

A Biochemical Denominator in the Primary Prevention of Alcoholism

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Introduction

The primary prevention of alcoholism and/or the alcoholic syndrome, like the primary prevention of any other so-called "health" problem, hinges upon the awareness of two fundamental ingredients. First, to wipe out the occurrence of the problem requires the identification of the constellation of risk factors. Secondly, it then follows that there must be an elimination of some if not all of these risk elements.

Risk Factors

There seems to be little or no disagreement regarding these two strategic points to accomplish primary prevention or prevention of occurrence. There is, on the other hand, considerable confusion as to what

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constitutes a risk factor. Serum cholesterol, to pick a popular parameter, is viewed as a risk agent in the genesis of certain types of cardiovascular pathosis. Serum uric acid, as a second example, is regarded as a risk variable for gout. However, the question then to be resolved is what is it which makes for hypercholesterolemia and hyperuricemia? And so, at best, the blood cholesterol and uric acid levels can be viewed as secondary risk factors. We now know that the serum cholesterol and uric acid concentrations are a function of physical activity, tobacco consumption, coffee/tea intake, certain dietary indiscretions as well as other already defined and other still-to-be identified lifestyle characteristics. These lifestyle components are the true or primary risk factors. For those students of predictive medicine, no matter what the syndrome, it is possible to identify a mosaic of primary and secondary risk factors (Cheraskin and Ringsdorf, 1977). It would follow that such must be the case when one examines the alcohol-prone person.

Ecology of Health and Sickness

There is one additional not-generally-

considered point which is critical to this discussion of primary prevention. In the final analysis, health or disease is a function of the mosaic of environmental challenges and the organism's capacity to cope with the external milieu. The copability ingredient is variously termed *constitution*, *predisposition*, or *tissue tolerance*. The terms most frequently utilized are *host resistance* and *host susceptibility*. For most investigators, resistance and susceptibility are simply viewed as antonyms. Thus, it matters little, by this definition, whether one's resistance goes down or whether one's susceptibility goes up. However, when viewed analytically (Schneider, 1951), resistance may be regarded as any agent which, when administered, tends to discourage the development of disease. When absent, however, it encourages disease. For example, vitamin B₁ (thiamin) may be regarded as a dietary resistance agent, for its administration tends to discourage the development of beri-beri, and its absence causes it. In a sense, therefore, resistance agents, dietary and nondietary, are pluses. They should be added to our lifestyle if not already a part of it. In contrast, a susceptibility agent invites disease when present and discourages the development of disease when it is withdrawn. Thus, sugar is to be viewed as a dietary susceptibility agent because its introduction tends to encourage dental caries, and its absence exerts a preventive action. Hence, in one sense, susceptibility agents, dietary and nondietary, are minuses. They should be subtracted if they exist as part of our lifestyle. Parenthetic mention should be made that an agent is never a resistance factor for one disease or one system or organ or site and a susceptibility factor for another. Since vitamin C, for example, is known as a resistance agent for scurvy, it would seem that it should be a resistance agent for other syndromes. On the other hand, since sugar is viewed as a susceptibility factor in the mouth, it is likely the same for the whole body.

Proneness Profiles

Over the past few years, we have been studying primary prevention in a number of systems and have already reported an oral disease proneness profile (Cheraskin, Ringsdorf, Hicks, and

Romano, 1975), mental illness proneness profile (Cheraskin and Ringsdorf, 1973), musculoskeletal disease proneness profile (Cheraskin, Ringsdorf, Medford, and Hicks, 1977), and the syndrome of sickness profile (Cheraskin and Ringsdorf, 1971). The resistance agents for each of these systems are strikingly the same. Likewise, for all systems, the susceptibility factors are identical. It would follow, if there is indeed a wisdom of the body of man, that these same resistance and susceptibility factors should prevail in the alcohol proneness profile.

A Common Denominator in Alcoholism

Apropos to alcohol consumption, it is generally agreed that different individuals drink alcohol for different reasons. Some people drink because they like the taste of alcohol. Within this group, some such persons may eventuate as alcoholics where some will not. Others will drink because of the relaxing and other tranquillizing benefits derived from alcohol. Within this second group, some may eventually turn to alcoholism but the majority will not. Third, there are those who drink because of real or supposed social pressures. Here again, some few may become alcoholic; others not. Finally, there is a group which drinks because of an urge, a chemical craving, to drink. This thirst is critical for without it alcoholism and the alcoholic syndrome do not exist.

