ETHANOL METABOLISM IN HUMANS

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ABSTRACT

This thesis outlines the development of breath alcohol measurement and investigations of the rate of absorption, equilibration and elimination of alcohol from the body using breath analysis. After a historical outline, the methods of alcohol detection are reviewed and a comparitive study of some modern breath alcohol testing instruments detailed. The results show that the gas chromatograph Intoximeter was the most reproducible and accurate instrument. Of the fuel cell instruments, the Alcolimiter gave reproducible readings but with a higher frequency of mechanical breakdowns and the Alcometers failed to hold a calibrated value on repeated testing. The chemical analysis of the Borkenstein Breathalyzer offered portability and freedom from calibration but with a lowering of accuracy.

No instrument offered the degree of flexibility required for laboratory investigation of factors affecting breath alcohol concentrations. Consequently a gas chromatograph was modified for breath sampling at 30 second intervals. The partition coefficients for alcohol between air and blood were found to be related to the water content of the blood sample. Breath alcohol concentrations increased with expiration volume and were related to a rise in breath temperature. After correcting to a standard temperature of 34^{o}, a linear increase in alcohol concentration remained which was greater with higher blood alcohol levels.

Equations for estimating the distribution volume of alcohol in the body were derived and the Widmark factor 'r' was found to be related to the ratio, body water over blood water. The blood alcohol time curves resulting from a fixed dose of alcohol given to semi-fasted subjects were analysed to determine the apparent distribution volumes in the body. Volumes exceeding physiological limits were found in some subjects and ascribed to either a faster rate of metabolism during the absorptive phase or to anomalies in equilibration. A markedly non-linear alcohol elimination curve was seen in one alcoholic. Faster rates of alcohol oxidation were discussed in relation to the Michaelis-Menten kinetics of enzymatic catabolism and it is suggested that some subjects

have a second enzyme for alcohol metabolism which operates at a higher Km than normal.

The fluctuations of blood alcohol level during the absorptive phase were examined by measuring the abundance of a tracer dose of deuterated alcohol given orally after a loading dose of unlabelled alcohol. The fluctuations were ascribed to contractions of the pyloric sphincter releasing alcohol into the duodenum in an irregular fashion.

The studies were extended to subjects drinking in a private bar. The rate of alcohol absorption appeared to keep pace with the rate of drinking which was spread over at least a three hour period. The rates of alcohol elimination from the blood were faster than in a previous study with a lower dose of alcohol. This is explained by lower blood alcohol levels from a smaller dose and is consistent with the enzyme kinetics of alcohol catabolism. An equation was derived to enable the estimation of blood alcohol levels from amount consumed which compared favourably with traditional methods for this calculation.

The accuracy, rapidity and ease with which breath alcohol analyses could be made to determine alcohol concentrations in the body enabled its use with large groups of people consuming alcohol at party situations or in hotel bars and two examples of such studies are presented in the appendix.

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TERMINOLOGY

Throughout the text, "alcohol" is used as synonymous with ethanol. All blood alcohol concentrations have been expressed in milligrams per 100 millilitres. This terminology is still commonly used by workers in the fields of medicine, alcohol abuse, psychiatry and alcohol and traffic safety to whom the present study could be of interest.

With the adoption and increasing use of SI units in recent years by the scientific community, blood alcohol levels expressed in millimoles per litre are becoming increasingly common. The equivalent value for 10 millimoles per litre (mmol/l) is 46 mg/100 ml. The results of breath alcohol analyses have, in the main, been expressed as blood alcohol concentrations based on the blood : breath distribution ratio of 1 : 2,100 as explained in the text. Recent legislation in New Zealand has made it an offence to drive a motor vehicle with a breath alcohol level greater than 500 µg per litre, and eventually it is expected that breath rather than blood alcohol concentrations will be widely used.

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CHAPTER 1

INTRODUCTION

Scientific studies on the metabolism of alcohol in human subjects date back to investigations in the late 19th century according to Jacobsen (1952). Prominent among early experimenters was Anstie, whose sulphuric acid - potassium dichromate mixture for the colorimetric estimation of alcohol in biological samples is in use to the present day, forming the basis of the method used in the "Breathalyzer" and in the screening devices for measuring breath alcohol with mixtures impregnated on silica gel, e.g. Drager tubes (cited by Harger et al 1956). In 1874, Anstie wrote a paper in the 'Practitioner' that he had founded in 1868, entitled, "Final Experiments on the Elimination of Alcohol from the Body" (cited by Jacobsen, 1952), a title which was clearly optimistic since work on alcohol elimination is still continuing at the present time and it is clear from the literature that the factors involved are still incompletely understood.

With the development of motor vehicles in the early part of this century, interest centred on the effect of alcohol on driving skills and Widmark (1914) published his important paper entitled "Alcoholic Excretion in Urine and a Simple Clinically Applicable Method for Diagnosing Alcoholic Intoxication in Drivers". At that time, methods for the estimation of alcohol in various biological samples were based on the analysis of alcohol concentrations in distillates by chemical methods (Jaulmes and Brun, 1970).

During the First World War, Mellanby was commissioned by the Central Control Board (Liquor Traffic) of Great Britain under the auspices of the Medical Research Council to investigate circumstances under which alcohol could lead to intoxication. He published his report in 1919 describing the work which had been performed entirely on dogs. Later, he repeated some of his experiments on human subjects with similar results. In the experiments with dogs, the animals had been deprived of food and water for 20 hours before an alcohol dose was given by stomach tube. Mellanby showed that there was a rapid absorption of alcohol into the blood and a slow linear blood level decline subsequently. He also found that absorption was delayed from dilute alcohol solutions or beer or when food, as milk, was given before alcohol. From this study probably arose the idea that milk

was a most effective foodstuff to delay absorption. Signs of intoxication in the dogs were not seen until blood levels reached 0.345ml/100g blood, (267mg/100ml).

In 1922, Miles, working in Boston, reported on the levels of alcohol in urine, blood and plasma in human subjects for some time after the consumption of 0.5g/Kg body weight of alcohol. He discussed the new concept of relating intensity of physiological and psychological effects of alcohol to its concentration in the blood and in subsequent papers centred his studies on the impairment of work related tasks at various blood alcohol levels. His paper published in 1922 was concerned mainly with the relationship between urine and blood levels, and he provided a simple method for determining blood alcohol concentrations during psychological studies as well as showing that urine samples directly reflected the concentration of alcohol in the blood. It was noted that the rate of alcohol absorption was increased in habitual drinkers and his results were in general agreement with those reported by Mellanby. In 1925, Southgate reported a delayed absorption of alcohol after food with human subjects and suggested that the lower maximum blood alcohol levels obtained were due to the failure of a considerable proportion of the alcohol to enter the bloodstream.

Subsequent developments in alcohol studies in the United States were closely associated with the names of Harger (Indiana University) and Haggard (Yale University). The Centre of Alcohol Studies was established at Yale University with Jellinek as its first director and by 1940, the Quarterly Journal of Alcohol Studies was founded by Haggard (cited by Keller 1975).

An early conflict over the interpretation of results came when Harger and Hulpieu (1935) challenged the conclusions of Haggard and Greenberg (1934) that it took at least 6 hours for alcohol to be absorbed when taken orally. Harger and Hulpieu showed that, in dogs, one and a half hours after a dose of 3g/Kg of alcohol an average of 93.4% of the alcohol had been absorbed, by comparing the alcohol concentration in the gut after intravenous and oral administration. No account appears to have been taken of the earlier work of Southgate in 1925, who described a disappearance of alcohol which had been added to

faecal suspensions attributable to adsorption rather than catabolism. While basic information on alcohol absorption and elimination was being obtained, attention continued to be directed to the impairment of driving skills by alcohol. In 1938, Haggard et al commenced a paper with the statement, "Alcohol is involved in a considerable proportion of fatal motor accidents". They noted that in Sweden this problem had been met more directly than elsewhere, due mainly to the efforts of Widmark (University of Lund) who had been regularly blood testing drivers apprehended by traffic officers.

Although these blood analyses were providing valuable information, the advantages of having methods for obtaining body alcohol concentrations without the need for taking blood samples were being considered. Venesection could be an unpleasant procedure before the advent of disposable needles and syringes and it is clear that Miles in 1922 was considering urine alcohol levels as an attractive alternative to taking and analysing blood samples. In 1927, Bogen became the first investigator to propose the analysis of breath according to Harger et al (1938). It was recognised that alcohol in the pulmonary arterial blood would be in equilibrium with the air in the alveoli of the lungs. Samples of alveolar air could be readily obtained towards the end of an expiration when the air in the dead space of the upper bronchial tree had been displaced. If a sample of this air was bubbled through a heated solution of iodine pentoxide, the alcohol present reduced the oxidant and liberated free iodine which could be estimated quantitatively. In 1934, Haggard and Greenberg reported studies with subjects who had been trained to blow directly into reagents for alcohol analysis. In these early studies, breath alcohol concentrations were converted to blood levels using a coefficient of distribution which when multiplied by the amount of alcohol in 1 ml of air, gave a value for the equivalent amount of alcohol in 1 ml of blood. Liljestrande and Linde (1930) determined empirically a value for this coefficient of 2,000 from simultaneous alcohol measurements in both blood and breath samples. While it was agreed that there was a relationship between breath and blood alcohol levels, there were differences on the value for the distribution coefficient and the effect of temperature. Haggard and Greenberg (1934) obtained a coefficient value of 1,150 at 37.5^{o} by an *in vitro* technique

and later reported studies on both blood and breath alcohol levels using this value (Haggard et al, 1938). They made the statement that "..... there was also precise agreement between the values so obtained", although data supporting this contention were not reported. A later paper by the same authors, (Haggard et al, 1941) stated that they had not taken into account the effect of water condensation in their apparatus and they revised the value for the coefficient, now measured at 35° to 1,550, previously, at this temperature, the value had been given as 1,204.

In 1938, Harger et al adopted a different approach using the coefficient of 2,000 reported by Liljestrande and Linde (1930). They obtained samples of mixed tidal and alveolar air and determined simultaneously the concentration of both alcohol and carbon dioxide in a breath sample. The alcohol concentrations were converted to alveolar air concentrations assuming a 5.5% carbon dioxide content. The literature on blood/breath distribution coefficients was later reviewed by Harger, Raney et al (1950) who redetermined the coefficients for both air: water and air: blood. They noted that the temperature of the breath as it left the mouth averaged 34° and at this temperature, the distribution coefficient was 2,028, approximately the same as that reported twenty years earlier by Liljestrande and Linde (1930). The iodine pentoxide method was eventually superseded by a reaction involving the oxidation of alcohol by either dichromate, (Jetter et al, 1941) or permanganate, (Harger et al, 1938) in sulphuric acid. The permanganate method was used by Harger, Forney and Barnes, (1950) in their analytical device called a "Drunkometer". They found an average distribution coefficient of "about 2,100", which when correction for the carbon dioxide content of the air was made, enabled an estimate of blood alcohol levels ranging from -28% to + 32% of blood samples taken simultaneously. The poor correlations between the breath and blood levels for alcohol were ascribed to (a) differences in breath temperature, (b) fluctuations in carbon dioxide levels and (c) the use of venous blood for the determinations. The use of a carbon dioxide correction factor was eventually dropped. Haggard et al (1941) had noted that what they termed "venous air", or air obtained after a short period of rebreathing was nearly identical to alveolar air. This was also confirmed by Harger, Forney and Barnes, (1950)

who proposed that breath samples should be collected in a warmed aluminum bag and alcohol concentrations determined from the volumes of breath required to decolorise a set volume of a standard solution of potassium permanganate. With appropriate modifications to the "Drunkometer", Harger et al (1956) were able to reduce the errors of their previous estimates while still confirming the distribution coefficient of 2,100. At the same time, Borkenstein, (cited by Harger et al, 1956) developed his now well-known "Breathalyzer" which although a patented name for an instrument has, in fact become a new word in the English language. The Borkenstein instrument permitted the analysis of the last portion of breath which had passed through a heated solution of dichromate in sulphuric acid. The subsequent colour change was measured photometrically and translated into blood alcohol levels using the distribution coefficient value of 2,100.

