

Alcoholics' Odd Blood Suggests Genetic Disease

The blood of severely alcoholic men contains a substance that is not found in the blood of social drinkers, indicating that alcoholics may use a unique physiological pathway for the breakdown of ethanol, the intoxicating ingredient of drink. According to government and Harvard University scientists, these findings provide additional support for the ascendant view that serious alcoholism is a disease controlled, at least in part, by one's inherited genes.

A research group headed by Harvard epidemiologist David D. Rutstein — and including biochemists at the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in Rockville, Md., and the Centers for Disease Control in Atlanta, Ga. — studied a group of men who had been hospitalized for acute alcoholism and compared them with a group of social drinkers. Based on their analysis of blood samples taken before and after drinking, the scientists conclude (and report in the Sept. 3 LANCET) that following drinking, nearly 80 percent of the alcoholic subjects had elevated blood levels of a chemical called 2,3 butanediol; only one of the controls showed such an effect.

Earlier studies with rats have indicated that when the normal pathway for metabolism of ethanol is artificially blocked, the ethanol is broken down by way of a second pathway; this alternative way of clearing the toxin (through chemical reactions in the brain and testes) produces 2,3 butanediol as a by-product. The presence of this substance in the blood of alcoholics, the researchers say, is consistent with the idea that alcoholics metabolize ethanol using a different sequence of biochemical steps than those normally involved in alcohol metabolism.

The most likely explanation for these findings, the researchers say, is that there is a defect in the enzymes normally involved in alcohol metabolism; this defect, they add, could be genetic or it could be caused by chronic consumption of alcohol. However, according to NIAAA biochemist Richard L. Veech, who conducted the animal studies, it remains unclear whether or not the 2,3 butanediol found in humans is a by-product of ethanol metabolism; without clinical studies of human subjects, he notes, it is impossible to know for certain how alcoholics and non-alcoholics break down ethanol.

Epidemiological evidence has consistently indicated that severe alcoholism runs in families, and these findings, the researchers say, lend further support to the idea of a hereditary component to the disorder. If alcoholism were exclusively a social or psychological phenomenon, they

point out, all of the alcoholic subjects would be expected to have acquired the same biological abnormality; 20 percent did not. Further studies of alcoholic and non-alcoholic twins will be necessary to verify the genetic contribution, Rutstein says.

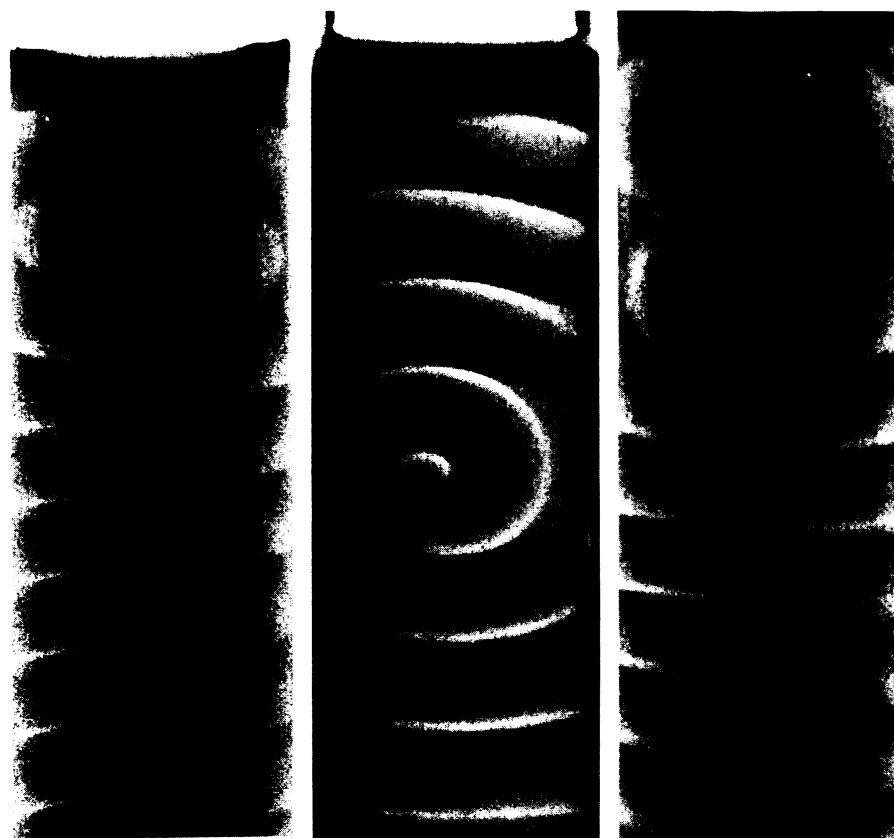
Other biochemical abnormalities associated with alcoholism have been reported in the past, but many have not held up, and those that have lack explanatory value. One major problem with such research is that alcoholic beverages contain thousands of so-called congeners, products of the fermentation and distillation process, that contaminate research. The substance 2,3 butanediol, one such congener, is found in wine and beer but not, according to the researchers, in distilled spirits, which were used exclusively for this study.

If indeed the normal pathway for al-

cohol metabolism is somehow blocked in alcoholism — through genetic or alcohol-related damage to the liver's natural enzymes — then it is reasonable to hypothesize that 2,3 butanediol is a product of an alternative metabolic pathway, perhaps (as with rats) involving the brain and testes; the brain and testes are particularly susceptible to alcohol damage in humans. But even if this process were verified, the researchers say, they cannot even speculate on how such an abnormality might be related to habituation and addiction. The greatest promise of this finding is that the abnormality might serve as a marker for people who are predisposed to alcoholism, they suggest. The potential of such a test was made clear even in the preliminary study: the single control subject who showed an elevated level of 2,3 butanediol was subsequently treated for alcoholism.

—W. Herbert

Test-tube toroids and other chemical waves



Weish, Gomatiem, Burgess/Nature

The grayish swirls visible within the dark liquid in the test tubes shown provide direct evidence for the formation of three-dimensional chemical waves. The reaction that generates these slowly evolving patterns is a variation of the Belousov-Zhabotinskii reaction, one of the first examples discovered of an oscillating chemical system (SN:9/19/81, p. 188). Lightly tapping the test tubes sometimes produces unusual wave forms out of the initial disorder. Researchers at the Glasgow College of Technology in Scotland, reporting in the Aug. 18 NATURE, say their design is easy to implement and lends itself to time-delay photography.