Coronary Project: Negative Results

Cardiologists would very much like to see definitive evidence that lowering blood cholesterol concentrations can prevent heart attacks, the leading cause of death in the United States. They did not find it in the results of the Coronary Drug Project. The study showed that the drugs niacin and clofibrate do not improve the long-term survival of heart patients—even though these agents decrease blood cholesterol.

Epidemiological studies have shown a strong and consistent association between high concentrations of cholesterol in blood and increased susceptibility to heart attacks. Nevertheless there is still some dispute about whether the relationship between the two is causal. One way to settle the dispute is to show that decreasing blood cholesterol concentrations also decreases the risk of having a heart attack or prolongs the lives of people who have already had one. The latter was the aim of the Coronary Drug Project, a nationwide study sponsored by the National Heart and Lung Institute (NHLI) at a cost of $40 million.

The study, which began in 1966, included more than 8300 men who had already suffered one or more heart attacks, and involved the participation of 55 clinical centers. Five drug regimens known to lower blood cholesterol were originally included in the study. Three had to be discontinued because they were doing more harm than good. Patients taking clofibrate or niacin remained in the project for 5 to 8 years, during which time their conditions were carefully monitored and compared to those of controls, who received a placebo medication.

Both drugs produced modest reductions (an average of less than 10 percent) in the blood cholesterol concentrations of the men. But neither drug significantly decreased mortality compared to that of patients taking the placebo. Patients treated with niacin did have slightly fewer nonfatal heart attacks than the controls. Niacin and clofibrate were associated with unpleasant or hazardous side effects such as disturbances in heart rhythms. Thus, the study showed that the benefit-to-risk ratio for using the agents after a heart attack was generally unfavorable.

These drugs are the two most widely used agents for lowering blood cholesterol. About 4 million prescriptions for clofibrate and 2.5 million for niacin were filled in 1973. (Niacin may be prescribed for conditions other than high cholesterol.) How the results of the project will affect usage of these drugs remains unclear.

The situation is, of course, complicated. According to Jeremiah Stamler of Northwestern University Medical School, chairman of the steering committee for the Coronary Drug Project, a low-cholesterol, low-fat diet can reduce blood cholesterol concentrations by about 10 percent. But not all patients stick to their diets. And some have very high cholesterol concentrations so that both diet and drug therapies may be indicated. Also, certain individuals may give much more dramatic responses to clofibrate than the average seen in this study.

Moreover, both Stamler and Robert Levy of NHLI emphasized that the results of the Coronary Drug Project cannot be used to draw any conclusions about whether lowering blood cholesterol will prevent first heart attacks—which kill the majority of their victims. It may be that by the time a heart attack has occurred it is too late for a modest lowering of blood cholesterol to significantly prolong the life of the patient. The role of cholesterol in primary prevention may be clarified by studies now in progress. In one, the effect of cholestyramine, another cholesterol-lowering drug, on coronary disease and mortality is being examined.

Despite the negative findings of the Coronary Drug Project, Stamler and Levy said that the participants were encouraged by what they learned. They cited two accomplishments as positive results. The project proved the feasibility of such large-scale cooperative ventures. And clinicians discovered a great deal about the natural history of coronary heart disease and about predicting a patient's prognosis after a heart attack.—JEAN L. MARX

portation study might represent a questionable use of the CIA's resources, but that the idea seems well within the customary bounds of propriety. As for contracting work out to private companies rather than to Commerce or Transportation, Scoville noted that "there are some advantages to not relying entirely on a bureaucracy with an ax to grind."

The possibility arises that the Transportation Department asked for the R & D study in the first place. Although this could be neither confirmed nor refuted, it should be noted that the department has been under pressure from the Office of Management and Budget to trim its research on exotic technologies. In mid-January, the department let it be known that it was virtually stopping its support of ultrahigh-speed rail technology, including projects involving air-cushion and magnetic levitation vehicles, subjects of prime interest in the proposed CIA study. A report with the CIA's imprimatur hinting at potential disaster for U.S. transportation markets in the 1980's would not have hurt the department's case for continuing this research. The CIA memo does not say who is to receive the resulting information, but it does ask the contractor to "present a reasonable number of oral briefings . . . to certain government agencies upon successful completion of each task."

Does all of this add up to industrial espionage at the taxpayer's expense? The fact that the proposal comes from the OSI and is unclassified suggests the study was a fairly innocuous undertaking that the OSI itself couldn't be bothered with.

On the other hand, some cryptic wording in the memo could be taken to mean that a little espionage would not be out of order. The contracting firm is supposed to search the open literature, review the results of U.S.-foreign technology exchange agreements, and riffle through its own files for information. But the contractor is also instructed to "acquire technical information using his available resources."

What's more, the CIA notes, technical publications on R & D programs in some countries may not be "readily available." In this case, reads an underlined section of the memo, "the contractor's discussion and proposed approach to these problems will form a primary area of proposal evaluation."

The forthcoming Senate inquiry may help clear up the CIA's murky intentions.—ROBERT GILLETTE