

ALCOHOLISM

Roger Williams and his co-workers at the Biochemical Institute of the University of Texas are tackling this age-old problem in a new and revolutionary way

A GOOD MANY people still think alcoholism is a sign of moral depravity. Others recognize it as a disease, but consider it a mental one. Recent research at the University of Texas, however, has begun to produce evidence that alcoholism, after all, may have a physiological basis.

In 1946 Roger J. Williams, Director of the Biochemical Institute of the University of Texas, wrote a book called *The Human Frontier*, in which he proposed the development of a new branch of applied science—humanics—to undertake a comprehensive study of individual human beings.

It was Williams' conviction that most scientific studies of man were concerned with a non-existent "average" man—whereas what we really needed was a science of human beings to help us cope with such social problems as marriage, health, employment, crime, group bigotry, alcoholism and war.

Having expressed this conviction, Williams determined to do something about it. Obviously it was impossible to try to learn everything about everybody all at once. In order to make any headway at all he would have to tackle some specific problem, and after considerable cogitation and discussion he settled on a study of real people in connection with alcoholism.

Williams suspected that the differences which people exhibit with respect to alcohol—and the fact that some people develop a craving which they cannot control—had a genetic basis, as well as a physiological basis. So, with his co-workers at the Biochemical Institute at the University of Texas, he began to explore the problem of alcoholism in relation to differences between people and to inborn difference.

The work began with studies of the metabolic patterns—the body chemistry—of various individuals. Though the body chemistry of human beings is broadly the same

This article has been adapted from "Alcoholism as a Genetotropic Disease," a Hixon Lecture delivered by Dr. Roger J. Williams at the California Institute of Technology on January 31, 1952



Dr. Roger J. Williams, Director of the Biochemical Institute of the University of Texas, who has been studying the effects of nutritional deficiencies in relation to alcoholism

from individual to individual, and the same chemical reactions take place in each of us, nevertheless individual human beings can differ greatly in the degree of effectiveness with which they carry out the various reactions. Different individuals, for instance, react differently not only to alcohol but to drugs, anesthetics, coffee, and nicotine.

The studies revealed at once that the metabolic pattern of each individual is quite different from that of all other individuals. But the investigators soon discovered that some of these patterns were significant from the standpoint of different groups. Highly significant differences were found between schizophrenics from a state hospital and normal individuals, between children from feeble-minded institutions and normal children, between morons and imbeciles—and between alcoholics and non-alcoholics.

Alcoholics and non-alcoholics compared

Alcoholics and non-alcoholics were compared with respect to some 62 items that could be measured. Urine and saliva samples were collected from the two groups five times a week for a period of four weeks, and analysis of these samples revealed, for example, that the sodium content of the saliva of alcoholics was extremely high. Uric acid in both the urine and the saliva of alcoholics was also high. Gonadotropin and citrilline in the urine of alcoholics were low.

The evidence was by no means watertight, but it was sufficient to indicate to Williams that many of these metabolic patterns were to a considerable degree genetic

in origin. Could the inheritance of a specific pattern of endocrine gland activities, for example, be responsible for alcoholic tendencies?

The next step in the studies was animal experimentation. In order to study the tendencies of animals to consume alcohol, a group of rats was put into individual cages. Each rat was given two drinking bottles—one containing 10% alcohol, the other water. The positions of the bottles were shifted each day so that the rats would have to make a deliberate choice each time they took a drink.

All social influences had to be eliminated. (“The rats were not allowed to give parties,” Dr. Williams wryly observes, “—nor were they given the opportunity to look over each other’s records or anything like that.”)

The principal difference between this experiment and most animal experimentation was that the investigators here were interested in observing *individual* rats. The usual thing, of course, would be to take a group of rats, average them together, and come up with a result. At the risk of being considered unscientific, Williams and his co-workers watched each rat by itself.

They found immediately that the rats showed a great degree of individuality in their response to alcohol under this particular set of conditions. One rat, for example, consumed alcohol at a substantially high level—continuously, from the first time it was offered to him. Another rat was, as far as any of the investigators could observe, a teetotaler. He didn’t touch a drop of alcohol during the 60 days he participated in the experiment. A third rat was a very moderate drinker, taking just

enough for the investigators to be able to tell that he was drinking alcohol at all.

