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EXPERT COMMITTEE ON ALCOHOL

First Report

		Page
1.	Definitions formulated by the Expert Committee on Drugs Liable to Produce Addiction and by the Alcoholism Subcommittee of the Expert Committee on Mental Health . .	3
2.	Concepts pertaining to the pharmacological position of alcohol	3
3.	The approach to alcoholism by animal experiments . . .	7
4.	Metabolism of alcohol	11
5.	Alcohol and traffic	14
6.	The need for further discussion	16

WORLD HEALTH ORGANIZATION

PALAIS DES NATIONS

GENEVA

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EXPERT COMMITTEE ON ALCOHOL

First Session

Geneva, 5-10 October 1953

Members :

L. Dontcheff, Docteur ès Sciences, Laboratoire de Physiologie générale de la Faculté des Sciences, Université de Paris, France

Dr. L. Goldberg, Associate Professor of Pharmacology, Karolinska Institutet, Stockholm, Sweden

Dr. E. Lundsgaard, Professor of Physiology, Medical Faculty, University of Copenhagen, Denmark (*Chairman*)

L. D. MacLeod, B.Sc., Burden Neurological Institute, Bristol, England (*Rapporteur*)

Dr. J. Mardones, Professor of Pharmacology, Medical Faculty, University of Chile, Santiago, Chile (*Vice-Chairman*)

Dr. H. W. Newman, Associate Professor of Medicine, Stanford University School of Medicine, San Francisco, Calif., USA

Representative of the International Labour Organisation :

Dr. W. Norman Taylor, Occupational Safety and Health Division, ILO, Geneva

Secretariat :

Dr. G. R. Hargreaves, Chief, Mental Health Section, WHO

Professor E. M. Jellinek, Consultant on Alcoholism, WHO

Dr. P. O. Wolff, Chief, Addiction-Producing Drugs Section, WHO (*Secretary*)

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EXPERT COMMITTEE ON ALCOHOL

First Report *

The first session of the Expert Committee on Alcohol was held in Geneva from 5 to 10 October 1953.

Dr. H. S. Gear, Assistant Director-General, welcomed the members of the committee on behalf of the Director-General, Dr. M. G. Candau, who was away from Headquarters. He expressed the appreciation of the World Health Organization for their readiness to provide technical guidance on the important subject to be discussed, and also outlined the general principles established by the World Health Assembly and the Executive Board defining the status of and procedures for expert committees.

1. Definitions Formulated by the Expert Committee on Drugs Liable to Produce Addiction and by the Alcoholism Subcommittee of the Expert Committee on Mental Health

The committee noted the various definitions formulated by the Expert Committee on Drugs Liable to Produce Addiction and by the Alcoholism Subcommittee of the Expert Committee on Mental Health.

The Secretary explained the difference between the Alcoholism Subcommittee and the Expert Committee on Alcohol—namely, that the former was concerned with psychiatric clinical and social aspects of the question, while the latter was concerned with the physiological, pharmacological, and biochemical properties of alcohol.

2. Concepts Pertaining to the Pharmacological Position of Alcohol

2.1 *Tolerance to alcohol*

The committee recognized the existing state of confusion arising out of the indiscriminate use of the term " tolerance ". It was felt necessary

* The Executive Board, at its thirteenth session, adopted the following resolution : The Executive Board

1. NOTES the first report of the Expert Committee on Alcohol ;
2. THANKS the members of the committee for their work ; and
3. AUTHORIZES publication of the report.

(Resolution EB13.R14, *Off. Rec. Wld Hlth Org.* **52,** 6)

to make a distinction between the use of the term tolerance in connexion with addiction-producing drugs of the morphine type, and that required for consideration of the problems which arise in connexion with the use of alcoholic beverages.

In the case of alcohol, which, in the form of alcoholic beverages, is consumed by many people as a social custom, a concept of tolerance is needed which describes differences in the inherent susceptibility of individuals to the effect of the substance on the function of the nervous system. It was therefore agreed to regard tolerance to alcohol as the capacity of the organism to function with alcohol in the blood without measurable deterioration in nervous function.

That considerable individual differences in tolerance to alcohol in this sense exist has been demonstrated in experimental work upon animals and man. Various functions of the nervous system have been tested by suitable procedures, such as fusion frequency determination, the use of the pursuit meter, electro-encephalography, quantitative measurement of standing steadiness, and many others. By administering different amounts of alcohol, and following by serial determinations both test performance and blood alcohol concentration, it has been possible to correlate the response of the organism, as measured by these tests, to blood alcohol concentration.

