demonstrated, but the number of atoms and confinement time are still low. An additional wrinkle is the use of low-cost infrared laser diodes rather than comparatively expensive visible dye lasers. Making optical trapping less costly undoubtedly enlarges the number of researchers who might want to try their hand at this kind of experiment.

The JILA researchers exploit the phenomenon of optical pumping. One form of optical pumping is normally a complicating factor in laser cooling. It arises because of the existence of a hyperfine splitting in the atomic ground state; that is, the energy is different when the electron and nuclear spin angular momenta are parallel and antiparallel. During cooling, the laser excites atoms in only one of the hyperfine states, but the atoms can decay back to either state. The result is that the atoms quickly end up in the wrong state and can absorb no more light, so that cooling stops. If two beams of unequal intensity are used, one to excite each hyperfine state, the stronger beam will end up doing the optical pumping.

For optical trapping of cesium, the optical pumping is not between hyperfine states but between Zeeman substates when the atoms are in a constant magnetic field. Circularly polarized beams traveling in opposite directions are each focused to points on the far side of the trap relative to the lasers. Optical pumping of an atom on the left side of the trap, for example, prevents absorption of the more intense light coming from the right but allows it from the weaker light from the left. Similarly, an atom on the right can only absorb light coming from the right. Once again, all the atoms feel a force pushing them toward the center.

All in all, more and more researchers are getting interested in trapping atoms with the result that some of the promised fruits of the technique should be ready for picking in the not too distant future. ■

ARTHUR L. ROBINSON

Study Bolsters Case Against Cholesterol

A new study shows that aggressive cholesterol-lowering therapy can halt the growth of lesions and in some cases shrink them

THE benefits of lowering blood cholesterol levels have become almost gospel over the past few years. Clinical trials, involving thousands of subjects, have shown that lowering blood cholesterol can reduce the risk of coronary heart disease and heart attack. But what has not been clear is the mechanism: Does lowering cholesterol actually improve the condition of coronary arteries that have become clogged with fat deposits, called lesions?

Now new evidence, perhaps the strongest to date, comes from a 2-year trial by David H. Blankenhorn and his colleagues at the University of Southern California School of Medicine.* They report that a drastic reduction in blood cholesterol levels, achieved through an aggressive diet and combination drug therapy, can slow the progression of atherosclerotic lesions and in some cases even shrink them. At last, says Blankenhorn, the mechanism is clear.

The results of this trial, the Cholesterol-Lowering Atherosclerosis Study (CLAS), were reported in the 19 June *Journal of the American Medical Association* and announced with much fanfare at a news conference at the National Heart, Lung, and Blood Institute (NHLBI), which supported the study along with the Upjohn Company. Heart institute director Claude Lenfant hailed the study as "significant new information" that presents "for the first time . . . evidence regarding regression of lesions in humans."

According to Blankenhorn, this study showed a "strong and consistent therapy effect—the first seen in humans at the level of coronary arteries—from cholesterol lowering."

To Robert I. Levy, former director of the heart institute who is now at Columbia University College of Physicians and Surgeons, the study results are "exciting" if not unexpected. "It confirms and extends the factual evidence," he says. "Every new bit of evidence makes the conclusions firmer, but I didn't think they were soft before."

Several primate studies have demonstrated that lesions regress in response to both diet and drug therapy, he and others say. And, Levy adds, previous human trials, including the NHLBI Type 2 Coronary Intervention Study, have clearly indicated that the progression of atherosclerotic lesions can be slowed by lowering cholesterol levels. Human studies have also strongly suggested that lesion regression may occur.

But those earlier human trials were inconclusive, according to Basil M. Rifkind, chief of the lipid metabolism branch at NHLBI, who calls the Blankenhorn study the "first conclusive study with clear-cut results in humans."

One key finding of the new study, researchers agree, is that diet and combination drug therapy can achieve substantially greater reductions of blood cholesterol than previously demonstrated. And that, according to heart institute officials, suggests a larger role for drugs in the future treatment of coronary heart disease, which affects some 5 to 6 million Americans, and perhaps in the treatment of those with elevated cholesterol levels.

