Observations on the Distribution of Alcohol in Blood, Breath, and Urine

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Brit. med. J., 1966, 1, 196–202

The effect of ethyl alcohol on the central nervous system is similar to that of a general anaesthetic, but fortunately, because of its high solubility in water, the amount required to produce the degree of saturation necessary for narcosis is greatly in excess of that commonly consumed. In practice, therefore, ethyl alcohol has only slight effects on the brain. These slight effects, however, may have important repercussions in certain circumstances ; for example, there is evidence that even small amounts of alcohol in blood are sufficient to impair the performance of tasks demanding skill and accuracy (Drew, Colquhoun, and Long, 1958). The amount needed to produce such impairment varies from one individual to another (Cohen, Dearnaley, and Hansel, 1958), but since performance begins to deteriorate with blood-alcohol concentrations of the order of 20–30 mg./100 ml. (Drew *et al.*, 1958) the factor of individual susceptibility is less important than the amount of alcohol in the blood.

When the task is one which exposes others to risk, such as driving, then impaired ability becomes a social problem. It is for this reason that Governments in many countries have imposed a statutory limit on the amount of alcohol a driver may have in his blood. The law in these countries does not suggest that a driver with a blood alcohol in excess of the statutory limit is drunk ; it simply states that it is an offence to drive when the blood alcohol exceeds the stipulated level. The situation is exactly analogous to that which exists when a speed limit is imposed. The law does not state that a driver is incompetent when he exceeds the speed limit ; it merely states that an offence is committed when he does.

The arguments in favour of restricting the alcohol intake of drivers are unanswerable, and in the near future legislation will be introduced in this country to make it an offence to drive with more than a given amount of alcohol in the blood. It is therefore important to know whether a direct determination of blood will be needed for law-enforcement purposes or whether the blood-alcohol level can be deduced from the amount present in breath or urine. Accordingly the studies to be described were undertaken to examine the relationship between alcohol levels in arterial and venous blood and those in breath and urine.

Methods

Experiments in Dogs

The first experiments were carried out on 10 mongrel dogs of both sexes weighing between 6.7 and 15.5 kg. After induction of anaesthesia with thiopentone 5 mg./kg., given intravenously into a foreleg vein, the dog was intubated and anaesthesia maintained with a 4–5 litre flow of a 50% mixture of nitrous oxide and oxygen supplemented when necessary by 0.5–1% halothane and administered through a semi-closed non-rebreathing system.

Once anaesthesia was established a 50-cm. polyethylene tube was passed through the mouth into the stomach in three dogs. In the remaining seven dogs the tube passed into the stomach was guided into the duodenum through a small incision about 5 cm. long in the midline of the upper abdominal wall immediately below the sternum. A second 5-cm. incision was made in the midline of the lower abdomen through which both ureters were mobilized and tied immediately above their insertion into the bladder. Both ureters were opened immediately proximal to the ligature and polyethylene catheters of 2.08 mm. external diameter and 10 cm. in length inserted for a distance of about 5 cm. before being tied in position. The distal end of each catheter was led out through the abdominal wound and connected to a second catheter of the same length, which was allowed to drain continuously into a test-tube. Urine samples were collected by clamping the proximal end of the distal catheter, disconnecting, and draining the urine into a suitably graduated pipette.

In three experiments the ureters were catheterized just distal to the pelvi-ureteric junction opposite the lower pole of the kidney, but in this position the catheters were easily dislodged by respiratory movement, and on two occasions bleeding from the kidney pelvis made the urine analyses worthless.

In all animals catheters were placed in the left femoral artery and vein for the collection of samples of arterial and venous blood. In some animals catheters were placed in the internal jugular vein, in the right ventricle, in the pulmonary artery, and in the inferior vena cava just before it enters the heart. The position of these catheters was confirmed at post-mortem examination after completion of the experiment.

The blood-pressure was measured by means of a glass cannula placed in the right carotid artery and connected by a column of heparin-saline to a mercury manometer recording on a smoked drum.

When the necessary preparations had been completed alcohol 1–3 g./kg. in various dilutions of water was washed through the polyethylene tube into the duodenum ; thereafter arterial and venous blood samples and urine samples were collected for analysis at 20-minute intervals. The urine samples were collected as described ; the blood samples were collected anaerobically into 10-ml. syringes the dead space of which had been filled with heparin-saline 10 mg./ml.

Experiments in Human Volunteers

The second series of experiments was carried out on 24 male volunteers between the ages of 19 and 62 years. On arrival in the department after a light breakfast each volunteer was shown the equipment used and the nature of the experiment was explained to him. At this stage each subject was given the opportunity to withdraw from the study if he so desired.

In 14 volunteers the radial artery was cannulated percutaneously immediately proximal to the wrist-joint after infiltration with 1% lignocaine of the overlying skin and the tissues around the vessel. For this purpose a Braun needle and cannula (size 1) were used. Once the needle had penetrated the artery the overlying cannula was advanced gently until about 3–4 cm. lay within the lumen of the vessel, when the needle was withdrawn. A three-way tap was connected to the cannula, which was filled with heparin-saline solution 10 mg./ml. Usually the left radial artery was catheterized, but if the volunteer was left-handed the right was preferred.

With the use of a similar percutaneous technique a polyethylene catheter was placed in a convenient superficial vein

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on the forearm of all volunteers ; in those with a radial catheter in position the insertion was made on the same forearm. As soon as the catheters had been inserted control blood samples were taken anaerobically into 10-ml. syringes, the dead space being filled with heparin-saline solution (10 mg./ml.). A control specimen of urine was collected about the same time. This was done by asking the volunteer to void urine through a filter funnel attached to a 20-cm. length of polyethylene tubing ; a mid-stream sample was obtained by clamping the tube at both ends and disconnecting from the filter funnel.