Devices such as the "Drunkometer" and the "Breathalyzer" presented increased opportunities to use breath-testing to detect motorists driving with an excess of alcohol in their blood and by 1959, the "Breathalyzer" was in routine use with the Royal Canadian Mounted Police. Over the next 15 years, many papers, (reviewed by Harger, 1974) were published comparing simultaneous breath and blood tests. The value of blood tests has been consistently overemphasised, as it is to the present time, in spite of the convincing work of Forney et al (1964) and Payne et al (1966) who showed that there could be considerable differences in alcohol concentration of venous bloods taken simultaneously from different sites 15 minutes after drinking and that there were also arterial-venous differences for up to 2 hours. Dubowski, (1960, 1962) gave safeguards necessary for breath collection and in commenting on the empirical nature of the distribution coefficient emphasized the need for adequate instrument calibration and standardisation procedures.

From 1970 onwards, newer methods of analysis based on gas chromatography, infra-red absorption and fuel cells began to be used in instruments for the measurement of breath alcohol levels, (Lovell, 1972. Jain and Cravey, 1974). Controversy existed over the use of a breath test for evidential purposes in a court of law. Payne (1974) pointed out the failure of investigators to demonstrate that the distribution

coefficient for alcohol between air and blood was constant even in the same individual and expressed concern that breath tests were, on the whole, underestimating the levels in the blood. While there are still some opponents to the use of breath tests who say that blood and breath levels cannot be equated, Mason and Dubowski (1974) suggested that breath analysis for law enforcement purposes should be based on the amount of alcohol in a unit volume of alveolar air.

During the period when breath alcohol measurement techniques were being developed, investigations were still continuing on the way in which alcohol was absorbed, distributed and eliminated from the body. The work up to 1953 was reviewed by a special committee of the World Health Organisation (Lundsgaard, 1953). The work of Widmark (1932) and others was cited with particular reference to his formulae which enabled the calculation of the amount of alcohol eliminated from the body in unit time. Later work by Widmark (1933) was also discussed where he had shown a marked lowering of the blood alcohol curve where alcohol was consumed with or immediately after food. No satisfactory explanation was put forward apart from the possibility of alcohol oxidation in the gastro-intestinal tract or a faster rate of oxidation in the liver during the absorptive phase. Work with cats, reported by Eggleton in 1940 had suggested that the rate of oxidation of alcohol could be more rapid at higher blood alcohol levels, but a similar situation had not been demonstrated unequivocally in man. In recent years a pharmacokinetic approach has been made to the problems of alcohol absorption and elimination using various mathematical models (Wagner et al, 1976). While the formulae used can simulate very closely the blood alcohol curve in subjects who have been drinking, the factors underlying the lower blood alcohol levels from a given dose of alcohol when taken with food or diluted as beer have not been clearly defined. In practice it should be possible to determine blood alcohol levels using the Widmark formulae if the alcohol doses and body weights are known. However, in fact, it has been found that widely different doses can give the same equilibrium blood concentration.

Despite the very large amount of work which has been published on alcohol metabolism in human subjects, it is clear from the literature that there are still many important unanswered questions which would

justify the continuation of experimental studies. Many of the earlier studies had been carried out with subjects who consumed alcohol as rapidly as possible under laboratory conditions. By comparison, little emphasis was placed on differences which may occur under conditions where alcohol was consumed more slowly and approaching normal social drinking situations. Since it is difficult to readily obtain blood samples where social drinking conditions are being maintained, it was considered possible that accurate breath alcohol analysis might provide a significant advance in collecting reliable data. Results with a fuel cell device for measuring breath alcohol levels in an earlier study on alcohol metabolism (Couchman, 1974, MSc thesis) had been promising and led to work reported in this thesis on improving breath testing instruments; studies on factors affecting accuracy and the application of the procedures developed to give more information on the relationship between alcohol dose and blood alcohol levels under a wide variety of drinking conditions.

2.1 MEASUREMENT OF ALCOHOL IN BREATH SAMPLES

Expired air will normally be similar in composition to atmospheric air with slight changes in oxygen and carbon dioxide composition and an increase in water vapour. Other substances which may be present in appreciable quantities are usually volatile organic compounds which have been ingested such as alcohol or inhaled such as anaesthetics or solvents, (Dubowski, 1974). Volatile metabolites, such as acetone may be found in increased quantities in subjects with diabetes mellitus or who are in a fasting state. Breath samples from subjects who have consumed alcohol will contain alcohol in proportion to the amount in the blood and the breath concentration can be used to estimate the blood alcohol concentration. The relationship between blood and breath concentrations is given by the distribution coefficient, which at a breath temperature of 34^{o} is near 1 : 2,100 (Harger et al 1950b). Accordingly, the amount of alcohol in 1 ml of blood will be contained in 2.1 litres of alveolar air and when the blood levels are 100mg/100ml there will be nearly 500 µg of alcohol in one litre of air. In normal subjects, acetone concentrations are not greater than 1 µg per litre of breath but for untreated diabetics, the amounts can increase up to 370 µg/litre, (Stewart et al, 1964). Acetaldehyde, a volatile metabolite from alcohol, rarely exceeds 5 µg/litre and then only when the breath contains much higher levels of alcohol, e.g. above 500 µg/litre, (Freund et al, 1965).

Methods for measuring alcohol in breath samples should, ideally, not be affected by atmospheric air including water vapour. However, while specificity of a method for alcohol may be essential in legal evidence, less specific methods may be very valuable for screening studies. The chemical methods for the detection of alcohol have been reviewed by Jaulmes and Brun (1970) and the most useful of these is the oxidation of alcohol by a sulphuric acid/potassium dichromate mixture resulting in a decrease in intensity of the yellow dichromate colour. In this method, calibration is dependent on the concentration of reagents and the volume of the breath sample used. The reaction is not specific for alcohol but the reaction velocity is much greater than those for other alcohols or fatty acids, (Jaulmes et al, 1970).

Gas-liquid chromatography, (GLC) has been used extensively for the identification and quantitative estimation of mixtures of volatile substances. With this technique, alcohol may be readily separated from atmospheric gases and water vapour on solid support materials such as Porapak Q (Waters Associates Inc., U.S.A.) and then detected by flame ionisation and other methods. Because of the very small quantities of organic constituents in breath samples, rapid analyses may be made with very short columns.

Infrared spectrophotometers are available which measure the absorbance of organic constituents in a vapour phase caused by stretching or bending of the C-H or O-H bonds. Alcohol vapour has 5 absorption bands between 2.7 μm and 9.6 μm of which the most useful are those at 7.1 - 7.3 μm and 8.0 - 8.1 μm. Acetone has a similar infrared spectrum and therefore cannot be differentiated from alcohol. Differences occur at 2.7 μm where there is also strong absorption by water vapour, and at 9.5 μm where there are absorption bands due to the silica of the spectrophotometer cell windows. These instruments depend on long light paths through the vapour samples which may be achieved by multiple reflection between two mirrors in the chamber containing the breath sample. A large breath sample may be required. However there are the advantages of immediate readings and the requirement for only infrequent calibration.

Alcohol may be oxidised to acetic acid using the region of a potential controlled electrode where neither the reduction of oxygen nor oxidation of water takes place, (Bay et al, 1972). Alcohol vapour diffuses onto an electrocatalytic surface in a fuel cell where oxidation occurs and a current flow between the cathode and anode is obtained which is proportional to the alcohol concentration in the sample. Such cells do not give an appreciable reaction with acetone but they do give reactions with aldehydes and other alcohols.

Semiconductors containing N type sintered silicon oxide decrease electrical resistance when combustible or reducing gases are absorbed onto their surfaces. They are very sensitive to a wide range of gases which are found in atmospheric air including exhaust fumes and petrol from motor vehicles. Their reliable use as detectors of alcohol in breath samples presupposes an inaccessibility of other volatile

substances to the semiconductor. They are inexpensive and stable for a long time requiring low voltages with simple circuitry for their operation. Resistance changes are comparatively large for small changes in alcohol concentration.

By 1975, a range of instruments designed for the measurement of alcohol in breath samples using each of the methods described in the previous paragraphs had become commercially available. A research grant from the Licensing Trust Fund enabled the department to purchase at least one instrument incorporating each of the different principles, except for the infrared device. The instruments were all delivered during the following eighteen months and are listed in Table 2.1. and illustrated in Figures 2.1, 2.2 and 2.3.

2.2 TESTING PROCEDURES

Tests on each instrument were based on the procedures set out in the following sections. However, due to unique features in some of the instruments, additional tests were carried out which were not applicable to other instruments and the methods used in these cases have been included with the results obtained.

2.2.1 Breath Volume

The minimum volume of breath required by the Alcolimiter was measured by connecting a spirometer to the outflow of the breath sample from the test instrument. As there was no single breath outlet on the Intoximeter, minimum breath volumes were measured indirectly by connecting an air supply to the mouthpiece of the instrument. The air pressure was adjusted to the minimum required to activate a pressure sensitive switch within the instrument and the sampling time measured. The air supply was then connected to a spirometer through an adjustable restriction to obtain the same air pressure and the volume was measured with the same sampling time.

2.2.2 Tests with a Breath Alcohol Simulator

All instruments were calibrated to give equivalent blood alcohol levels using a distribution coefficient value of 2,100. They were tested initially by blowing ten consecutive breath samples from a subject with a zero blood alcohol level through a Stephenson simulator (Smith and Wesson Inc. U.S.A.) containing water plus alcohol. The air

TABLE 2.1

BREATH ALCOHOL TESTING INSTRUMENTS

Principle	Trade name	Manufacturer	Size, cm.	Cost NZ$ (1975)
Fuel cell	Alcolimiter	Energetics Science Inc USA	15x15x27	750
Fuel cell	Alcolmeter	Lion Laboratories UK		
	Pocket APST-M1		3x6x12	209
	Evidential AE-M2		11x20x24	644
	Evidential AE-D1		13x15x29	1152
Fuel cell	Alcosensor	Intoximeter Inc USA	3x6x12	370
Gas chromatography	Intoximeter MkIV	Intoximeter Inc USA	27x40x45	3,700
Colorimetric	Breathalyzer 900A	Smith and Wesson USA	21x26x20	770
	1000		20x36x51	1760

Figure 2.1

A range of fuel cell instruments. From left to right; Alcolmeter AE-M2; AE-D1; Alco-Limiter with the Alco-Sensor II and Alcometer PET in the foreground.

Figure 2.2

The gas chromatograph Intoximeter Mark IV with mixed hydrogen/nitrogen gas supply on the right and breath alcohol simulator on the left.

