

Some Pharmacological Actions of Alcohol

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The contribution which alcohol may make to a man's nutrition varies considerably. Alcohol is not an essential dietary constituent, but it is commonly consumed, and unlike most foods it has notable subjective and objective effects in quantities which contribute trivially to the total daily calories. Moderate drinkers are much commoner than those who consume to excess, and it will therefore be most interesting and most relevant to consider the effects of small doses of alcohol on healthy subjects.

When alcohol is taken by mouth, it is absorbed rapidly from the stomach, especially if the stomach is empty, and it enters the blood stream and thence is widely distributed in the body. Some 95–98% is removed by oxidation in the liver and elsewhere, and the rest is excreted unchanged in the urine and by exhalation. As a rough approximation the rate of removal, by one channel or another, is about 10 ml./h in a healthy adult and is less dependent on the concentration in the body fluids than might be expected. (See Jacobsen (1952) for review.) The concentration of alcohol in the blood during or after drinking therefore depends particularly on the dose, on the duration of consumption, and on whether the stomach is empty or full; a given dose of alcohol will produce only about half the peak concentration of alcohol if it is taken on a full stomach instead of an empty one (Mellanby, 1919). Individuals vary in their metabolism of alcohol as well as in their response to a given amount, and on the whole habitual drinkers of large amounts metabolize alcohol a little faster than more moderate drinkers; but with these factors in mind it is roughly possible to predict fairly reliably the course of the blood-alcohol concentration curve after a drink or drinks. Conversely, from a knowledge of the concentration of alcohol in the blood or urine, it is possible to predict with reasonable certainty the minimum amount of alcohol the subject must have consumed to attain such a level—a point of some forensic importance.

One of the earliest effects of consuming alcohol is the recognition of its characteristic taste and smell, or that of the liquid which contains it: and with stronger drinks this is followed by mild epigastric sensations when the material reaches the stomach. These effects are important experimentally, because it is very difficult to produce a dummy alcoholic drink which is pleasant to consume but contains no ethanol. The point is important because it makes distinction almost impossible between the effects of ethanol *per se* and the effects of drinking, with all the emotional and cognitive associations involved. The difference does not matter much in considering the practical consequences of drinking, but it considerably complicates the psychological and pharmacological problems in unravelling exactly how alcohol acts on the brain. Many attempts have been made to provide proper dummy

controls, but they have not been very profitable. For instance Rivers & Webber (1908) used a drink flavoured with capsicum, cardamons, chloroform and peppermint, which they demonstrated to disguise up to 10 ml. of alcohol: this is not very much and they found their drink unpleasant to consume. Nevertheless, they found it to be devoid of effect on muscular work, whereas distinct effects were obtained by drinking the same amount of alcohol in the more palatable form of whisky. Hollingworth (1923*a,b*) used beer freed from alcohol by a special (undescribed) process, but his genuine beer contained only 2.75% ethanol, and was regarded as poor stuff by his subjects, who had to drink several pints of the liquid. There have been a number of other attempts, sometimes described without comment as to their adequacy.

When alcohol has been absorbed, its main effects are on the central nervous system, and these effects will be discussed shortly. Alcohol stimulates salivation and gastric secretion, and the stimulation of the oropharyngeal region by highly alcoholic liquids such as brandy probably underlies some of the therapeutic use of this substance as an analeptic. Alcohol dilates blood vessels, and in the absence of much external stimulation, such as contributes to many of the common manifestations of mild inebriation, this effect may be the most noticeable one. It promotes diuresis, and although this effect has been well known for a long time (Shakespeare, 1623) the underlying mechanism has been identified relatively recently as the inhibition of the secretion of the posterior pituitary hormone (Edkins & Murray, 1931; van Dyke & Ames, 1951). Sexual reflexes are depressed, and depression has also been demonstrated objectively in dogs (Gantt, 1940) in support of subjective impressions in man. In large doses alcohol interferes with most functions of the central nervous system, and death can occur acutely from respiratory failure. But the most interesting actions are probably those of much smaller doses on the central nervous system, sufficient to produce mild changes of activity and consciousness but considerably short of serious disorganization of physical and mental functions.

