THE DIAGNOSIS OF DRUNKENNESS FROM EXCRETION OF ALCOHOL AND THE GENERAL DISTRIBUTION OF ALCOHOL IN TISSUES

by

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It is recognised by all medico-legal authorities that the ordinary tests for drunkenness are very unsatisfactory. No two men behave in the same way under the influence of alcohol, and the result often is, that many cases charged with drunkenness, where motor accidents have occurred, are dismissed for want of convincing evidence. The very fact of the shock of arrest sometimes produces an apparent and astonishing sobriety in people who, a short time before, have been quite evidently drunk. These persons generally acquit themselves well in routine tests. If, however, an analysis be made of the blood or urine of accused persons, and a high concentration of alcohol be found, it useless for them to protest that they have had no alcoholic liquor or only a very small amount. From this point of view at least the examination of urine supplies indubitable evidence of the imbibition of alcohol, and also to some extent, of the amount taken. In cases of gross intoxication the state is obvious and analysis hardly necessary, although advisable, as even in these cases it is often contested that the condition was not brought about by alcohol.

As long ago as 1892 Kraepelin stated that it required a lapse of 12 to 24 hours after even a moderate amount of alcohol before mental equilibrium was reinstated.
reinstated. In his work on alcohol elimination Gréhant (1900) proved that with a dose of alcohol of 1 cc. per kilo. of body weight the time for elimination of the alcohol from the blood was 8 hours. 2 cc. per kilo. took 10 to 11 hours to disappear, and 5 cc. per kilo. 20 to 22 hours. A dose of alcohol of 1 cc. per kilo. is a moderate amount to take, but 2 cc. per kilo. might be termed a fairly large dose. On the other hand 5 cc. per kilo. is a very large dose. Combining Gréhant's times of elimination of alcohol and Kraepelin's statement, it would seem that as long as there is alcohol in the blood a person is not mentally normal.

Schweisheimer (1913) showed that the curve for the concentration of alcohol in blood was parallel with the intensity of intoxication.

It is generally believed that a small amount of alcohol does no harm either to the consumer or anyone else. This may be so, but some workers claim, and have substantiated their claims, that in answer to accurate efficiency tests, a person who has consumed only a small quantity of alcohol, will not respond quite normally.

But it is when a slightly greater amount of alcohol has been consumed that danger arises, and with it a difficulty in diagnosing drunkenness. In this stage/
Stage a person often becomes excited and there is loss of self control and will power. When a large quantity of alcohol has been consumed the effects are quite apparent and the case presents no difficulties if trouble has occurred.

McDougall and Smith (1919) tested their subjects by counting the number of errors made on a dotting machine, and by memory tests for related words. With both these tests the number of errors increased greatly even after taking only a moderate amount of alcohol although the subject might be convinced he was performing the tests very well. These tests were applied to fatigued subjects who had been given alcohol, as well as to normal ones. In some cases of fatigue the alcohol acted as a stimulant for a short time and improved the work done. This was never found with the normal rested subjects and not always, nor even very frequently, with the fatigued ones.

In his psychological tests for the effects of alcohol Mellanby (1920) found that incoordination appeared very soon after taking alcohol, generally within 30 to 40 minutes. The effects, however, began to disappear immediately after the alcohol in the blood had reached a maximum, even if the blood-alcohol value was still high.

In/
In a publication on alcohol and efficiency Miles (1921) stated that the general conclusion was that alcohol gave a decreased human efficiency soon after its ingestion. He observed the effect of alcohol on the number of typewriting errors, using trained stenographers as subjects. There was an increase in the number of errors by 25 to 30 per cent and a loss of speed. He noticed that alcohol had its maximum effect on the work from 30 minutes to 1½ hours after complete ingestion, that is, over the maximum part of the blood alcohol concentration curve. The effect was more prominent when concentrated doses of alcohol were used than with dilute ones. The taking of food just before or with the alcohol causes a marked decrease in its effects, and this is also noticed if a quantity of non-alcoholic liquor is taken one hour before or one hour after the alcohol. If the alcohol is taken in portions over a period of an hour there is decidedly less alcohol effect than if it was all ingested in 10 minutes.

Professor Sydney Smith (Henderson Trust Lectures, 1930) did not observe loss of efficiency with doses of less than 30 ccs. of alcohol. A factor which entered largely into his experiments, and of which other workers make little or no mention, is the imposing of the conscious will on their failing faculties by his subjects. If the cells of/
of the brain are damaged by alcohol as is supposed, how a mental process such as "willing" can decrease the effect of the alcohol is a mystery, but there is no doubt that persons under its effects can "pull themselves together" by a conscious effort and give results approaching normal in their tests.

All these workers were using only small and moderate doses of alcohol, and applied their tests to many types of subjects. Total abstainers, moderate drinkers and steady drinkers were all used for their experiments. The amount of alcohol given was varied in dilution, administered one time on a fasting stomach and at another on a full stomach, and water given sparingly one time and generously another. The reaction conditions were varied most comprehensively, but in every case the general conclusion is one of decreased efficiency, especially in skilled work.

Up to 1915 no work appears to have been carried out on the concentration of alcohol in urine as a measure of drunkenness. An examination of the blood of a person under the influence of alcohol gives, in many cases, a fair idea of the state of drunkenness he is in. Workers both before and after this time allow that there is a definite correlation between the state of drunkenness and the amount of alcohol/
alcohol in blood, at least for some time after ingestion of alcohol. Some hours after taking alcohol an analysis of either the blood or urine is of very little value as a guide to drunkenness, for reasons that will be given later.