Figure 2.3

The Breathalyzer 900A (left) and the 1000 (right) with the Mark IIA breath alcohol simulator in the foreground.

which came from the simulator contained standard amounts of alcohol vapour giving an equivalent concentration of 100mg alcohol/100ml blood. The simulator contained a stirrer, immersion heater and a thermostat to maintain the water-alcohol solution at $34^{o} \pm 0.2$. The alcohol solution was prepared freshly each day or after a series of tests by diluting a stock solution of 60.8 g alcohol /litre which had been standardised by freezing point osmometry (Redetski, 1973). For every increment of 10mg/100ml of blood level required to be simulated, one millilitre of the stock solution was used and the total diluted to a volume of 500ml. In the remainder of this section, the results of breath tests are referred to as the concentration of alcohol in 100ml of blood.

2.2.3 Maintained reliability

All instruments were intially calibrated with a 100mg/100ml standard. At intervals over a period of 28 days, they were retested and the deviations from the intial level recorded.

2.2.4 Linearity of response

The linearity of response of each instrument was checked by determining the mean of 3 simulator tests at each of several alcohol levels in a range from 0 to 250mg/100ml. Higher levels tended to overload the fuel cell instruments. However, the range could be extended to 500mg/100ml for the Breathalyzers.

2.2.5 Breath test on subjects

Breath alcohol estimations were carried out on subjects who had consumed alcohol and whose blood alcohol levels were declining at a constant rate. Since it was not convenient to obtain blood samples from the subjects at the times they were tested, crosschecks of results from other instruments were obtained. In an initial study, six subjects ingested alcohol as vodka in lemonade over a one hour period approximately four hours after a light lunch. Breath testing commenced one hour later using the Intoximeter and then on the next exhalation, one of the other breath testing instruments. Subsequently, in a study in which only the digital Alcolmeter and a modified gas chromatograph (described in the next chapter) were used, breath tests were obtained on subjects either from consecutive breath samples or from the same breath sample by connecting the Alcolmeter mouthpiece to

the inlet of the breath sampler on the gas chromatograph. The sampling valve on both instruments were operated simultaneously capturing a portion of breath from the stream of exhaled air with an intervening volume loss of only about 5ml.

2.3 RESULTS

2.3.1 Alcolimiter

The Alcolimiter is operated by blowing into a heated chamber in the instrument through a mouthpiece containing a small segment of pipe cleaner to absorb any saliva. A pressure-sensitive switch starts a timer and an "analyse" light is turned on after 5 seconds of continuous blowing at a minimum breath pressure. The 20ml sample retained in the container, which is the last portion exhaled, is then passed through the fuel cell by switching on a pump in the instrument and an electrical signal resulting from the catalytic oxidation of alcohol is displayed on a meter showing as a blood alcohol level.

The first instrument was received early in 1974 and a second instrument in May 1975. An instruction manual was supplied with each detailing the principles of operation. Although changes had been made in the instrument, the servicing and instruction manuals were identical. The second instrument contained thermostats which were enclosed in the heated chamber and could not be adjusted and a protection diode had been added to the 12 volt supply line making the heater inoperative unless the supply was of the correct polarity. In addition, the operation of the light which indicated when the instrument was at the correct temperature had been reversed. Apart from the operations related to these changes, the manual was adequate for some maintenance but inadequate to handle electronic problems.

With the first machine, it was possible to analyze after the expiration of only 60ml of breath. In practice, larger breath samples are required and so the internal tubing connectors were modified to a wider bore to increase the minimum volume. This meant that both instruments would then operate at a minimum breath pressure of 30mm Hg and ensured that at least 450ml of breath was vented to the atmosphere before an analysis was recorded.

The specifications for these instruments had quoted a standard deviation of 3mg/100ml on a breath level of 100mg/100ml which is in agreement with the results of the simulator tests given in Table 2.2. Fuel cell devices require a period of several minutes to recover after an analysis. If a second reading follows immediately, the result will be falsely elevated. The mean recovery time on ten consecutive tests was 8 minutes. It was found that the instruments could be used at closer intervals in time providing the reading observed immediately prior to breath sampling was subtracted from the final reading. A further ten consecutive tests each three minutes apart using this procedure gave the same mean value and a lowering of the standard deviation from 1.5 to 0.9 mg/100ml. Table 2.3 shows a decline in calibrated value with time. As the fuel cells aged, they had to be calibrated upward by increasing the amplification of the signals. Eventually, no further such adjustments could be made. The cells were usable for a period of 9 months before they were replaced. Their life exceeded the specification of 4 months but this may have been due to a lower level of use than that employed by the manufacturers. During the 9 months, alcohol-free breath samples showed increasing small readings up to 10mg/100ml and recovery from a high alcohol test was slower. Linearity fell off above 100mg/100ml, becoming more marked as the cell aged, (Table 2.4).

Both Alcolimiters developed a series of small but important faults during use so that it was necessary to have both in operation at any one time, with one as a reserve instrument for the other. The faults which were largely mechanical, occurred in (a) the thermostat of the heated chamber in both models resulting in a temperature drop, (b) the internal tubing became loose causing breath leakage and (c) a circuit board containing the batteries developed a hairline fracture which was difficult to locate. Other electrical problems also occurred. Both models repeatedly developed these faults and rather more so with the newer model. The use of these instruments was abandoned in late 1975 when devices from other manufacturers became available.

2.3.2 Alcolmeters and the Alco-sensor

There were five different versions of this fuel cell device produced over a 3 year period. Breath sampling with all five instruments

TABLE 2.2 Results of ten consecutive tests with a simulated breath alcohol standard corresponding to 100mg/100ml blood.

Test	Alcolimiter 1	Alcolimiter 2	Alcometer 1	Alcometer 2	Alcometer 3	Alcometer 4	Intoximeter	Breathalyzer 900	Breathalyzer 1000
1	98	100	97	115	100	105	99	100	97
2	100	102	90	105	100	102	100	105	100
3	100	100	84	95	98	97	101	100	99
4	99	99	78	85	98	99	102	95	103
5	97	99	76	85	92	97	100	100	100
6	101	102	78	80	90	97	100	100	95
7	98	102	75	75	94	95	99	100	98
8	91	100	70	70	92	93	97	95	105
9	97	102	73	70	90	94	99	100	100
10	94	98	70	70	88	92	98	105	101
mean	97.5	100.4	79.1	85.0	94.2	97.1	99.5	100.0	99.8
s.d.	3.0	1.5	8.8	15.6	4.5	4.0	1.4	3.3	2.9

Notes:-

Alcolimiters 1 early model
2 late model

Alcolmeters 1 Alco-sensor II, digital
2 APST-M1 pocket, meter
3 AE-M2 evidential analogue
4 AE-D1 evidential digital

Readings on the Alcolmeter 2 and Breathalyzer 900 were made to the nearest 5mg/100ml.

TABLE 2.3 Deviations in mg/100ml from a standard simulator test of 100mg/100ml at various intervals during a one month period.

Day	Alcolimiters		Alcolmeters			Intoximeter	Breathalyzer	
	1	2	2	3	4		900	1000
1	0	0	20	0	0	0	0	0
4	0	0	15	0	0	0	[illegible]	-3
5	0	0	10	0	2	2	5	-3
6	0	0	15	-5	0	-3	0	-1
7	-5	-3	10	-7	-1	-1	-5	2
15	-4	-7	5	-5	2	-3	-5	0
21	0	-20	5	-10	0	0	0	0
28	10	-20	5	-10	3	0	0	1

The notes at the foot of table 2.2 apply

TABLE 2.4 Linearity of instruments. Results of standard alcohol vapours from the simulator.

Value of standard, mg/100ml	50	100	150	200	250	300	400	500
Alcolimiter, new cell	53	98	145	190	233			
Alcolimiter, old cell		95	135	170	205			
Alcolmeter, AE-M2	50	97	130	160	190			
Alcolmeter, AE-D1, digital	50	103						
Intoximeter	50	103	154	205	260			
Breathalyzer 900A		95		205		295		
1000		100		190		277	371	459

operated on the same principle; the subject blew through an open tube attached to the sensor head and at a point decided by the operator, a button was depressed releasing a spring-loaded syringe to take a small sample of the breath flowing through the tube directly into the fuel cell chamber. The breath tube contained a large hole which was intended to provide a whistling sound during expiration; a decrease in the note indicated the approaching end of the expiration when the sample should be taken. There was no resistance to blowing in these tubes and it was difficult to judge the correct time at which to take the specimen. This tube has recently been replaced with a conventional whistle offering some resistance to blowing and making it easier for the operator to determine the end of an expiration.

The earliest instrument tested was a pocked model with a small meter scale from 0 to 300mg/100ml. The performance of this instrument was very unsatisfactory and the results are not presented here. It was replaced by an improved version, the APST-M1 which had a more stable meter. It was recommended that this device should be used only when the indicated temperature on a liquid crystal display was between 20 and 36^{o}. A small instruction manual was included with the instrument detailing operational and calibration procedures.

At this time an evidential instrument, the AE-M2, also became available from the manufacturers and one of these was purchased. It operated on the same principles as the pocket model but contained a heating compartment in which the sensor could be placed to maintain it at a temperature which appeared to be between 30 and 40^{o}. The results were displayed on a large meter contained in a carrying case to which the the sensor was attached by a flexible cable. The operating manual was reasonably comprehensive with an electronic circuit diagram, but there was no mention of the heating compartment. The use of a NALCO standard gas (alcohol in argon) was recommended for calibration and pressurised cans or cylinders were commercially available. Although the instructions stated that the outlet of the NALCO container should be connected to the sampling port of the sensor, it would seem that this connection should have been made through an open tube, similar to the breath tube but without the large hole in the top.

The third instrument purchased from these manufacturers displayed

the result in digital form, the AE-D1, and the temperature of the sensor head compartment was approximately 60°. The instruction manual included a servicing section with circuit diagrams as well as an instrument evaluation section. The specifications were the same as for the meter model.

The last instrument was purchased from Intoximer Inc. U.S.A. which was a pocket instrument, the Alco-Sensor II, using the same fuel cell and basic design but with a digital display. The operating manual, though small, was both clear and concise and the calibration procedure well illustrated with a photograph.

For the intial pocket Alcolmeter, it was suggested that the fuel cell life would be between 6 and 12 months, but in later instruments it was stated that a minimum of 1000 tests could be performed before replacement was necessary. The specifications of the evidential devices gave an alcohol range from 2 to 300 mg/100ml with a reproducibilities of 5% and an accuracy of predicting a blood alcohol level of 10%. All four instruments showed losses of calibrated value on ten consecutive tests at 100mg/100ml (table 2.2), even when these tests were spaced 15 minutes apart. The loss of linearity in the higher ranges was no doubt due to an inability for the instruments to hold a calibrated value (Table 2.4). This fall in performance appeared to decrease with the higher operating temperatures of the fuel cell.

2.3.3 Intoximeter Mk IV

The Mark IV model of the Intoximeter delivered in September 1975 is a gas chromatograph with automatic breath sampling. The subject is required to blow through a flexible unheated tube about 40 cm long through which a stream of air continuously flows to keep it free of condensation. A minimum breath pressure is required to stop this airflow and activate a pressure sensitive switch to start a timer. The breath overflows through a sample valve so that the last portion of exhaled air becomes the test sample. If the breath pressure is less than the minimum level within 4 seconds, the sample is not accepted. Otherwise the valve closes automatically after 7 seconds with a minimum breath volume having been expired of 600ml. After a brief delay, the breath sample is released onto a short chromatographic column filled with Porapak Q in an oven at a temperature of approximately 95°.