Another rat started at a low level of consumption but, after 20 or 30 days, showed a high consumption. A number of the rats reacted in this way. Sometimes it would be four or five weeks before they would begin to take alcohol in substantial quantities, sometimes only a couple of weeks.

Spasmodic drinkers

Some of the rats were spasmodic drinkers. They would drink for a day or two, then go on the wagon for a week or more, only to come back and drink heavily for a couple of days again.

The behavior of the rats was, in a word, individual. As Williams points out, if the investigators had taken a group of rats (and the larger the group the worse the results would have been, he adds) and averaged them all together, they would have found a pattern of behavior that *no* rat exhibited.

But *why* did the rats behave so variously? They were on identical diets, and they were under as nearly identical conditions as possible. Did diet have something to do with it?

To find out, the rats were put on a stock diet—a diet which was marginal on B vitamins only. On this marginal diet it was found that *all* the rats would drink alcohol. Some began to drink from the start; others delayed, but eventually all the rats came up to a fair level of drinking.

Drinking on an abundant diet

As a follow-up to this experiment, the rats were put on an abundant diet, which included everything they could conceivably want. None of the rats drank alcohol at a high level.

The researchers then tried the obvious experiment of putting the rats on a marginal diet, allowing them to drink at a high level, while giving individual rats various supplements to see how each would behave. The responses of the rats to this treatment were, again, highly individual.

One rat, for instance, started out at a very high level of alcohol consumption. After several weeks, the rat was given a supplement containing ten vitamins, which it was thought might bring his diet up to a satisfactory level. His alcohol consumption rate dropped overnight. Because of this striking response, the treatment was carried on over a long period of time. The rat showed no tendency to go back and try the alcohol again.

The behavior of this particular rat is not something that can be duplicated with every rat, of course, though it is a fact that most of the rats in the original group chosen for these studies reacted in this manner. As the work progressed and different strains of rats were brought in, however, this particular assortment of added vitamins was not sufficient to keep them off the alcohol. Other nutritional supplements had to be added to their

diets. But the more supplements that were added, the more rats were prevented from consuming alcohol.

Probably it was just a fortunate coincidence that the original group of rats used in these experiments gave such conclusive responses. It is an interesting sidelight that, when the researchers began to run out of these rats, they had to borrow others from the Home Economics Department at the University of Texas. These proved to be much heavier drinkers, and were much harder to cure.

Some people, of course, blamed this on environmental influence—though the researchers continued to suspect genetics. They reasoned that the Home Economics rats reacted differently because these animals had in their makeup a possible genetic block which increased their nutritional demands. For instance, if an animal has a mechanism—genetically received—involving riboflavin deficiency, then it may require more riboflavin to make the system work efficiently. So rats, it was argued, may differ in their needs for riboflavin or other vitamins, amino acids or minerals.

Alcohol and nutrition

Presumably, some of the original rats did not consume alcohol because the stock diet furnished them with all the nutrients they needed. And some took to alcohol from the start because this diet was deficient for them in certain respects. Why deficiencies should cause an appetite for alcohol is still not too clearly understood, but it is nevertheless an experimental fact in regard to these rats.

Dr. Williams and his co-workers have made a number of studies to find out which vitamins are most effective, and whether amino acids, minerals or other nutrients have much effect. In general, they have found that a lack of thiamine, riboflavin, pantothenic acid or pyridoxine is particularly effective in producing an alcoholic appetite. When animals are put on a deficiency diet of any of these substances, the animals drink; when the vitamins are supplied, the animals stop drinking.

An individual matter

It doesn't always work out as cleanly as this. Sometimes when the researchers produce a diet deficient in riboflavin only, the diet is apt to be marginal in respect to some other things. But all the results fall in with the hypothesis that each animal has different needs from a quantitative standpoint. The researchers have found that they are not able to give rats generally—all strains and all kinds of rats—all the things which are important in their nutrition. But, as far as rats are concerned, when this *can* be done, alcohol consumption will pretty much disappear.

