Original Articles.

ALCOHOL IN THERAPEUTICS.

THE VALUE OF ALCOHOL AS A THERAPEUTIC AGENT IN MEDICINE.*

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THERE is no drug in the pharmacopeia in regard to the therapeutic use of which there is a greater variety and divergence of opinion and practice among the medical profession generally than alcohol. To exemplify this diversity let me cite the opinion existing at the present time in regard to the action of the drug upon the heart and nervous system. In many of the leading textbooks upon therapeutics (Harc, White, Wood⁴) we find alcohol spoken of as a nerve and heart stimulant and advised for use in conditions of heart weakness, and it is the custom of a large number of practising physicians to regard the drug in this light and to use it for purposes of stimulation, more or less continuously, during the course of acute diseases in which signs of heart weakness occur. Other physicians, among them the pharmacologists who base their opinions upon the results of pharmacological research with the drug, are of the opinion that the action of alcohol upon the nervous system and heart, taken in its total effect, is always depressant in kind, and that its use for purposes of heart stimulation is, therefore, irrational.

Another instance of radical divergence is found in the opinions in regard to the food value of alcohol. It is a more or less general idea held by physicians and laymen that alcohol is an excellent food substance of equal value with the recognized fuel foods, the starches, sugars and fats. Pharmacological research, however, while indicating that alcohol, since it is oxidized in the body and to some extent, spares the body tissues, or some of them, is undoubtedly a food, considered in the chemical sense of the term, indicates with equal definiteness, and with this the opinion of almost all the leading physiologists of the world is in accord (G, H, K, M, T), that it is not a good food from a hygienic point of view, or a food in any sense comparative in its value to the recognized food substances, since it cannot protect the body tissues in the same extent as these, and possesses poisonous properties which so affect the body, acting through the nervous system or by direct action upon the tissue cells, that it is impossible to feed the individual with it, under ordinary conditions at all events, to the extent of affording any substantial aid to nutrition without at the same time poisoning him. Thus, Van Leyden,¹¹ in his textbook upon dietetics, classes it not with the foods, but as an *erfrischungsmittel*, since, as he says, its drug effects bar its use as a food.

The reason for this extreme diversity of opinion lies principally in the careless attitude in

which the profession has received and continues to hold the drug. Owing to the very general use of alcoholic liquors as beverages in conditions of health, there has always been, and still is, among physicians a tendency not to consider alcohol seriously as a drug whose pharmacological action has to be considered in its administration, as in the case of strychnia and digitalis and other substances used solely as drugs. As a result, practitioners have not learned the pharmacology of the drug accurately or, having learned it, have disregarded its teachings, not feeling obliged to apply the same rigid principles of rational therapeutic procedure in this case, which they are accustomed to use in their general therapeutic practice.

This careless and unscientific attitude in regard to the use of alcohol which exists more or less unconsciously in medical practice, is clearly a wrong one, and is totally unjustifiable in the present condition of medical knowledge.

A drug should be used rationally or not at all. The wide use of alcohol, its well-recognized poisonous properties, and the extensive moral and social influence which the abuse of this drug, following the acquisition of the habit of using it, exerts, all unite to make a rational use doubly imperative in the case of this drug. The pharmacology of alcohol has been thoroughly worked out by extensive experimental research, and is today as definite as that of most drugs in the pharmacopeia. It should be possible, therefore, by collecting this pharmacological knowledge and that obtained by clinical observation of its use in the treatment of disease, and the theories and practices in regard to its employment which have come down in traditional use, and considering them together in the court of judicial medicine, to thresh out the false from the true, and determine for the use of the drug as rational and intelligent an attitude and procedure as exists in the case of most active drugs in modern medicine.

Considered pharmacologically, that is as a drug pure and simple, alcohol belongs to the group of narcotics or anesthetics, substances which act as intoxicants upon the higher nerve centres of the body (Schmiedeberg,⁷ Cushny⁶). The drugs with which it is most closely allied in its drug action are perhaps ether, chloroform and chloral of the same group. These substances, especially the first, produce, as alcohol in small doses or in the beginning of administration, a condition of apparent cerebral excitement which is followed, as more of the drug is taken or as its final effect is accomplished, by depression and anesthesia.

The action of alcohol upon the nerve cells, by which it produces its drug effects, is undoubtedly a poisonous one, and places the drug among the narcotic poisons (Wharton and Stille²). It has been claimed by some writers that alcohol should not be classed as a poison (Atwater³) since it can be taken in small doses without producing demonstrable poisonous effects. These advocates urge that all substances are poisons when taken in sufficient quantity, and that the term should be ap-

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plied to such substances only as always do harm to the body, that is, are poisonous in all doses. Such a claim cannot, however, hold for pharmacological classification, or even for practical consideration of a drug. For few, if any substance known, even among the most deadly poisons, causes *demonstrable* injury in all doses and all conditions. Strychnia and arsenic may be taken with benefit in proper doses. Morphia, like alcohol, may be oxidized in the body and in increasing quantities as the subject becomes more immune to it (Faust¹⁰). In scientific terminology the term poison applies to any substance which, when incorporated into the blood or applied to the body surfaces in relatively small quantities, produces disturbance of any body function (Fick,¹¹ Abel). Under this definition alcohol is certainly a poison (Fick,¹¹ Schafer,¹² Tigerstadt,¹³ Abel¹⁴). For its most characteristic drug properties its depressant or narcotic effects upon the nerve centres are present, and can be demonstrated experimentally under the use of quantities of the drug, which, when the quantities in which it is commonly used among men are taken into consideration, are comparatively small. The extent of immunity to the poisonous action varies with individuals, as with all poisons, and it can apparently become increased by the use of the drug. In medicine it certainly deserves this title of a poison, for it is one of the most common poisons with the effects of which the medical profession has to deal.