A mixture of hydrogen and nitrogen gas carries the sample through the column, where separation of alcohol from other volatile components occurs, to a flame-ionisation detector. The signal strength from the detector is proportional to the alcohol concentration. This signal is automatically integrated and converted to a digital form for display.

The accompanying instruction and maintenance manuals are detailed and clearly illustrated with complete circuit diagrams for the electronic circuitry. There were no specifications for performance but the results of consecutive tests show a low standard deviation (Table 2.2) and the deviations from calibrated value over a one month period were also small (Table 2.3). Readings with standard alcohol vapours were linear over a range from 50 - 260 mg/100ml with a deviation no greater than 4% (Table 2.4). The Intoximeter has been used extensively over a two year period for many hundreds of tests under various social and laboratory drinking situations. It has been notably trouble-free during this time and apart from routine servicing, the only modification has been the replacement of a potentiometer to make resetting of the calibrated value more reliable. This is the best performing instrument in all respects of linearity, reproducibility and stability.

2.3.4 Breathalyzer

Two models of the Breathalyzer, the 900A and the 1000 were obtained with separate comprehensive instruction and maintenance manuals. In the model 900A, the subject blows through a mouthpiece, incorporating a saliva trap, into a 52ml heated chamber within the instrument. This chamber contains a piston which is raised by the inflowing breath to uncover holes in the top of the chamber through which excess breath is vented. When the breath flow ceases, the piston drops slightly to cover these holes and is held in this position by a magnet so that the last portion of breath exhaled is retained in the cylinder. With this design, the volume of breath exhaled before capturing a sample can be very variable.

To overcome this deficiency in the Model 1000, the breath overflows into a second chamber of 400ml capacity also containing a piston so that a minimum volume of 450ml is required and the last portion of breath is retained in the smaller chamber as before. Although the requirement for a minimum breath volume has been met, there can be

considerable variation above this volume because a lamp indicating that the second chamber is full does not light until the subject stops blowing.

In both instruments, the sample of breath in the 52 ml chamber is slowly bubbled through an ampoule containing the reaction mixture by releasing the weighted piston and the amount of alcohol in the breath is measured by the changes in absorbance of the mixture. These ampoules contain 3.0 ml of a 0.25 mg/ml potassium dichromate in 50% sulphuric acid and a catalyst of silver nitrate at a concentration of 1 mg/ml. The following reaction takes place:-

$$2K_2Cr_2O_7 + 8H_2SO_4 + 3C_2H_5OH \xrightarrow{14AgNO_3} 2Cr_2(SO_4)_3 + 2K_2SO_4 + 3CH_3COOH + 11H_2O$$

The original Breathalyzer used a heated dichromate mixture to speed the reaction, but with the addition of a silver catalyst, the reaction was essentially complete at room temperature in 90 seconds at alcohol levels below 200 mg/100 ml, but it was found that 240 seconds were required at equivalent blood alcohol levels of 500 mg/100 ml. In the model 1000, changes in absorbance readings were made automatically at 90 seconds so that the high alcohol levels were slightly underestimated resulting in some loss of linearity (Table 2.4). These low readings could be corrected by a simple calibration curve. The problem was not so evident in the model 900A as the readings were registered manually after an indicator light came on.

As the Breathalyzer is essentially a colorimeter, its performance could be checked against a standard laboratory spectrophotometer (a Hitachi model 101). Breath tests were made in the model 900A in the usual manner from a range of simulator standards. After the reaction period, the contents of the test ampoules were transferred to square cuvettes of 1 cm light path and the transmission read in the spectrophotometer at a wavelength of 440 nm. A similar set of ampoules was prepared by pipetting 50 µl volumes of an alcohol solution, equivalent to the amount of alcohol contained in 52 ml of breath at the various blood alcohol levels, into the dichromate/sulphuric acid solution and the reaction allowed to proceed to completion. Tables 2.5 and 2.6 show the mean percentage transmission of 5 tests at each alcohol level. The conversion from transmission into blood alcohol levels was made by linear

TABLE 2.5 Results from ampoules prepared from simulated breath tests in the Breathalyzer 900A.

Breath standard, mg/100 ml blood	100	200	300
Spectrophotometer % transmission, mean (n = 5)	55.8	61.4	66.0
Conversion to blood alcohol mg/100 ml	106	205	289
Standard deviation	20.6	29.3	26
Coefficient of variation %	19.4	14.3	9.0
Breathalyzer 900A reading, mean (n = 5)	103	197	285
Standard deviation	9.7	16.0	9.4
Coefficient of variation %	9.4	8.1	3.3

TABLE 2.6 Results from ampoules prepared by pipetting 50 µl alcohol into the dichromate solution.

Breath standard, mg/100 ml blood	100	200	300
Spectrophotometer % transmission, mean (n = 5)	56.0	61.4	66.3
Conversion to blood alcohol, mg/100 ml	99	206	295
Standard deviation	11.7	3.1	17.4
Coefficient of variation %	12.0	1.5	5.9
Breathalyzer 900A reading, mean (n = 5)	98	200	298
Standard deviation	10.9	12.7	2.7
Coefficient of variation %	10.9	6.4	0.9

regression analysis. The results show that the Breathalyzer gave more consistent readings than the spectrophotometer, but the standard deviations were smaller with ampoules prepared from alcohol solution than from simulated breath tests in the Breathalyzer.

There were no major problems with either of the Breathalyzers. The model 900A breath collection cylinder required washing out after extensive use as recommended in the maintenance manual. A transformer of the printer on the model 1000 became faulty but did not preclude the use of the instrument for breath tests.

A major disadvantage with Breathalyzers is the use of ampoules containing 50% sulphuric acid which need to be thin-walled since they are, in effect, cuvettes in the colorimetric estimation. A poor design point in the model 1000 is the ampoule compartment which is made of aluminium and very prone to attack by sulphuric acid in spite of a protective coat of paint. The corrosion swellings on compartment walls cause jamming of the ampoules. They became so difficult to remove, that on occasions, the instrument had to be dismantled to release the ampoule and clean the compartment.

2.3.5 Results on subjects

Results of comparative breath tests with five instruments carried out on consecutive breath samples from the same subject are given in Table 2.7 as a percentage of the Intoximeter result. For a second series of tests using the digital Alcolmeter and a gas chromatograph described in Chapter 3, the results from three subjects are combined in a correlation diagram in Figure 2.4. When the Alcolmeter inlet was attached to the gas chromatograph inlet so that the breath was sampled simultaneously by both instruments, the correlation between the two results were within experimental error. However, when the Alcolmeter test was made independantly of the gas chromatograph, but on the consecutive breath sample, the results of the Alcolmeter were consistently higher and with a wider degree of scatter.

These tests were made with a 20 minute recovery period between each use of the Alcolmeter so that a deterioration in calibration was not apparent. When there was only a 5 minute interval between tests on one subject using the simultaneous sampling technique described above, the Alcolmeter readings dropped from 104% of the gas chromatograph

TABLE 2.7 Comparative tests on consecutive breath samples.
The results are expressed as a percentage of the Intoximeter result.

SUBJECT	Test:- 1	2	3	4	AVERAGE
	Alcolimiter 1				
S	-3	4	-5	9	2
B	13	29	15	49	32
J	6	15	13	52	33
K	-6	-4	-11	-9	-10
A	-3	3	-5	6	0
C	7	13	16	35	25
	Alcolimiter 2				
S	-17	-6			-11
B	-4	0			-2
J	3	6			4
K	-13	-4			-8
A	-9	-4			-6
C	4	1			2
	AE-M2				
S	9	1	15	2	8
B	20	10	29	15	22
J	-7				-7
K	2	3	4	7	5
A	-23	4	-44	11	-15
C	10	8	20	19	20
	APST-M1				
S	-14	-20			-17
B	-10				-10
J	-6	-11			-8
K	-19	-10			-15
A	-9	-13			-11
C	-3	-12			-7
	Breathalyzer 900A				
1	-23	-19	-12	-20	-4 -16
2	-7	6	-2	-8	-9 -4
3	21	-23	0	-7	-4

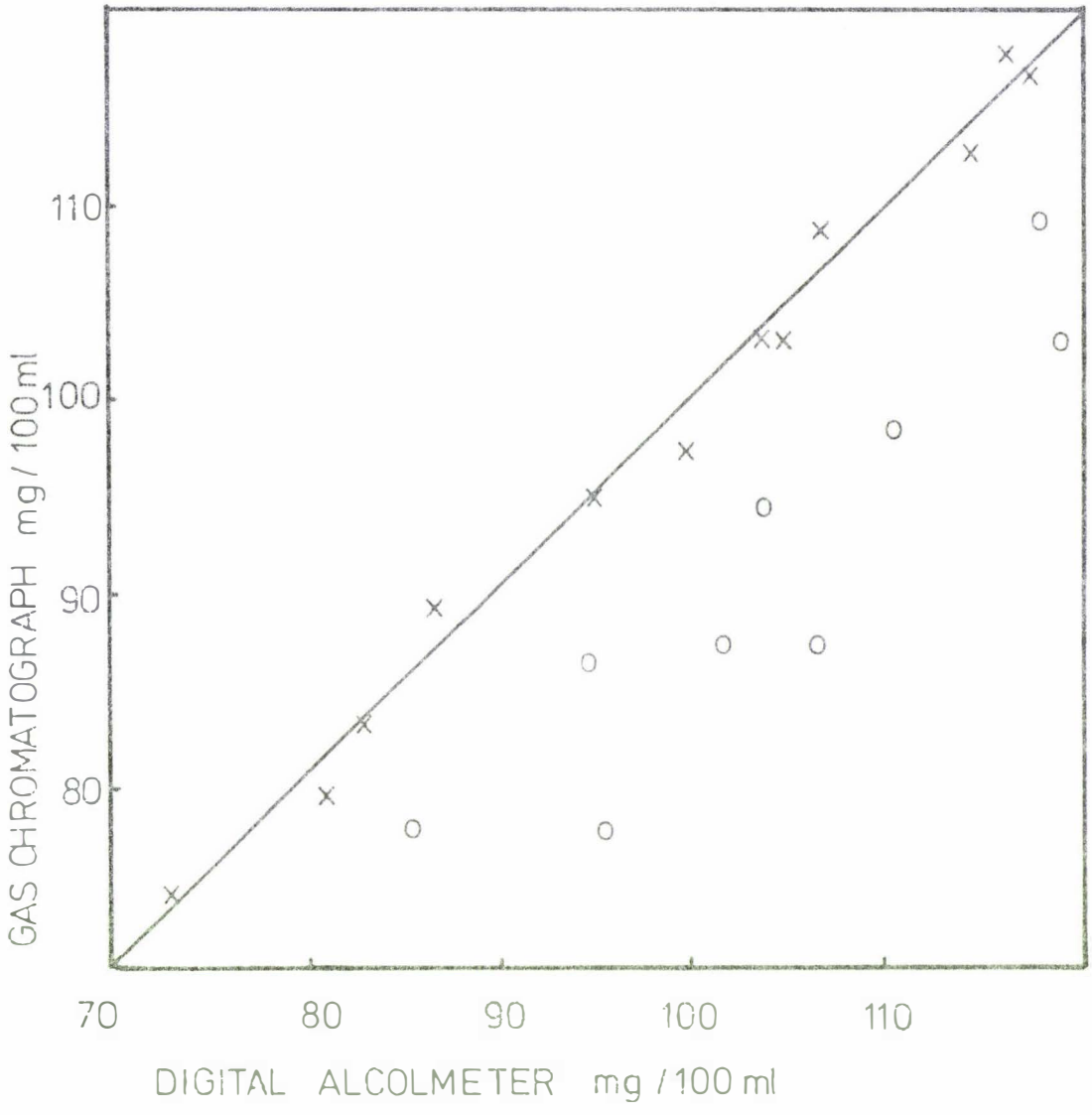


FIGURE 2.4

Correlations between breath test results obtained from a digital Alcolmeter and a gas chromatograph. Alcolmeter tests taken 20 minutes apart.