These effects are rather difficult to investigate. They involve the higher parts of the nervous system, and so are suitable for study only in man: and methods for this sort of study are still fairly naïve. One cannot study even a simple physical system without altering it in some way, and human behaviour is particularly susceptible to being the object of observation by other human beings. Also, human beings vary considerably from individual to individual, both in their general mental constitution and in their experience of alcohol, so it is not surprising that the literature is full of somewhat divergent findings, especially about threshold effects. But these actions of alcohol are of great practical importance, because men and women perform complicated and potentially lethal actions, like driving cars, under its influence, and it is desirable to know whether they perform such actions better or worse in the circumstances.

As far as the practical issue of driving is concerned, although completely direct evidence is lacking, there is very little doubt that the effect of alcohol is generally harmful. Completely direct evidence on this point depends on a difference between two proportions: the proportion of persons involved in road accidents who have a

detectable amount of alcohol in their body and the proportion of a comparable group of road users not involved in accidents who have similar amounts of alcohol in their bodies. If there is no difference in these proportions, it is unlikely that alcohol makes a serious contribution to road accidents, however much evidence there is that it interferes with judgement or co-ordination under experimental conditions. On the other hand, if the people involved in accidents contain a higher proportion of those who have recently consumed alcohol, the causal relation is strongly supported. It is very difficult to obtain figures of this kind. In this country, for instance, nobody can be obliged to give scientifically adequate evidence about how much alcohol he has consumed or contains, even if he is involved in an accident, and once a voluntary element comes into the method of sampling the population the evidence becomes invalid on the overall question. The best evidence on this point appears to be that of Holcomb (1938), who made a survey at various times and positions in a particular city of the United States and succeeded in persuading all but twenty-four out of 1750 drivers whom he stopped to give samples of expired air for analysis for alcohol. In this way he found that 12% of the drivers had consumed detectable amounts of alcohol and 2% had probably got blood-alcohol concentrations exceeding 0.1%. He also obtained comparable data from drivers who had been involved in accidents, and found quite different results. Of these drivers involved in accidents 47% (instead of 12%) had consumed detectable amounts of alcohol, and 25% (instead of 2%) had a blood alcohol above 0.1%. Numerous criticisms are possible of these startling figures and especially of their applicability to other conditions, but it is difficult to find any possible collection of reasons that can completely account for the differences. It is much more likely that their general trend applies to other centres of western civilization; and there is a good deal more evidence from various countries which correlates the times when road accidents are commonest with the times shortly after alcohol consumption is maximal.

Also, the less direct evidence provided by observations made on drivers under test conditions is quite consistent. Most experiments of this sort have been carried out with quantities of about 30–50 ml. alcohol, corresponding to about two or three large whiskies. Various kinds of measurement have been made: of the accuracy with which cars can be driven to prescribed marks or parked in confined spaces, of the speed with which drivers react to stimuli demanding emergency responses, or of the speed with which given courses can be covered with a specified precision (Bahnsen & Vedel-Petersen, 1934; Newman, Fletcher & Abramson, 1942; Bjerver & Goldberg, 1950). One measurement which appears not to have been made is of the precision with which a course can be followed when the driver is instructed to take it as slowly as he likes and to concentrate on care and not speed. This measurement needs making because there are occasions when a conscientious person who has consumed an appreciable amount of alcohol wishes to drive a car, and it is important to know whether his care and deliberation can overcome the effects of alcohol. In other words, is the argument 'I have had some alcohol; I know alcohol makes me drive worse even if I think I am driving better. I shall therefore be

particularly cautious, to correct for these effects', accompanied by driving objectively better or worse than usual?

