Enzymes and alcoholism: Blood simple?

Is there a relatively simple blood test that can help verify whether someone is an alcoholic? According to a new report, the answer may be yes.

The test combines measures of two chemical compounds, known as enzymes, that are found in blood platelets, say molecular pharmacologist Boris Tabakoff of the National Institute on Alcohol Abuse and Alcoholism in Bethesda, Md., and his colleagues. After taking blood samples from 95 male alcoholics and 33 nonalcoholic men, and saturating the samples with alcohol, the researchers found that the activity of one enzyme, monoamine oxidase, decreased significantly more among the alcoholics. The activity of the other enzyme, adenylate cyclase, was substantially lower among the alcoholics than among the nonalcoholics after blood samples were exposed to cesium fluoride, a substance that stimulates this enzyme.

Furthermore, adenylate cyclase activity stimulated by cesium fluoride was abnormally low among 10 alcoholics in the sample who had abstained from alcohol for one to four years.

The tests correctly identified three-quarters of the alcoholics and nonalcoholics when calculations of the enzyme responses were combined for each subject, the scientists note in their report in the Jan. 21 NEW ENGLAND JOURNAL OF MEDICINE.

Further refinement of the test procedures can be expected, writes psychiatrist Theodore Reich of the Jewish Hospital of St. Louis in an accompanying editorial, "so they hold great promise for the development of convenient specific laboratory measures of alcohol abuse and dependence."

This approach might simply provide a means for identifying individuals who drink a lot—certainly a welcome advance for physicians trying to uncover the alcohol consumption histories of their patients, says Tabakoff.

It is also possible, says Tabakoff, that the abnormal enzyme activity marks an inherent predisposition to alcohol abuse. To test this possibility, he is now organizing a study of children of alcoholics to see if abnormal platelet-enzyme activity is present among people thought to be genetically susceptible to alcoholism.

There is reason to suspect, notes Tabakoff, that alcoholics in the present study had a less heritable form of the disorder, known as Type I alcoholism, in which environmental stress plays a larger role and close relatives are often not alcoholic. Type I alcoholism occurs in both men and women, often after age 25. Type II alcoholism, on the other hand, has a greater hereditary influence. It appears mainly among sons of male alcoholics before age 25, along with frequent bouts of aggressive and violent behavior.

Although alcoholics had abnormal monoamine oxidase activity after their platelets were saturated with alcohol, the activity of this enzyme before alcohol saturation was comparable in alcoholics and nonalcoholics. Other researchers have found that baseline measures of monoamine oxidase activity are abnormally low only among Type II alcoholics.

Tabakoff is currently analyzing enzyme-test responses of Type I and Type II alcoholics who were studied in a collaboration with Swedish researchers.

Another goal of further research is to establish whether the lapses in enzyme activity occur only among alcoholics or if they also appear in individuals with related psychiatric diagnoses, such as depression. *— B. Bower*

Pattern B another genetic heart risk?

A recent study suggests that about one-third of the population in the United States carries a yet-unidentified gene associated with an increased risk of heart disease, a scientist involved in the study said last week. Other scientists, however, say that there is no satisfactory proof that the observed genetic trait actually translates into any amount of increased risk.

Speaking at the American Heart Association's 15th Science Writers Forum in New Orleans, Ronald M. Krauss of the University of California at Berkeley suggested that roughly 30 percent of the U.S. population has a preponderance of particularly heavy forms of low-density lipoproteins (LDL) circulating in their blood. Lipoproteins are complexes of lipids and proteins used by the body to transport fats, and the LDL types are considered "bad" in terms of depositing cholesterol in the blood vessels. Using a superfast centrifuge to separate LDL factions according to their size and weight, Krauss and his co-workers had previously found four major LDL subgroups. Since that discovery, they have used a more sophisticated method to measure the relative concentrations of the different LDL types in more than 2,000 individuals.

What they found were two distinct LDL patterns, or profiles. Approximately 70 percent of those tested had higher relative concentrations of the lighter, larger LDL types (a profile called the A pattern), while the remainder had more of the smaller, denser LDL types and were said to have the B pattern. Krauss says that, based on subsequent family studies among 300 Mormons in Northern California, "there appears to be a major single gene in the population . . . which appears to regulate, or at least influence, whether or not an individual falls into [the B] category."

The Berkeley scientists, with researchers at Harvard University, then looked at A and B patterns in about 120 patients with heart disease, as well as those in an equal number of normal controls. Their results—which have been submitted for publication — suggest that the B profile is more common among heart patients, and therefore closely tied to an increased risk of heart disease. This does not necessarily mean, however, that the B individual is definitely predisposed to cardiovascular problems, says Krauss.

He says that because a person can use diet and exercise to convert B to A, this particular factor can be controlled. In general, he says, everyone age 20 or younger appears to be an A in terms of LDL patterns. With increasing age, however, the B blood pattern begins to appear, becoming common by middle age.

Although the Berkeley/Harvard group originally concluded there was a threefold increased risk of having heart disease among those with a B profile, the scientists have been reevaluating the magnitude of this increased risk, Krauss told SCIENCE NEWS. He says the possibility that heart drugs called beta-blockers can artificially cause a B pattern has cast some doubt on the clinical implications of A and B profiles.

Ernst J. Schaefer of Tufts University in Boston agrees that medication may indeed influence clinical findings. He said in an interview that independent studies by his research group show that, when subjects taking beta-blockers are eliminated from clinical studies, no increased risk of heart disease is evident among those with B profiles. Beta-blockers, which are used in about 80 percent of heart patients following a heart attack, can themselves increase the concentration of dense LDL, says Schaefer. Until much larger studies are completed taking into account the drugs' actions, he says, researchers will not know whether the B profile equals increased risk.

Both Krauss and Schaefer agree that there are many unanswered questions regarding the clinical importance of the new studies. While the B pattern "deserves a lot of attention," it may actually just be a marker for the impaired clearance of fats that are the true risk factors, says Krauss. Schaefer, however, says he cannot yet discount the possibility that dense LDL is somehow directly related to heart disease. His group has found significant amounts of the dense LDL in 44 percent of normal middle-aged males in one small study, as compared to only 15 percent of the study's female subjects. This sex difference, along with the fact that heart disease is more common among men, may be evidence supporting the Berkeley/Harvard data, says Schaefer. *— D.D. Edwards*