In addition to its most characteristic drug influences, its depressant or narcotic effects upon the nerve centres of the body, in accordance with which it is classed pharmacologically among the anesthetics, alcohol influences the body in a variety of ways.

Its most immediate action when introduced to the body by the mouth is its local irritant action upon the mucous membranes of the mouth and stomach. As a result of this irritation a hyperemia of the membranes occurs and a reflex excitation of nerve centres, and, through those, of certain body functions, as the circulatory, or muscular, or digestive functions may be induced. Following this, after it is incorporated into the blood by absorption from the alimentary tract, it acts directly upon the nerve centres, most immediately the higher nerve centres, and through this action upon the centres governing special functions of the body, most particularly those of circulation, motion and respiration, influences these functions. Finally, the alcohol is in great part (95%) oxidized in the body, through this oxidation plus its effect upon the nerve centres and its destructive (poisonous) action upon the protoplasm of the tissue cells, influencing the metabolism of the body.

The special purposes for which alcohol is most generally used as a therapeutic agent in medicine today are: (1) As a heart stimulant; (2) as a nerve stimulant or general tonic; (3) as a digestive stimulant; (4) as a food; (5) as a general remedial agent in acute infectious conditions.

Let us now consider these various therapeutic uses of the drug which we see advised and practiced in the medicine of the present time, and determine how far each is rational in the light of our experimental knowledge of the action of the alcohol. (By experimental knowledge we mean here knowledge gained by deduction from either pure experimental work or clinical experience, in the determining of which proper scientific methods have been followed.)

ALCOHOL AS A STIMULANT.

The purpose for which alcohol is perhaps most frequently and generally used in medicine today is for the stimulation of the heart. It is used for this purpose for short periods in collapse from whatever cause; continuously for days during the course of acute diseases, as pneumonia and typhoid, where signs of heart failure are thought to be present; and by some physicians in cases of dilatation or valvular disease of the heart. It is classed as a heart stimulant in textbooks of medicine,¹⁵ and many leading physicians consider it as such and advise it for this definite purpose. Is this use rational in the light of the most competent experience with the use of the drug?

A study of our evidence in regard to the question as to whether or not alcohol acts as a heart stimulant points to the conclusion that the best evidence at hand is against its possessing such action, always excepting the initial effect resulting from its irritant action, and certainly force us to the opinion that the use of alcohol for *this purpose of heart stimulation*, especially in continuous doses for periods of one or more days, as it is practised in the case of acute diseases or conditions of debility, is irrational, such use tending rather to defeat than accomplish this purpose.

The theory that alcohol is a heart stimulant has for its principal foundation the special facts of clinical observation, that acceleration of heart beat and apparent increase of pulse strength follow its administration. The fallacy explained below, into which a misinterpretation of these facts has led the profession, serves as a good example of the danger of following the indications of clinical impressions alone in determining the action of a drug, a habit to which much of our confusion and error in therapeutic practice generally has been due. To my knowledge, there is today no evidence which can stand to prove that alcohol given regularly can increase the capacity of the heart to work, that is, that it is a heart stimulant. The only stimulant effect which it can produce is a reflex effect, which may result in a momentary increase of work by the heart, which, however, is soon overbalanced by the total effect of the drug, and therefore always gives a sum total effect of depression (Brunton¹⁶). Such an action may fit the drug for use in single doses in emergencies where momentary action is desired at any cost, but does not give it any value for continued use, to strengthen the heart.

The results of the most accurate experimental investigation in regard to the action of alcohol

upon the heart and the circulation are as follows:

Single doses of alcohol (20 to 60 gm.), if given in ordinary non-diluted form and under ordinary conditions, may cause a temporary acceleration of the heart action followed in measure with the size of the dose by a depression of the action.

If, however, the alcohol is given in well diluted form to avoid the irritant action upon the mucous membranes, and the subject is kept quiet to avoid increased nerve and muscular excitement, which are associated with the ingestion of the drug, it is found that no acceleration of heart action occurs (Zimmerberg, Jacquet). In these conditions small doses have no demonstrable effect upon the heart action; large doses cause depression of this action (Zimmerberg,⁸ Jacquet,¹ Martin and Stevens²). The same facts are true of the effects of the alcohol upon the character of the pulse and blood pressure. With ordinary administration a greater fulness of the pulse may be observed. If precautions against irritant action and restlessness are taken, however, this effect is not obtained, the blood pressure remaining either unaffected or becoming depressed. Small doses of alcohol have no effect upon the blood vessels; larger doses dilate the vessels.

