THE ACTION OF ALCOHOL ON THE CIRCULATION.

BY W. E. DIXON, M.A., M.D.

(From the Pharmacological Laboratory, Cambridge.)

FEW drugs have received so much attention as alcohol; yet its exact action is not clearly defined. To take for example the case of the heart, there are those who would have us believe that alcohol has a depressant action only, and there are others who produce experiments to show that it has a right to the title 'cardiac stimulant.'

Previous work dealing with the action of alcohol on the circulation is very extensive and the more important papers only can be referred to here. For convenience of description the action will be taken under four sub-headings, (1) the rhythm of the heart; (2) the cardiac output; (3) the vessels; (4) the blood-pressure.

Effect on cardiac rhythm.

Zimmerberg[1] experimented with frogs, cats, dogs, and men, and concluded that, when proper precautions were taken to avoid local irritation, alcohol did not alter the pulse rate. Von de Mühll and Jaquet[2] experimented with eight convalescent men and concluded that alcohol in amounts varying from 50 to 100 c.c. diluted to 20 per cent. had practically no action on the heart or circulation. Maki[3], and Hemmeter[4] also state that alcohol does not alter the rhythm of the heart. Parkes and Wollowicz[5], Marvaud[6], Binz[7], Foster[8], and

[1] For an account of Zimmerberg's work published in 1869 and of other observers who have come to similar conclusions, see *Der einfluss des Alkohols auf den Organismus*, by G. Rosenfeld, 1901, 50–52.

[2] *Correspbl. Schw. Aertze*, XXI. 457. 1891.

[3] *Dissertation Strassburg*, 1884.

[4] *Trans. Med. and Chirur. Faculty Maryland*, 1889, p. 230.

[5] *Proc. Roy. Soc. London*, XVIII. 362. 1869–70. Also Parkis, *ibid.* XXII. 172. 1873–4.

[6] *L'alcool, son action physiologique.* Paris, 1872.

[7] "Lectures on Pharmacology." *New Syd. Soc.* 1895, p. 320. Also see Binz u. v. Jaksch, *Der Weingeist als Heilmittel*, 1888, p. 4.

[8] *Text Book of Physiology*, Part I. p. 375. 1893.

others state that alcohol increases the pulse rate. Martin and Stephens[1], gave 15 c.c. of alcohol to a young man, taking due precautions as to dilution; they failed to notice any change in the pulse rate.

Ringer and Richards[2] state that in health alcohol slows the pulse, whilst Lichtenfels and Fröhlich and von Jaksch describe a preliminary slowing followed by acceleration. Von Jaksch[3] administered 8 c.c. of brandy to a number of children; he found decrease in the pulse rate in nine cases, an increase in one, and no change in two. After 3·2 grms. alcohol, properly diluted, the results were of the same character.

From this medley of observations it is at once evident that whatever the changes in pulse rate may be they are neither constant nor of any great significance. The amount of time which has been expended on such observations is out of all proportion to their importance; but it was formerly believed that if it could be shown that alcohol accelerated

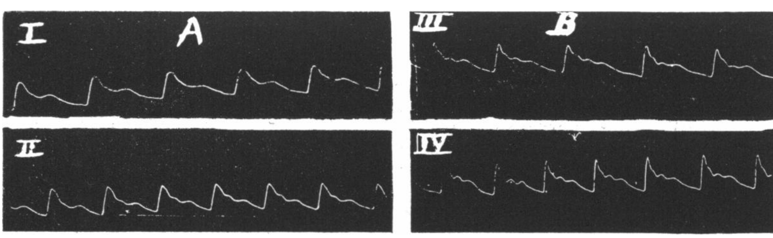

Fig. 1. Sphygmographic tracings of two men. I is normal and II is taken about 30 secs. later after holding in the mouth a little 50 % alcohol. III and IV are records from a second man under identical conditions. The time is constant throughout.

the pulse, it had a right to the title 'cardiac stimulant.' When concentrated alcohol, 20 to 50 per cent., is taken by the mouth the pulse during the space of a minute or two is always accelerated; this is not an action peculiar to alcohol and it can be observed after the administration of any irritant such as mustard and water, or even after water alone if it is sufficiently hot. As is well known any mild peripheral stimulation causes acceleration of the pulse.

To test the value of these statements I have performed a number of experiments on men using different stimulants. The subject was placed in as comfortable a position as possible; one radial artery was adapted

[1] *Studies from the Biol. Laboratory, Johns Hopkins University*, II. 213. 1887.

[2] *Lancet*, II. 209. 1866.

[3] *Der Weingeist als Heilmittel*, 1888, 23.

to the sphygmograph so that the pulse could be recorded at will. Whilst the record was being taken the man was required to hold in his mouth for a few seconds, or to swallow, some of the stimulant. By this means it was easy to show that alcohol as a 50 per cent. solution was a more efficient "stimulant" than the other substances (mustard, essential oil, hot water) which were tried and that it quickened the heart considerably. If the alcohol was retained in the mouth a few seconds only and was then spat out, the effect quickly passed off, but if it was taken into the stomach the acceleration was prolonged for half an hour or longer. When the same amount of alcohol is given well diluted these effects are not seen.

If moderate doses of alcohol well diluted with water be administered to animals or men the pulse rate does not alter. I have tried these experiments over and over again and always with the same results. The popular fallacy that alcohol quickens the pulse is clearly derived from the conditions under which alcohol is usually taken. It is well known that excitement of any kind quickens the heart and alcohol is generally taken under exciting circumstances.

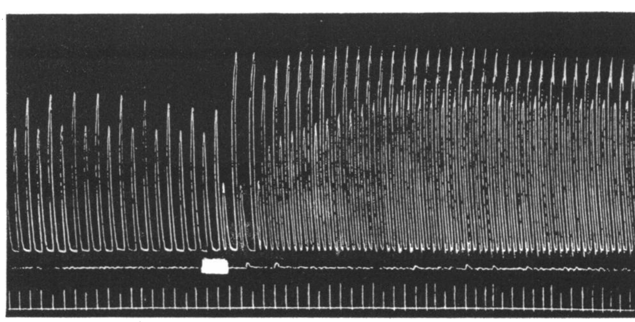

Fig. 2. Record of rabbit's heart perfused with oxygenated Ringer's solution. The heart had been perfused for an hour and at the indicated mark the fluid was changed for one containing 0·1 % alcohol. Time = secs.