Although of recent years the analysis of the urine of persons on trial for drunkenness has received much attention, Widmark (1915) appears to have been the first person to use this method of diagnosis. He analysed the urine of 27 people arrested for drunkenness and found alcoholic contents varying from 200 to 450 mg. per 100 cc. of urine. None of these persons were grossly intoxicated. If an alcoholic concentration of 450 mg. per cent had been obtained as a value for the alcohol in blood, the person would have been very obviously intoxicated, if not actually in coma. In 1916 Widmark published a paper comparing the blood and urine values of people who had been given alcohol experimentally. He found that for the first half hour after ingestion of alcohol the values for urine and blood were much the same. After this, the urine had an alcoholic value above that of blood, unless the concentration of alcohol in urine excreted over short periods was taken, when it agreed very nearly with the concentration of alcohol in the blood.

Chabanier/
Chabanier and Ibarra-Loring (1916) published a paper in the same year claiming to have substantiated Widmark's work independently.

Miles (1922) carried out extensive work on a comparison of blood and urine alcoholic concentration. Most of his subjects were young men in perfect health. Non-drinkers, moderate drinkers, habitual and occasional heavy drinkers were all used for his experiments. He found that for 20 to 40 minutes after ingestion of alcohol the concentration of the alcohol in the blood might even be slightly higher than that in the urine. After this time, and up to 120 minutes after consumption of the alcohol the concentration in urine exceeded that in blood.

While working on the effects of alcohol and its fate in the body Southgate (1925) found in the analysis of samples of blood and urine taken simultaneously that over a period of 1 to 6 hours after ingestion of alcohol the urine concentration exceeded the blood concentration by 40 to 50 percent, but that the ratio of these two concentrations, with urine always in this excess, was fairly constant over that period.

In 1930 Widmark published another paper on the excretion of alcohol and again found that the alcoholic/
alcoholic concentration in urine exceeded that in blood by 15 to 20 per cent for simultaneous estimations of these two fluids. He also found a definite comparison holding between whole blood and urine over a considerable after ingestion.

In a recent paper Smith and Stewart (1932) state that they do not regard the analysis of urine as a very valuable aid to a diagnosis of drunkenness. Carter takes .2% of alcohol in urine as the dividing line above which alcoholic value anyone is drunk. Widmark's earlier work, however, shows otherwise. Also, Smith and Stewart had cases who were excreting urine containing more than .2% of alcohol, and yet were classed as sober by police and psychological tests. From my experiments I would place the marginal value slightly higher - about .25%. Above this value nearly every subject was undoubtedly drunk. This at least was so in my work on animals.

It is not so difficult to set a value of alcoholic concentration above which drunkenness of quite definite, but it is almost impossible to set one below which everyone is sober. Smith and Stewart in their experiments had one case, where drunkenness had almost reached the state of coma, and yet the concentration of alcohol in the urine of this subject never reached .2%. Non-drinkers, not necessarily totally
total abstainers, but those who only take alcohol occasionally and in small amounts, nearly always show signs of intoxication when the concentration of alcohol both in their blood and urine is very much lower than it would have been in a person accustomed to alcohol and showing the same degree of alcohol effects.

There is another factor now generally recognised. Miles (1924) brings it forward in his report. This is, that the effects of alcohol are much more apparent on the rise of the concentration curves in blood and urine than on the fall. The psychological effects wear off much more rapidly than the concentration curves fall off. For the same concentration of alcohol in the blood or urine, it after the maximum as before, there is generally far less apparent effect, and far fewer errors occur in applied tests. Turner and Loew (1932), in their experiments on dogs, show that although alcoholic intoxication is quite definite at .25% of alcohol in the rise of the blood concentration curve, on the fall of the curve the animal may appear quite normal even although its blood has this value, or even higher. From this they suggest that the analysis of blood as a diagnosis of drunkenness is only of use if the sample is taken during the first two hours after ingestion.

The/
The same thing was found in the experiments quoted here. When a large dose of alcohol was administered to the animal, it generally passed into an alcoholic coma within half an hour of being dosed. In most cases it had at least partially recovered in 3 hours, and in 3½ to 4 hours after ingestion had apparently returned to normal. But even 4 hours after receiving the dose of alcohol the blood alcohol concentration was very little lower, if any, than when the animal passed into coma. Another set of experiments on the effect of alcohol on the oxygen uptake of brain (Robertson and Stewart, 1932) was being carried out simultaneously with these experiments on the distribution of alcohol in blood and tissues. The same animals were used for the two sets of experiments. Even 3½ hours after dosing with alcohol the oxygen uptake of the animals brain had not returned to its normal value but was rather lower. If fine enough tests could be devised it might be found that the return to normal was only “apparent” and that the abnormal brain metabolism was still producing a psychological effect, although not necessarily of the same kind as at the beginning of the experiment. No speculation or theory can be put forward on this subject until much further work has been done.

From the above data it is seen that with both human beings and animals the psychological effects/
effects of alcohol apparently pass off long before it is eliminated from the body. This holds both for small doses administered to human beings and for the large doses given to animals. Unfortunately large amounts of alcohol have to be given to the animals before alcoholic effects can be observed. Loss of muscular control, unless in trained animals, was the first observable effect. Alterations in breathing may be seen earlier than muscular effects but this comes outside the scope of my experiments. Such differences make a comparison between human and animal experiments very difficult.
METHODS.

A simultaneous set of experiments on the effect of alcohol on the oxygen uptake of brain was being carried out along with those on alcoholic concentration in tissues. The rabbits used for these experiments were also used for the oxygen uptake experiments. The method of dosing the animals is described in a paper published on the oxygen uptake work by Robertson and Stewart. In the distribution experiments, however, estimations were also made when the rabbit had been given a dose of alcohol of 4 ccs. absolute alcohol per kilogramme weight, and also when the dose had been administered by stomach tube instead of per rectum, as had been done for all the experiments on oxygen uptake work. When the alcohol was given by stomach tube there was no attempt to obtain an empty stomach by starvation of the animal, as even after three days without food the stomach was still not quite empty. The animals, as a rule, were used just after having been fed, so that uniformity was gained in that they all had full stomachs.