Once the control samples had been obtained the volunteer was allowed to settle comfortably in a dental chair facing the infra-red analyser and given his choice of whisky, gin, or rum. Six volunteers swallowed in one draught 60–100 ml. of their choice diluted with an equal volume of water. The remainder consumed between 150 and 360 ml. similarly diluted with water over a period of 25 to 60 minutes.

Arterial and venous blood samples were collected at intervals of 20 to 30 minutes for two to three hours after drinking, as were urine samples whenever possible. Breath samples were analysed more frequently, in some instances at four-minute intervals.

Measurement of Alcohol Vapour in Breath

The volunteer breathed out forcibly through a low-voltage electrically heated metal tube maintained at 38° C. into a conventional Luft-type non-dispersive infra-red gas analyser, the optical portion of which was thermostatically controlled at 38° C. Since the volume of the tube was 12 ml. and that of the sample cell 100 ml., at least 112 ml. of alveolar air was needed for the analysis. The alveolar nature of the expired air was confirmed by observing the carbon dioxide plateau traced out on the recorder of a rapid-response infra-red carbon dioxide analyser. For the purpose of sampling carbon dioxide a catheter was placed at the inlet of the heated tube together with a thermocouple for measuring the temperature of the expired air at the mouth.

The infra-red alcohol-vapour analyser, which has a full-scale sensitivity of 400 parts per million by volume of ethyl alcohol vapour, was calibrated against known mixtures of alcohol vapour in air produced by means of an accurately made slow injector system (Hill and Newell, 1965). For this purpose a power-driven syringe loaded with saturated alcohol vapour and fitted with a suitable wick to ensure full saturation was used to inject the vapour into a metered gas-stream. The vapour concentration achieved could be calculated from a knowledge of the syringe dimensions, the rate of travel of the piston, the saturated-vapour pressure of alcohol, and the temperature of the syringe. The absolute accuracy of this calibration method is plus or minus 10% and its reproducibility plus or minus 5%. With this system it was shown that the analyser had a linear response over the range 0–400 p.p.m. v/v. In practice the gain controls of the analyser were adjusted to give a known deflection when a standard alcohol vapour-in-air mixture was fed into the analyser from a cylinder under pressure. Little variation in the gain settings required was found from day to day. The actual alcohol-vapour concentration contained in the cylinder was determined by interpolation against known mixtures generated by the syringe. When a cylinder mixture of 300 p.p.m. of alcohol vapour in air was sampled repeatedly it was found that successive readings did not deviate by more than plus or minus 3 p.p.m. Sampling successive breaths from subjects did not give this degree of reproducibility, and suggests that the variation lies in the breath. The alcohol-vapour concentration indicated by the analyser was easily converted into milligrammes of alcohol vapour per 100 ml. of air, since the gramme-molecular weight of vapour occupies 22.4 litres at normal temperature and pressure.

A blood/breath partition coefficient of 2,060/l. at 34° C. was derived from the data of Harger, Raney, Bridwell, and Kitchel (1950), and this ratio was used to convert the concentrations of alcohol measured in breath to the corresponding blood concentrations. From the data of Harger *et al.* (1950) it was found that this value falls by 5.8% per degree rise in temperature, assuming a straight-line relationship between the partition coefficient and temperature over the range 30–37° C. The mouth temperatures recorded in this study ranged from 34 to 36° C., and the appropriate adjustment to the partition coefficient was made when necessary.

Because the infra-red alcohol-vapour analyser exhibited a deflection of 6% of full scale for water vapour in the breath, the zero of the instrument was set on the alcohol-free breath of a member of the laboratory staff before each reading was taken. For future work it is planned to incorporate optical-interference-type filters in the analyser to remove the effect of water vapour in the breath. Before the start of each experiment the subject was asked to breathe into the analyser. This revealed any deflection arising from the prior drinking of alcohol or from the presence of methane or acetone in the breath. After each reading the analyser was purged with dry air to remove any accumulated moisture or breath from the system.

To check the accuracy of the analyser further, known concentrations of alcohol in water or blood were placed in a two-litre Perspex tonometer which was maintained at 34° C. for two hours. At the end of this period the vapour in the tonometer was ejected into the analyser ; at the same time samples of the water or blood were removed for analysis. The analyser readings obtained agreed with the calculated values to within 5% for water and 10% for blood. It is believed that the accuracy of this method of calibration can still be improved, and further work is already in progress in this connexion.

On 17 occasions the volunteers were asked to blow through Alcotest tubes calibrated for breath levels equivalent to 100, 70, and 50 mg./100 ml. of blood when the infra-red analyser indicated these levels.

Measurements of Alcohol in Blood and Urine

In dogs' blood and urine the alcohol concentration was determined by a modification (Ryan, Nolan, and Conway, 1948) of the microdiffusion technique of Winnick (1942). Studies *in vitro* showed that an extraction rate of at least 95% could be expected when known quantities of alcohol were added to dogs' blood. But when the method was applied to human blood the extraction rate fell, and it was often impossible to recover more than 90% of the added alcohol when the alcohol content was above 100 mg./100 ml. This extraction rate was regarded as unsatisfactory for the degree of accuracy required for this particular study, and accordingly the Nickols (1960) modification of the macro-Cavett method was tested. With this technique *in-vitro* studies gave an extraction rate higher than 95% with good repeatability on duplicate samples, and it was therefore adopted for the determination of the alcohol levels in the blood and urine samples of the volunteers.