There is no question but that alcohol is a chemical agent. As such, the desire for the first drink and, more importantly, the desire created by the first for the second and third one, stems from a deranged cellular metabolism. Setting aside for the moment the pathologic consequences, the wish for one and then another alcoholic drink is similar to the urge for water when the tissues are dehydrated and for food when the tissues are starved. However, under physiologic conditions, once the tissues are satisfied, the individual stops drinking water and eating food. This is not the picture in the heavy drinker following a spree. Notwithstanding the cause for the celebration, be it

social pressure, or psychotrauma, or whatever else, it is well-documented that the hangover is devastating. Yet, a common "solution" is more alcohol!

The phenomenon of more and more alcohol in alcoholism is not unique. If it were pathognomonic, then it might be possible to explain away alcoholism on a specific psychological basis rather than in physiologic terms. After all, morphine, cocaine, and nicotine are also habit-forming drugs. These agents have in common with alcohol the fact that one dose produces an appetite for more and more of the same. Such cravings have never been shown to be psychological or mental in nature. Rather, these bizarre appetites stem from a derangement in cellular metabolism induced by one or another chemical agent.

Just as elevated serum cholesterol is one, surely not the only, secondary risk factor for certain cardiovascular syndromes and just as high uric acid is one, certainly not the only, secondary risk factor for gout, it would follow that there should be biochemical repercussions of deranged metabolism in alcoholism and in the alcoholic syndrome. And so it is. Low blood sugar appears to be one, clearly not the only, chemical parameter serving as a secondary risk factor. It is estimated that about 70 percent of alcoholics have reactive hypoglycemia and that the dysglycemia existed before the addiction to the alcohol. The question now to be resolved is what are the primary risk factors which explain the deranged cellular metabolism?

There is a body of knowledge, admittedly not large but exciting, in both lower animals and in man, which suggests that dietary factors might well represent some of the most serious primary proneness factors in the development of alcoholism and the alcoholic syndrome.

Lower Animal Observations

Doctor Jorge Mardones, of the Institute of Pharmacology and the Institute of Research on Alcoholism at the University of Chile in Santiago, almost 20 years ago (1960) and subsequently Professor Roger Williams and his colleagues at the Clayton Institute of Biochemical Research at the University of Texas in

Austin (1959), in brilliant monumental reviews examined the experimentally induced changes in the free selection of alcohol in lower animals.

First and foremost, the point was emphasized that lower animals, like man, possess a "wisdom of the body." The overall conclusions drawn from many studies on the self-selection of foods was that the rat, for example, chooses the best combination of foods for physiologic growth and reproduction. Also, it is abundantly clear that food choice predictably compensates for pathologic imbalances, thus, rats will regularly and reliably increase their salt consumption after adrenalectomy and reduce carbohydrate intake after pancreatectomy.

The most relevant conclusions may be summarized in the following three statements. First, the quantity of alcohol consumed under free-choice conditions varies in different laboratory animals. Second, the deprivation of most of the water-soluble vitamins invites an increase in ethanol consumption. Third, when sugar solutions or a fat emulsion is offered as a third choice, ethanol intake decreases. There are also other conclusions which will not be discussed because of the serious time and space constraints.

A second direction of investigation has looked at the possible effects of ordinary human diets upon alcohol intake in lower animals. Doctors Register, Marsh, Thurston, Fields, Horming, Hardinge, and Sanchez from the Departments of Nutrition and Biochemistry of the School of Health and the School of Medicine at Loma Linda University in California conducted (1972) a series of studies to ascertain whether a typical teenage-type American diet, generally held to be marginally suboptimal in certain nutrients, could provoke alcoholic behavior in rats similar to the observations obtained with the purified diets mentioned earlier. Additionally, included in these same testing schedules, an attempt was also made to examine the possible effects of other lifestyle elements such as coffee and caffeine upon drinking behavior. In one such study, the Loma Linda group

provided a choice of 10 percent alcohol versus water under rigidly controlled circumstances. Bottles of these two fluids were made equally available in the cages so that there was no technical reason for choosing one versus the other liquid. One group of rats were fed a typical teen-age-type American diet which is usually relatively high in refined-carbohydrate foodstuffs and marginally low in most of the vitamins and minerals. A second group received a control diet containing adequate concentrations of all nutrients as compared with recommended intakes for adolescents plus additional vitamins and minerals. A comparison of these two groups showed that, in a matter of a few short weeks, the subjects with the typical teen-age type diet consumed five times as much alcohol!