Whether the dose was 4 ccs. or 5 ccs. per kilo, it was made up to three times its volume with distilled water. These doses correspond roughly to/
to 400 and 500 mgs. per cent, administered in a concentration of 30% alcohol. Small doses were not experimented with at all. The concentration of alcohol given may seem rather high, but results were more quickly obtained by this means and that was what was desirable. It was wished to produce a definite state of drunkenness in the animals in 15 to 30 minutes after administration of the alcohol, and this it was found could only be obtained with concentrated solutions. In practically every case where the dose was 5 ccs. per kilo, extreme drunkenness was produced in 10 to 20 minutes after administration. Most of these animals went into coma within 30 minutes of being dosed. After being dosed the animal was put back into a cage and observed closely for the first half hour and a note made of the clinical symptoms produced by alcohol.

The rabbit, after sitting quietly in its normal position for about five minutes, in many cases then became restless and moved about the cage. Generally in 8 to 10 minutes after dosing it was incapable of moving without falling over sideways, and in 10 to 12 minutes it fell over on its side and remained in that position for at least 2 hours. Its breathing during this period was shallower and more rapid than usual. In quite a few cases where 5 ccs. alcohol per kilo had been given, the rabbits passed completely/
completely into a state of coma about 30 minutes after the dose. Most of them showed some signs of recovery from their stupor or coma in about 2 to 2½ hours after going into it - i.e. 2½ to 3 hours after having been given alcohol - and had apparently almost completely recovered in 4 hours, although the concentration of alcohol in the blood was still high. In some cases, however, the animal was still incapable of sitting in a normal position even 4 hours after alcohol, although in no case was the coma prolonged until that time. The rabbits were killed by a sharp blow on the back of the neck which snapped the spinal column. The brain was removed at once for the oxygen uptake experiments. The chest and abdominal cavity were then opened up. Blood was obtained from the heart and portal vein, and urine taken from the bladder with a syringe. Liver, kidney, muscle and fat, if it was obtainable, were removed for analysis. These were put into a small basin, covered with a watch glass and kept in the refrigerator until needed. Storing the tissues until they were needed at a low temperature would prevent, to a great extent, evaporation of alcohol from the tissues.

Estimations were carried out on animals which were killed ¼, ½, 1, 1½, 2, 3 and 4 hours after being dosed with alcohol. No blood was taken from an animal for an intermediate result - i.e. to obtain/
obtain the alcoholic content of its blood – say at 1 hour after being dosed when the animal would not be killed until 2 hours after its dose. All the results given here were obtained from tissues and fluids taken from the animals after death.

As well as the experiments on animals which had been given a dose of alcohol, control experiments were carried out on animals which had had no alcohol at all. In every case, both for the alcohol experiments and controls, an average was taken of several experiments where the same dose had been used and the same lapse of time between dose and killing had occurred. The average for the control experiments was subtracted from each of the averages for alcohol estimation. These control experiments were necessary as the results obtained from the normal tissues and fluids, calculated as ethyl alcohol, were by no means negligible.

2 ccs. each of blood and urine were used for estimation, and 2 gms. of tissue. The blood and urine were pipetted into tubes for analysis. The tissues were carefully weighed on a watch glass, transferred to an agate mortar and ground up finely with sand. The ground tissue was then transferred to the tube for analysis by washing it in with as little distilled water as possible.

The/
The alcohol was estimated by a method of Southgate's, described in a communication by Dr. Godfrey Garter. For these experiments, however, a simpler type of apparatus was used, than is described by Southgate in the Biochemical Journal, (1927). This apparatus is shown in Figure I.

The apparatus consists of two large boiling tubes of about 100 ccs. capacity. The inlet tubes of both A and B extend almost to the bottom of these two boiling tubes, that of B terminating in a Sinter glass sprinkler. A and B are connected together as shown, by a piece of rubber tubing. The outlet tube from B is connected to a filter suction pump. By this means a current of air is drawn through the whole apparatus, which is immersed in a water bath at 80°C. Alcohol exists as vapour at this temperature, and so is sucked over from A to B.

In tube A is placed the blood, urine or tissue for analysis. Tube B contains 10 ccs. $\frac{N}{10}$ potassium dichromate and an equal volume of concentrated sulphuric acid. The alcohol vapour is sucked over from A to B and is broken into fine bubbles by the Sinter glass sprinkler, so that good contact is ensured between it and the dichromate-sulphuric acid mixture. In tube B the alcohol is oxidised to acetic acid by the dichromate-sulphuric acid mixture, according/
Figure I:

Apparatus used in these experiments for the estimation of alcohol in blood, urine and tissues.

- Water bath at 80°C.

A B

To suction pump.
ing to the equation -

\[ \text{CH}_3\text{CH}_2\text{OH} + 2(0) = \text{CH}_3\text{COOH} + \text{H}_2\text{O} \]

Alcohol \hspace{1cm} \text{Acetic Acid}

The suction is continued until the contents of A have been evaporated to dryness. The distillation is then stopped and the contents of B washed carefully and thoroughly, with distilled water, into a titration flask. The excess of potassium dichromate left after the oxidation of the alcohol has been completed is then estimated volumetrically. This is done by adding excess of an approximately 0.04% solution of potassium iodide to the acid-dichromate mixture washed into the titration flask from B. The acid-dichromate solution liberates iodine from potassium iodide in an amount equivalent to the amount of potassium dichromate present. This free iodine is at once titrated with \( \frac{N}{10} \) sodium thiosulphate solution, the iodine disappearing in equivalent amount to the thiosulphate added. Starch solution is used as an indicator for the end-point of the titration. The starch is not added until the brown colour of the iodine is becoming very faint. It is inadvisable to add starch while the iodine is present in large amounts, as in concentrated iodine solutions the blue iodide of starch tends to be precipitated in the solid form which is less readily acted upon by the thiosulphate.