From these and similar results it is concluded that alcohol is generically a depressant of the heart and circulatory mechanism. Where quantity sufficient to cause any influence in either direction is administered, the sum total of effect is always a depression. Where an initial stimulation is obtained it is due, as Brunton⁷ says, to the act of ingestion of the substance and to its irritant and reflex effects. The ingestion of any food or even of water causes results similar in kind (Brunton, Zimmerberg). These indirect effects of the administration of the drug are a part of its action, but not the whole of it, and it must be judged by its total effect. They are, of course, to be taken into account in a consideration of its use, but they must not be permitted to mask the true generic character of the drug, which is always depressant in kind and soon gets the upper hand of the effect of the reflex action.

This action of alcohol upon the circulatory system as accomplished in medical administration is entirely a result of the action of the drug upon the nerve centres controlling the heart and blood vessels. Evidence of direct action upon heart muscle is obtained only when the amount of alcohol in the blood reaches one-eighth to one-fourth of 1% of the blood, a quantity never present in human blood in medical administration (Diabella⁴). Such direct action obtained in animals is always depressant.

It is not intended by this statement to imply that the use itself of alcohol in these cases of acute disease is necessarily irrational, but simply that its use for this definite purpose of heart stimulation, and in this way mentioned, is so. Alcohol may have other actions which make it useful in certain of these conditions. And in a condition of collapse, as already stated, where it is desired

to produce a momentary excitation of the nerve centres, or vital organs through a shock to these nerve centres, alcohol, on account of the reflex effect of its irritant action upon the mucous membrane of the stomach, may, in a single concentrated dose, be of use, according to both clinical and pharmacological evidences.

It may, and undoubtedly will, be urged by some men that, since these pharmacological results are obtained principally in conditions of health, they cannot serve for indications in regard to the action of the drug in disease, where the conditions are different; in other words, that a substance which is a heart depressant in health may be a heart stimulant in a given diseased condition. In consideration of such a claim we will point out:

(1) That our pharmacological evidences are collected from conditions of both disease and health, and are so far identical in quality in both^{44 46}; (2) that we have no scientific records of any drug possessing a directly contrary pharmacological action in disease from that which it has in health, the difference of action, if any, being simply quantitative*; (3) that since we have, in regard to this particular point at issue, no evidence of a clinical or of any other character pointing to a stimulant action which will bear the test of judicial examination, there is no occasion as yet to raise such an issue upon this subject.

A second character, in which alcohol is advised in practice, is that of a general nerve tonic. Continued use of small doses is considered to be useful in keeping up the body tone, or to help the individual in the accomplishment of continuous or arduous nerve and muscular expenditure in conditions of debility, chronic and acute diseases.

In regard to the generic effect of alcohol upon the nervous system there are two theories held today by physiologists and pharmacologists. The first, that of Binz and his followers, is that alcohol, when incorporated into the blood, first stimulates, then depresses, the nerve centres. According to others (Schmiedeberg and Bunge), and this is the view most generally held among pharmacologists today, it depresses the centres from the start. According to this latter school, of which Schmiedeberg is the most prominent authority, the apparent excitation which occurs as a preliminary stage in the action of the drug is in reality an increased action of certain subordinate centres, resulting from a removal of control or inhibition through the depression or paralyzing influence of the alcohol upon the higher centres, which normally exert a certain inhibitory control over these lower systems. The higher centres, being most delicately organized, are most easily affected by the drug, and the lower centres, being liberated from higher influence, run free for a moment, just as a heart runs free with paralysis of the vagus. Then these lower centres, being af-

* In fever, for example, research shows that metabolism follows the same lines, the oxidation processes having, however, more activity. More alcohol may, therefore, be oxidized in fever conditions, but this cannot change it from a depressant to a stimulant.

fects in their turn, show a depression which, being the sum of the loss of the reserve strength incident upon their period of free action and the final depressant effect of the drug upon them, more than counterbalances the initial excitation, so that the total effect of the drug action upon the body forces is a depression (Schmiedeberg,⁷ Binz,⁸ Bunge⁹). It will be noted that under both of the above theories the final effect of the alcohol is considered to be a depression. The difference of opinion is simply in regard to the detailed action of the drug in accomplishing its total effect.

This question of the intimate action of alcohol upon nerve forces has been the subject of a large amount of investigation. Kræplin and his pupils have conducted a series of over 2,000 experiments to study the influence of alcohol upon psychical and psychomotor processes. The results of these experiments show that with small single doses of alcohol (15 to 30 gm., one-fourth to one-half bottle of wine) there is on the average, the results differing with individuals, a slight initial increase in the activity of certain simple psychomotor processes, as, for example, a shortening of the reaction time of simple motor innervation, as moving a finger, lasting from one-fourth to one hour.

With psychical processes, where the subject is obliged to dwell upon or compare sensations or perform less simple psychomotor labor, as, for example, the addition of columns of figures, or those involved in typesetting, the reaction time is increased, the depression of the nerve processes occurring with all doses. With doses of over 30 to 40 gm. of alcohol, all types of brain action are depressed.