The equivalent levels in blood for given values of alcohol in urine were determined by means of the urine/blood ratio of 1.32/l. recommended by the B.M.A. Special Report (1965).

Results

Experiments in Dogs

In the three dogs given alcohol into the stomach absorption was relatively slow ; the peak concentrations of alcohol in blood were reached between 45 minutes and two hours after administration. The absorption trend is shown in Fig. 1, which also demonstrates the close agreement obtained between the blood-alcohol levels of the inferior vena cava, the femoral artery, and the internal jugular vein. The increase in the amount of

alcohol in peripheral venous blood occurs more slowly, but ultimately comes into equilibrium with the other values.

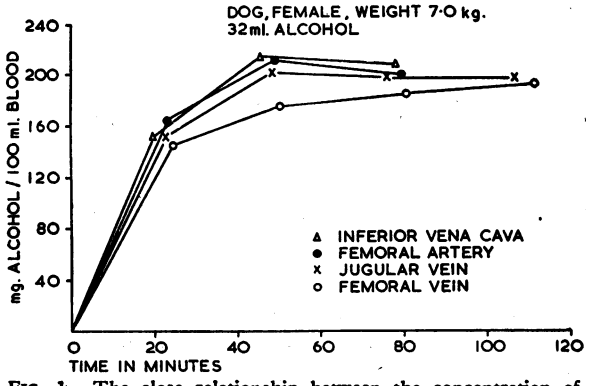

FIG. 1.—The close relationship between the concentration of alcohol in the blood of the inferior vena cava, the femoral artery, and the jugular vein is clearly seen in a dog given undiluted alcohol into the stomach. The alcohol concentration in the femoral vein climbs more slowly and had still not reached its peak when the last sample was taken.

In the remaining dogs given alcohol into the duodenum the rate of absorption was more rapid, and in most instances the peak concentrations occurred within 20 minutes after administration. Fig. 2, which demonstrates one of the slower rates of uptake from the duodenum, illustrates this pattern of absorption. It also shows that during absorption the amount of alcohol in the right ventricle is slightly higher than that in the femoral artery, whereas that in the peripheral venous blood remains relatively low until the arterial level begins to decay. In most instances once this had happened the amount of

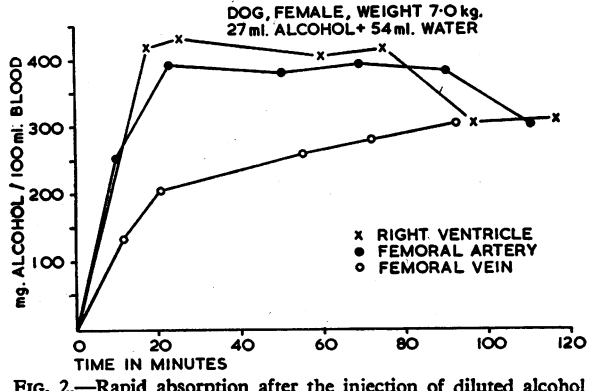

FIG. 2.—Rapid absorption after the injection of diluted alcohol into the small intestine of a dog. The close relationship between the concentration of alcohol in the right heart and the femoral artery is apparent. Although their absorption peaks were reached within 30 minutes, the femoral-vein concentration had still not reached its peak one hour later.

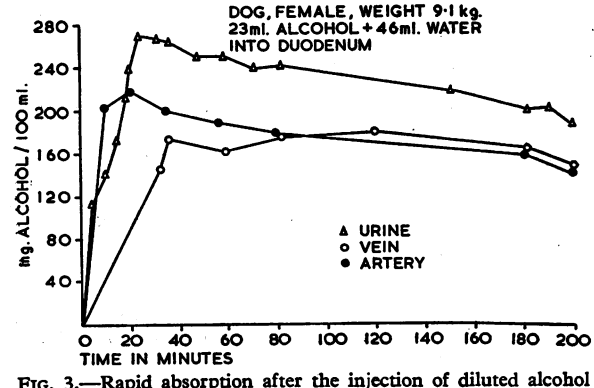

FIG. 3.—Rapid absorption after the injection of diluted alcohol into the small intestine of a dog. The concentration of alcohol in the femoral artery reached its peak within 20 minutes and the peak urine concentration was reached nearly as rapidly. Typically the femoral-vein concentration peaked more slowly but ultimately rose slightly above the arterial concentration.

alcohol in arterial blood fell slightly below that in peripheral venous blood. In all experiments where the downward trend had become well established this "cross-over" effect was seen (Fig. 3). The trend also appears in Figs. 1 and 2. The time at which the cross-over occurred varied between 100 and 180 minutes after the administration of the alcohol.

In addition to demonstrating the relationship between the amount of alcohol in arterial and peripheral venous blood, Fig. 3 also shows the relationship between the amount of alcohol in urine and blood. In the seven experiments in which serial urine samples were obtained the peak alcohol concentrations were reached at times varying between 10 and 180 minutes after its administration. When the urinary output was high the peak concentration was reached early. In every experiment once the maximum concentration in urine had been reached subsequent values were invariably higher than those in both arterial and venous blood, so that the ratio of urine concentration of alcohol to blood concentration was always greater than unity and varied between 1.045 and 1.36.

Experiments in Human Volunteers

The rate of alcohol absorption in the volunteers varied considerably. In five of the six subjects who swallowed their alcohol in one draught the highest concentration in arterial blood was achieved within 30 minutes of drinking, but in the remaining subject the peak concentration was not achieved until approximately 50 minutes after drinking.