\( \frac{N}{10} / \)
N sodium thiosulphate is equivalent to $\frac{N}{10}$ potassium dichromate, so that the number of ccs. of thiosulphate used in the titration will give the number of ccs. of dichromate unreduced by the alcohol vapour. This number is subtracted from the original amount of potassium dichromate taken, thus giving the number of ccs. of $\frac{N}{10}$ potassium dichromate reduced by the alcohol in 2 ccs. of blood or urine, or in 2 gms. of tissue.

From the equation -

$$\text{CH}_3\text{CH}_2\text{OH} + 2(\text{O}) = \text{CH}_3\text{COOH} + \text{H}_2\text{O}$$

it is seen that 1 molecule of alcohol requires 2 atoms of oxygen. Now 1 litre of N potassium dichromate yields $\frac{1}{2}$ an atom of oxygen, and, therefore, is equivalent to $\frac{1}{4}$ of a molecule of alcohol - i.e. $\frac{46}{4}$ gms. of alcohol are equivalent to 1,000 ccs. N potassium dichromate. Therefore, 1,000 ccs. $\frac{N}{10}$ potassium dichromate equals $\frac{46}{40}$ gms. of alcohol - i.e. 1.15 gms., so that 1 cc. $\frac{N}{10}$ dichromate equals 0.00115 gms. of alcohol. The number of ccs. of potassium dichromate reduced during the distillation, which is obtained from the titration, multiplied by 0.00115 will give the number of grammes of alcohol contained in the 2 ccs. of blood or urine, or the 2 gms. of tissue. This value multiplied by 50 will give the alcoholic contents of the fluid or tissue as a percentage.
RESULTS.

The maximum alcohol concentration in blood.

It is generally stated that the maximum concentration of alcohol in blood is not reached until 60 to 90 minutes after the ingestion of alcohol. Cushny (Pharmacology and Therapeutics) states that the maximum concentration of alcohol in the blood is reached 1 hour after ingestion, but Schweisheimer (1913) obtained his highest values 1½ to 2 hours after taking alcohol. Mellanby (1919), on the other hand, showed that the maximum blood concentration for alcohol occurs sooner than this. He obtained a maximum value about 1 hour, or even a little earlier, after consumption of the alcohol, and found that the maximum reached is proportional to the amount administered. His experiments were done using dogs. Although the maximum was reached very rapidly the disappearance of alcohol from the blood is very slow. At an earlier date than this Gréhant (1899) also worked on alcohol elimination experiments, using dogs as the subjects, and he obtained a maximum concentration of alcohol in blood about 1 hour after ingestion. He also found that for a considerable time after the maximum was reached the concentration of alcohol in blood did not fall very much below the maximal/
maximal value. This prolonged high region in blood-alcohol concentration curves became known as "Gréhant's Plateau". The larger the dose of alcohol administered the more quickly the maximum is reached and the longer the blood-alcohol value stays in the region of "Gréhant's Plateau". This worker also found that the elimination of alcohol from the blood was very slow.

Cushny and Schweisheimer were quoting re-experiments on results obtained from human beings, where relatively small doses had been administered but the last two workers mentioned were both experimenting with animals and were using much larger doses, so that an earlier maximum of alcohol concentration in the blood would be expected.

In my experiments, where rabbits were used as the subjects, the maximum for the blood-alcohol concentration occurred about 30 minutes after administration of the alcohol, where the alcohol had been administered per rectum, and about 40 minutes after ingestion when it had been given by stomach tube. This, although slightly earlier than the time obtained by Mellanby and Gréhant in their experiments was not unexpected, as a higher dose of alcohol was being given than in any of Mellanby's experiments or most of Gréhant's. The latter when using the same dose of alcohol as was administered in this work - i.e./
- i.e. 5 ccs. absolute alcohol per kilo. of body weight, found that his animals generally passed into a state of coma and that the blood alcohol concentration remained in the plateau region for a period of 1 to 2 hours. As will be seen from the diagrams given later this was obtained in my work.

The actual maximum reached in these experiments was very high, but this was to be expected with the large and concentrated doses that were being given.

When a dose of 5 ccs. of absolute alcohol per kilo. of rabbit was given the fall in the concentration of alcohol in the blood from the maximum value was very slow. The "Grehant Plateau" extended over a period of 2½ hours and even after that the fall in the curve was very gradual. As long as 4 hours after dosing with alcohol the value for blood was still very little lower than the maximum value. Grehant (1900, 1903) gives the time of elimination of alcohol from the blood for a dose of 5 ccs. of absolute alcohol per kilo., given by stomach tube, as 20 to 23 hours. If the curve obtained for a 5 ccs. per kilo. dose, given per rectum, in these experiments was extended to meet the base line, the blood alcohol value would reach zero about 23 to 2¼ hours after ingestion.

When/
When this dose was administered by stomach tube instead of per rectum, the maximum concentration of alcohol in the blood reached was almost as high as that obtained with a rectal dose. The value fell off a little more rapidly however, than in the former case, but had only fallen to a value 50 mgs. below its maximum value in two hours after ingestion of the alcohol.

If 4 ccs. of absolute alcohol per kilo. was the dose given, whether per rectum or by stomach tube, the fall of the curve for the concentration of alcohol in blood, from the maximum value, was very much more rapid than when the larger dose had been administered, although the actual maximum reached was very little lower. There was no "plateau" when a dose of 4 ccs. per kilo. was used. The fall from the maximum was more rapid when the dose was administered by stomach tube, than when it had been given per rectum. There was a slight trend for the maximum blood-alcohol value to occur a little later when the dose was given by the stomach. This is due to delayed adsorption of the alcohol from the stomach, in reason of the food contained in it.

In general I found that the maximum concentration of alcohol in the blood was reached a little earlier than is stated by those workers who were using human/
human beings as subjects, and giving only moderate doses of alcohol, but was comparable to the time the maximum was reached by workers using animals and administering doses of the same order as those stated here.

The actual curves obtained for the concentration of alcohol in blood, with different doses and different methods of administration are shown in Figure II.