Such experiments have demonstrated that there is a critical level or threshold of alcohol concentration in the blood at which performance begins to show deterioration. This threshold is characteristic of the individual tested and of the particular test employed. Tolerance to alcohol can thus be measured by that concentration of alcohol in the blood at which a demonstrable effect on the performance of a given test of nervous function first becomes apparent.

Since this precise method of measuring tolerance to alcohol exists, it was considered that the term tolerance should not be used in other senses such as, for example, the following:

(*a*) the amount of alcohol required by an individual to produce euphoria;

(*b*) the amount of alcoholic beverages ingested by an individual without the appearance of signs of intoxication;

(*c*) the mere ability to ingest large quantities of alcohol irrespective of whether such quantities result in intoxication or not.

The main reason for the rejection of the above forms of usage was because they relate the effects of alcohol to dosage. This is undesirable since variation in the rate of absorption and other aspects of the metabolism

of alcohol, as well as the period over which ingestion takes place, may change the relation between dosage and blood alcohol levels.

It appeared to the committee particularly undesirable to introduce the concept of tolerance in connexion with the phenomenon known as " loss of control " as defined by the Alcoholism Subcommittee. [1]

2.2 *Acquired increase of tolerance to alcohol*

It has been shown that to produce the same effects, as measured by objective tests, a higher blood alcohol level is required in habitual heavy drinkers than in moderate drinkers and abstainers. That this increase of tolerance is acquired is shown by its disappearance after a period of abstinence. There is, furthermore, experimental evidence that in animals subjected to prolonged administration of large doses of alcohol the blood alcohol level required to produce the same symptoms must be increased.

Since the term tolerance had been reserved to denote the inherent susceptibility of the individual to alcohol, another term was needed to describe the change in resistance to the drug brought about by habitual intake. It was recommended that this be referred to as " acquired increase of tolerance ". This usage would correspond roughly to the term " acquired tolerance " as employed in the case of addiction-producing drugs of the morphine type.

In view of the variation in the acquired increase of tolerance to alcohol, even among heavy drinkers, the committee suggested that research on the determining factors should be undertaken. Such research might be greatly facilitated if it were found possible to adopt a standard set of tests in order to permit of comparison between the results obtained by different workers.

Prolonged heavy intake of alcohol does not decrease the rate of absorption nor does it increase the rate of oxidation or excretion of alcohol. There is no evidence to show that the permeability of the haemato-encephalic barrier to alcohol is lowered. Two other possible explanations have been put forward for the increase in resistance to alcohol.

Conditions may arise that make the nervous system more resistant to alcohol, or the individual may compensate for the effects of intoxication through the process of learning. Frequently, these two possibilities are regarded as though mutually exclusive, but it does not appear necessary to make this assumption. No doubt continued experience with the effects of alcohol can enable an individual to offset them to a limited degree. However, in view of the results of experiments with objective tests both in man and in animals it is the opinion of the committee that, although

[1] See *Wld Hlth Org. techn. Rep. Ser.* 1952, **48**, 33.

the biological mechanism of the change is not fully understood, the total phenomenon cannot be accounted for solely by compensation based on learning, and in addition requires for its explanation a changed physiological response of the organism to alcohol.

The committee felt that special emphasis should be laid on the fact that acquired increase of tolerance to alcohol was of a lower order of magnitude than the corresponding phenomenon known to occur with addiction-producing drugs of the morphine type. The morphine addict may develop (an increase of) tolerance enabling him to withstand several times the lethal dose. An increase of this degree has not been observed with alcohol.

While knowledge is beginning to accumulate on the action of alcohol in the unaccustomed organism, as judged by the application of a number of physiological, pharmacological, and other methods in animals and man, very little is known about the underlying mechanism of acquired increase of tolerance in the habituated organism. The committee believed that basic research in this field was very desirable.

2.3 *Withdrawal symptoms*

The existence of withdrawal symptoms in alcoholism is a controversial question. As far as animal experimentation is concerned, no evidence has come forth as yet of the existence of specific symptoms following abrupt withdrawal of alcohol. Thus, the question can be discussed only on the basis of clinical observations.

Upon interruption of an acute alcoholic episode certain symptoms are not infrequently observed. The symptoms are largely in the category of psychomotor excitement, but convulsions of the " grand mal " type are also seen.

The committee feels that a sharp distinction must be made between these symptoms and those which are produced by the withdrawal of morphine-type drugs. The symptoms after sudden withdrawal of alcohol are of short duration and, in the absence of serious organic disease, do not usually have grave consequences. Such symptoms may be tentatively regarded as involving a process of physiological readaptation, requiring a comparatively short time for its accomplishment.