If a heart is beating very feebly alcohol invariably accelerates the rhythm quite apart from the reflex effects just described; for example, at the end of a long perfusion experiment, small doses of alcohol not only improve the quality of the beat but increase the rate. This is shown in Fig. 2, which records a rabbit's heart that had been perfused during one hour with oxygenated saline; the beat had become very weak and slow, no doubt largely on account of the absence of any form of foodstuff. At this time the solution was changed to one containing 0·1 per cent. of alcohol and the rate of the beat increased immediately. In similar cases I have obtained a like effect on the heart by the administration of glucose.

Large doses of alcohol administered to the normal animal slow the heart beat. This action is not obtained on the isolated heart nor when the vagi have been severed, but only in an animal having an intact medulla. Now alcohol administered in large doses behaves in many respects like chloroform, and belongs to the same group of narcotics. It differs from chloroform because within certain limits it is oxidised in

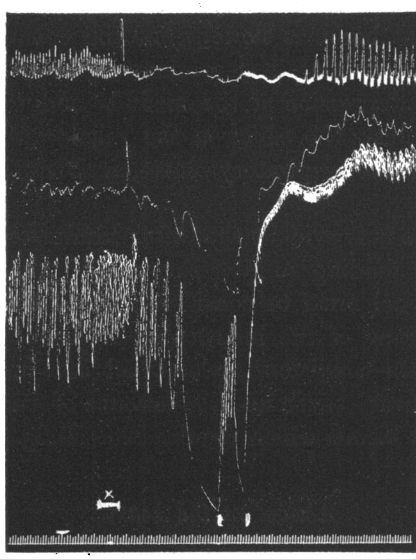

Fig. 3. Dog. Cerebrum destroyed but medulla uninjured. Record of respiration, intestinal volume, and blood-pressure. At the mark, 10 c.c. 30 % alcohol was injected into the femoral vein. At the two smaller marks the right and left vagi respectively were severed. Time = secs. × ½.

the tissues. If then it is required to determine its action upon nervous structures neither chloroform nor other anæsthetic substance should be present in the tissues. Large doses of alcohol administered to an animal under the influence of chloroform have little power of slowing the heart, but to the unanæsthetised animal the slowing may be very decided, or there may be even complete inhibition. Fig. 3 shows such a condition. The animal in this case was decerebrate but its medulla was intact and respiration active. It will be seen from this figure that the injection of the alcohol caused complete standstill of the heart, but that recovery is complete on section of the vagi. From this experiment it is clear that alcohol stimulates the medulla directly or indirectly, *i.e.* reflexly.

Cerna[1], Jaquet[2] and others have denied that alcohol excites the medulla, but in view of the conclusive experiments conducted by Binz and his colleagues[3] on respiration it must be conceded that alcohol to both men and animals is a decided stimulant to the medulla. Such stimulation being granted, Schmiederberg and his pupils would regard it as due to dissolution of the higher centres and not a primary effect on the medulla. My experiments show, conclusively, that large doses of alcohol increase the activity of the medulla for a period during which the heart-beat becomes slower; and this effect cannot be due to dissolution since the animal is decerebrate. Large doses of alcohol ultimately produce depression of the medulla and the heart quickens again. In smaller doses the effect on the vagal centre is not apparent though the effect on the respiratory centre, as Binz has clearly shown, is decided.

From these facts it is evident that after administering alcohol many factors are at work tending to alter the rate of the heart. First the strength of the alcohol must be considered, concentrated doses exciting the mucous membrane of the mouth and stomach and causing reflex acceleration; then the conditions under which it is imbibed, exciting or otherwise; the quantity taken and the amount of peripheral dilatation are other important factors which require controlling.

Action on the heart.

Martin and Stevens[4] perfused the dog's heart by the method devised by Martin. They found that 0·125 per cent. alcohol by volume in the perfusing blood had no effect, but that double this strength diminished the work of the heart in one minute. They assumed that this amount of alcohol was equivalent to taking 5 ounces of brandy. Hemmeter[5] and Bock[6] confirmed these results; they considered that alcohol had no special effect on the heart. Hemmeter[7], working with Ludwig's Stromuhr, showed that alcohol increased the velocity of the

[1] *Physiological Aspects of the Liquor Problem.* Boston, II. p. 102.
[2] *Arch. de Pharm.* II. 107. 1896.
[3] *Centralbl. f. Klin. Med.* 1895. *Berlin Klin. Woch.* 1903, 45 and 79.
[4] *Studies from the Biol. Lab. Johns Hopkins Univ.* II. 213. 1887.
[5] *Studies from the Biol. Lab. Johns Hopkins Univ.* IV. 5. 1889.
[6] *Arch. f. exp. Path. u. Pharm.* XLI. 158. 1898.
[7] *New York Med. Rec.* 1891, p. 292.

circulation in the dog's carotid; and this has been confirmed by Wood and Hoyt[1]. Loeb[2] perfused the isolated cat's heart with saline and found that alcohol, in amounts varying from 0·13 to 0·3 per cent., generally increased the force of the beat. Larger doses depressed the

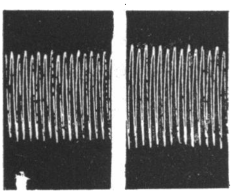

Fig. 4.

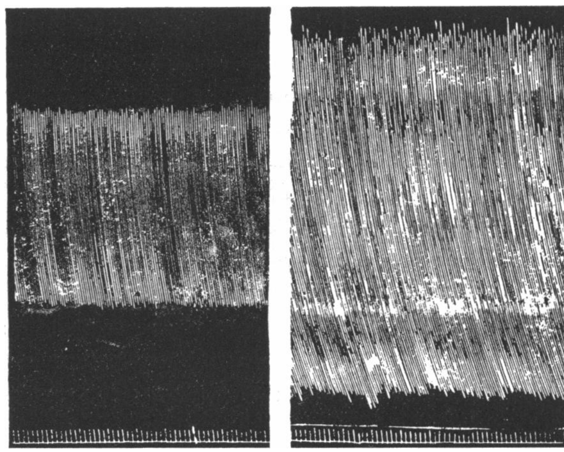

Fig. 6.