With a dose of 4 ccs. of absolute alcohol per kilo. administered by either method, and 5 ccs. per kilo. administered by stomach tube, experiments were not done on animals which had had alcohol for longer than 2 hours. The more rapid decrease in the concentration of alcohol in the blood, from the maximum value, when the smaller dose has been administered, is quite apparent in the curves shown.

A correction has been applied in the curves given here for the value of ethyl alcohol in the blood from control experiments.

**Comparison between the alcohol in blood and urine.**

Earlier workers had made extensive comparisons between the concentrations of alcohol in blood and urine, in an attempt to gauge the alcoholic content of blood from that of urine. If a determination of the amount of alcohol in urine can give a fairly/
Concentration of alcohol in blood with doses of 4 ccs. and 5 ccs. of absolute alcohol per kilo., administered by stomach tube and per rectum.
fairly accurate measure of the amount of alcohol present in the blood at the time the urine sample is taken, the analysis of urine as a diagnosis of drunkenness would be of great value, as it is held that, for at least 2 hours after ingestion of alcohol, the curve for the concentration of alcohol in blood is parallel to the intensity of the effects of alcohol. Schweisheimer said that the concentration in blood is parallel throughout its whole course with the intensity of intoxication. Now, however, as will be shown later, it is thought that this parallelism only holds for about 2 hours after the ingestion of the alcohol.

From any person arrested for drunkenness a urine sample can, as a rule, be easily obtained, but this is not always the case if a blood sample is desired. The accused person can refuse to allow a sample of his blood to be taken.

Widmark, Southgate and Miles all obtained urine values of a higher alcoholic concentration than those of blood, obtained at the same time. This superiority of the alcoholic concentration in urine over that in blood, persists over a period of 1 to 6 hours after ingestion of alcohol. All these experimentors used human beings for their work. Miles, in the earlier stages of alcoholic intoxication, that is up to 40 minutes after taking the alcohol, stated that the concentration of alcohol in the blood had a higher value than that of the urine, but that the urine/
urineconcentration soon rose above the blood level, and continued there for some hours. He found that blood and urine both reached their maximum concentration at about the same time, and that while the two values were not identical, the concentration of alcohol in urine is useful as a comparison for the blood value, and the effects of alcohol on the central nervous system.

The curve for the concentrations of alcohol in blood and urine in my experiments, is shown in Figure III. These values were all obtained from animals which had had a dose of alcohol of 5 ccs. per kilo., given per rectum.

The values obtained for the concentration of alcohol in urine in these experiments were, at least when the animals had been killed a short time after ingestion of alcohol, not at all comparable with those for blood. The alcoholic concentration in the urine did not rise rapidly to a sharp maximum, as it did in blood, but rose very gradually and was only approaching its maximum value about three hours after ingestion of the alcohol. As long as 2 hours after the dose had been administered, the concentration of alcohol in the urine was still decidedly lower than that in blood. From these results no idea of the amount of alcohol in blood could be obtained from an analysis of a urine sample for at least 2 hours after the start of the experiment. From 2 to 4 hours after ingestion/
Figure III:

Concentration of alcohol in blood and urine with a dose of 5 ccs. per kilo, given per rectum.
ingestion of the alcohol the concentrations in blood and urine are tending towards one-another, and in this region a rough estimate of the blood value might be obtained from a urine analysis. At about 4 hours after ingestion, beyond which time no experiments were carried out, the urine alcohol concentration curve shows a tendency to cross the blood curve and proceed on a higher level. The alcohol in urine in these experiments did not exceed that in blood until a much later time than was usually found. It was generally found that urine had a higher value of alcohol than blood from 40 minutes after ingestion of the alcohol, whereas in these experiments at no point did the urine value actually exceed the blood, but only seemed, from the curves obtained, to be still increasing after 4 hours had elapsed, by which time the blood alcohol concentration was steadily decreasing.

It must be remembered that these experiments were being done with animals and no information as to the state of the bladder at the beginning of the experiment was sought, whereas the other workers were using human beings and so had control over such factors.

The animals would have had to be catheterised in order to obtain an empty bladder at the beginning of the experiment, and this was thought inadvisable on account of the nervous upset to the animal. Brain/
Brain metabolism experiments were being done using these same animals, and on account of this as little mental disturbance as possible was desired, either at the beginning of, or throughout the experiment. It was desired that, if possible, all alteration in the oxygen uptake of the brain tissue should be able to be ascribed to the effects of the alcohol, and to that only. This would hardly have been so, if the animal had been subjected to any mental strain, such as would have taken place during catheterisation. Such a disturbance might or might not upset the oxygen uptake of the brain to any appreciable extent, but it was undesirable to risk any alteration for other causes than the one under observation.

The lack of control of this factor may offer some explanation of the discrepancy of my results from those obtained by other people. With human beings the experiments could be started, and as a rule were, after the bladder had been emptied, and this could also be done at regular intervals, and urine samples obtained when desired. The length of these intervals could be regulated to the requirements of the experiment as was desired. In my experiments the bladder may have been in any state from empty to very full, at the beginning. Also, complete retention of urine, throughout the time that elapses between dosing and killing, could not be guaranteed, and in work lasting several hours this very seldom happened. The rabbit, as/
as a rule, in experiments lasting longer than 2 hours, at least partially emptied its bladder. No attempt was made to procure a specimen of this urine evacuated, and subject it to analysis for alcoholic content, as only results at the end of a stated period were desired. These uncontrollable factors were bound to affect the results obtained.

