Coffee and Heart Disease: Is There a Link?

"Everything I enjoy in life," runs the ancient lament, "is either illegal, immoral, or fattening." A steady accretion of evidence is now beginning to suggest, unfortunately, that the old lament should bear a new addendum: "and hazardous to the heart."

The list of factors associated with the development of heart disease has grown in recent years. It now includes, among other items, lack of physical activity, obesity, hypertension, smoking, a low concentration of dissolved minerals in the community water supply, and the ingestion of foods containing excessive quantities of saturated fats, cholesterol, and sugar. The most recent addition to the list—and one that has been both widely publicized and highly controversial—is the consumption of large amounts of coffee.

The controversy began last December when Hershel Jick, Dennis Slone, and their associates at the Boston Collaborative Drug Surveillance Program of Boston University Medical Center reported (*1*) an observed association between heavy coffee drinking and myocardial infarction. Myocardial infarction is the degeneration of heart muscle tissue that results when the tissue's blood supply is restricted by clogged or blocked blood vessels. Jick and Slone estimated that the risk of developing this disease is about twice as great for heavy coffee drinkers as it is for individuals who drink no coffee at all. This conclusion was confirmed by a second, larger study reported last month (*2*) by the same authors, but their results have been sharply criticized because they contradict several previous studies by other investigators showing no correlation between coffee and heart disease.

A Large-Scale Screening Program

Jick and Slone's investigation was not originally aimed specifically at coffee. The Boston Collaborative Drug Surveillance Program, established in 1966, is a large-scale screening operation designed to obtain information about the therapeutic and adverse effects of commonly used drugs. Trained interviewers at cooperating hospitals obtain information about each newly admitted patient's prior use of drugs, including pharmaceuticals, drugs of abuse, tobacco, alcohol, coffee, and tea. This information, in conjunction with the patients' hospital records and diagnoses upon release from the institutions, then provides a large body of data for detecting statistical correlations between drugs and diseases. The association between myocardial infarction and heavy coffee drinking is only one of the correlations observed in the ongoing study.

In their first report, Jick and Slone compared 276 myocardial infarction patients (subjects) from eight hospitals in the United States, Canada, New Zealand, and Israel with 1104 closely matched control patients with other diseases. In the second, independent study, they compared 440 white, middle-aged (40 to 69 years old) subjects from 24 Boston area hospitals with a matched control series of 12,319 patients hospitalized with other diseases. In each study, they found that patients who drank one to five cups of coffee daily ran an approximately 50 percent greater risk of developing myocardial infarction than did those who drank no coffee, and patients who drank six or more cups daily ran about a 110 percent greater risk.

Close comparison with the control patients showed that this increased risk could not be attributed to many other factors that might also be associated with an increased risk, including age, sex, diabetes, occupation, smoking, and the use of sugar in the coffee. The relation between coffee and myocardial infarction was, however, apparently most pronounced among patients who were already predisposed toward development of the disease by these other factors; that is, the greatest increased risk associated with heavy coffee drinking was observed among those patients who already ran the greatest risk for other reasons. There was no data in the study concerning any possible roles of personality, diet, or exercise.

The association between myocardial infarction and coffee was the only correlation the Boston group observed for coffee among common diseases. Surprisingly, the group found no associations between heavy coffee drinking and such closely related infarction progenitors as obesity, hypertension, and coronary insufficiency. Such correlations might reasonably be expected to occur if there were a definite causal association between coffee and myocardial infarction, and their absence has been one source of criticism of the studies. The group also found a slight negative correlation with heavy coffee drinking among subjects with a previous history of infarction or angina pectoris, a type of heart disease associated with a reduced oxygen supply to heart tissues. This association is consistent with a voluntary or medically prescribed reduction of coffee drinking after the initial heart episode.

Less Risk from Smoking

Jick and Slone found a strong correlation between coffee drinking and cigarette smoking, but their results showed only a slightly increased risk of infarction associated with smoking and a lesser overall risk associated with smoking than with coffee. This observation, Jick says, is consistent with previously published reports that smoking engenders the greatest risk of heart disease among individuals who are otherwise healthy, and that the risk associated with smoking decreases as the risk from other factors increases. More than 90 percent of the subjects in the Boston study were predisposed to heart disease by other factors.

Interestingly, the Boston group was unable to find any association between heavy tea drinking and any heart or other disease. This result suggests that the link between coffee and infarction does not stem from the effects of caffeine, as other investigators have previously suggested. (Apparently, none of the many investigators seeking the causes of heart disease have examined the possibility of an association with cola beverages, which contain an amount of caffeine similar to that in tea or coffee.)

The source of the link between coffee and myocardial infarction is still very much a mystery, Jick and Slone concede, but several possible explanations are available. These include the possibilities that personality traits might predispose certain individuals toward both heavy coffee drinking and development of the disease, that unidentified

ingredients in coffee might increase the concentration of lipids in the blood, and that unidentified ingredients might inhibit fibrinogenolysis or fibrinolysis (the dissolution of large proteins that participate in the formation of blood clots). In any event, Jick and Slone caution that the available evidence is not sufficient to justify an interpretation that coffee is a cause of myocardial infarction.