Fig. 4. Rabbit's heart perfused with Ringer-Locke solution. The second part of the tracing shows the effect of perfusing with 0·08 % alcohol. The effect is typical.

Fig. 6. Record of rabbit's heart perfused with Ringer-Locke fluid. This rabbit had been previously dosed with alcohol for some 3 weeks. The second portion of the tracing shows the effect on the heart 10 mins. after perfusing with 0·1 % alcohol.

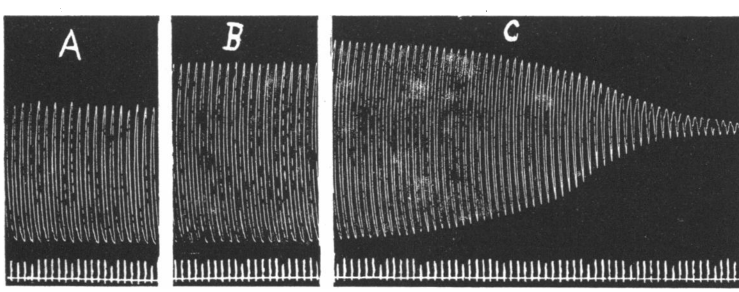

Fig. 5. Record of rabbit's heart perfused with Ringer-Locke solution. *A* is the normal beat. *B* shows the effect after perfusing for 2 mins. with 0·4 % alcohol. *C* shows the effect of increasing the alcohol to 0·8 %: the heart beats at first more vigorously but the toxic effect is soon obtained. The muscle retains considerable tonus. Time = secs. × $\frac{1}{3}$.

[1] *National Acad. of Science, U.S.A.* x. 43. 1905.

[2] *Arch. f. exp. Path. u. Pharm.* LII. 459. 1904.

heart. Somewhat similiar results have also been obtained by Kochmann[1]. Tunnicliffe and Rosenheim[2] with the same methods obtained little effect on the rabbit's heart.

The first series of experiments were conducted upon the isolated rabbit's heart perfused with Ringer-Locke's solution by means of the Langendorff apparatus. The hearts were allowed to record for about one hour and when the beat was quite constant the saline solution was changed to one containing the alcohol. It was found that certain strengths of alcohol generally increased the amplitude of the contractions. This effect was observed in strengths varying from 0·05 to 0·3 per cent. in the rabbit. It was most marked in feeble hearts which had been beating for some hours without nutriment, and was least marked or even entirely absent from vigorous organs, especially when these were freshly isolated or provided with nourishment such as glucose. Fig. 4 shows a record of the movements of the left ventricle in a heart which had been beating with saline solution alone for half an hour; by the addition of alcohol to 0·08 per cent. a permanent effect was produced as shown in the second half of the tracing. Fig. 5 shows the effect on another heart which had also been beating for about half an hour; first 0·4 per cent. of alcohol was used and then 0·8 per cent. It will be seen that for a short period the stronger alcohol increases the force of the beat but that this is quickly followed by decided weakening, the heart nevertheless retaining considerable tonus. Fig. 6 shows the effect of perfusing 0·2 per cent. of alcohol through the heart of an immunised rabbit: the animal had previously for the space of three weeks been given daily doses of alcohol by subcutaneous injection. At first 1 gramme per kilo body weight was given and this was later increased to 1·5 grammes. It will be noticed that the increase in the heart beat is in this case very considerable. This experiment was repeated in another case and the effect was of the same nature but not so decided. Without laying too much stress on these two experiments there can be little doubt that within certain narrow limits the heart can adapt itself so as to deal with and make use of the alcohol just as we know the body as a whole is able to do. But complete proof of this will only be forthcoming when it is shown that the alcohol in the perfusing fluid disappears in part or whole after passing through the heart: such experiments are being arranged in this laboratory.

[1] *Arch. Internat. Pharmacodynamie et de Therapie*, XIII. 329. 1904. (Literature.)
[2] *Proc. Phys. Soc.* This *Journal*, XXIX. 15. 1903.

If alcohol in greater concentration such as 2 per cent. be perfused through the coronary vessels for a short period such as 30 seconds the force of the beat is greatly diminished; the muscle fibre is not injured however because when the alcohol is replaced by saline not only does the heart recover completely but the beats become much more vigorous

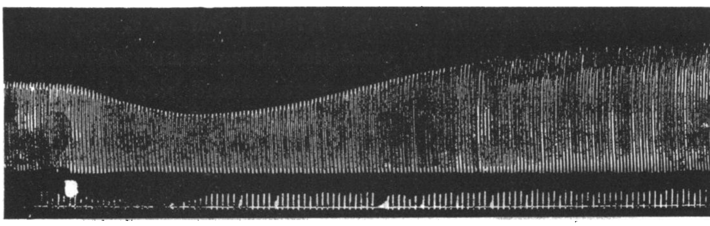

Fig. 7. Record of rabbit's heart perfused with Ringer-Locke solution. Shows the typical effect of injecting alcohol into the side tube (1 c.c. 2 %). There is no alteration in the rate. $\times \frac{1}{3}$.

than before (Fig. 7). These experiments on the isolated rabbit's heart have been repeated on the cat and the results obtained are of the same nature.

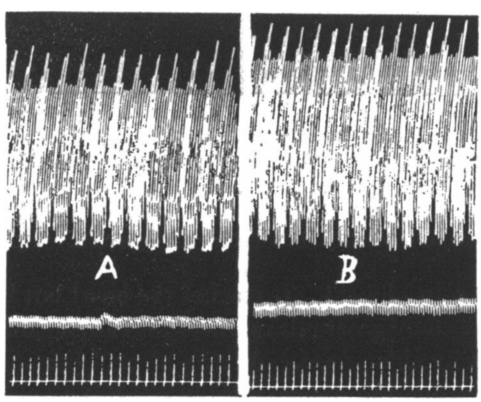

Fig. 8. Dog, 12 kilos, pithed (brain and medulla completely destroyed). Morphine. Cardiometer and blood-pressure. *A* is the normal. *B* shows the effect 3 mins. after the injection of 10 c.c. of a 30 % solution of alcohol into a vein. (Note the increase of cardiac output, and the rise in B.P.) Time=secs. $\times \frac{1}{5}$.