X Simultaneous breath sample

O Consecutive breath sample

results to 89% over 14 tests (Table 2.8) showing a similar loss of calibration found with simulator standards.

2.4 DISCUSSION AND CONCLUSIONS

Although comparisons between blood and breath were not made in this study, some useful information was obtained concerning the different breath testing instruments. Variations in breath test results between machines can be attributable to either the electrical and mechanical operation of the instruments or to the factors involved in breath sampling related to the physiological functions in the subject.

Firstly, consideration will be made of the electrical and mechanical operation. The Breathalyzers have an advantage over all of the other instruments in that the calibration is dependent on the volume and concentration of the contents and the size of the ampoules, both of which can be standardised by the manufacturers through quality control procedures. In addition, the mechanism of the Breathalyzer itself which translates the movement of the light source between the photcells into blood alcohol levels is a very reliable system. Providing the instruments are properly maintained, they may be used at any time with known tolerance limits on the degree of error. In all the other instruments tested, calibration may depend on the state of the sensor, its associated amplification circuitry and the electrical supply. All amplifiers used in these instruments are subject to variations due to movement of the calibration potentiometers caused by vibration in transit from one site to another. Tolerance limits for breath tests in these devices can only be determined on a probability basis from standardised tests on many instruments over a period of time. It might then be possible to quantify the chance of a result being outside certain limits within a time period after calibration. Such probability methods may not be acceptable in a court of law and it may be necessary to obtain a reading on a standard alcohol vapour at the time of a breath test. It is understood that such a system using the Alcolmeter fuel cell is under developement by Intoximeter Inc. Such tests, unless completely automated, add to the complexity of the breath testing procedure.

At the present time, it would appear from the results in this study, that there is a major problem with variations in results between instruments independent of changes in calibration values. Such

TABLE 2.8 Results of simultaneous breath samples taken with a gas chromatograph and the digital Alcolmeter, mg/100 ml.

GC	AE-D1	% difference from GC
68	71	4
77	81	5
82	84	2
82	84	2
96	95	-1
99	95	-4
96	91	-5
90	85	-6
93	88	-5
95	88	-7
88	82	-7
93	83	-11

problems are clearly associated with breath sampling procedures. During the experiments, it was noted that although well briefed on giving a breath test, the approach of each subject was different. For some, the breath was blown as vigorously as possible into the instrument, while others barely attained the minimum breath pressure required to operate the instrument. While each achieved the minimum breath volume, some would greatly exceed this volume so that the breath tests could have been carried out on expirations varying between 0.5 and 2.0 litres. It is likely that alcohol concentrations are dependent on the expired breath volume before sampling as well as on tidal air effects. Such a conclusion may be deduced from the comparative study of breath testing instruments using subjects who had been drinking alcohol. In Table 2.7 it can be seen that some subjects gave test results which were consistently lower with a particular device than the Intoximeter, yet at the same time, another subject would have high test results. In the comparison between the digital Alcolmeter and a gas chromatograph (Fig 2.4) there was a high degree of correlation between the two results when the same breath was sampled with both instruments. When a separate breath sample was used for the Alcolmeter, the correlation showed a wider degree of scatter and all readings were consistently higher than those obtained from the gas chromatograph. These higher readings may be explained by differences in expired breath volume. With the gas chromatograph, the breath sample was obtained after an expired air volume of one litre as determined by either a spirometer or a one litre bag. When the Alcolmeter was used by itself, the expired air volume depended on the instrument operator judging the approaching end of the expiration before manually actuating the sampling mechanism. The design of the Alcolmeter tubes was such that a large portion of the lung volume of some 2 - 3 litres could be expelled in a few seconds which suggests that larger breath volumes were used with the Alcolmeter by itself than when connected to the gas chromatograph intake. With the larger breath volume, it appears that the alcohol concentration also increases. Such an increase has been shown by Jones et al (1974) in Figure 4 of their paper. It has been implicitly assumed until now that the concentration of alcohol in the breath is constant after the expiration of the tidal air. While it may be expected that the air in the alveoli of the lungs comes into equilibrium with the blood from the pulmonary artery, tidal air is that portion that is recently inhaled

and occupies the relatively large air spaces of the upper respiratory tract where complete equilibration would be difficult to achieve. Some manufacturers of breath testing instruments have appeared to assume that once the tidal air has been expired, the remaining breath has a constant alcohol concentration throughout its volume. Quite clearly, this point will have to be re-examined and modifications to the design of breath sampling devices made. Another factor which may have some bearing on these changes in alcohol concentration in expired breath is the effect of temperature. Harger et al (1956) have shown an approximate 7.5% change in alcohol concentration in vapours for every degree centigrade change in temperature while Dubowski (1974b) has shown that breath temperature increases with expiration volume. In view of these factors it was decided to carry out further investigations on the effects of volume and temperature on the alcohol concentration in the breath before embarking on further studies of alcohol metabolism using breath tests to determine blood alcohol levels.

3.0 INTRODUCTION

The results from the comparative study of various breath-testing instruments, described in Chapter 2, suggested that it could be worthwhile to study in more detail the factors influencing the concentration of alcohol in breath. To study different factors, it was considered that there may be advantages in measuring the volume, pressure and rate of flow of expired breath together with accurate analyses of alcohol concentrations at any time during an exhalation. Since breath temperatures can influence breath alcohol concentrations, it was essential to record these temperatures during exhalations. Observations obtained with the Alcolimiter suggested that there were physiological fluctuations in breath alcohol levels occurring over a period of several minutes. Accordingly, it was decided that the measurements of alcohol concentration should be made within very short time intervals.

3.1 METHODS

3.1.1 Alcohol measurement by gas chromatography

The rapid, repeated measurements of alcohol in breath samples were achieved by making modifications to a standard gas chromatograph, model AGC 211 manufactured by Carle Instruments Inc, U.S.A. (Figure 3.1). The basic instrument, (dimensions 180 x 450 x 450 mm) contained two columns leading to a single flame ionisation detector. The electronic components were housed in a separate compartment (dimensions: 450 x 100 x 100 mm). A so-called 'mini volume' valve (Carle Inc.) containing a 1.0 ml sample loop was fitted into the column oven. Because narrow passageways in the valve restricted flow, it was not possible to exhale freely through the valve. Accordingly, breath samples were captured by blowing through a 4mm internal diameter copper T piece with one arm connected to the valve inlet and the other venting to the atmosphere. By varying the restriction to flow on the vent arm, it was possible to bypass more or less breath through the valve. An exhalation rate of 12 litres/ minute at a pressure of 30 mm Hg resulted in a flow through the loop of 10 ml/ second; at 6 litres/ minute and a pressure of 10mm Hg, a loop flow of 10 ml in 4 seconds was obtained. From these figures, it is apparent that the sample loop was flushed at a high rate under normal exhalations without increasing the breath pressure beyond 30 mm Hg.

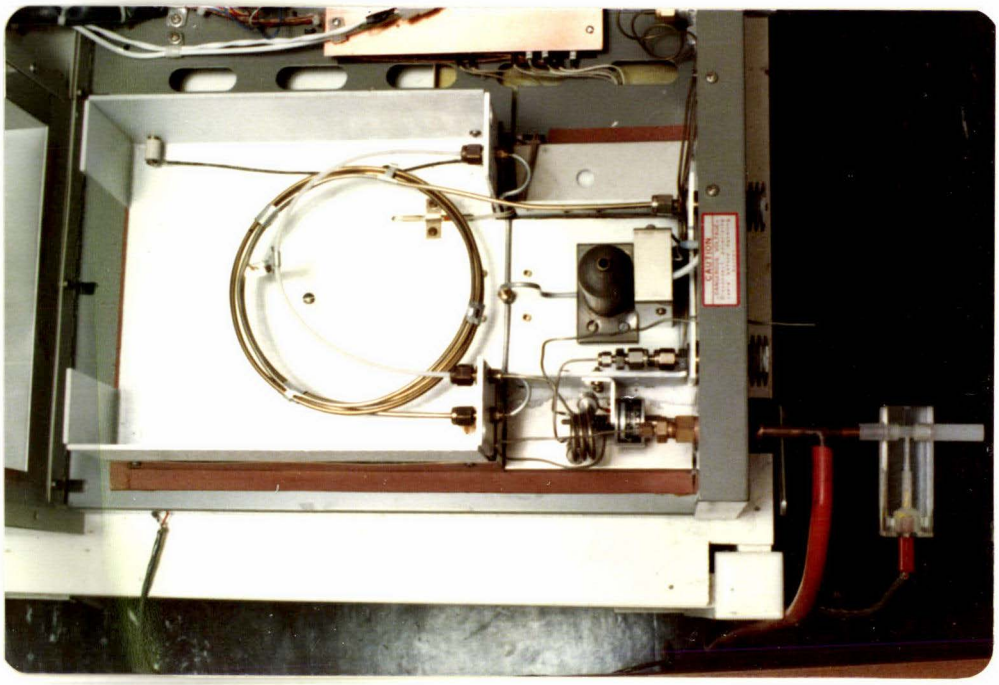


Figure 3.1

A plan view of the modified Carle gas chromatograph to show the interior. The lower coil is a 2 meter column operating from the right hand injector and the upper half-loop is the 150 nm teflon column connected to the left-hand injector via the gas sampling valve. The breath inlet, (lower right) shows the copper T piece with its connection to the spirometer and attached is the perspex block containing the breath temperature thermistor.

The arm of the T attached to the sample valve within the oven transmitted heat to the other two arms projecting outside the instrument and prevented condensation of water vapour from the breath. Where a thermistor was used to measure breath temperature at the point of entry into the valve, the heated arm helped maintain the thermistor ambient temperature between 25 and 29°. In the 'purge' position of the valve, breath flowed through the loop while carrier gas passed through the gas chromatograph column in the normal manner. On switching to 'inject', the loop was connected into the carrier gas flow thus applying its contents to the head of the column.

Rapid analyses were made with a column made of 'Teflon' 200mm long and 1.5mm internal diameter. It was filled with Porapak Q (Waters Associates Inc., U.S.A.) and had a carrier gas flow of 30 ml/ minute. A one metre by 2mm internal diameter column also containing Porapak Q was placed in the second position and used for blood alcohol estimations by the headspace method. The carrier gas was a mixture of hydrogen and nitrogen in the optimal ratio for the detector of 4 : 6 and supplied from a single cylinder with less than one part per million of organic contamination, (N.Z. Industrial Gases). The flame ionisation detector received the gas flows from both columns at a combined optimal gas flow rate of 60 ml/minute. A typical chromatogram of a simulated breath sample corresponding to a blood alcohol level of 200mg/100ml is shown in figure 3.2. The retention time for alcohol was 16 seconds and acetone, if present in sufficient concentration, was a shoulder on the declining alcohol slope at 21 seconds. Baseline recovery was rapid and the instrument was ready for a further analysis in 30 seconds. At the usual electrometer settings with the range at 10^2 and the attenuator at x16, water vapour and acetaldehyde were not detected. Immediately on switching the sample valve, a reversed peak was recorded corresponding to the pressure drop in the column and this was followed 3 seconds later by a larger reversed peak probably due to cooling of the flame by the water vapour in the sample. The concentration of alcohol in a sample was calculated from prior calibration of peak heights on the chart recorder.