In an attempt to simulate further the human experience, another group of animals were supplied the very same teenage diet plus spices. A comparison of the alcohol intake in this group versus those on the teen-age diet alone showed no difference. In other words, the increased consumption of alcohol with the typical American teen-age diet was not significantly altered by virtue of the spices.

In a third instance, and once again designed to duplicate if possible the typical human lifestyle, a group of rats were supplied with the same teen-age diet plus the spices and coffee equivalent to 18 cups per day. Under these circumstances the alcohol intake was higher by 13 percent with coffee with the teen-age diet than with the diet alone and sixfold greater than the alcohol intake with the so-called good (control) diet! It would appear that the addition of coffee encourages significantly greater alcohol ingestion. Parenthetic mention should be made that this experiment resembles the experiences in limited human studies.

In order to establish what it is in coffee which contributes to the desire for alcohol, two other studies were performed. In one instance, the typical teen-age diet plus spices was supplied along with caffeine (instead of coffee) and, in another experiment, the caffeine was substituted by decaffeinated coffee. In the case where caffeine was added to the teen-age diet, the consumption of alcohol was very much like

that observed with coffee. In other words, caffeine and coffee behaved very much alike. In the experiment in which decaffeinated coffee was utilized, the results approached those of the teen-age diet alone. Hence, within the limits of these studies, it appears that the active ingredient in coffee which makes for greater alcohol consumption is caffeine.

Finally, and once again in an attempt to simulate the human experience, the teenage diet plus spices and coffee were supplemented with vitamins and minerals. Under these conditions, there was a significant reduction in alcohol intake even though the diet was not grossly deficient in any one nutrient fraction.

Human Implications

On the basis of the reports cited here and others not included in the interest of expedition, many investigators view these results as evidence of "experimental alcoholism". It should, however, be underlined that, while there are many glaring similarities, there are striking differences between the observations reported in lower animals and the experiences in man.

It is well known that the craving for alcohol observed in the human is usually overbearing and critical. The withdrawal syndrome includes insomnia, anxiety, tremor, and a host of other psychologic symptoms and signs which are, to a degree, alleviated for a time by supplementation with additional alcohol. This overriding desire for alcohol is almost pathognomonic of the behavior of the human alcoholic subject. On the other hand, the desire for alcohol in laboratory animals is much less intense. This point obviously sets apart "human alcoholism" from "experimental alcoholism".

Second and generally speaking, alcoholics consume alcohol until they are intoxicated and this is demonstrated by changes in their behavior (the alcoholic syndrome). Generally speaking, laboratory animals do not display any overt signs of intoxication. Perhaps the only similarity between the lower animal and human studies is the fact that both,

sooner or later, demonstrate liver damage.

A third fundamental difference between human alcoholism and experimental alcoholism is the presence of withdrawal symptoms after cessation of drinking in the human organism. Parenthetical mention should be made that the symptomatology observed in the alcoholic syndrome is encountered in other so-called psychologic disorders. In contradistinction, the clinical picture of tremulousness, nausea, perspiration, insomnia, convulsions, hallucinations, and delirium are not observed in laboratory animals.

On the other hand, there are actually more similarities than differences in human versus experimental alcoholism. The urge to drink is a function of the diet and other lifestyle characteristics (Williams, 1978). Individuals with suboptimal dietary regimes are more prone to become alcoholics. Persons who engage in suboptimal physical activity, who drink coffee and tea, and who consume tobacco are more alcohol-prone. As a matter of fact, it is not infrequent to observe that, when individuals cease drinking alcohol, they turn to a greater consumption of refined carbohydrate foods (foods made primarily of sugar and white flour), a larger intake of coffee and caffeinated beverages (cola drink, cocoa, tea), and an increase in nicotine intake. Therefore, the mere fact that one can eliminate alcoholism (defined as the cessation of alcohol consumption) may not necessarily mean the elimination of the alcoholic syndrome since, as we have just seen, the individual simply switches his or her "fix" from alcohol to food indiscretions, coffee/tea, nicotine, and sugar.