Another series of experiments was conducted on the hearts of cats and dogs with the circulation intact. In these experiments the brain was usually destroyed, but in a few cases the animals were anæsthetised with chloroform and urethane. The heart was enclosed in a glass cardiometer and the movements of the air recorded, so that as the heart fills with blood the recording lever rises and during systole of the heart the lever falls. The results of such experiments show that the action of alcohol, whether administered intravenously or subcutaneously, is to increase the output from the heart; relaxation is greater than before and the systole is somewhat increased. Fig. 8 shows the effect of injecting 10 c.c. of 30 per cent. alcohol into the femoral vein of a dog, the second portion of the tracing shows the condition three minutes after injection. The cardiac output is considerably augmented and blood-pressure is increased. Fig. 9 shows the typical effect of a large dose of alcohol injected

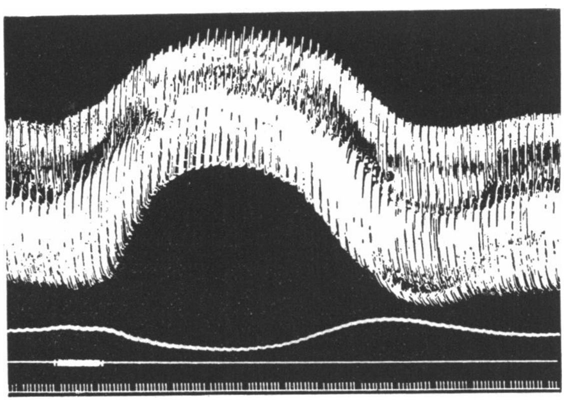

Fig. 9. Cat. Brain and medulla completely destroyed by pithing. Cardiometer and B.P. Shows the effect of injecting 2 c.c. of 30 °/₀ alcohol. This large dose at first causes the typical toxic action with dilatation of the heart. As the alcohol becomes diluted recovery occurs and the heart as recorded on the right of the tracing is working much more efficiently than before the injection. × ½.

into the jugular vein of a cat. It reaches the heart but little diluted and its first effect is to cause great relaxation of the cardiac muscle very similar to that induced by chloroform. As the alcohol becomes more dilute a stage is reached when the amount in the blood corresponds to less than 0·5 per cent., and this amount no longer interferes with the cardiac systole. And it will be seen that when this stage is passed the output of blood from the heart is much greater than it was before the injection of the alcohol. The height of the record in the first or normal stage is 43 mm. During the stage of depression, when according to calculation there should be between 2 and 3 per cent. of alcohol in the blood, it measured only 37 mm. In this state the heart is gorged with blood, the muscle being unable to contract upon it. In the final stage the record measures 48 mm. and the effect is of a permanent character. In other words the alcohol, after temporary depression due to the large percentage present in the heart, increases the output by about 10 per cent. for a period of ten or fifteen minutes. In some other cases an increase of 15 and 20 per cent. has been recorded.

The initial depression is commonly absent in the dog. In Fig. 10, 5 c.c. of 30 per cent. alcohol was injected at '*A*'. It will be noticed that in this case the systole becomes more and more efficient and the tonus of the heart is increased, the total effect is considerable augmentation of output.

Two facts are evident from these experiments. First that when alcohol is present in the blood in moderate amounts say about 0·1 to 0·2 per cent. the efficiency of the heart is increased, but that when it is present in the blood in amounts greater than 0·5 per cent. the efficiency of the heart is diminished. How are these facts to be accounted for? It is clear that alcohol possesses two entirely different actions, it excites in small doses but depresses in larger ones. In this respect it resembles no other drug, for when we increase the dose of other drugs the effect is at first exaggerated and only with enormous doses does paralysis ensue. But with alcohol there is a definite limit to the dosage, to overstep which is depression. In other words to increase the dose with alcohol is to cause a different type of effect.

It is well known that alcohol is oxidised in the body and yields energy; and the experiments of Atwater and Benedict[1] have made it abundantly clear that the alcohol is not burnt up uselessly but that it can be isodynamically substituted for carbohydrates or fats. In this sense then, alcohol is a food. But the tissues can oxidise only a limited amount and if this is exceeded the toxic effect of the alcohol becomes evident. Immunity to organic substances such as morphine and alcohol is the expression of the increased ability of the tissues for their oxidation[2]; and the tissues may be cultivated to a greater or less tolerance by the continual administration of the drug.

The 'stimulant' action of small quantities of alcohol on the heart is readily explained by regarding it as an expression of the food value of the drug and for the following reasons:—First we know it acts as a food to the tissues as a whole, why then should it not so act to each separate tissue, *e.g.* the heart? In animals rendered somewhat immune to the action of alcohol, it behaves as a more decided stimulant to

[1] *Memoirs National Acad. of Science*, VIII. Washington, 1902.

[2] Faust. *Arch. f. exp. Path. u. Pharm.* XLIV. 217.

the heart than in control animals, thus suggesting that the heart behaves like the tissues as a whole. And moreover its action on the heart shows many resemblances to certain other foods such as sugar, the effect being most decided when the heart has been beating for some time whilst deprived of food. The addition of sugar to the perfusing saline fluid during a Langendorff experiment is to cause an increase in the excursion of the lever, and the same effect though less defined is obtained with alcohol. But alcohol differs from sugar because if the

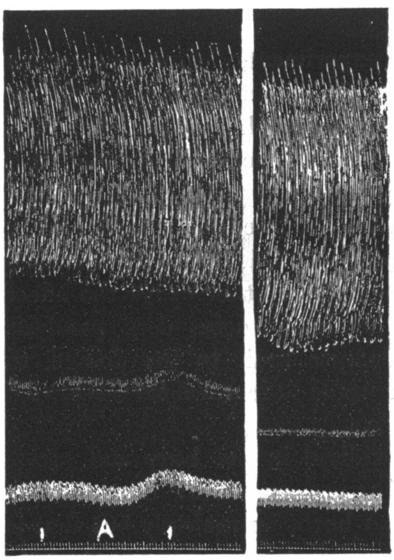

Fig. 10.