Continued daily administration of from 40 to 80 gm. of alcohol in twenty-four hours caused after a few days a marked decrease in the usefulness of such psychical functions as memory or mathematical figuring, which soon disappeared when the alcohol was removed. Kræplin concludes that alcohol may, in small doses, stimulate for short periods certain motor centres, while it depresses all other brain centres, the sum total of effect, considering the whole psychical capacity, being a depression. In no condition, the author expressly states, does the alcohol enable the individual to perform a greater total of work in a daily or greater period (Kræplin,⁹ Baratynsky¹¹).

Experiments upon the effect of alcohol upon muscular power bring us to the same conclusion in this regard. Thus, experiments upon the effect upon single muscular action, as, for example, those of Partridge with the ergograph and dynamometer upon the muscular power of the finger or hand muscles, show that with small single doses there is, in some cases, an initial increase of work for one-half to one hour, with a subsequent depression, in some cases by a decrease from the start. Shafer found that the increase occurred only where plenty of nutritive material was present for the muscles, otherwise a decrease was present (Shafer,¹² Schumberg¹²). In no ex-

periments which will bear inspection was a total increase of power for work an evidence of any dynamogenic quality of alcohol obtained. The same initial increase was obtained by the ingestion of bicarbonate of sodium or nitrate of silver (Gutrickson), and followed the ingestion of sugar before time for oxidation elapsed, and is probably a reflex effect of ingestion of food. Mayer obtained similar results with introduction of water into the stomach.

By far the most conclusive results in regard to the nature of the action of alcohol upon the nerve functions and the power of the body for neuromuscular work are, however, those which are obtained, not from a determination of the effect of the drug upon special processes for special periods, but from a comparison of the total output of labor or neuromuscular force which the individual is enabled to put forth under the use of alcohol and that which he can produce in abstinence. The most accurate and complete experiment of this nature which we possess is that of Aschaffenburg,¹³ upon the work of typesetters. A comparison of the results obtained from these men in periods of abstinence and periods of indulgence in moderate quantities of alcohol (35 to 40 gm. in 24 hours, equivalent to 2 ounces of whiskey) shows that at least 15% less work was performed in the alcohol periods.

Experiments upon the marching records of regiments, performed in the armies of the several nations, invariably give results which point to a similar conclusion. The same men can march less far and endure labor less well with regular moderate rations of alcohol than when using no liquor of any kind (*vid.* Parkes,¹⁴ Baer,¹⁵ Woodhead on Kitchener's Campaign; Hall, Kaffir War).

These results would then indicate definitely that alcohol is not in continued use a tonic to nerve or muscular action. In this finding pharmacological and physiological experiments are in keeping with practical experience among intelligent members of military and exploring expeditions, that alcohol does not increase the power for work, but simply induces a spirit which uses up energy faster, and is more than offset by the depression following, and that its use where any work is to be done is distinctly harmful.

In this connection the results of the use of alcohol upon the nerve cells, as studied by Dehio and by Stewart, are of interest. These researches showed that retrograde changes in the cell substance appeared regularly after the administration of the drug (Dehio,¹⁶ Stewart¹⁷).

These facts certainly prove that the still too common custom of the use of alcohol as a tonic for nerve or muscular work in conditions of debility or chronic disease is irrational and probably harmful. They also, to my mind, give us food for thought in regard to the continued use of the drug in acute diseases, where a substance which lessens the capacity for endurance of nerve or physical labor is *a priori* the last thing which we wish to use.

ALCOHOL AS A NARCOTIC.

From the point of view of pharmacology the rational use of alcohol for the purpose of its effect upon the nervous system is as a narcotic; for this is the characteristic action of alcohol which it possesses, as far as investigation has gone, under all circumstances and in all doses which have any effect upon the body whatsoever. Of course therapeutic experience must determine for us whether it is a useful narcotic and where. All narcotics are poisons, and we choose in our case that which will produce the greatest benefit in the case with the least danger. If in a given case alcohol is the narcotic which answers best to this requisite, it should be given. It is to my mind undoubtedly to this special influence of alcohol that the majority of the medicinal effects, variously interpreted as stimulation and tonic effects, which are obtained with the use of the drug, are due, always excepting the momentary effects of its irritant action. The higher nerve centres are depressed and thus the nervous excitement which accompanies acute disease or fatigue quieted, and this relief from nerve strain is rest to the patient and he feels better. The effect of the drug in conditions of shock which are reported may be explained in this way, if we adopt the theory so commonly advanced, that shock is a condition of nerve inhibition of the vital functions. Alcohol, in depressing or paralyzing the higher centres which control these inhibitory forces, relaxes the extreme inhibition which has obtained, and the results of shock are ameliorated.

ALCOHOL AS A STOMACHIC.