The study also makes a strong case, Blankenhorn says, for reducing blood cholesterol to a level below 200 milligrams per deciliter, the level now recommended by both NIH and the American Heart Association. "These findings suggest that the target level should be on the low side of 200—between 185 and 200," Blankenhorn says.

The study was conducted on 162 men, aged 40 to 59, who had previously undergone coronary bypass surgery for treatment of atherosclerosis. (Bypass patients were selected both because they could benefit from cholesterol reduction and because the researchers believed they would be highly motivated to comply with the rather rigorous study requirements.) None of the subjects smoked, although some had previously, and all had blood pressure within normal range, thus eliminating the two other major risk factors for heart disease.

The men were randomly assigned to two groups. Half received the cholesterol-lowering drugs, colestipol and niacin, and were placed on a stringent diet that limited fat intake to 22% of total calories and cholesterol to less than 125 milligrams a day. The other half received a placebo and were

*His colleagues are Sharon A. Nessim, Ruth L. Johnson, Miguel E. Sanmarco, Stanley P. Azen, and Linda Cashin-Hemphill.

placed on a moderately restrictive diet.

The study was designed not so much to evaluate this particular therapy as to assess the results of a dramatic reduction in blood cholesterol levels. The specific goal of the drug therapy was to reduce overall blood cholesterol and low-density lipoprotein (LDL) cholesterol and to increase high-density lipoprotein (HDL) or "good" cholesterol. High levels of LDL cholesterol lead to fatty buildups on artery walls. In contrast, HDL cholesterol is beneficial because it aids in removing cholesterol. In combination, colestipol and niacin, both of which have been used for years, affect both LDL and HDL cholesterol. Colestipol, a resin drug, reduces LDL cholesterol. Niacin is a vitamin when administered in milligram doses, but when administered in extremely high doses, a gram or more a day, it lowers LDL cholesterol and elevates HDL cholesterol.

By all accounts, the drug therapy produced and maintained a remarkable reduction in cholesterol levels. Most previous trials achieved about a 7 to 15% reduction in total cholesterol. The CLAS achieved a 26% reduction in the drug group (from an average of 246 milligrams per deciliter to 180 milligrams per deciliter) compared with a 4% decrease in the placebo group. These figures mask the magnitude of the cholesterol change, however. In the drug group, LDL cholesterol decreased 43%, and HDL cholesterol increased 37%. In the placebo group, LDL dropped 5%, and HDL increased 2%.

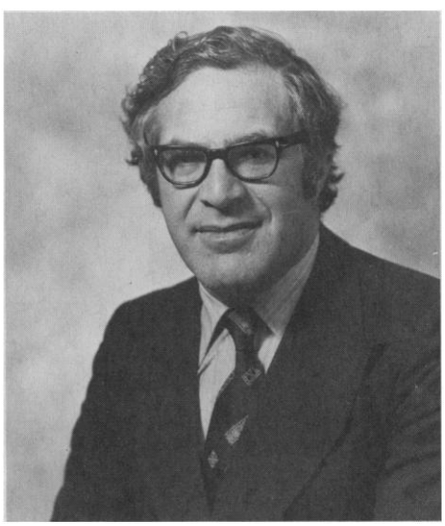
To assess the effects of this therapy, angiograms of both bypass grafts and natural coronary arteries were taken before treatment began and after 2 years. A panel of angiographers evaluated the two films for each subject without knowing whether the subject had received the drug or the placebo or which angiogram had been taken first.

In the drug group, 61% showed stable or improved coronary status at the end of 2 years, as opposed to 39% of the placebo group. Moreover, regression of lesions was evident in 16.2% of the drug group and in only 2.4% of the placebo group, the researchers report. These benefits were observed in both grafted and ungrafted arteries. They were also evident whether the subjects' base line cholesterol levels (before therapy) were high (more than 240 milligrams per deciliter) or moderate. The average starting blood cholesterol level was 246 milligrams per deciliter but ranged from 185 to 350. It is this finding—that beneficial effects occur even at the relatively low cholesterol level of 185 milligrams per deciliter—that suggests that persons with cholesterol levels below 200 should be considered for vigorous therapy, Blankenhorn says.