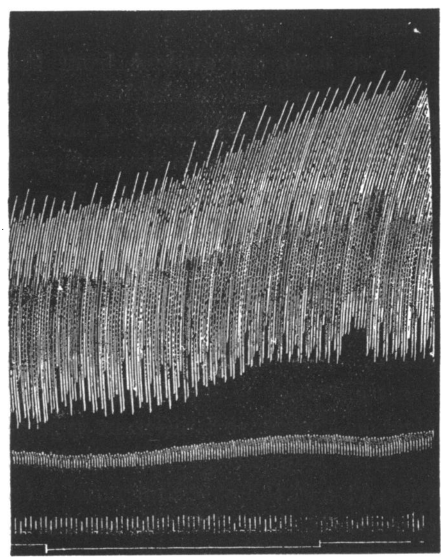

Fig. 11.

Fig. 10. Dog, 14 kilos. Complete destruction of the brain and medulla by pithing. Cardiometer. Limb volume. Blood-pressure. At *A* 5 c.c. 30 $^0/_0$ alcohol was injected intravenously. Time = secs. Between the two parts of the tracing is an interval of 3 mins.

Fig. 11. Dog, 10 kilos. Complete destruction of the brain and medulla by pithing. Cardiometer. Blood-pressure. Shows the effect of injecting 5 c.c. 60 $^0/_0$ sucrose into the jugular vein. Time = secs.

dose is increased toxic effects come into play. The effect shown in Fig. 2 is one which is not uncommon after the administration of either alcohol or sugar. Alcohol given by the mouth has this advantage over other foods that it very rapidly finds its way into the circulation and unlike sugar it can be absorbed directly from the stomach. Fig. 11 is a cardiometric tracing of the dog's heart, and shows the effect of injecting 2 grms. of sucrose into the circulation; the output from the heart is considerably augmented. In many respects this effect resembles that of alcohol. For these reasons I favour the view that alcohol in moderation provides a food for the heart but that in excess its effect is depressant and tends to resemble that of chloroform. It is doubtful however whether this acute depression can occur in life since Grehant[1] has shown (for dogs) that drunkenness is associated with about 0·5 per cent. of alcohol in the blood. Larger amounts of alcohol than this are necessary to cause serious depression of the dog's heart, since if the amount did not exceed 0·7 % recovery occurred.

Finally I would point out that alcohol is normally found, though in minute quantities, in the fresh tissues of man and animals that have received no alcohol. It can be distilled off from the liver, muscle, brain and other tissues[2]. Since we know that small quantities of dextrose and alcohol are readily oxidised in the tissues it is not improbable that dextrose is oxidised in successive stages and that the oxidation passes through the alcohol stage, energy being liberated at all stages in the oxidation. As we are daily obtaining more and more evidence that the so-called "vital" phenomena are in reality fermentations it seems to me feasible that such oxidations might be brought about by a series of co-ordinated ferment actions. That such an explanation is possible is seen from the fact that the ferments in yeasts will oxidise dextrose to the stage of alcohol, and those in Mycoderma aceti will continue the oxidation.

Action on the vessels.

When administered to the intact animal, alcohol does not affect all vessels in the same way. But if it is perfused through the vessels of organs which are isolated from the body the effect is the same in all cases. In frogs, ½ % alcohol in the perfusing fluid determines an immediate though moderate constriction which is very permanent in character but which is removed by substituting pure Ringer's solution for that containing alcohol (Fig. 12). In mammals small amounts of alcohol such as 0·1 or 0·2 % cause very slight dilation when perfused through isolated vessels; if the percentage be stronger, about 1 or 2 %, then constriction, quite considerable in extent, first ensues followed later by dilation. All vessels, pulmonary and coronary as well as systemic,

[1] *Gaz. méd. de Paris*, 1882, p. 95.

[2] Rajewski. *Pflüger's Arch.* II. 122. Hoppe-Seyler. *Handbuch der chem. Anal.* Berlin, 1893, p. 40. Ford. This *Journal*, XXXIV. 431. 1906.

are affected in just the same way so that the action must be on muscle. In part these results agree with those of Kobert[1] who found that alcohol in dilute solution, 0·1 and 0·2 °/₀, had little effect when perfused through the renal vessels.

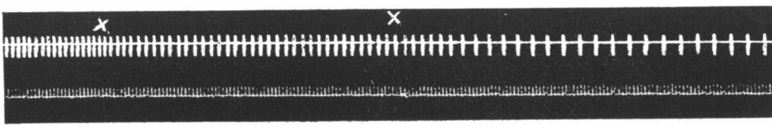

Fig. 12. Perfusion of the systemic vessels of a frog. Drop record. At the first cross alcohol 0·15 °/₀ was substituted for the pure Ringer's solution. At the second cross 1·5 °/₀ of alcohol was perfused. Time = secs.

These experiments show that the action of alcohol upon the blood vessels must be partly central. Drugs which affect the centre do not influence all blood vessels in the same way. Thus atropine excites the medulla and basal ganglia in the brain, but whilst constricting the splanchnic vessels it dilates the superficial ones. Alcohol also dilates the skin vessels very rapidly, and at the same time tends to constrict the vessels in muscle-tissue, and to a less marked degree in the splanchnic area.

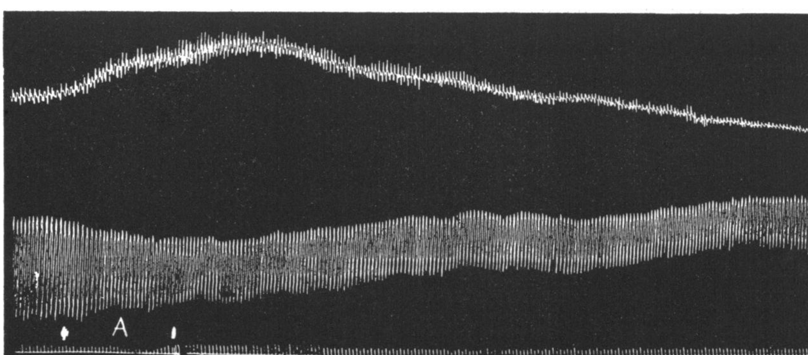

Fig. 13. Dog, 14 kilos. Morphine, chloroform. Limb volume. Blood-pressure. At the indicated mark 30 c.c. of well diluted alcohol was administered by the stomach tube. Time = secs. (This experiment should be compared with those of Gutnikow.) × ⅓.