If the bladder was full at the commencement of the experiment, one would expect a low concentration of alcohol in the urine obtained from the bladder, although the urine being excreted from the kidney might have a high alcoholic concentration. This would probably be especially noticeable in those experiments where the animal was killed a short time after being dosed. In fact, if this were the case, the concentration of alcohol in the urine in the bladder would assume a lower level even in those experiments where the animal was not killed until 2 or 3 hours after it had been dosed, provided the bladder had not been emptied during that period, than would have been obtained from an analysis of the urine actually being excreted from the kidney, if such an estimation had been possible. The higher values obtained in the experiments where the animal had been under the influence of alcohol for 3 or 4 hours before being killed might ascribed to the fact that, as has been stated, the animal had generally emptied its bladder, at least partially, by this time. The urine obtained/
obtained for analysis at the end of 3 or 4 hours would therefore, be showing the true value, or at least one nearer the truth, of the alcohol in the urine excreted from the kidney. Earlier values for the alcoholic concentration of the urine were really values for an amount of alcoholic urine diluted with urine already in the bladder before alcohol was introduced into the system.

It is more than likely that the curve for the alcoholic concentration of urine obtained under the conditions of working stated here, gave an entirely false record of the amount of alcohol being excreted into the urine, although the results given show the actual concentration of alcohol in the urine, contained in the bladder at the time the animal was killed.

A "calculated", or theoretical curve for the concentration of alcohol in urine was worked out. It is assumed for the purposes of calculation of this curve that urine is being excreted from the kidney into the bladder at a steady rate. It is of course, understood that this would not be so, as alterations in blood pressure, nervous disturbances and the addition of water to the system in dosing with the alcoholic fluid, would all alter, in one way or another, the secretion of urine. Miles states that the amount of urine excreted per minute appears to have little effect on the concentration of alcohol in the urine, when the urine is collected over short intervals.
He does not state that this would hold for urine samples collected over a long period.

The first results obtained in these experiments, were for the concentration of alcohol in urine \(\frac{1}{4}\) of an hour after the animal had been dosed with alcohol. The average of these results obtained at \(\frac{1}{4}\) of an hour was used as a basis for the calculation of the theoretical curve. The basic result used for this calculation should really be the concentration of alcohol excreted during the first minute after dosing. Such a short interval of time would probably have given very inaccurate results, so it was decided to use the earliest results obtained as the standard. It is not suggested that the theoretical curve is a true representation of the excretion of alcohol in urine, but that it is probably nearer the truth than the alcoholic excretion represented by the curve for the concentration of alcohol in urine obtained from these experiments, and shown in Figure III. The theoretical curve obtained by calculation is shown in Figure IV.

Both in Figures III and IV a correction has been applied for the blank values of blood and urine.

The average concentration of alcohol in urine for the first 15 minutes after the dose of alcohol had been administered, was 105 mgs. per 100 ccs. of urine. This value used as the basis of the calculation for the theoretical curve. Let it/
Theoretical curve for the excretion of alcohol in urine.
it be supposed that the urine is being excreted at the steady rate of "a" ccs. every 15 minutes. Figure V shows the method of calculation of this theoretical curve.

In the first \( \frac{1}{4} \) of an hour after the dose has been given, X mgs/ per 100ccs. of urine is the concentration of the alcohol in the urine. Therefore, \( \frac{ax}{100} \) is the amount of alcohol contained in a ccs. of urine in the first \( \frac{1}{4} \) of an hour. In \( \frac{1}{4} \) an hour 2a ccs. of urine have been excreted into the bladder. From Figure V it is seen that Y mgs. of alcohol per 100 ccs. of urine is the concentration of alcohol actually obtained, but \( \frac{2ay}{100} \) mgs. is the amount of alcohol excreted into the urine in half an hour. Therefore, during the second \( \frac{1}{4} \) of an hour \( \frac{2ay - ax}{100} \) mgs. of alcohol are excreted into "a" ccs. of urine, i.e. \( \frac{a(2Y - X)}{100} \) mgs. of alcohol. The values for X and Y may be obtained from the actual curves for the concentration of alcohol in urine given in Figure III. The percentage concentration of alcohol in urine excreted in the second \( \frac{1}{4} \) hour is, therefore, \( \left( \frac{a(2Y - X)}{100} \times \frac{100}{a} \right) \) mgs., or \( (2Y - X) \) mgs. per 100 ccs. of urine.

In this way it was calculated what percentage of alcohol should have been excreted each successive \( \frac{1}{4} \) of an hour, had the excretion of urine remained constant throughout the experiment.

The theoretical curve for the concentration of/
Graph demonstrating the method of calculating the theoretical curve for the concentration of alcohol in urine.
of alcohol in urine gives a urine value lower than that of blood up to 1 hour after ingestion of the alcohol. From 1 to 2 hours, or even \(2\frac{1}{4}\) hours after ingestion, the values for the alcoholic contents of blood and urine certainly could be said to be approximately equal, but all the time the alcohol in urine is mounting to a value above the concentration of alcohol in blood. Beyond the 2 hour period the concentration of alcohol in urine is always distinctly higher than that in blood, or at least is so up to 4 hours after ingestion of alcohol, after which time no experiments were carried out. Such a high percentage difference as that obtained by Miles, who got his urine values 40-50% higher than his blood, was never reached by this theoretical curve. He, however stated that if the alcohol is taken in a concentrated form, the urine value, although still above that of the blood, is not so much so, as if the alcohol had been taken in a dilute form. The dose used in these experiments was very concentrated, being almost 30% of alcohol, and that may, therefore, account for the close approximation between the two curves for alcoholic concentrations, or at least in part account for the low urine alcohol values. Miles also found that if the secretion of urine is slight, the concentration of alcohol in the urine may be depressed almost to the blood level. In the majority of cases it by no means happened that the bladder/
bladder was very full when the animal was disected, but often there was hardly enough urine to be obtained, for an analysis, and in a few cases none at all.

From these results, as from the work of Miles and Widmark, it will be seen that an analysis of urine for the concentration of alcohol in it, is not of very much use as a guide to the concentration of alcohol in blood, and therefore, as a diagnosis of the state of drunkenness in an accused person. All that really can be proved from such an analysis is that the person has inbibed alcohol, and of course, if the concentration of alcohol in the urine is very high, considerable alcohol must have been taken. If it was known what time had elapsed since the ingestion of the alcohol and approximately the concentration of alcohol in the beverage which had been consumed, a better diagnosis could be made from an urine analysis. Such data, however, are almost impossible to obtain.