The CLAS has clear and major implications for coronary bypass patients, say heart institute officials: aggressive treatment with cholesterol-lowering drugs and diet may halt the progression of their coronary heart disease. Some 200,000 Americans undergo bypass surgery each year, in which veins from the leg are implanted to bypass clogged arteries and provide a new supply of blood to the heart. Within 3 to 4 years, however, atherosclerotic lesions may begin to build up in the grafts, and about 44% of bypass patients need a second operation within 10 years. Bypass patients are typically put on fat-restricted diets, but if that therapy proves insufficient, says NHLBI's Rifkind, drug treatment should clearly be considered in light of the new study. In addition, he says, all bypass patients should be put on an aggressive cholesterol reduction therapy, whether or not their cholesterol levels are high.

"This study offers the patient with coronary disease some hope," says Levy. "Even as recently as last fall I was hearing comments that you probably can't do anything about secondary prevention. But Blankenhorn's study suggests that if the individual changes his life-style and diet—and if necessary, takes drugs—it looks like one can resolve the existing disease."

For individuals with moderately elevated cholesterol levels, diet remains by far the preferred approach. Rifkind suspects that a vigorous cholesterol-lowering therapy, using diet and drugs, might be beneficial to the 40 million Americans with moderate to high cholesterol levels (more than 240 milligrams per deciliter) who are now free of coronary heart disease. But the risks of colestipol and niacin, which can cause gastrointestinal distress, joint inflammation, and other side effects, may outweigh the benefits for this group, he says.



Basil M. Rifkind: *"The first conclusive study with clear-cut results in humans."*

He and other heart institute officials predict that a new class of drugs, HMG coenzyme A reductase inhibitors, "may transform the whole cholesterol picture—if they prove safe." These drugs, one of which is currently being reviewed by the Food and Drug Administration, are far more effective at reducing cholesterol than existing drugs such as colestipol, cholestyramine, and niacin and appear to have fewer side effects, Rifkind says.

A number of questions remain, however, about the CLAS study in particular and cholesterol management in general. Although Blankenhorn believes that his study has finally demonstrated that lowering cholesterol directly affects the arteries, others are not yet convinced. Katherine Detre, a biostatistician at the University of Pittsburgh who worked on the NHLBI Type 2 study, calls Blankenhorn's findings "very important." But she says that too much information is missing from the published paper for her "to feel comfortable with" his conclusion. "I'm not saying he's not right. It makes sense that if you lower cholesterol it should slow progression. But to say that slowed progression is due to cholesterol lowering—we need more information."

Many factors can influence the rate at which lesions progress, says Detre, including the subjects' symptomatology at the start of the study, how many lesions they had, the size of the lesions, and whether the lesions were in grafted or ungrafted arteries. "I'm not really convinced that the two groups were comparable in regard to those factors," she says.

In an accompanying editorial in *JAMA*, Eugene R. Passamani of NHLBI raises other questions as well. While stressing the importance of this study for the treatment of bypass patients, he says that the implications for other patients are not clear. In addition, he writes, it is not known whether the drug therapy worked solely by lowering cholesterol levels. Nor is it known whether HMG drugs will have a similar effect on atherosclerotic lesions, or whether even more vigorous therapy, leading to greater LDL reduction and HDL elevation, would yield more improvement in coronary arteries. These and other questions, he says, may be answered by the continuing analysis of CLAS data (more information will be published later) and by the publication of other, similar studies now under way.

Meanwhile, the heart institute has a persuasive new weapon to use in its campaign to change American eating habits. Given the difficulty of doing that, says Levy, "all of us welcome additional confirmatory studies."

■ LESLIE ROBERTS