The effect on the skin-vessels has been investigated by the plethysmographic method on the ears of dogs and rabbits; in anæsthetised animals alcohol caused decided constriction, whilst the volume of the limb in the dog also diminishes (Fig. 13). And this effect is obtained

[1] *Arch. f. exp. Path. u. Pharm.* XXII. 90. 1887.

no matter whether the drug is injected under the skin or given by the mouth. Fig. 14 shows the volume of a loop of gut and the corresponding blood-pressure at certain stated intervals. The effect of a subcutaneous injection of alcohol is to produce a gradual rise in blood-pressure, with but little apparent change in the condition of the vessels.

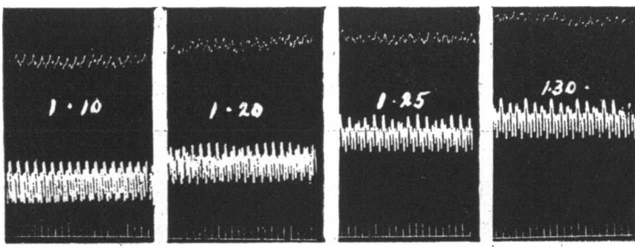

Fig. 14. Dog, 7 kilos. Morphine. Cerebral hemispheres destroyed. Medulla intact. Intestinal volume. Blood-pressure. Shows the effect of injecting 16 c.c. 90 % alcohol, diluted to 1 in 3, subcutaneously. The injection was made at 1.15 p.m. Time=secs. (There is considerable rise in B.P. The dilatation of the splanchnic vessels is not in proportion to this rise.) × ½.

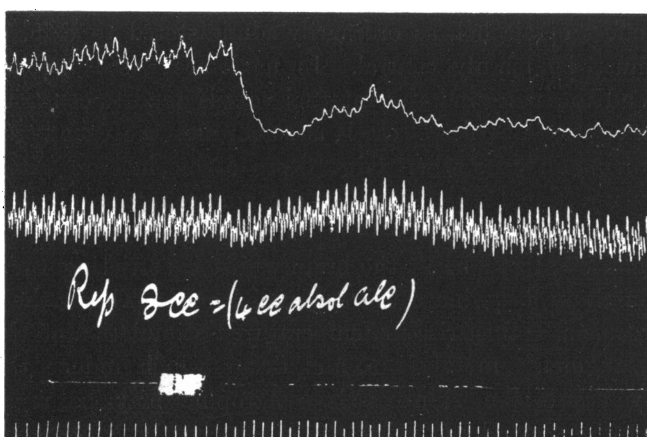

Fig. 15. Dog, 16 kilos. Morphine, chloroform. Intestinal volume. Blood-pressure. Shows the vaso-constriction produced by a big injection (8 c.c. 50 %) of alcohol. × ½.

In this case there must be a marked tendency towards constriction since if the vessels were in their normal state they would become considerably dilated, passively, from the rise in blood-pressure. In Fig. 15 the effect of a large dose of alcohol is shown to cause immediate constriction of the splanchnic area. By perfusion experiments it has been already demonstrated that this effect may be peripheral on the vessel walls; but it is more likely partly central. It can easily be shown that alcohol exerts a stimulant action on the brain by injecting a little, well diluted with Ringer, up one carotid artery towards the brain. Fig. 16 shows an experiment on a dog in which first 5 c.c. of 30 per cent. alcohol was injected into the jugular vein; this produced great weakening of the heart-beat and a large fall in blood-pressure. During recovery an exactly corresponding dose was injected up one carotid under similar conditions; it caused a considerable rise in pressure which was not followed by a fall.

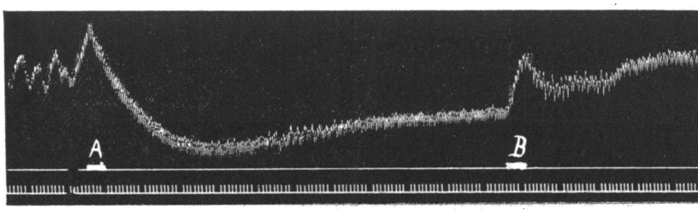

Fig. 16. Dog. Morphine, chloroform. Blood-pressure. At '*A*' 5 c.c. 30 % alcohol was injected into the jugular vein. At '*B*' the same dose was injected up the carotid towards the brain. $\times \frac{1}{2}$.

The effect of alcohol, as ordinarily administered to man, on blood vessels must be mainly central. In moderate doses the superficial vessels tend to dilate and the internal vessels tend to constrict. This dilatation of the superficial vessels is sometimes the exact opposite to that occurring in dogs when large doses of alcohol are administered either by injection (Fig. 10) or by the stomach tube (Fig. 13); the explanation of this is simple. We know that drugs which excite the medulla and basal ganglia of the brain whilst constricting the internal vessels simultaneously dilate the superficial ones. This is the reaction of the organism against rise in temperature: stimulation of the corpus striatum augments metabolism, and drugs which induce this effect invariably dilate the skin-vessels. Atropine may be regarded as a typical drug which by exciting the brain centres causes constriction of the internal vessels and dilatation of the superficial. Now small doses of alcohol, as we have already pointed out, excite the medulla and should tend to dilate the superficial and constrict the splanchnic vessels. This effect is obtained in animals if certain precautions are taken with regard to keeping the medulla as normal as possible and giving only a small dose of alcohol, and that for preference by the mouth; it is the effect which is generally observed in man. It might be suggested that the alcohol was quickly oxidised in a useless fashion and produced a sudden output of heat and so dilatation of the skin vessels. This is not the case for we know that alcohol is oxidised as it is required by the body and may be substituted in a diet, isodynamically, for starch or sugar. In Figs. 10 and 13 (last half), the more typical effect on superficial vessels is reversed because the peripheral action of the alcohol overshadowed the central effect, in the former case because the centre was destroyed, and in the latter because it was fatigued by chloroform and morphine.