In nine volunteers who drank between 150 and 360 ml. of 70° proof spirits the highest concentration of alcohol in arterial blood was obtained between 35 and 95 minutes after the start of drinking and between 8 and 35 minutes from the end. When drinking was slow the peak concentration tended to be reached soon after the drinking ceased (Fig. 4); with rapid drinking it developed more slowly (Fig. 5).

Of the 14 subjects in whom simultaneous arterial and venous blood samples were obtained the arterial concentrations of alcohol were always higher than those in venous blood until after the peak concentrations had been passed. As the fall-off in concentration became established the arterial concentrations declined more rapidly than the venous concentrations. In eight subjects the arterial concentrations of alcohol fell slightly below the venous concentrations between 50 and 90 minutes

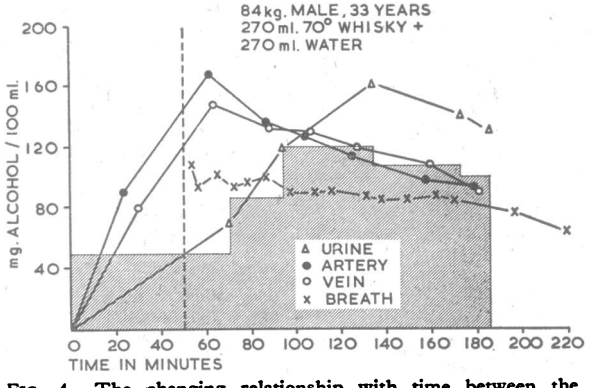

FIG. 4.—The changing relationship with time between the alcohol concentration in arterial and venous blood, breath, and urine in a 33-year-old man. The dotted perpendicular line indicates the point when drinking ceased. The urine:blood ratio of 1.32 has been used to convert the alcohol concentrations in urine to blood. As the urine figures represent the mean values of the altering concentrations during secretion the conversion to blood has been plotted as the mean value against time and is represented by the shaded areas. The peak blood concentrations were reached soon after the end of drinking; the urine peak was not reached until over an hour later, after which good agreement with blood was obtained. A cross-over point between arterial and venous blood levels is obvious. The breath values are lower than those in blood, but they come closer together towards the end of the experiment.

after drinking (Figs. 4, 6, and 7). In a further three this cross-over effect appeared later, between 120 and 140 minutes (Fig. 8) after drinking, and in the remaining three subjects the experiments were discontinued before any cross-over effect was seen.

In the 10 subjects in whom only venous blood samples were obtained the peak concentration of alcohol in venous blood occurred between 45 and 180 minutes after the start of drinking and between 30 and 155 minutes (Fig. 9) from the end of drinking.

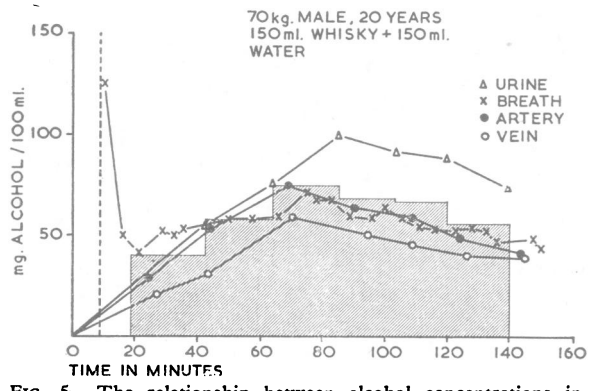

FIG. 5.—The relationship between alcohol concentrations in blood, breath, and urine in a 20-year-old man. Plot as in Fig. 4. Drinking was completed in 10 minutes and the peak concentrations in arterial and venous blood occurred about an hour later, followed after a further 20 minutes by the urine peak. There was good agreement between breath and arterial blood.

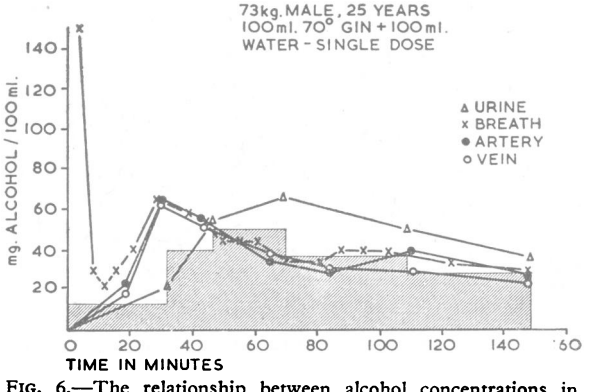

FIG. 6.—The relationship between alcohol concentrations in blood, breath, and urine in a 25-year-old man. Plot as in previous Figs. Peak concentrations of alcohol in arterial and venous blood were reached about 30 minutes after drinking and in urine a further 30 minutes later. An arteriovenous cross-over point occurred early, but the arterial level peaked again nearly two hours after drinking. In this subject there was good agreement between blood, breath, and urine after the urine peak.