Actually, sugar is such a powerful reinforcer of behavior that it may be the mother of addictions. Controlled laboratory experiments cited by Dr. Michael B. Cantor of the Department of Psychology at Columbia University of the City of New York convincingly demonstrate the power of sweet taste to determine behavior. These lower animals and human studies show that the higher the concentration of sweetener, the greater the preference and the more avid the behavior in its pursuit.

Citing John Falk and his colleagues at Rutgers,

Dr. Cantor illustrates the unusual power of sweetness to control behavior and raises the question of whether it is appropriate to consider sweetness as addictive (Cantor and Eichler, 1977). In an attempt to wean rats from ethanol, Falk found that only a sweet taste could compete with the alcohol dependence. When five percent ethanol was pitted against three percent dextrose, alcohol was preferred. When the concentration of dextrose was increased to five percent, it was preferred over alcohol. In choosing the sweet taste over ethanol, the animals drank so much sugared water that they suffered convulsions and faced death from malnutrition. Since Falk's animals were addicted to alcohol and this was supplanted by overindulgence in sugar, may one conclude that these animals gave up one addiction for another?

Summary and Conclusions

There is no question but that the alcohol problem, like any other problem, is multifactorial.

If one surveys the literature, the overwhelming body of fact suggests that alcohol proneness is the result of psychologic, social, economic, ethnic, religious, cultural, and spiritual factors. There are only a few publications dealing with the biochemistry of alcohol-proneness.

On the other hand, if one examines the research funding process, it becomes clear that the ratio of monies is fairly proportional to the ratio of nonchemical versus chemical studies.

It would be interesting in the coming years to inaugurate the following experiment. Let us, for once, shift our emphasis, meaning our time and money skills, from our present strivings to discover more non-chemical denominators in the genesis of alcoholism to a study of the risk potential of the air we breathe, the water we drink, and the food we eat. We predict, if this is done properly, we shall unearth a boundless fountain of fascinating and fruitful data in support of the chemistry of alcohol-proneness.

PRIMARY PREVENTION OF ALCOHOLISM References

- CANTOR, M.S. and EICHLER, R.J.: Sweetness: a Supernormal Reinforcer. *Chemtech*. 7 (4), 214-216, April 1977.
- CHERASKIN, E. and RINGSDORF, W.M. Jr.: Fabric of Man. *J. Amer. Soc. Prevent. Dent* 1 (4), 10-12,15-17, July 1971.
- CHERASKIN, E. and RINGSDORF, W.M. Jr.: Predictive Medicine. New Canaan, Keats Publishing, Inc., 1977.
- CHERASKIN, E. and RINGSDORF, W.M. Jr.: The Mental Illness Prone-ness Profile. *Alabama J. Med. Sci.* 10 (1) 32-45, January 1973.
- CHERASKIN, E., RINGSDORF, W.M. Jr., HICKS, B.S., and ROMANO, D.M.: The Prevention of Oral Disease. *J. Internat. Acad. Prevent. Med.* 2 (11,22-52, First Quarter, March 1975.
- CHERASKIN, E., RINGSDORF, W.M. Jr., MEDFORD, F.H., and HICKS, B.S.: The Musculoskeletal Disease Proneness Profile. *ACA J. Chiro-pract.* 14 (51,41-51, May 1977.
- MARDONES, J.: Experimentally Induced Changes in the Free Selection of Ethanol. *Internal. Rev. Neurobiol.* 2,41-76,1960.
- REGISTER, U.D., MARSH, S.R., THURSTON, C.T., FIELDS, B.J., HORMING, M.C., HARDINGE, M.G., and SANCHEZ, A.: Influence of Nutrients on Intake of Alcohol. *J. Amer. Dietet. Assn.* 61 (2). 159-162, August 1972.
- SCHNEIDER, H.A.: Nutrition and Resistance-Susceptibility to Infection. *Amer. J. Trop. Med.* 31 (2), 174-182, March 1951.
- WILLIAMS, R.J.: Alcoholism: The Nutritional Approach. Austin, University of Texas Press, 1959.
- WILLIAMS, R.J.: Alcoholism: The Nutritional Approach. Austin, University of Texas Press, 1978.