Action on blood-pressure.

No observations on the action of alcohol show greater discrepancies than those dealing with blood-pressure. These may possibly be explained by the very different conditions under which the various experiments were conducted. Those of Zimmerberg[1], Dreser[2], and Abel[3], were performed on anæsthetised animals, and on the whole agree with one another, the main effect being a fall of blood-pressure. Experiments on anæsthetised animals cannot be regarded as showing the exact action; and especially would anæsthetics hide the delicate effects produced by alcohol as a food substance on account of their known action on metabolism[4]. Another error is the tendency of observers to give excessive doses of alcohol. Thus Gutnikow[5] says that alcohol produces a fall of blood-pressure in the curarised dog; but to produce this effect he administered 250 grammes of 50 to 70% alcohol and does not mention the weight of his dog. The majority of observers state that small doses of alcohol cause some rise of blood-pressure, and some that this is followed by a more considerable fall[6]. Dogiel[7] and Cerna[8] did not employ anæsthetics in their experiments: they describe an increase of blood-pressure. Schafer[9] has recently shown how very decidedly alcohol acts in preventing the fall of blood-pressure caused by chloroform.

[1] *op. cit.*
[2] *Archiv. f. exp. Path. u. Pharm.* XXIV. 236. 1888.
[3] *Physiological Aspects of the Liquor problem,* II. 73.
[4] Barcroft and Dixon. This *Journal,* XXXV. 182. 1907.
[5] *Zeit. f. klin. Med.* XXI. 168. 1892.
[6] Haskovec. *Wied. med. Woch.* 1901, 14–18. Also *Arch. de Méd. exp. et d'Anat. path.* 1904, 539.
[7] *Pflüger's Arch.* VIII. 605. 1874.
[8] *op. cit.* p. 68.
[9] *Transactions Roy. Soc. Edin.* XLI. 337. 1904.

The present experiments were performed on cats, dogs, and rabbits; anæsthetics were not usually administered, but the animals were in each case killed by pithing, the cerebral hemispheres being completely destroyed. In some cases the medulla was destroyed, and in others, especially in experiments dealing with vaso-motor phenomena, it was kept intact; in the latter case the animal's respiration was natural.

Large injections of alcohol into a vein cause an immediate fall in blood-pressure, this is shown in Figs. 9 and 16: in the former experiment, in which a cat was employed, it is quite evident that the effect is produced by the deficient systole of the heart. As soon as the heart is acted upon by the concentrated alcohol the muscle fibres lose their power of contractility and the organ becomes gorged with blood; but as the alcohol becomes diluted the force of systole increases and the blood-pressure rises again. Fig. 16 shows a similar effect in the dog. This initial fall of blood-pressure is due to cardiac failure and is analogous in every way to that caused by chloroform. It is however of little significance practically since the enormous amount of alcohol necessary to produce this effect is such as never occurs in life.

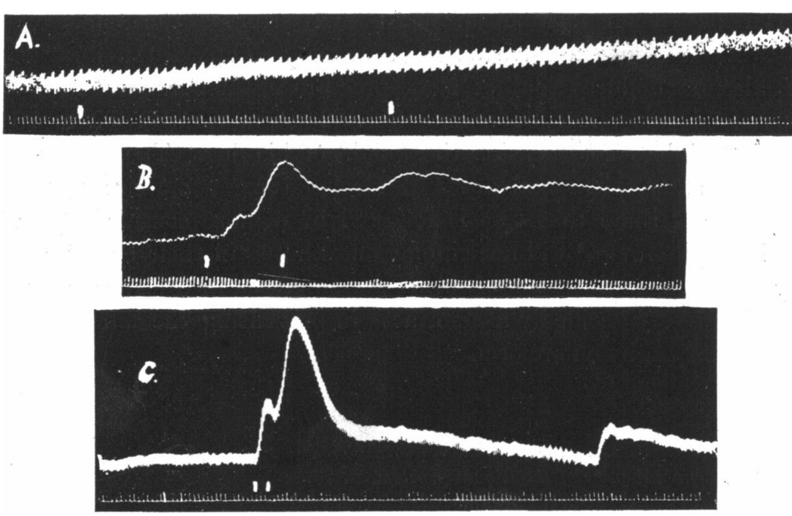

Fig. 17. Record of blood-pressure in three cats which had been killed by pithing. Complete destruction of brain and medulla. Artificial respiration. *A* shows the effect of injecting 5 c.c. 1 % alcohol very slowly. *B* and *C* show the effect of 1 c.c. 33 % alcohol more rapidly. The injections were made into the jugular vein. Time = secs. $\times \frac{1}{3}$.

Smaller injections of alcohol, sufficiently diluted, usually cause a slight rise in blood-pressure. Fig. 17 records the action of alcohol on the blood-pressure in three separate cats. Tracing *A* shows the effect of injecting 5 c.c. of a 0·4 per cent. solution into the jugular vein; the rise in blood-pressure is very gradual, and closely resembles the type of rise following the administration of digitalis. Tracing *B* shows the effect of injecting the alcohol more rapidly; in this case 1 c.c. of a 33 per cent. solution was injected, and the rise in pressure was both considerable and prolonged. Tracing *C* shows an exactly similar injection made still more rapidly; the initial large increase of pressure soon passes off, but some permanent increase remains. In the rabbit also alcohol raises the blood-pressure: this is shown in Fig. 18 after the injection of 2 c.c. of 25 per cent. alcohol. The injection of alcohol into