The object of the theoretical curve was to see if a totally different concentration of alcohol in the urine would have been obtained if the experiments had been carried out under conditions such as were used by the workers with human subjects. The assumption of a steady secretion of alcohol, and all that is implied to ensure this condition, was the device selected to get the desired result.

**Distribution of alcohol in tissues.**

It/
It is generally agreed that alcohol is to be found in all the tissues of the body in considerable amount quite soon after ingestion of even a moderate amount of alcohol, except in the fat and bone, the former taking up very little, on account of its poor blood supply, and the latter practically none at all. It has been thought, however, that all tissues might not contain alcohol in the same amount, but that some might have a preferential absorbing power to others.

Fridmann (1901), in a thesis, stated that he obtained a concentration of alcohol in brain tissue higher than in any other tissue. Vollmering (1912) obtained the same results from his analysis of the concentrations of alcohol in tissues. Both these workers were using animals for their experiments. Neither of these two theses could be obtained for further investigation, and Miles in his publication of the Carnegie Institute of Washington (1924) gave no further reference to their work. In a series of experiments on the alcoholic content of the tissues of fowls, Carpenter (1919) gave results for many tissues. The alcohol, in this case, was administered by inhalation. The alcoholic content of the tissues in his experiments, in a descending order of magnitude, are, blood, heart, brain, kidney, muscle, liver and fat. Figure VI shows the curves obtained for the alcoholic contents of the various tissues used in these/
Concentration of alcohol in tissues and blood, at various times after ingestion, when a dose of 5 ccs. per kilo, had been given.
these experiments here.

In my experiments blood, brain, kidney, liver, muscle, fat and urine were analysed. The alcoholic contents of these tissues and fluids, excluding urine, in a descending order of magnitude, are blood, brain, kidney, liver, muscle and fat. Heart tissue was never analysed for alcoholic content in my experiments.

At the peak of the concentration curves the brain value exceeds the kidney, as is stated, but later on the kidney value is slightly in excess of that obtained for brain.

Carpenter found that muscle had a higher alcoholic content than liver, which is the reverse order from that obtained in my experiments. But he mentions that his fowls remained active throughout the time of the inhalation of the alcohol, and, therefore, their muscle would attain a higher alcoholic content than that of an inactive or comatose animal. He carried out some experiments with rabbits which he had rendered comatose with alcohol, and found that the alcoholic content of the muscle was the lowest of all the tissues except fat. Nearly all the animals used in my work were in a state of coma, or at least so far under the influence of alcohol as to be totally inactive. The reverse order of the muscle and liver contents for alcohol from these quoted by Carpenter in his experiments on/
The shape of the curve, in Figure VI, for the alcoholic content of muscle, lends itself to this theory. With those experiments where the animal had had alcohol only a short time, say up to 1½ hours before it was killed, they were all in coma. When there was a lapse of 3 or 4 hours between administration of the alcohol and the killing of the animal, it had come out of its coma, in the majority of cases, and if not exactly what could be termed "active", it was at least moving about a little. The alcoholic content of muscle is very small up to 1½ hours after dosing the animal. Its value is much below those of other tissues. With the animal killed after a longer interval, the concentration of alcohol in muscle is of the same order as that of the other tissues.

It will be seen from Figure VI that the concentration of alcohol in tissues follows that in blood very closely, although at a lower level. This is especially so of the alcoholic contents of brain and kidney, which are parallell to that of blood throughout the whole of their course. Gettler and Tiber (1927) say that the alcoholic content of the brain gives the best and most consistent indication of the degree to which the alcohol has influenced the subject. In persons, however, such an estimation is impossible unless they have died of alcoholic poisoning. Since the/
the blood and brain curves for the concentrations of alcohol contained in them are entirely parallel; an analysis of the blood alcohol concentration would give a measure of the brain alcohol concentration, and so an indication of the intensity of the effects of alcohol.

The points shown on the alcohol concentration curves in Figure VI, except at $\frac{1}{4}$ of an hour and 1 hour after ingestion, for the values of brain matter show an alcohol content of about 250 mgs. %. The value at $\frac{1}{4}$ of an hour is just over 200 mgs. % and is the average of several values. All the animals with a concentration of alcohol in their brain of 200 mgs. per 100 gms. of tissue, or over, were extremely drunk. This holds good not only for a dose of 5 ccs. per kilo., but for a dose of 4 ccs. per kilo., and for the two methods of administration. When a dose of 5 ccs. per kilo. given per rectum, was used there is no record of an animal being classed as anything else but extremely drunk, until 3 hours after ingestion. The animals which had had alcohol 3 and 4 hours before being killed, were classed as moderately drunk, as a rule, although their was one case where the animal was still very drunk after 3 hours.

A diagnosis of the animal's state is extremely difficult. Only the most obvious signs of intoxication can be used as a guide. If a person could not move without falling over, then they would be classed/
classed, not as moderately drunk, but as very drunk. By comparison with animals in a much worse plight, a rabbit, which could sit in its normal position, even although on the slightest movement or with the gentlest of pushes, it "staggered", and generally fell, was termed moderately drunk.

In several cases it was recorded that the animal showed no signs of intoxication at all. All these cases had been given a dose of 4 ccs. per kilo., by stomach tube. Neither the blood or brain values had reached 200 mgs. %, in fact the average brain values for these cases was 140 mgs. %, and blood about the same. The blood value did not exceed the tissue values be a large amount, as had been the case when the animal was grossly intoxicated and had high blood and tissue alcohol contents.