3.1.2 Alcohol measurement in vitro

The effect of any delay in switching the valve to inject the

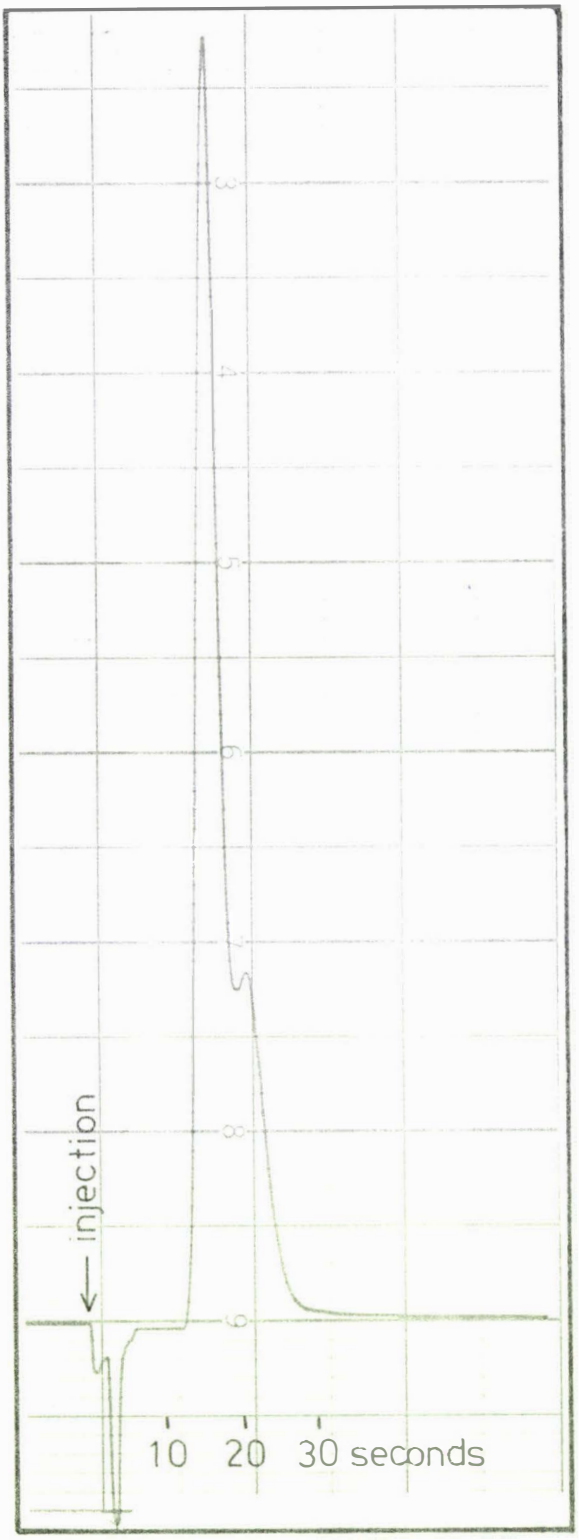


Figure 3.2

Alcohol and acetone peaks obtained with the Carle gas chromatograph equivalent to 200 mg alcohol and 12 mg acetone / 100 ml blood. chart speed at 6 cm/minute.

sample onto the gas chromatograph was examined by comparing samples switched immediately and after a delay of 5 seconds. There were no differences between the means and standard deviations from both procedures. Performance was checked by ten tests at each of four simulator levels from 0.243 to 1.824 g/litre (Table 3.1). Peak heights were converted to alcohol concentrations after linear regression analysis of the 40 results on the expected alcohol concentrations in the vapour phase from the simulator at 34^{o} and no significant departure from linearity was seen over the range covered.

The high degree of reproducibility (Table 3.2) and rapidity of analysis made this modified gas chromatograph ideally suited for the investigations to follow.

3.1.3 Partition coefficients

Standard alcohol vapours were obtained from a Stephenson simulator as described in Chapter 2. The concentration of alcohol in the air from the simulator can be calculated from the partition coefficient:-

$$K_t = \frac{\text{weight of alcohol per unit volume of air}}{\text{weight of alcohol per unit volume of water}}$$

where t is the temperature of equilibration. The coefficients for a wide range of temperatures, but not 34^{o}, have been determined by Harger et al (1950b) and these produce a curvilinear regression of K on t. This data was rectified by logarithmic transformation of K and a value of 393×10^{-6} was obtained for 34^{o} from the least squares fit of the transformed data, (Figure 3.3). Jones, (1974) found a value of 391×10^{-6} using a gas chromatographic method. The coefficient shows that when water contains 1 gram of alcohol per litre at 34^{o}, the air in equilibrium with that water will contain 393 µg alcohol per litre.

The partition coefficient for air over blood or plasma was determined with the Carle gas chromatograph by the following method. Erythrocytes were separated from the plasma of outdated blood donated for transfusion purposes (2 weeks old). To 500ml of blood, plasma or water was added 10ml of the standard 60.8 g/litre alcohol solution to make three solutions of identical alcohol concentration of 1.216 g/ litre. No haemolysis occurred in the blood when the alcohol was added slowly with stirring. Two drops of anti-foam A

TABLE 3.1 The alcohol concentration of simulator solutions and the resulting peak heights of gas chromatographic analysis of the vapour phases.

Volume of standard 60.8 g/l alcohol diluted to 500 ml in the simulator (ml)	2	5	10	15
Alcohol concentration in the aqueous phase g.l	.243	.608	1.216	1.824
Peak heights in mm, mean	23.8	59.0	122.2	184.7
s.d.	0.167	0.275	0.632	1.059
C.V.%	0.7	0.5	0.5	0.6

TABLE 3.2 The range of alcohol concentrations in the vapour phase from simulator solutions. Calculated from the data summarised in Table 3.1

Alcohol concentration in the vapour phase µg/litre	95	238	478	717
minimum estimate µg/litre	98	232	471	712
maximum estimate µg/litre	99	236	478	724

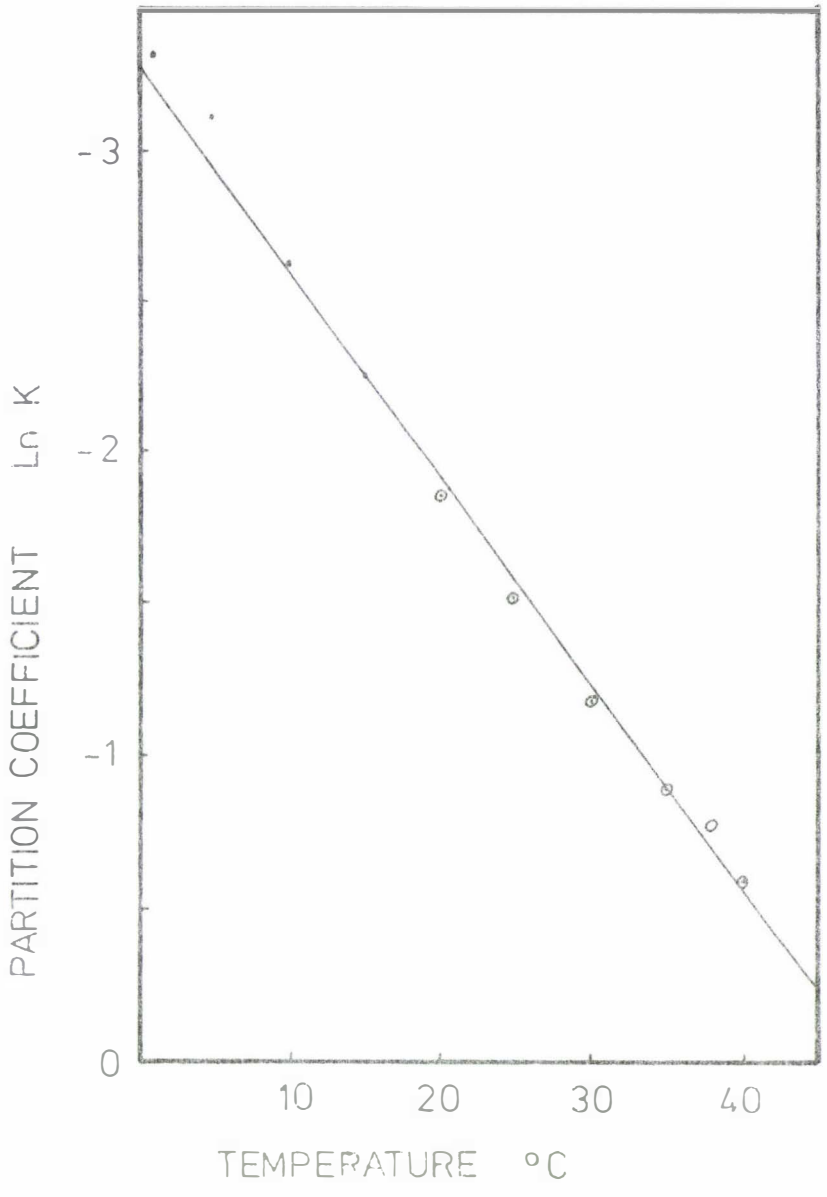


Figure 3.3

A plot of the logarithmic transformation of partition coefficients for alcohol between air and water at various temperatures. Data from Harger et al (1950b), __ . __ ; and Jones (1974), __ o __.

concentrate (Sigma) were added to each solution to prevent frothing. The simulator outlet was then attached to the gas chromatograph and a steady stream of breath blown through it for at least 5 seconds before activating the sampling valve.

Alcohol concentrations in each of the vapours from the three solutions were determined from the peak heights from at least five estimations with each solution. The blood was then diluted with the plasma to give two lower haemotocrit values and alcohol concentrations in the vapour phase determined, (Table 3.3).

The haematocrit of the blood was determined with a micro-haematocrit centrifuge by standard procedures, (Dacie and Lewis, 1975) and the water contents of blood and plasma by weight difference after drying over sulphuric acid, (Figure 3.4). The water content of blood showed a negative correlation with the haematocrit, ($r = 1.000$) and in the range of blood samples studied could be calculated from the regression formula:-

% water in the blood = 92.4 - 27.5 x the haematocrit value

The concentration of alcohol in the vapour phase from the aqueous solution can be calculated from the partition coefficient of Harger (1950b):-

concentration of alcohol / unit volume of aqueous phase x partition coefficient = concentration of alcohol / unit volume of vapour phase

or $1.216 \text{ g/litre} \times 393 \times 10^{-6} = 479 \times 10^{-6} \text{ g/l.}$

As the alcohol concentration in the vapour phase is proportional to peak height and the alcohol concentrations in water, plasma and blood samples are identical, peak heights can be directly related to partition coefficients taking the mean peak height of the 30 estimations on the aqueous sample equivalent to 393×10^{-6}. The partition coefficients for the plasma and blood samples were calculated from the mean peak height ratios (Table 3.4). The mean partition coefficient for blood with an average haematocrit value of 0.45 was 461×10^{-6} which is close to the mean value for males of 462×10^{-6} reported by Jones (1974) and 486×10^{-6} reported by Harger (1950b). When the partition coefficients were plotted against the water contents of the samples, there appeared to be a linear relationship and statistical analysis gave a regression

TABLE 3.3 Alcohol peak heights obtained from gas chromatographic analysis of the vapour phases from alcohol concentrations in the simulator of 1.216 g/litre of water, plasma and blood at three different haematocrits.