A third common use of alcohol is as a stomachic. This use would appear to be to some extent borne out by the results of pharmacological studies. These studies show that alcohol produces in the stomach, through its irritant action, a hyperemia of the membranes. This may undoubtedly, if the irritation is not too great, cause an excitement of appetite. Through this irritant action and a reflex from it, an increased secretion of saliva in the mouth and of gastric juice in the stomach occurs. A similar increase of less extent is produced when alcohol is injected into the blood without contact with the stomach.

The total effect of alcohol upon the digestive process is a matter of controversy. The presence of 5 to 10% of alcohol in the stomach retards digestion markedly (Chittenden). With ordinary doses, Kretschy and Buchner found digestion retarded, while Eichenberg and Wolffhardt claim that it is accelerated. Klempner states that the mobility of the stomach is increased by alcohol. According to Brandl and Scanzoni the absorption of the fluid substances in the digestive tract is accelerated by small doses of alcohol. Zuntz and Magnus Levy in their experiments found absorption impeded. Mehring found that solutions of sugar and other substances in alcohol were absorbed from the stomach more rapidly than solutions in water. This evidence, combined with the experience of the wine-drinking nations, would indicate that alcohol taken with food may serve

digestion in the character of a *genusmittel*, a substance which by its pleasant taste and slight irritant effect may stimulate appetite. That it has any other influence upon digestion is not proven (Chittenden and Mendel,¹⁸ Chittenden, Mendel and Jackson,¹⁹ Buchner,²⁰ Scanzoni,²⁷ Magnus Levy,²⁸ Brandl,²⁶ Eichenberg, Gluzinsky and Mehring).

ALCOHOL AS A FOOD.

A fourth character in which alcohol is much used and advocated in medicine is that of a food. It is given for this purpose in conditions of debility, chronic diseases, in acute diseases, and is even advised by some men for this purpose in health. The question as to whether or not alcohol should be considered as a food has been a matter of much controversy among physiologists and scientific men. This matter can be determined only by a study of the effect of the use of the drug upon tissue metabolism. The results of such a study are as follows:

If a given quantity of alcohol (50 gm. hydroxid in 24 hours), for example, be ingested the greater portion (90%, at a minimum, 94 to 96% as an average) is oxidized, the remainder passing through the body and being eliminated as alcohol (Atwater,²⁸ Stassman²⁹). The influence of this substance thus utilized in the body upon the metabolism of the tissues is twofold. In the first place, the alcohol, in becoming oxidized, liberates energy which is thus supplied to the body. This energy serves to replace an equivalent amount which, in the absence of the alcohol, would have to be supplied by the oxidation of the body fats, and thus spares a certain quantity of fat in the body. Alcohol thus acts in the metabolism as a tissue-sparing substance or food. This fact has been demonstrated by competent experimental research (Zuntz and Geppert^{28 29}). In the second place, the alcohol in circulating among the tissue cells produces certain derogatory or poisonous effects upon them which destroys a certain amount of protoplasm. Alcohol thus acts in the metabolism as a poison to the body. Evidence of this latter fact may be obtained in several ways. First, if a man be given a large quantity of alcohol there will be a marked increase in the nitrogenous waste of his body. This in itself occurring while a man is taking sufficient food to maintain nitrogenous equilibrium under ordinary circumstances is evidence of this poisonous property of alcohol for protoplasm. If the quantity of alcohol used is lessened, or as the individual becomes more immune to its use, the loss becomes less, and with small quantities becomes so slight that it falls within the limits of error of experimental records, or is so counterbalanced by the tissue-protecting effect of the alcohol that it is not apparent in results of experimentation. These facts in regard to the poisonous action of alcohol upon protoplasm are well illustrated in the numerous experimental researches which have been made to test the tissue-sparing influence of alcohol. For these experiments an individual who has been brought

to a condition of nitrogenous equilibrium upon a regular diet consisting of a mixture of proteids, carbohydrates and fats, has a certain portion of the carbohydrate and fat food replaced by an isodynamic quantity of alcohol, and the records of his metabolism in this alcohol period are compared with those of his regular food period. In these experiments it is practically invariably found (in sixteen out of seventeen performed upon men up to 1901) that on the day after the substitution of the alcohol for the regular food, the condition of nitrogenous equilibrium is destroyed, the body losing nitrogen, this loss continuing for four to six days, the period of most experiments, so that the average of the alcohol period shows a decided loss of tissue to the body. Upon the return substitution of the fat food for the alcohol the equilibrium is again restored. Now these results are distinct evidence of the poisonous action of the alcohol upon protoplasm; and they prove that this action can be demonstrated with moderate quantities, the quantities used being from 50 to 70 gm. of alcohol in twenty-four hours. For we know that alcohol spares isodynamic quantities of fat to the body; and we know that this tissue fat can spare a certain quantity of proteid (V. Noorden⁴⁰). Why, then, is the proteid loss not controlled by the fat in the body spared by the alcohol when the alcohol is being administered, as it is when the body fat is protected by sugar of fat in the diet? Clearly because there is greater loss during the alcohol period. The fat protected by the alcohol does serve to protect proteid to its full extent just as it does when sugar or fat are taken. It is insufficient, however, to protect it against both the regular loss and also the extra loss due to the alcohol poisoning, and hence the loss of equilibrium under alcohol (Kassowitz⁴¹). Equilibrium can be maintained in such cases, as shown by Stammreich, von Noorden and Roseman, only by giving the individuals quantities of proteid, more than sufficient for their needs, which will serve to make up for the extraproteid destruction. This point is further elucidated by some recent experiments of Neumann and of Roseman. These authors show that in individuals thus experimented upon the loss of nitrogen which is seen in the first four to six days of feeding with alcohol grows less after this period until it becomes the same as with the feeding of fat or is at all events less than in the control period when the patient is on a diet which is equal to the regular diet used minus the caloric value of the alcohol. That is, the individual after the first few days becomes accustomed to the alcohol so that the poisonous effects are less and can be offset by the proteid-protecting effect of the alcohol consequent upon its oxidation in the body.