The symptoms occur only on abrupt withdrawal and are not observed during either voluntary or enforced abstinence. This latter point distinguishes markedly the effects of withdrawal of alcohol from those following withdrawal of drugs of the morphine type. For this reason, the committee recommends, in connexion with alcohol, the use of the term " withdrawal symptoms " alone; the term " abstinence syndrome " is justified in the case of drug addiction of the morphine type.

While the processes behind the appearance of these withdrawal symptoms are not clear, the occurrence of convulsions accompanied by characteristic electro-encephalographic changes (patterns of diffuse slow rhythms immediately after the convulsion) strongly suggests that some symptoms at any rate have an organic basis although emotional disturbances may play a part in their appearance.

Further study of such withdrawal symptoms in the human subject appears to be necessary. Although alcohol withdrawal symptoms have not, hitherto, been observed in animals, there is a possibility that more-adequate methods of investigation will reveal them.

3. The Approach to Alcoholism by Animal Experiments

3.1 *General considerations*

The phenomenon of increased voluntary consumption of alcohol by animals under different experimental conditions has been reported by a number of workers. Among these conditions may be mentioned vitamin deficiency, toxic agents (including those producing obvious liver damage), and states of conflict induced by conditioning procedures.

This phenomenon is occasionally referred to as " experimental alcoholism ", but the committee considers the use of this term to be undesirable. In the present stage of knowledge it is not possible to extend such observations upon animals subjected to vitamin deficiencies or toxic influences directly to the problem of alcoholism. The latter condition involves considerably more than a mere increase of alcohol consumption. The relief by alcohol of experimentally induced neurotic manifestations in animals represents a somewhat closer approach to alcoholism, but important features of the latter are not represented in such an experimental situation, since the preference for alcohol does not persist after resolution of the conflict. Similarly, the demonstration in rats of the genetically determined character of alcohol drinking behaviour cannot be directly applied to the human problem.

3.2 *Specific organogenic approaches*

Present knowledge of the basic mechanism of acute alcoholic intoxication is meagre. This constitutes a difficulty in the investigation of the corresponding long-term changes induced by alcohol. Various proposals have, however, been made to elucidate certain aspects of alcoholism by means of experimentation to the more recent of which brief reference may now be made.

3.2.1 *Nutritional deficiencies*. In recent years, attention has once more been focused on the possible role of dietary factors by a number of investigators, mostly using autoselection techniques applied to rats. The preference displayed in a restricted choice situation has an inherent weakness for which reason the identification of increased voluntary consumption of alcohol under such conditions with that occurring in alcoholics may not be justified. On the other hand, it might be maintained that a preference for alcohol shown in autoselection experiments could be an indication of the presence of a need which, exaggerated under pathological conditions, might gain the attributes of craving in the sense of irresistible desire. The committee feels that this point is far from settled.

3.2.2 *The approach via endocrine studies*. On the basis of clinical reports indicating reduced adrenocortical function among alcoholics and stimulation by alcohol of the pituitary-adrenal system, craving for alcohol has been interpreted as arising from the need for substances of the adrenal cortex which, according to the results of certain experiments carried out on animals, may be released following ingestion of alcohol. It has been surmised, although not as yet demonstrated, that alcoholism might result from a disturbance in the control of the pituitary affecting adrenocortical secretions. The evidence in the literature is, however, conflicting.

3.2.3 *Other concepts*

(*a*) According to some authors, craving has been interpreted as the need for lengthening of chronaxie by the depressant agent, alcohol. The generalization to the entire nervous system of observations on the flexor-extensor relationship in peripheral nerve seems highly dubious. In alcoholics variable effects of alcohol on chronaxie were found, and earlier ideas on the influence of acid-base equilibrium were invoked as an explanation of the chronic toxic states believed by that particular group to account for the phenomena of chronic alcoholism. Such ideas undoubtedly account for later attempts to implicate pyruvate as the toxic factor in (chronic ?) alcoholic states.

(*b*) Upholders of the view that alcohol possesses antigenic properties have suggested, on the basis of the treatment by intravenous administration of alcohol, that circulating antibodies require the consumption of increased amounts of alcohol.

(*c*) Attempts have been made to explain craving for alcohol as the result of hyperactivity of cerebral centres vis-à-vis the mid-brain or medullary centres. The resultant disequilibrium may, according to such ideas, be overcome either by the depressant action of alcohol on the cortex or by stimulation of the lower centres by apomorphine.