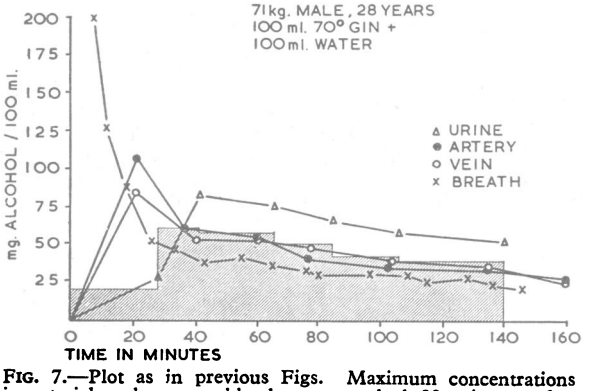

FIG. 7.—Plot as in previous Figs. Maximum concentrations in arterial and venous blood were reached 20 minutes after drinking and in urine 20 minutes later. The arteriovenous cross-over point occurred after a further 20 minutes. Good agreement was obtained between blood and urine, but the breath values were consistently lower except during the initial period after drinking, when they were artificially high.

A general observation was that when absorption was rapid the peak concentration tended to be high, with a rapid fall-off, whereas when absorption was slow the peak concentration was lower and the fall-off more gradual.

During the initial period after alcohol has been swallowed breath analysis gives an artificially high reading due to contamination of the breath by alcohol retained in the mouth. At least 15 minutes were needed to ensure removal of this source of contamination. Occasionally a much longer time was needed; Fig. 10 illustrates the effect of drinking gin on the breath of four volunteers. Though the alcohol content dropped rapidly in three, the fourth subject retained a very high alcohol content in his breath for approximately 45 minutes.

In 21 of the 24 volunteers repeated breath analyses were carried out throughout the study. After the initial period of high readings the pattern of the concentration of alcohol in breath followed the trend of the alcohol concentration in arterial blood but was nearly always lower (Fig. 7). No breath pattern was ever consistently higher than the arterial concentration, but there was sometimes good agreement, especially when the arterial concentration of alcohol did not exceed 70–80 mg./100 ml. (Fig. 6). There was also a tendency for better agreement to occur between breath and blood levels towards the end of an experiment (Fig. 8).

In one subject, approximately 40 minutes after drinking, the alcohol concentration in breath suddenly rose independently of the blood level beyond the limit of the recorder and remained off-scale for approximately 15 minutes before falling just as rapidly to the anticipated level.

The correlation between the direct estimations of alcohol concentrations in blood and those derived from breath was

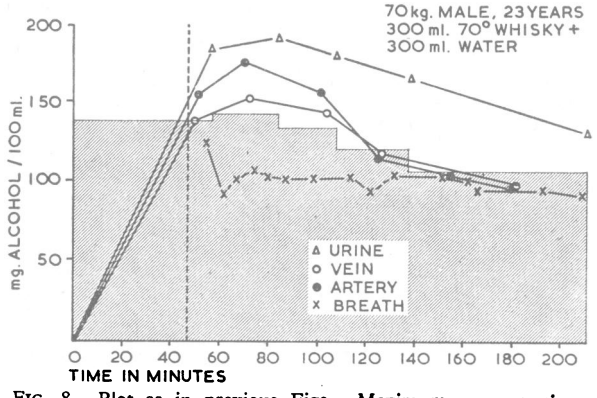

FIG. 8.—Plot as in previous Figs. Maximum concentrations of alcohol were reached in arterial and venous blood and urine within 20 minutes of each other. Arteriovenous cross-over point occurred about two hours after drinking. Breath concentration was lower than blood in the early stages, but better agreement was obtained shortly after the cross-over point.

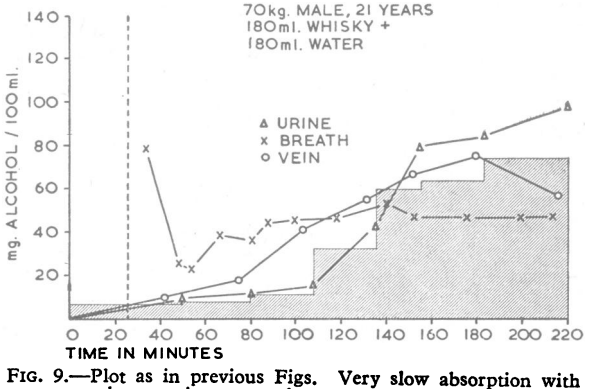

FIG. 9.—Plot as in previous Figs. Very slow absorption with venous peak occurring more than two and a half hours after drinking and urine peak at least 40 minutes later. Breath pattern, originally higher than the venous level, presumably reflecting a higher concentration of alcohol in the arterial blood, fell below the venous concentration and remained at a constant level for the remainder of the experiment.

determined from values obtained once the contamination effect of mouth alcohol had been shown to have disappeared. This was done by excluding all values obtained before the breath levels had begun to rise after the initial fall-off. The tendency towards low values for breath analyses is clearly seen in Fig. 11.

When calibrated Alcotest tubes were used at the appropriate blood levels as indicated by the infra-red analyser good and consistent agreement was obtained.

Urine samples were collected usually at intervals of 20 to 30 minutes from 21 of the 24 volunteers included in the study. In the six subjects who swallowed the alcohol in one draught the peak concentration in urine was reached between 30 and 120 minutes after drinking, between 8 and 52 minutes after the arterial peak had been reached, and between 6 and 50 minutes after the maximum venous value.

In the remainder the urine peak was reached between 84 and 220 minutes after drinking had begun and between 37 and 190 minutes after it had ceased. In these subjects the peak urine concentration was reached between 14 and 96 minutes after the peak of the arterial concentration and between 6 and 80 minutes after the venous peak. In one subject the urine peak preceded the venous maximum by 43 minutes.

During the period of absorption no direct relationship could be shown between the amount of alcohol in urine and that in blood (Fig. 12). But once the peak concentration in urine had been reached good agreement was usually obtained between the blood levels derived from urine and those determined directly; Fig. 13 illustrates this relationship. The urine: arterial blood ratio varied between 0.29 and 2.22 and the urine: venous blood ratio between 0.05 and 2.12.