The evidences of the action of alcohol upon the body metabolism thus indicate that alcohol is thus acting in the body at the same time as a food and a poison, the oxidized portion serving to protect the body tissues, the circulating portion tending to destroy them. Where small quantities are

used so that the poisonous unoxidized residue is small, the individual may be or becomes so immune to the poisonous action that the alcohol may help, if given with plenty of proteid food, to maintain the tissue equilibrium (v. Noorden and Stammreich,³⁵ Roseman,⁶⁰ Neumann⁶¹).

References: Roseman, Pflüger; Arch., 1901, Bd. lxxxvi, S. 307^x, gives a record and critical review of all recent experiments upon men and animals and a complete summary of the subject of the food character of alcohol.

The results of scientific investigation at the present time would then indicate that alcohol is to be considered as a food from a physiological point of view. This being established, the only further question for medicine to determine is whether it is a good food for use in disease or in any special diseased conditions. The first point, whether alcohol is a good food for use in disease generally, can be very promptly settled. Both experimental and clinical observation and study have proven to us that alcohol, in addition to its food properties, possesses certain drug properties, as a result of which it tends to produce disturbance of the nervous system and destruction of tissue protoplasm. Also the study of pathology has shown that the continued use of alcohol tends to produce certain changes in the tissues of certain of the body organs harmful to the integrity of the organs and their function.

These facts, determined principally by the observation of the effect of alcohol upon individuals in a condition of health, have definitely established the opinion in which we find practical unison among all scientific men today,—physiologists, pharmacologists and dieteticians,—that alcohol can play no rôle, and is not to be considered as a food substance for use in health under ordinary circumstances. For it is not rational to use for a food a substance which possesses poisonous properties, and which, when given in quantity sufficient to aid materially in the nutrition of the body, will exert these properties and produce disturbance of the body functions when we possess and can utilize other food substances which can be used in sufficient quantity without producing results other than beneficial to the organism* (Foster,⁷ V. Leyden,⁸ Roseman, loc. cit., p. 273, Fick,⁹ Bunge,⁶ Schafer,¹¹ Tigerstadt,¹² Howell,¹³ Halliburton.¹⁴)

And this same reasoning which applies to the use of alcohol in health applies to its use generally in disease. In most diseased conditions which come under our care, the conditions of metabolism do not vary greatly from those of health, or vary only quantitatively (Weber,⁴⁴

* Different individuals possess varying degrees of immunity to the poisonous action of alcohol. Small quantities may be taken by many individuals without producing demonstrable evidences of any poisonous influence. And this immunity may perhaps be increased by continued use of the drug, as with morphia. In many cases the poisonous action can be demonstrated with doses of 20 gm. of alcohol (12 gm. Tigerstadt), an amount equivalent to about an ounce of cognac or six to seven ounces of wine, with a caloric value of 140 cm. And the quantity which the average individual, in America at all events, can take with immunity is certainly, at a maximum, 50 gm. in twenty-four hours, equivalent to a half-pint of 10% wine, a quantity which has a caloric value when utilized of less than 350 calories, one-eighth to one-ninth the food necessary for body combustion (Tigerstadt¹²).

Svenson⁴⁶). The drug which depresses the nervous system or wastes protoplasm in health will do so here. The patient can utilize the regular food substances in one form or another in full quantity or to the extent that he can take any food whatsoever, and there is no necessity or excuse, from the point of view of providing a food, of including alcohol in the diet. These statements will apply to the use of the drug for food purposes in conditions of debility, phthisis and most chronic diseases, and to its use generally in any and all diseased conditions.

In the case of special diseased conditions, however, the matter may wear another aspect. Among such conditions we may have, for example, a condition, in pneumonia or typhoid for example, where the patient cannot utilize the ordinary food substances and can utilize alcohol. In such a case it is, of course, rational to use alcohol as a food. We have, of course, to give in such a case quantities far above the normal limits of immunity to the poisonous effects of the drug, and we must expect to produce to some extent these effects. But we are perfectly willing to risk these for the sake of the nutritional value of the drug.