	Water	Plasma	Blood Haematocrit:		
			0.25	0.45	0.65
n	30	10	5	5	5
mean	140.6	150.9	158.3	164.9	175.4
s.d.	3.5	2.8	1.9	2.9	2.1
C.V.%	2.5	1.9	1.2	1.8	1.2

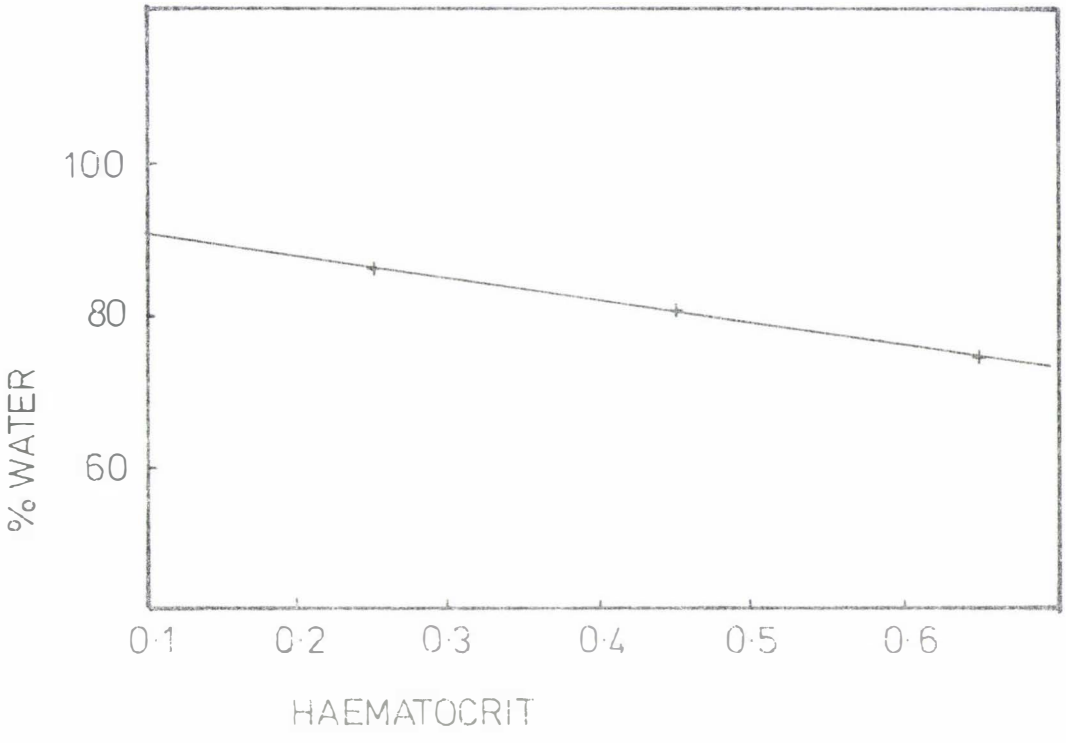


Figure 3.4

A plot of the water content of blood against haematocrit

TABLE 3.4 Partition coefficients for alcohol between air and water, plasma and blood at three haematocrit values.

	Water	Plasma	Blood haematocrit:- .25	.45	.65
Mean x 10^{-6}	393	422	442	461	490
minimum		410	433	447	483
maximum		430	447	466	497

coefficient of -3.62 and an intercept of 756, (Figure 3.5). This linear regression suggested that the amount of alcohol in the vapour phase is inversely proportional to the water content of the medium and that there are no apparent cell, salt or lipid interactions.

The water contents within the normal ranges of haematocrit values for males and females and the partition coefficients were calculated from the appropriate regression formulae, (Table 3.5). The reciprocals of the partition coefficients are the distribution ratios which give the volume of air containing the same amount of alcohol as present in 1ml of the aqueous phase, (Table 3.5).

3.1.4 Respiration measurements

Breath volumes were measured in a spirometer attached to the breath bypass tube on the gas chromatograph (Figure 3.6). A mercury manometer was interposed between a variable restriction on the bypass line and the breath inlet point to monitor breath pressure. Breath temperatures were recorded from the amplified output of a glass bead thermistor having a response time of 0.1 seconds. The bead projected into an air channel 6 mm diameter cut into a perspex block which fitted onto the T inlet. The thermistor temperature was maintained between 25 - 29°. A polythene mouthpiece 20 mm long, which was fitted into the inlet of the block, ensured that temperatures were measured as close to the mouth as possible.

3.1.5 Breath alcohol levels in drinking subjects

Six volunteers were given alcohol as vodka diluted *ad libitum* with lemonade at doses of 0.5 or 1.0 g/Kg body weight after a light lunch. The subjects consumed the alcohol over a 20 - 30 minute period. For the breath tests, the subjects were asked to make a normal inspiration, hold the breath for 2 seconds and then blow out through the mouthpiece of the gas chromatograph, maintaining a pressure on the manometer at 10 mm Hg. The sampling valve was operated after the passage of the required volume of air. A set sequence of tests was adhered to at various intervals after drinking. The subjects were required to make 6 expirations into the apparatus 1 - 2 minutes apart. The alcohol concentration in the first breath sample was measured after the expiration of 250 ml of air and successive breath samples after 500, 750, 1000, 1500 and 2000 ml of air.

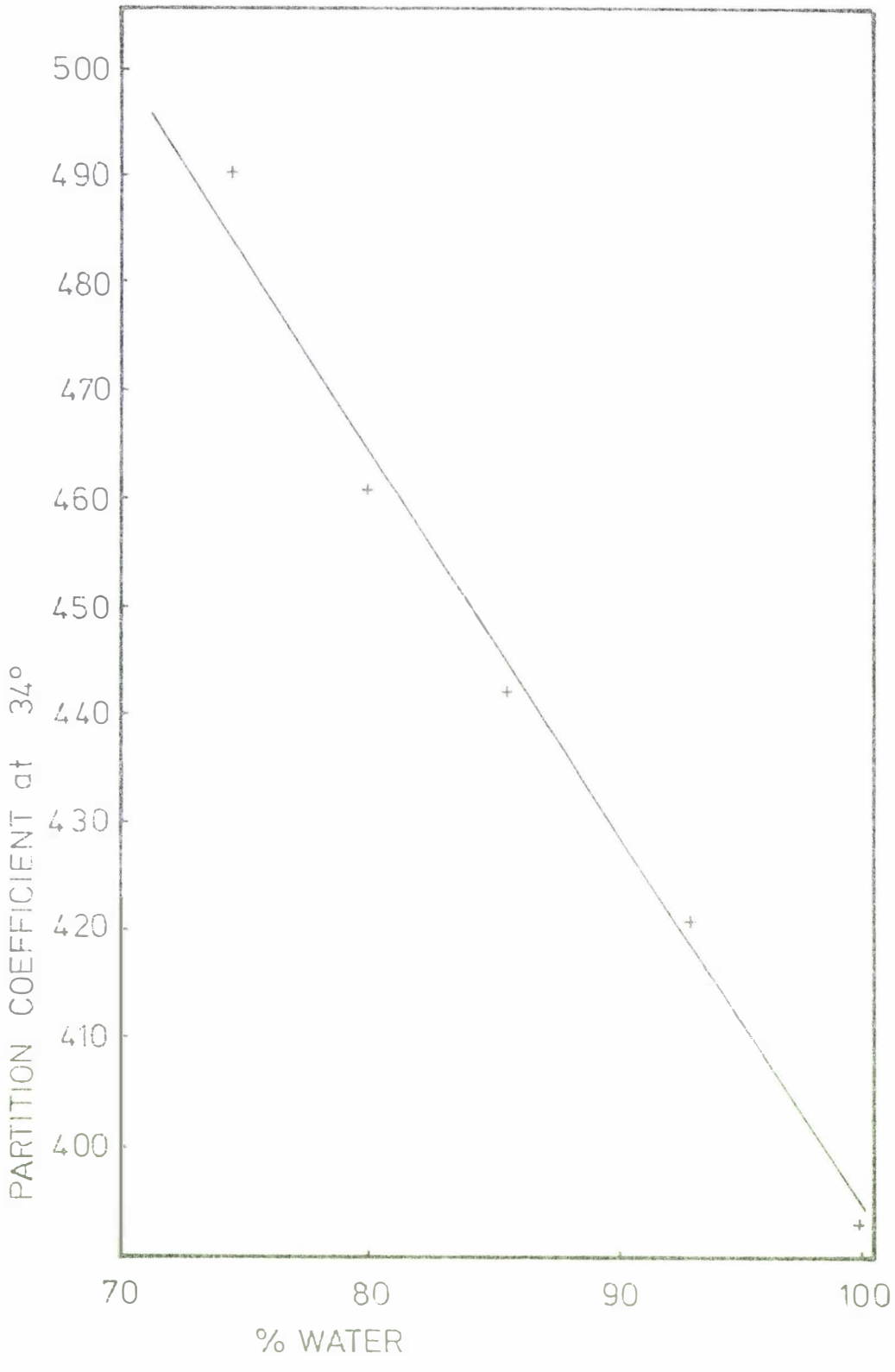


Figure 3.5

A plot of the partition coefficients for alcohol between air and blood, plasma and water at 34° against the water content.

TABLE 3.5 The calculated values of water contents, alcohol partition coefficients and distribution ratios for blood with a normal range of haematocrit.

		Haematocrit	% water	Partition coeff $\times 10^{-6}$	Distribution ratio
males	max	.54	79.5	475	2105
	mean	.47	77.5	468	2137
	min	.40	81.4	461	2169
females	max	.47	77.5	468	2137
	mean	.42	80.8	463	2160
	min	.37	82.2	458	2183

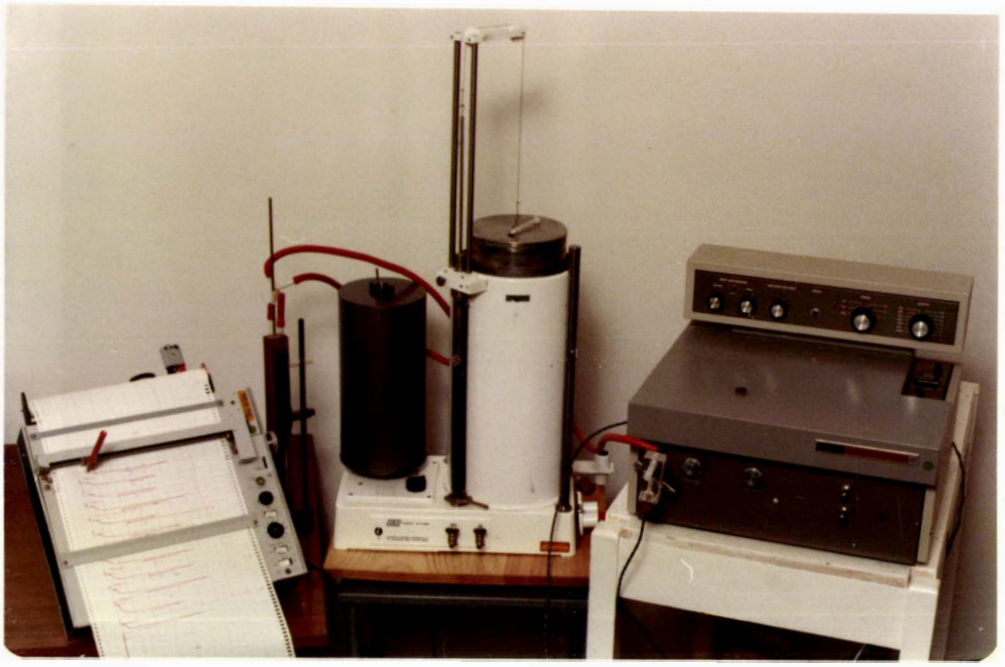


Figure 3.6

The modified gas chromatograph with a spirometer, mercury manometer and chart recorder.