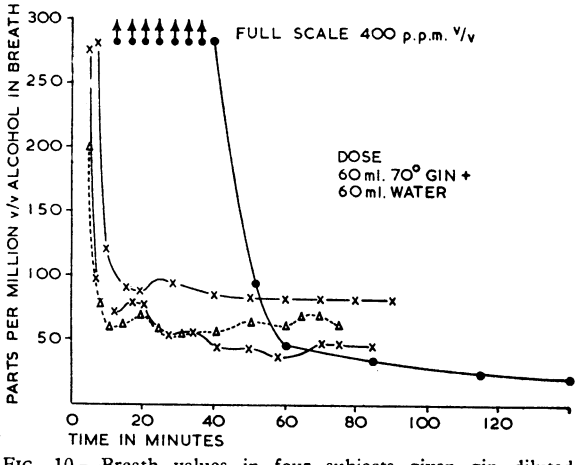

FIG. 10.—Breath values in four subjects given gin diluted with water. In three the mouth-alcohol effect disappeared within 15 minutes, but in the fourth subject the breath concentration remained off-scale for at least 40 minutes.

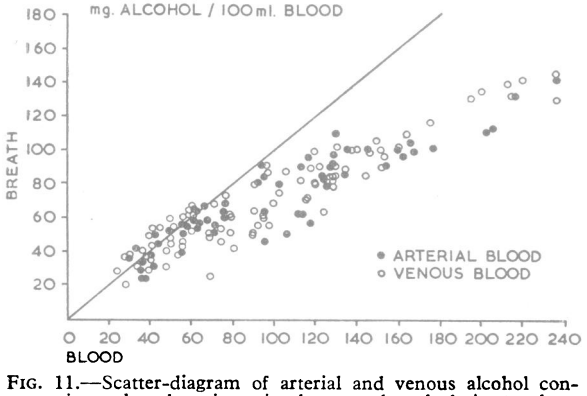

FIG. 11.—Scatter-diagram of arterial and venous alcohol concentrations plotted against simultaneous breath-derived values. The tendency for breath analyses to underestimate the blood values is obvious.

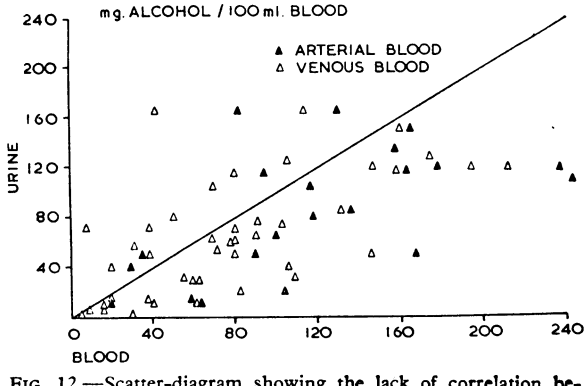

FIG. 12.—Scatter-diagram showing the lack of correlation between alcohol concentrations measured directly in blood and derived from urine before the peak concentration in urine has been reached.

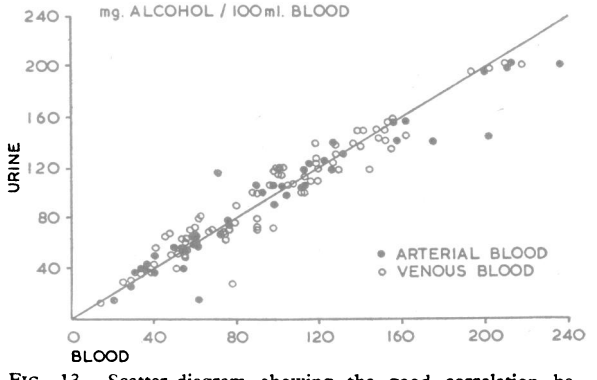

FIG. 13.—Scatter-diagram showing the good correlation between alcohol concentrations measured directly in blood and derived from urine once the peak concentration in urine has been reached.

Discussion

The observation by Mellanby (1919) that once alcohol had entered a dog's stomach its maximum concentration in blood was reached 30 minutes to two hours later has been substantiated, but it has also been shown that when alcohol is passed directly into the small intestine the uptake is much faster. Under these circumstances the peak concentration of alcohol in the blood of seven dogs studied was attained within 30 minutes. This is in agreement with the work of Elmslie, Davis, and White (1964), who showed that in man after gastrectomy the absorption of alcohol reached its peak within the same period.

By repeated sampling of blood it has been possible to determine in more detail the pattern of arterial and venous blood levels during the absorption, distribution, and elimination of alcohol in dogs and man. The results in dogs confirm the observation of earlier workers (Haggard and Greenberg, 1934; Harger, Hulpieu, and Cole, 1945) that the level of alcohol in jugular-vein blood very quickly reaches the same level as that in right-heart and arterial blood. The difference between the jugular-vein level and that in arterial blood presumably reflects the difference in alcohol content between the brain and its blood-supply, and the fact that this difference is reduced very rapidly implies that equilibrium is achieved quickly.

The lowest concentration of alcohol during absorption was recorded in peripheral venous blood; the alcohol level rose only slowly, and indeed did not come into equilibrium with the arterial blood until after the arterial peak had been passed for a varying period of time. It was, however, a characteristic feature of the studies, both in the dog and in man, that once equilibrium had been achieved a cross-over point was reached beyond which the peripheral venous concentration of alcohol remained just above the arterial concentration. In the studies in man a definite cross-over point occurred in 11 of the 14

subjects studied, and almost certainly had the experiment been continued the remaining three volunteers would have shown the same pattern.