Such conditions as the above, where alcohol is the only food which can be used, are conditions for the use of alcohol as a food, and they are to my mind, with a few special exceptions, the only conditions in which its use *for this purpose* is rational. In a majority of cases of acute disease the patient can take other foods. And if this is so, there is to my mind the same reason against its use here as in health. Metabolism in the acute diseases, according to what experimental data we have, differs quantitatively from that in health, and only thus. In febrile conditions the oxidation processes and nitrogenous waste are increased.⁴⁴ Diakanon, in the only experiments upon the effect of alcohol in febrile disease which we possess, experiments upon two cases of typhoid and one case of pleurisy, found that its influence upon proteid metabolism was no greater than in health.⁴⁵

The fact that oxidation is more active in fever, may result in a greater oxidation of alcohol in such conditions than in health, and may thus account for the commonly reported observation, that patients with fever can take more alcohol without showing signs of intoxication than individuals in health.

However this may be, it is only a question of increased immunity to poison, not of the absolute loss of the poisonous character by the alcohol, and to use a substance with poisonous properties for a food in conditions where other foods can be utilized is not rational medicine.

Among our special diseased conditions there are a few in which the changes in metabolism, as compared with the metabolism of health, are not only quantitative but also qualitative. In such conditions it is possible that alcohol may have a food or drug action quite separate from that in health. To determine this point experimental re-

search with the use of alcohol in each condition is necessary.

Work of this kind has been done in one of these diseases, Diabetes Mellitus, by Hirschfeld.⁴⁸ This investigation shows, like those upon health in some experiments, in some an increased loss of nitrogen with alcohol, in others a slight sparing of nitrogenous substances, and indicates, as do all researches with alcohol in disease so far reported, that the action of the drug upon metabolism in disease is similar to that in health.

So much for the consideration of rationality of the employment of alcohol in the more common special uses for which it is advocated and used in medicine generally.

In addition to this general use for specific actual or hypothetical pharmacological actions independent of the type of disease under treatment, as, for example, a heart stimulant in typhoid, as a food in acute febrile disease or diabetes, as a sedative for insomnia or in shock, the drug has a very extensive use as a special therapeutic agent in several definite diseased conditions, as, for example, pneumonia and other acute infectious diseases, phthisis, and conditions of sepsis from pyogenic infection. In many cases, in these conditions, it is used not from any special theory of stimulant or narcotic, or nutritive or any other definite pharmacological action,—for if it were proven that it had none of these special properties the physician would still use it in these cases,—but because extensive experience in its use in these conditions has proven to him that it has a beneficial influence on the course of that particular condition.

What can be said of the rationality of its use under such circumstances? Simply this: that as regards the final therapeutic value of a drug in the treatment of a definite diseased condition clinical experience must be the supreme guide.

We have today no definite scientific knowledge of the total action of alcohol in pneumonia or sepsis, such as we have in regard to the action of quinin in malaria or of thyroid in myxedema, cases where pharmacological investigation has covered the whole ground and where its results and those of clinical medicine are in accord.^{46 48} Additional research upon the use of alcohol in diseased conditions is needed. What results of scientifically conducted research with this use of alcohol we do possess indicate that its action here is similar to that in health. Pharmacology can at present prove to us that it is not rational to use alcohol for some special purpose in pneumonia, for direct heart stimulation, for example, or for a food in conditions where a more nutritious food may be taken, and that if we do use it for any purpose we must expect to produce a certain amount of nerve or heart depression, or if the kidneys are in bad shape a certain amount of deleterious action upon these organs and their function, and can thus serve to control our use of the drug in these conditions, but it cannot yet prove to us that the total effect of the use of the drug may not be beneficial. Drugs may have specific actions in

diseased conditions which pharmacology has at present no account of. For instance, alcohol may have a special antitoxic action in pneumonia or sepsis. Also its poisonous action may be less active in the changed conditions than in health.* On the other hand, they may be more active. So that for our final verdict in regard to the value of alcohol in special conditions, pneumonia, for example, in default of absolute experimental knowledge of the subject, we must fall back upon the evidence of our regular clinical experience.

This evidence of clinical experience appears in the shape of the opinions of physicians in general or hospital practice. If we collect these opinions we find, as stated at the opening of this article, that they show marked variance. Among the most competent men of the profession we find two equally assured sets of opinion in regard to the value of alcohol in these conditions in question, the acute infectious diseases, sepsis, phthisis, one affirming that the regular use of the drug in these cases, where infection is severe, is beneficial, the other claiming that such regular use is harmful. Still a third class, taking the stand that the evidence is not conclusive either way, do not use the drug in these cases, on the ground that unless we can have a definite reason for using drugs it is best to do without these elements in practical medicine. Which of these attitudes is the most correct it must be left to each physician to decide for himself while awaiting more complete clinical and experimental study of the matter.

My own clinical experience with the use of alcohol in one of the most common of these special conditions in which it is advocated, pneumonia, has in sum total left me with the opinion that there is not at the present time a balance of evidence in favor of its beneficial action, when used for periods of a day or more, sufficient to indicate such employment in this disease. And my study of the pharmacology and experimental work upon alcohol has tended to entrench me still more surely in this opinion.