The findings of the experiments that have been done agree well that, in one or more respects and often in all, performance is impaired, and if any tasks are performed faster than usual it is at the expense of accuracy. The other outstanding result of this sort of experiment is that the subject is commonly unaware of the demerits of his performance, and usually believes he has done better than usual. In the light of this evidence of dissociation between subjective and objective estimates, there is no justification for trusting the personal impression that 'I drive better when I've had a couple'.

More indirect evidence is given by pure laboratory tests of performance, and these also show a fairly consistent impairment of performance by alcohol. Laboratory tests of this sort—reaction-time measurements, word-association tests, tachistoscopes and so on—are much influenced by practice and fatigue effects and are difficult to control adequately, and much published work, particularly from the time when methods of statistical analysis were less well developed and appreciated, is rather unsatisfactory in these respects. The evidence was reviewed critically by Jellinek & McFarland (1940), and apart from Goldberg's studies (1943) not much has been added since. Goldberg's studies are particularly interesting because he did his tests at various times after administering alcohol to his subjects, and he related the test scores to the blood-alcohol concentrations at the time. In this way he found the threshold concentration for impaired performance in a number of tests, and it is notable that for most of them it lay between 0.04 and 0.06%. On the one hand, these concentrations are unlikely to be reached by drinking less than 1–2 pt. of beer, even on an empty stomach, and then they will not last long. On the other hand, they are substantially lower than levels at which drunkenness is clinically diagnosable, which is at about $0.15 \pm 0.05\%$ of alcohol in the blood (Jetter, 1938; Liljestrand, 1940). In view of the great variation between normal subjects, psychological tests would not necessarily be a better means of detecting whether a subject is under the influence of alcohol than ordinary clinical examination; but an estimate of the blood or urine alcohol is more useful, as it at least gives some evidence of how much liquor the subject has consumed, and if it is above 0.05% it suggests that his performance may be impaired at least in comparison with his normal ability.

At still lower levels, it must be noted that, although Goldberg found thresholds mostly around 0.04–0.06%, there are some very careful and convincing studies (e.g. Vernon, 1919; McDougall & Smith, 1920) which show that, in abstainers at least, as little as 10 ml. of alcohol can produce detectable changes in performance. On the other hand, careful observations sometimes suggest small objective improvements at this level (e.g. Newman *et al.* 1942), and on the whole there is very little solid evidence that the effects of up to $\frac{1}{2}$ pt. of beer are likely to be appreciable. But above this level deterioration is more likely than improvement, and in view of the repeated observation that subjects misjudge their performance in the direction

of thinking too well of it, no subjective beliefs about the effects on skill are likely to have any validity.

Finally, it may be worth briefly considering the long-term results of ingesting small or moderate amounts of alcohol. The disastrous effects associated with heavy drinking—addiction, cirrhosis of the liver, delirium tremens, for instances—are well known, and it is apt to be assumed that as large doses are very harmful small doses are mildly so. As in the matter of driving, completely satisfactory evidence on this point depends on comparison of the health and longevity of abstainers, moderate drinkers and heavy drinkers, not differing from one another in any other relevant respects. Evidence of this sort can be obtained from insurance statistics, but much of it is unsatisfactory because the different groups are not comparable in some important respects. The best data still appear to be those of Pearl (1924), who found that the greatest expectation of life occurred in occasional and moderate drinkers, that abstainers on the whole lived slightly less and that heavy drinkers lived substantially less long. As the various groups are of course self-selected, this correlation does not prove that small doses of alcohol prolong life: the characteristics that provoke a man to abstain may be associated with other characteristics which predispose to an early death. But the available facts suggest that a man must drink rather a lot before alcohol is seriously harmful to him, and that it is not impossible that the consumption of a little alcohol daily may even be a beneficial practice rather than the reverse.

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Vitamin Deficiencies in Alcoholism

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It is a matter of common experience that the drinking habits of different people vary. This profound observation explains why, for instance, the Boston City Hospital can fill a ward with cases of alcoholic neuritis drinking cheap wood spirit whereas