The failure of the alcohol concentration in peripheral venous blood to keep pace with the rising arterial concentration during absorption can be explained by the combination of the high solubility coefficient of alcohol in blood and tissues and the relatively poor blood-flow to resting muscle when compared with organs such as the brain and kidney. When substances are as soluble as alcohol slow perfusion of blood through muscle allows large quantities to diffuse out of the blood into the tissues. When absorption is finally complete and the arterial concentration begins to fall, the diffusion gradient between blood and tissues is reversed and alcohol passes back equally readily from the tissue and extracellular fluid into the capillaries and thence to the peripheral venous blood. Since excretion through the lungs and kidneys is slight and metabolism is relatively slow, the concentration of alcohol in the peripheral venous blood is likely to remain just slightly higher than the arterial concentration. In practice the difference was small, and in no instance after the peak had been passed did the concentration of alcohol in any venous blood sample exceed that in the preceding arterial sample.

The ability to demonstrate this close relationship between arterial and venous blood during the elimination of alcohol implies a high degree of accuracy in the extraction process; with a cruder method the pattern probably would not have been observed.

If it is accepted that the direct determination of alcohol concentrations in blood is accurate then there can be no doubt that estimates derived from breath analysis deviate significantly from the true values. This is made clear from a consideration of Fig. 11, which not only shows the tendency for values derived from breath to read low—no value over 70 mg./100 ml. read high—but it also emphasizes the tendency for the error to increase as the alcohol concentration rises.

The determination of blood-alcohol concentrations by breath analysis depends on the fact that a small fraction of any alcohol present in blood is excreted in the breath. When blood flows through the lungs alcohol diffuses into the alveolar air in proportion to the concentration present in blood if equilibrium between blood and air is achieved. This constant ratio, known as the partition coefficient, can be used to derive the blood concentration of alcohol if that in breath is measured.

Errors in breath analysis can arise, therefore, if (*a*) there are technical faults in the analysing equipment, (*b*) the partition coefficient is wrong, and (*c*) equilibrium is not reached between the alcohol content of blood and air.

Technical Faults in Analysing Equipment

Contamination of the infra-red analyser with moisture could lead to artificially low values being recorded, but the amount of moisture present in one forced expiration is small, and since the analyser was purged with dry air for several minutes between tests this is unlikely to be a source of error. Furthermore, the fact that good agreement was consistently obtained between the Alcotest tubes and the infra-red analyser over the tested range of 50–100 mg./100 ml. suggests that the fault does not lie in the analyser.

The calibration of the analyser was checked daily against known alcohol-vapour mixtures and shown to be consistent, but if the preparation of the mixture were faulty an error would be present in the reading. The injector-syringe system of preparation, however, has been thoroughly tested and shown to be reliable not only when used with saturated alcohol vapour but also with liquid alcohol (Newell, personal communication).

It can be concluded, therefore, that the infra-red analyser recorded accurately the amount of alcohol actually present in the breath of volunteers.

Partition Coefficient

The possibility that the air/blood partition coefficient could be wrong cannot be ignored, but the figure of 2,060 at 34° C. used in this study falls within the range determined by Harger *et al.* (1950) by a careful tonometric technique which is difficult to fault. Moreover, similar partition coefficients have been determined by Liljestrand and Linde (1930) and by Grosskopf (1954).

Equilibrium

The remaining possibility is that equilibrium between the pulmonary and alveolar air was not reached in most of our volunteers. Equilibrium can be achieved only if there is perfect distribution of the inspired air within the lungs relative to the pulmonary blood flow, but it is well recognized that even in apparently healthy individuals some degree of ventilation: perfusion ratio inequality exists in different parts of the lung. The attainment of equilibrium is further handicapped in the presence of conditions such as emphysema, which increase the physiological dead space still more.

The tendency in some of our subjects for closer agreement to be reached between blood and breath determinations an hour or so after drinking, even when the concentrations were still quite high, deserves further consideration. Because the blood-supply to the mucous membrane lining the bronchial tree is relatively poor it is likely that the alcohol concentration of the mucous secretions as well as of the cells themselves will remain lower than that in the pulmonary blood for some time. Thus, even if equilibrium were reached between pulmonary blood and alveolar air, the possibility exists that a proportion of the alcohol in the breath would be taken up by the mucous secretion as the breath passed along the bronchial tree, thereby reducing its concentration at the mouth.

Residual Alcohol in Mouth

Another potential source of error in breath analysis is the presence of residual alcohol in the mouth. Immediately after drink is taken there is enough alcohol vapour in the mouth to give artificially high levels on breath analysis. According to Grosskopf (1963) and Begg, Hill, and Nickolls (1964) this mouth-alcohol effect disappears 20 minutes after drinking, and while this is probably true in most instances, in one of our four subjects in whom it was specifically studied very high values in breath persisted for 45 minutes before falling suddenly to a more realistic value. In another of our subjects in whom a transient increase in breath alcohol not related to blood levels was observed 40 minutes after the consumption of alcohol, contamination of the mouth air by stomach contents was suspected but belching or regurgitation was denied.