For here I find it proven conclusively that alcohol, in whatever doses it is given, is never a heart stimulant or dynamogenic for nerve or muscular work, but that when used continuously, even in moderate doses, it acts as a depressant in these regards. And if alcohol, in conditions of health, depresses the functions and makes the body less able to work and endure strain, as instanced most conclusively by the experiments upon the type-setters or those upon the soldiers already mentioned, it is reasonable to adopt, and certainly difficult to dismiss *a priori* the supposition that it will exert this same action to some extent in disease.

And, therefore, without good evidence that it fails of such effect, or exerts some other effect, which in its general results more than offsets such action in this disease, it is certainly acting against our knowledge to give it in a condition like pneu-

monia, in which the work of the body and its exposure to nerve and heart strain are excessive.

This same reasoning would apply equally well to its use in other conditions of acute infectious disease and sepsis.

It is not the intention of this review to deny that alcohol has any value as a therapeutic agent in medicine, or that all of its traditional use in such a capacity is irrational, but simply to present a critical study of this use, in the light of our present knowledge, with the hope of promoting a more careful consideration of the subject among physicians, and a consequent more rational use of the drug in medicine than that which exists at the present time. There is, in my opinion, no drug in wide general use in medicine in the employment of which there is shown so much carelessness and disregard of its specific drug properties, or with which so much harm is done, as alcohol. This fault in the traditional use of this drug has long been recognized by careful observers, and as a result the use in medicine has been for some time undergoing gradual restriction, the quantity per capita given in practice generally today being probably less than one-half that employed twenty years ago. And it is my opinion that, with renewed consideration of the subject in the light of the knowledge and experience upon it which exist at the present time, this use will be much further restricted and corrected.

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A CLINICIAN'S ESTIMATE OF ALCOHOL AS A THERAPEUTIC AGENT.¹

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I SHALL preface the brief remarks which I can make now on this important subject with the statement of two premises, which seem to me sound:

(1) We cannot reason directly from the effects of alcohol in health to those in disease.

(2) There are facts clinical as well as facts chemical, physiological or pathological.

Under each of these heads I permit myself a few remarks. What experience of life I have had leads me to believe that the healthy man, under ordinary conditions, in this climate, does not require alcohol, although he can use it moderately and habitually for years without any apparent harm. Its use may, indeed, afford him a legitimate pleasure, especially if it is taken in a dilute form and at only one period of the twenty-four hours, preferably with food. Wine, in moderation, maketh glad the heart of man today as it did in King David's time. In excess it has the same disastrous effects as it did upon Noah of old.

At the same time the great difference in individual toleration of this, as of any other potentially harmful agent, should be always remembered.

And I should like to call attention to what I believe to be a fact—that while a single moderate dose of whiskey or sherry, for instance, is

pretty sure to taint the breath of a man in health, much larger and repeated doses may be given in acute or chronic infectious diseases without tainting the breath at all.

Is there anybody here present who has not seen an amount of alcohol taken in disease without any obvious ill or toxic effect, which, if given in health, would have produced more or less profound intoxication?

Among many personal observations I will cite only two:

A boy of seventeen with pneumonia, not wonted to alcohol, takes a bottle of brandy and two quarts of champagne during twenty-four hours with no more toxic effect than if it were water. He recovered and acquired no fondness for drink. A lady of seventy, always temperate, prostrated with grip, takes for several weeks whiskey at the rate of a bottle every three days, with benefit, to the best of her and my knowledge and belief, certainly without a suggestion of any toxic effect. Such facts as these cannot be blinked. And so numerous are they, derived from so many sources, that very convincing counter-evidence must be brought by those who maintain that alcohol is under no circumstances consumed in the system, and consequently useless or harmful.

I think I have seen persons take alcohol with avidity and benefit for a time, and become instinctively unwilling to take it as the indications which led to its use have passed away. If this observation be true it tends to show that alcohol may be useful as a drug. The difference between its use as a drug and as a beverage should be kept more clearly in mind than is always the case.

As physicians we are under responsibility to see that its use as a drug does not lead to its abuse as a beverage.

Its use as a drug in acute disease, in my opinion, involves small risk of the establishment of a vicious habit. The case is far otherwise in chronic disease. Here also it may be very useful, as I firmly believe, but its administration should be carefully guarded by a realization of its dangers.

I recall the case of an old butler of one of my families. He was of English birth, and, as a young man, had used alcohol to excess. His master made a strong appeal to him which elicited a promise of total abstinence. This promise was faithfully kept. In his old age a senile heart and other infirmities seemed to me to indicate moderate doses of alcohol. My suggestion that he should take a tablespoonful of whiskey three times a day met with absolute refusal from him. I then had the druggist "doctor" whiskey for him, and he took his dose thrice daily for the rest of his life, apparently never suspecting the nature of his medicine, but telling me, whenever I went to the house, how much good my medicine did him. I have not had time to run to earth the author of the saying that "wine is the milk of old age." Sir James Paget quotes it in advising his aged father to drink five or six glasses of port wine daily.

¹ Remarks made in connection with the Discussion on The Value of Alcohol as a Therapeutic Agent in Medicine, Clinical Section, Suffolk District Medical Society, Dec. 18, 1901.