Of course, Williams and his co-workers are not primarily interested in alcoholism in rats. ("It is not," Dr. Williams observes, "a really serious problem.") So, when they thought they knew something about what made animals consume alcohol, they began to turn their

attention to human beings. Possibly, they decided, a potential alcoholic is an individual who has rather high demands for certain vitamins, amino acids, minerals or other substances. Because of these high demands he is not nourished sufficiently on an ordinary diet. When he consumes alcohol he dilutes that diet. (It is a fact that some people *do* drink instead of eating; they don't drink in addition to eating. They take in so many calories a day, and if they take these in the form of alcohol they don't take them in the form of foods that contain vitamins, amino acids and minerals.) The more he drinks, the more he dilutes his diet, the more deficient he becomes, the more he drinks.

If it were possible to get these potential alcoholics to eating things they need, or if their diets could be supplemented with things they have high requirements for, the tendency toward alcoholism might disappear. It was on this basis that the Texas scientists began their experiments on human beings.

Human experiments

Soon after this work got under way a man came to them who had been an alcoholic for ten years, and a heavy drinker for 20 years. He was on his last legs. He had tried psychiatry and gotten no relief; he had tried Alcoholics Anonymous, but their program had not seemed to click with him, despite its general excellence. Now his wife had finally turned him out of their home.

It seemed like a long shot. "Suppose," said Williams, we could do something that would decrease your appetite for alcohol, or abolish it. Would you know it?"

The man was confident. Certainly, he would. He knew what the symptoms were; he was very conscious of his craving for drink.

So they started him out. They were careful not to try to sell him anything or promise him anything—in fact, they *couldn't* promise him anything. They gave him 15 vitamins to take regularly and asked him to report back from time to time.

At the end of a month the man reported that he was able to sleep better than he had for a long time. After several more weeks he announced that his craving for liquor was gone. The treatment was continued until, after four months of complete abstinence, the man insisted on proving that he was cured for good.

Acid test

It seemed risky and Williams tried to talk him out of it, but the man was determined to test himself.

"I'm going down to the beer parlor," he said, "and drink some beer and come back here sober."

He did. He drank a couple of bottles of beer with reasonable relish, forced himself to drink more to confirm the experiment, then reported back to Williams—sober.

Today, after three years, the man continues under treatment. He drinks moderately, but his compulsion is

gone. Williams thinks this may well be the first case on record in which an alcoholic has become a moderate drinker.

It was a matter of several weeks before this man reported any effects from his treatment, but in general—as with the rats—Williams has found that improvement often comes "overnight."

Case history

A young married student at the University of Texas came to Dr. Williams for help after hearing him give a talk. Since the war he had been unable to leave liquor alone. Though he had been working at a job he loved, he had lost it because of his drinking. Thinking that a change of environment would help him, he moved to Texas and went to law school. But it wasn't long before he was as bad off as ever, and he was unable to stay in school because of his drinking.

Williams put him under treatment. In less than two weeks his compulsion was gone, and, following his own inclination, he was able to spend an hour and a half dawdling over a bottle of beer, then leave it without wanting more. At last report, his condition was unchanged.

The Williams experiments with human beings are still just a little more than a year old. Overall results can hardly be expected to mean much yet, but Williams estimates that the partial successes and the complete successes are, to date, about equal in number. The work has already encouraged other researchers to enter the field, and has now received the cooperation of a number of physicians.

Parallel results

The fact that gives the Texas workers the greatest encouragement in connection with the human trials made so far is that the results parallel closely the clear-cut findings obtained with experimental animals.

"People have developed an unfortunate tendency," says Dr. Williams, "to think that a particular treatment will either alleviate a disease or fail to do so. If our basic findings are valid, our treatment of alcoholism in its present form is as certain to fail in particular cases as it is to succeed in others. If the results were different, if they were uniform in one direction or the other, our basic ideas would be seriously in question."

"We cannot say that we have fully demonstrated in a scientific manner the efficiency of nutritional treatment and that there is no room for doubt or questioning. We can say that in view of the animal experiments, which are clear cut, the inescapable logic of the genetrophic concept, and the striking results obtained with many of the alcoholics who have taken the treatment, we are convinced of its essential soundness and efficacy. We hold the opinion that any alcoholic wanting help will do well to arrange with his physician for a trial—a trial which at worst can do no damage."