Variations in Breath and Blood Analyses

Discrepancies between the results obtained by simultaneous breath and blood analyses have not been confined to this investigation. Examination of the data presented by Harger (1963) shows similar differences between breath and blood; and a tendency for both the breathalyser and the breathalyser bag to give readings below those obtained from blood is apparent in the report of Begg *et al.* (1964), who also investigated the Kitagawa-Wright instrument. In their hands this apparatus tended to read too low in the lower range of blood-alcohol concentrations and too high when the blood concentrations were high. In Melbourne, Bayly, McCallum, and Preston (1960) compared breath analyses with corresponding blood analyses in 100 subjects. They concluded that for a true blood level of 100 mg./100 ml. breath analysis would yield values ranging from 48 to 115 mg./100 ml.

The wide variations between breath and blood analyses virtually exclude the use of breath-testing for the accurate determination of the alcohol concentration in blood, but the fact that breath analysis usually underestimates the blood value makes it a useful screening test for law-enforcement work.

At first sight the close agreement shown in Fig. 13 between the values for blood-alcohol concentrations obtained directly and those derived from urine suggests that urine analysis can provide a suitable alternative to blood analysis and confirms the accuracy of the urine–blood ratio of 1.32.

It must be emphasized, however, that this good agreement held only after the peak concentration of alcohol in urine had been passed and that in all instances the bladder had been empty 20 to 30 minutes previously. Since sometimes the urine peak was not reached until two to three hours after drinking, the value of urine testing is obviously limited. Its value is further diminished by the observation that before the peak was reached no direct relationship between the alcohol concentration in urine and that in blood could be demonstrated (Fig. 12). This latter observation adds strength to the B.M.A. Special Report (1965) recommendation that when urine is required for medico-legal purposes two samples should be collected at approximately 30-minute intervals. We would go further and suggest that if the second sample contains more alcohol than the first then there is no guarantee that the urine peak has been reached, with a consequent loss of accuracy in the determination of the blood-alcohol value. If, however, the second sample contains less alcohol than the first then it is safe to assume that the peak has been passed and that the second value will therefore provide a substantially accurate estimate of the amount of alcohol actually present in blood.

Some Suggestions

On the basis of the work presented the following suggestions are made.

(*a*) Venous blood samples collected from a forearm give values for alcohol concentration in blood not significantly different from arterial samples after the venous peak has been passed. Before the peak the alcohol concentration in venous blood is always lower than that in simultaneously collected arterial blood.

(*b*) Breath analysis is not accurate enough for law-enforcement purposes if it becomes an offence to drive with more than a fixed amount of alcohol in the blood. But because breath analysis techniques tend to underestimate the true alcohol concentration in blood they could provide useful screening tests in police work. Their convenience is an added advantage in this connexion.

(*c*) Urine analysis provides an accurate determination of the alcohol concentration in blood only when the urine peak has been passed and when the bladder has been emptied within the preceding 30 minutes. Since the urine peak may not be reached for up to three hours after drinking, the application is limited. In practice at least two urine samples are needed about 30 minutes apart. The first is only a reference point, but if the alcohol concentration in the second is below that in the first it may be used to provide substantial collaborative evidence in doubtful cases. If the second sample is higher then it is of less value and may have to be disregarded.

Summary

In 10 dogs the distribution of alcohol in the blood and urine was studied and in 24 men the study was extended to include breath analysis.

In the dogs absorption from the stomach reached its peak between 45 minutes and two hours after administration, but when the alcohol was given directly into the duodenum the peak was passed within 30 minutes. Close agreement was obtained between the values for the alcohol concentrations in the blood of the inferior vena cava, the right heart, the pulmonary artery, and the jugular vein, but, especially when absorption was rapid, the alcohol concentration in peripheral venous blood remained substantially below the arterial concentration until after the arterial level had begun to decay. Almost invariably thereafter the arterial level dropped slightly below the peripheral venous level, and they fell in parallel. The peak alcohol concentration in urine was reached between 10 and 180 minutes after administration, and from that time the urine level was invariably higher than in arterial and venous blood.

In man the rate of absorption varied widely and was related to the dose and the rate of drinking. The alcohol concentration in arterial blood was measured in 14 volunteers, and in all of them it was always higher than in venous blood until after the peak concentrations had been passed. Thereafter there was close agreement between the arterial and venous levels, and in 11 a cross-over effect similar to that observed in the dogs was seen. Breath analysis was carried out in 21 of the 24 subjects studied ; blood-alcohol concentrations derived from the breath usually followed the trend of the direct determinations but were nearly always lower. Better agreement was often obtained at low concentrations and towards the end of an experiment even when the concentrations were high. During the period of absorption no direct relationship could be shown between the amount of alcohol in blood and that in urine, but once the peak concentration in urine had been reached derived values for blood agreed closely with those determined directly. Unfortunately the urine peak was often not reached until two to three hours after drinking.

It was concluded that for the accurate determination of the alcohol concentration in blood direct analysis of blood is required.

These studies were made possible by the co-operation of our volunteers, and we are particularly grateful to those officers and men of the Royal Air Force and Royal Army Medical Corps who submitted themselves to some pain, discomfort, and inconvenience to ensure their completion.

One of us (D. W. H.) would like to acknowledge the assistance of the Science Research Council in providing a grant for the study of methods for calibrating infra-red gas analysers.

We are also grateful to Mr. W. B. Bartley, of Hilger and Watts Ltd., who provided the infra-red analyser, and to the following for many useful discussions and advice: Messrs. E. G. Davies, H. A. Newell, and T. Powell, and Drs. K. Grosskopf, I. G. Holden, H. J. Walls, and B. M. Wright.

Finally, our thanks are due to Miss P. Taylor, Mr. A. Muir, and Mr. C. Tilsley for their technical assistance.

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