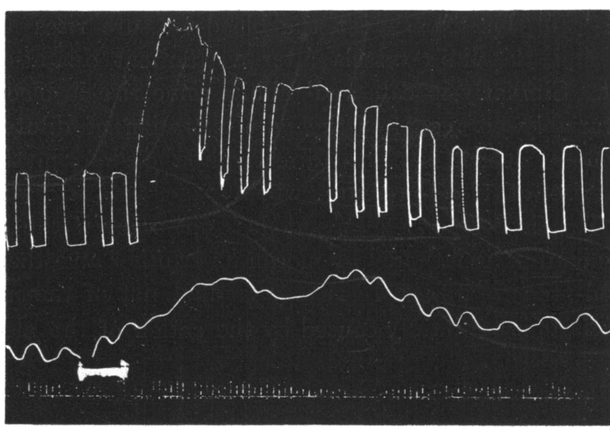

Fig. 18. Rabbit. Cerebral hemispheres destroyed. Respiration (natural). Upstroke = inspiration. Blood-pressure. At the mark, 2 c.c. 25 % alcohol was injected into the jugular vein. Time = secs. × $\frac{1}{3}$.

the circulation of dogs causes a less decided effect on the blood-pressure, thus in Fig. 10 little or no effect was caused by injecting 5 c.c. of a 30 per cent. solution into the jugular vein, in spite of the considerably augmented cardiac output; nor in Fig. 15 does 8 c.c. of 50 per cent. alcohol produce any significant alteration in height. Sometimes after the course of some minutes the blood-pressure assumes a higher level than normal and this is shown in Fig. 8, where three minutes after the injection of alcohol the blood-pressure is seen to be a little raised, probably entirely as a result of the increased cardiac output. Fig. 14 shows the effect of injecting 16 c.c. of 90 per cent. alcohol subcutaneously; the blood-pressure gradually rises and reaches a maximum twenty minutes after the first injection. Although some rise of pressure under these conditions is general, such a rise as is shown here is a little unusual. All these experiments have been carefully controlled by injections of saline solution, and the results obtained are not due to mere increase of fluid bulk.

A further series of experiments on pithed rabbits, cats, and dogs, was made, in which the alcohol was placed directly in the stomach by means of a tube; in some of these cases curare was given. In all cases this method of administration resulted in a decided action on the circulatory system. And especially was this the case when the circulation was failing as is apt to happen as the result of collapse some hours after the destruction of the brain. Fig. 13 shows the effect of placing 30 c.c. of alcohol diluted with 30 c.c. of water into the stomach of a dog by means of a tube. In this experiment the blood-pressure rises almost immediately and the limb vessels after a transient dilatation become constricted. Similarly in cats and rabbits some rise in blood-pressure almost invariably ensues after the administration of diluted alcohol. When absolute alcohol is placed directly in the stomach there is an immediate rise of blood-pressure, which passes off in two or three minutes. This is a reflex effect, and does not occur if the medulla is destroyed, nor if it is fatigued by morphine or other anæsthetics. The rise in blood-pressure in Fig. 13 is very gradual, not of the nature of a reflex, and is almost certainly caused by the action of the alcohol after absorption.

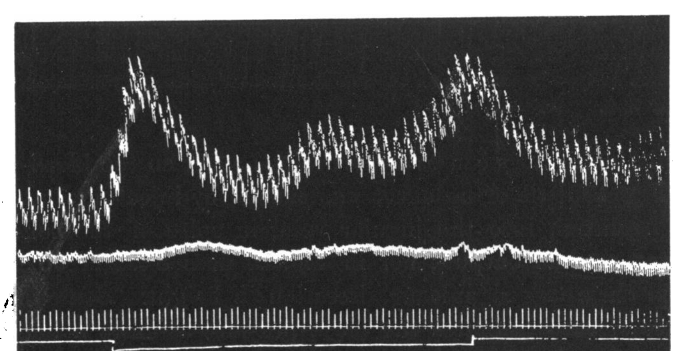

Fig. 19. Dog. Morphine. Brain and medulla completely destroyed. Pulmonary pressure in saline and systemic pressure in mercury. Shows the effect of injecting 3 c.c. 33 % alcohol. × ⅓.

Alcohol, no matter how it is administered, causes a small rise in pulmonary pressure. Fig. 19 shows the pulmonary and systemic pressures of a dog during the administration of alcohol. The systemic pressure is but little affected, yet the pulmonary pressure is distinctly raised. At this point the similarity between the action of alcohol and that of sugar on the blood-pressure may be pointed out. For this purpose Fig. 8, which I regard as showing the most typical effect of alcohol, may be compared with Fig. 11. In both the systolic pressure is raised to a trifling extent whilst the diastolic is less affected, but in neither is the rate of the heart materially altered; the effect in both cases may be regarded as due to increased cardiac output.

The blood-pressure is the resultant of the output from the heart and the condition of the vessels as a whole. The cardiac output is increased and the sum-total effect on the vessels is rather towards dilatation than constriction, so that the blood-pressure may either rise or remain constant according to which of these two factors holds the balance. But there is one effect which is seen fairly constantly in the blood-pressure tracing even when the systolic pressure is unchanged, that is the increased difference between systolic and diastolic pressures; this effect is also seen typically in Fig. 11, after the injection of sugar. In man the same condition is expressed by saying that the systolic pressure is a little increased or constant whilst the diastolic pressure falls. Indeed the conditions of the circulation of man, under the influence of alcohol and in the normal state, as shown by his blood-pressure, present considerable analogies to his blood-pressure in the recumbent and standing positions respectively. In other words alcohol facilitates the circulation. I do not, however, wish to dogmatise as regards man as my experiments are confined to two subjects.

CONCLUSIONS.

1. In moderate doses, and if well diluted, alcohol has little effect on the rate of the normal heart; in large doses it excites the medulla and slows the heart through the vagus. The failing heart is accelerated by alcohol. When taken by the mouth, in concentration, alcohol reflexly quickens the beat.

2. In moderate doses alcohol causes dilatation of the superficial vessels and some slight constriction, which after large doses is followed by dilatation, of internal vessels.

3. In moderate doses alcohol increases the activity and output of the heart. Reasons are given for suggesting that this effect is due, in whole or part, to the fact that alcohol is a readily assimilable food-substance. In large doses, strengths over 0·5 per cent. in the blood, alcohol depresses the heart; this is due to the direct toxic action of the drug.

4. Alcohol in moderate doses, administered to animals which show signs of circulatory failure, raises blood-pressure mainly on account of its effect on the heart. In normal animals and in man whilst the systolic pressure may rise a little or remain unchanged the diastolic tends to diminish: in other words the difference between the systolic and diastolic pressures tends to increase.