One major reservation in interpreting their results is the necessary exclusion from the studies of a substantial number of subjects. Published statistics indicate that as many as 60 percent of myocardial infarction victims die before they reach the hospital, and as many as 30 percent of the remainder die within 72 hours after admission. Since most interviews in the Boston program are conducted more than 72 hours after each patient's admission, there is a possibility that the association is based on selective early mortality of patients who drank lesser amounts of coffee. Such an effect would be consistent with an interpretation that heavy coffee drinking exerts a protective influence in infarction victims, perhaps increasing their chances of survival through its mild stimulant effect. There is little evidence to justify such an interpretation.

Retrospective vs. Prospective Studies

The strongest argument leveled against Jick and Slone's conclusion is that the conclusion is derived from a retrospective study in which the desired epidemiological evidence was gathered after the onset of the disease. Such studies are of value in the development of new hypotheses, but firm conclusions can rarely be drawn from the data they provide because of such complications as the questionable reliability of the respondents' memories and the possibility of hidden biases in the control group. Many scientists thus argue that conclusive evidence in support of any hypothesis can be gained only in a prospective study in which all the available evidence is accumulated prior to the onset of disease. The Boston group's results are in conflict with the conclusions of several prospective studies.

Perhaps the best known prospective study is the Framingham Heart Disease Epidemiology Study, directed by William B. Kannel and Thomas R. Dawber under the auspices of the National Institutes of Health. More than 5100 adult residents of Framingham, Massachusetts, have been monitored for nearly 20 years in an attempt to detect dietary, environmental, physiological, and personality traits that increase the risk of heart disease. This study, Kannel and Dawber say, has shown no relation between coffee consumption and any form of heart disease. One of the hospitals that provided data for Jick and Slone's second report is the Framingham Union Hospital, which also services the participants in the Framingham study; this suggests that, at least in part, different results are being obtained from prospective and retrospective studies of the same population.

In a similar fashion, Siegfried Heyden of the Duke University Medical Center, Durham, North Carolina, has monitored more than 2500 residents of Evans County, Georgia, for approximately 5 years. He has also found no evidence that heart disease of any type is more frequent among those individuals who drink large amounts of coffee. Heyden's results have not been published in the United States.

Oglesby Paul of the Northwestern University Medical School, Chicago, Illinois, has monitored the health of more than 1700 middle-aged men in the Chicago area since 1960. In 1963, he reported an increased incidence of heart disease among those subjects who consumed large amounts of coffee. After further study, however, he reported in 1968 that a major fraction of the association between coffee and heart disease could be attributed to an association between smoking and heart disease, since heavy smokers are generally also heavy coffee drinkers and vice versa. Interestingly, he found that the mortality rate among both smoking and nonsmoking myocardial infarction victims was lower for coffee drinkers than for nondrinkers, and that smokers who are heavy coffee drinkers run less risk of developing myocardial infarction than smokers who are nondrinkers.

Several smaller studies have produced mixed results. Lars Wilhelmsen and Gösta Tribblin of the University of Gothenburg in Sweden, have monitored the health of some 855 residents of Gothenburg since 1963. They have found no association between coffee and heart disease, but their results have not yet been published. Hans G. Thiel and his associates at the University of Oklahoma School of Medicine, Oklahoma City, retrospectively compared 50 subjects with an equal number of closely matched controls and found a significantly increased consumption of fluids, including coffee, among the myocardial infarction patients. Other small studies have generally revealed no link between coffee and heart disease, although nearly all investigators have noted strong correlations between coffee drinking and smoking and between smoking and heart disease.

Several other criticisms have been leveled against Jick and Slone's reports. Some investigators, for example, have criticized the use of hospitalized patients as controls. Such a population, Kannel says, may contain an excessive number of subjects with gastrointestinal or other diseases in which coffee drinking has been either voluntarily abandoned or medically proscribed. The Boston data indicates, however, that coffee consumption is not lower than normal among the gastrointestinal patients or in any other group. Nonetheless, many scientists argue that the coffee drinking habits of the hospitalized group cannot be accepted unequivocally as representative of the habits of the general population.

A Small Number of Subjects

A further criticism of the Jick and Slone results has been that some of their conclusions were drawn from data obtained from only a small number of subjects. Yet the total number of subjects observed by the Boston group is nearly three times as large as the number observed in the Framingham study, and much larger than that observed in any of the other studies. In fact, Jick argues, the major advantage of a retrospective study is that it is possible to obtain such large numbers of subjects to provide a useful data base.

Despite the great amount of criticism directed against the Boston studies, the difficulties of extrapolating from a hospital population to the population at large, and the inherent problems of a retrospective study, Jick and Slone's results clearly cannot be summarily rejected. Although there is little other available evidence to suggest either that coffee causes myocardial infarction or that heavy coffee drinking lowers the fatality rate among infarction victims, the ubiquity of both coffee use and heart disease in the United States suggests that a good deal more investigation is required.

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Additional Reading

1. Boston Collaborative Drug Surveillance Program, *Lancet* **1972-II**, 1278 (1972).
2. ———, *N. Engl. J. Med.* **289**, 63 (1973).
3. W. B. Kannel and T. R. Dawber, *ibid.*, p. 100.
4. O. Paul, *Postgrad. Med.* **44**, 196 (1968).