A curious point that strikes one in the graphs shown in Figure VI, is that there are two maxima. The first maximum occurs about 30 minutes after ingestion, and is regarded here as the true maximum. When the animals had been killed 1-1 ½ hours after being dosed with alcohol, a lower value is obtained, but when a longer period is allowed to elapse between ingestion and death, the concentration of alcohol in blood again rises and about 3 hours after dosing has reached another maximum. The second rise in the blood alcohol curve, and the tissue values too, is very gradual, and the second maximum not sharp and
and definite. In the case of blood there is only a rise of 12 mgs. of alcohol per 100 ccs. in 1½ hours. The maxima and minimum occur in tissues at the same times after ingestion as in blood, except in fat which has no second maximum. In every case except muscle, the second maximum is lower than the first. A possible explanation of the deviation of the curve for the concentration of alcohol in muscle from the usual type obtained, has already been put forward.

Turner and Loew in their graphs for the concentrations of alcohol in blood, obtained what they called a "staircase" descent, from their first maximum value. Figure VII is a reproduction of two of their graphs. In graph A the animal was given the dose of alcohol on a fasting stomach. The maximum concentration of alcohol was reached 1 hour after ingestion, and was approaching 0.4% of alcohol. When as in graph B the dose was administered half an hour after food, the blood alcohol concentration reached its maximum in ½ hour but only achieved a height of 0.21% of alcohol. In both cases 3 gms. of absolute alcohol per kilo., given in a 10% solution, was the dose administered. In the first case the fall from the maximum is fairly rapid but not entirely steady, a second, although lower maximum occuring 4 hours after ingestion. In the second case there is an irregular rise and fall of the concentration of alcohol in the blood until 6 hours after the animal/
Figure VII:

Turner and Loew's graphs:— Alcohol absorption in dogs: A - fasting; B - ½ an hour after a meal.

Ingestion of a 10% solution of alcohol in one dose.
animal has been dosed. Each rise after the initial maximum is lower than the one before it, but in the second case, where food had been taken, very little so.

The time of the maximum in the latter case, and the general outline of the graph for the concentration of alcohol in blood up to six hours after ingestion, is very similar to the results obtained in the experiments quoted here, for the alcoholic contents of blood and tissues of animals killed at times varying from \( \frac{1}{4} \) to 4 hours after being given alcohol. The actual level attained by the blood alcohol is very much higher than that got in Turner and Loew's experiments. They were using a dose of alcohol of only 3 gms. per kilo., whereas, in the other case, the dose was 5 ccs. per kilo., which is very nearly 5 gms. per kilo. A higher concentration both in blood and tissues would therefore be expected in my experiments. It has been stated that the animals used in my experiments were usually used just after having been fed.

The experiments demonstrated here did not go beyond 4 hours after ingestion of alcohol, and it had been assumed that after the second rise of the blood content at 3 hours, that the concentration of alcohol in blood fell to zero at a steady rate. Turner and Loew examined blood samples for alcoholic content up to 6 hours after ingestion and found, as can
can be seen from their graphs, that the slight fluctuations in the blood alcohol, continued up to that time.

Various explanations were sought to explain the results obtained in my experiments, but none were very satisfactory. Since it has been demonstrated that these irregularities occur for 6 hours after ingestion, and therefore, probably throughout the whole course of the fall in concentration of alcohol in blood and tissues, they are probably only due to slight bodily and mental disturbances in the animal, and not to any complicated chemical or physiological process that is taking place, except as a result of these disturbances.
DISCUSSION.

From the results given here, and from those of previous workers, it will be seen that a diagnosis of drunkenness from the excretion of alcohol into urine, is almost impossible. Even an analysis of the blood of a person arrested for drunkenness might be of no use at all. The personal reaction to alcohol is the most difficult factor to deal with. The fact that no two people react in the same way after consumption of alcohol makes a diagnosis of the amount they have consumed very difficult. Added to this, there is the fact that for the same dose of alcohol, the concentration of alcohol in the blood of two separate persons has rarely reached the same level after a similar lapse of time. The amount of alcohol consumed, its dilution, whether it is taken over a long period or gulped down, the person's mental and physical state at the time of ingestion—all these factors alter to a great extent the effect of the alcohol both physiologically and physically. By physically is meant the concentration of alcohol reached in blood and tissue and the amount excreted in urine. The lack of control over, and knowledge about, one physical factor—the state of the bladder—during experimentation is amply demonstrated in the/
the results given here. With this one piece of knowledge lacking the results obtained are useless for diagnostic purposes, and here all other factors such as the amount of fluid given and the time elapsed after dosing were perfectly controlled. The difficulties of drawing conclusions from urine analysis would be increased greatly if, as is likely to be the case, all knowledge of times, doses and methods of consumption were unknown. If a specimen of urine can be obtained that had been excreted over a short period after the arrest, then, some indication of the amount of alcohol in the blood could be obtained from it.

If a person had consumed a quantity of alcohol in a short period, and had had no further consumption of an alcoholic liquor, then an analysis of a blood sample would be of great use in diagnosing the extent of the effect of alcohol, provided the time that had elapsed since the ingestion of the alcohol was known. If, however, repeated doses of alcohol be taken, even if they are small ones, the maximum concentration of alcohol in blood is reached by a "staircase" ascent. Therefore, the highest maximum attained is not reached until a much longer time has elapsed from the start of ingestion, than if the alcohol had all been consumed in/
in a short period. Lacking a knowledge of such factors, however, it would be difficult even from an analysis of blood to obtain an idea of the intensity of alcohol effects from the concentration of alcohol obtained in the blood. Also, as has been stated, on the downward portion of the curve for the concentration of alcohol in blood, the blood may have a value higher than on the rise of the curve and the subject be showing effects of alcohol much less. For this reason the time that has elapsed since ingestion of the alcohol is important.

Although as an absolute diagnosis of drunkenness an analysis of blood or urine is valueless, such an estimation is very useful in that it will give the minimum amount of alcohol that must have been ingested. If a knowledge of the variable factors enumerated, which effect the rise of alcohol in the blood and its excretion in the urine, can be obtained, then the analysis might give an absolute measure of the effects of the alcohol. Persons arrested for drunkenness are rarely, however, helpful in supplying such details.
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