3.2 RESULTS OF IN VIVO TESTS

3.2.1. Breath temperature

The temperatures of the breath taken simulataneously with the sample for alcohol measurement were progressively higher as the expiration volume increased (Table 3.6) and the tendancy for the mean temperature to increase, although small, appeared to be constant throughout an expiration rather than to plateau after a constant volume of breath had been exhaled (Figure 3.7). The initial breath temperature no doubt, reflected ambient temperature so that if the room temperature was low, then the rate of temperature increase was high. A decrease in standard deviation as the breath volume increased, showed the tendency for breath temperatures to come to nearly the same value after a prolonged expiration.

3.2.2. Breath alcohol levels

Alcohol concentrations of breath samples increased with expiration volumes (Table 3.7). The alcohol concentrations were corrected to a standard temperature of 34^{o} (Table 3.8) by using a factor of 7.5% per degree, obtained from a linear interpolation of the data of Harger et al (1950b) between 32 and 36^{o} (Figure 3.8). The temperature-corrected and uncorrected alcohol curves from all subjects are shown in figures 3.9 a - f.

The mean breath alcohol concentrations over the complete time course of the experiment at each breath volume were calculated for both temperature-corrected and uncorrected alcohol levels from linear regression analysis (Table 3.9). It can be seen that after temperature correction, there was still a significant linear increase in breath alcohol concentration up to expiration volumes of 2 litres (Figure 3.10). There was a significant relationship between the change in breath alcohol concentration with volume and the mean blood alcohol level. Figure 3.11 shows that the breath volume effect is more important at higher blood alcohol levels than at lower and that this factor results in estimates of breath alcohol being lower by an increasing percentage as the blood levels increase.

As each of these breath concentrations reflect the same blood alcohol level, the distribution factor which converts the breath to blood levels must be different for every breath volume. It was assumed that the 2 litre temperature compensated breath alcohol levels

TABLE 3.6 Breath temperatures at the end of various expiration volumes.

Subject	Time (minutes) t	Breath Volume (litres) 0.25	0.5	0.75	1.0	1.5	2.0
NW	138	33.5	34.5	34	35	35	34.5
	168	33.5	34	33	33.5	34	34
	189	33.5	33	33	34	34	34.5
	256	32.5	33.5	34	34.5	34.5	34.5
	287	33	34.5	35	35	35.5	34.5
KJ	121	31	32.5	32.5	32.5	33	33.5
	156	31	32.5	33	33	33.5	33.5
	185	33	33.5	33.5	33.5	33.5	34
	220	32.5	33	33.5	33.5	33.5	34
	252	32.5	33	34	34	34.5	34.5
	278	33	34	34.5	34.5	35	35
	311	33	34	33.5	34.5	34.5	34.5
JP	86	34.5	34.5	34.5	34.5	34.5	35
	103	33.5	34.5	35	34.5	35	35
	140	33	33.5	33.5	33.5	33.5	34
	171	32.5	33	34	33.5	34	34.5
	201	33	33.5	34	33.5	34.5	35
VP	115	33	35	32.5	34	34	34
	170	32.5	33	33.5	33.5	34	34
	202	34	34	34	34	34	34.5
CW	66	33.5	34.5	34.5	34.5	34.5	35
	79	33.5	34	34.5	34.5	34.5	35
	94	34	34	34	34.5	34.5	34.5
	107	33.5	34	34	34	35	35
	129	33	34	34	34	34.5	35
	143	33	33.5	33.5	33.5	34	34
	166	33	33.5	33.5	34	34.5	34.5
	175	33	33	34	34	34.5	35
	190	33	34	34	34	34	34.5
RG	43	31.5	32	32	33	33	34.5
	59	31	31.5	32	32	33	33
	72	31.5	32	32	32	33	33
	93	31.5	31.5	32	32	32.5	33
	119	32	32	32	32	33	33
	133	30.5	31	31.5	32	32.5	33
	mean	32.8	33.3	33.5	33.6	34.0	34.3
	S.D.	0.88	1.0	0.93	0.87	0.76	0.67

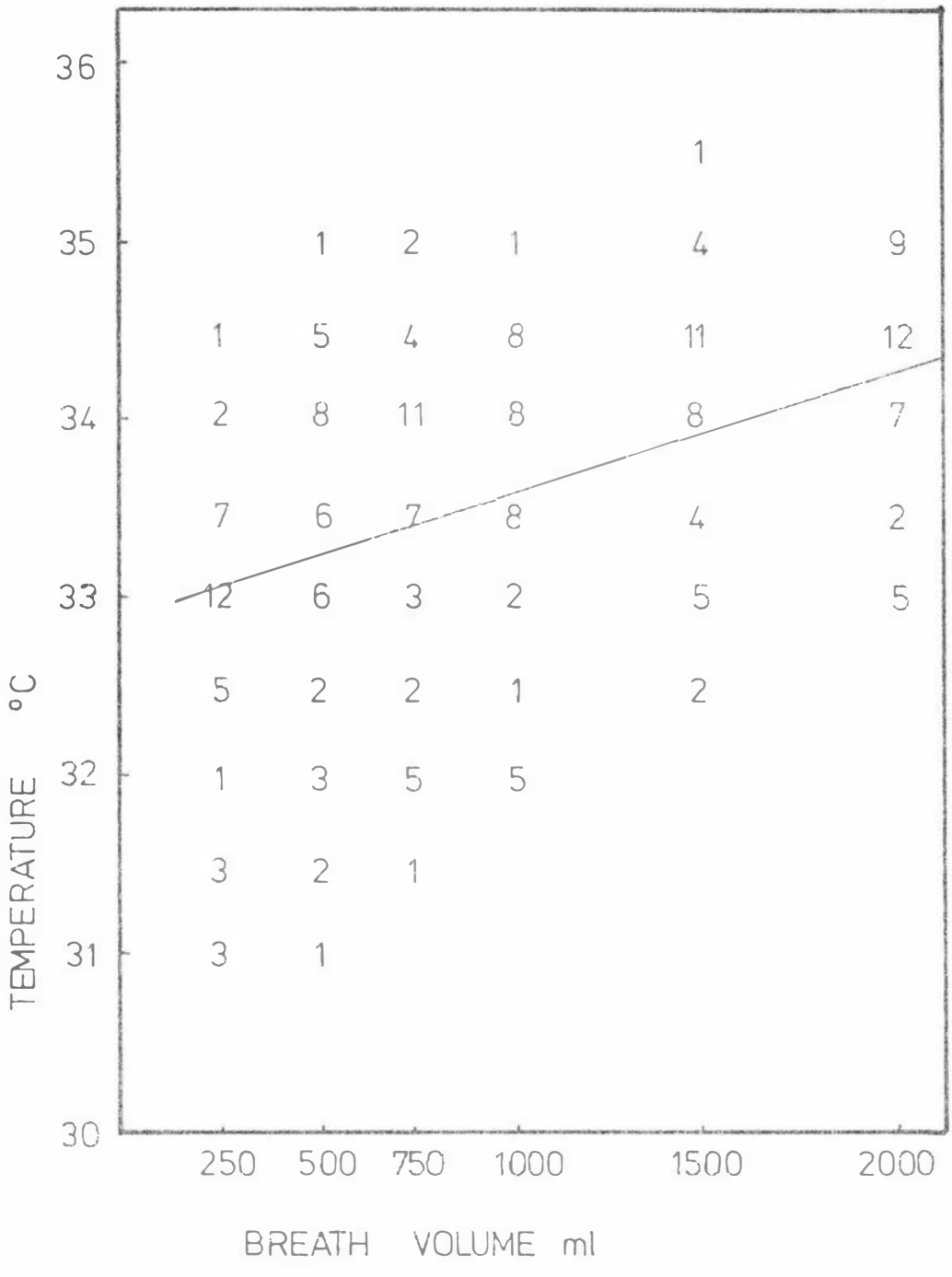


Figure 3.7

Frequency diagram of breath temperature at various expiration volumes. The line has been fitted by linear regression analysis of breath temperature on volume.

TABLE 3.7 Alcohol concentrations in the breath at the end of various expiration volumes, µg/litre.

Subject	Time (minutes)	Breath Volume (litres)					
	t	.25	.5	.75	1.0	1.5	2.0
NW	138	333	347	356	384	389	382
	168	293	314	308	318	329	331
	189	252	249	263	277	301	308
	256	142	171	177	185	206	209
	287	131	144	151	153	156	155
KJ	121	362	398	385	414	429	463
	156	328	344	376	381	415	427
	185	290	346	351	354	360	382
	220	236	275	300	311	316	317
	252	216	241	252	259	268	280
	278	195	211	219	236	249	252
JP	103	373	445	476	471	464	508
	140	338	364	369	390	390	432
	171	320	333	350	359	382	408
	201	274	277	316	322	342	343
VP	115	333	369	370	391	380	429
	170	288	305	330	351	353	367
	202	271	299	295	307	323	332
CW	66	174	191	197	205	206	208
	79	169	182	193	194	204	207
	94	145	169	181	179	188	184
	107	148	156	160	163	161	169
	129	121	137	134	140	148	152
	143	100	110	120	124	131	137
	166	93	101	105	112	120	121
	175	102	104	106	107	112	115
	190	71	87	88	91	92	98
RG	59	252	253	270	292	297	312
	72	214	245	252	250	262	284
	93	198	207	210	213	230	247
	119	145	155	175	178	188	193
	133	125	134	144	150	167	174

TABLE 3.8 Breath concentrations after correcting for temperature differences from 34°, alcohol µg/litre.

Subject	Time (minutes)	Breath Volume (litres)					
	t	.25	.5	.75	1.0	1.5	2.0
NW	138	345	333	356	355	360	367
	168	304	314	331	330	329	331
	189	261	267	283	277	301	296
	256	158	177	177	178	198	201
	287	140	138	139	141	138	149
KJ	121	443	443	429	460	461	480
	156	402	383	404	409	430	459
	185	311	359	364	367	373	382
	220	262	295	311	322	328	317
	252	240	259	252	259	258	269
	278	209	211	210	227	230	233
	311	143	170	168	176	180	181
JP	86	462	482	464	472	487	503
	103	387	428	440	453	429	470
	140	363	377	383	404	404	432
	171	356	358	350	372	382	392
	201	294	287	316	334	329	317
VP	115	358	341	411	391	380	429
	170	320	327	342	364	353	367
	202	271	299	295	307	323	319
CW	66	180	183	189	197	197	192
	79	175	182	185	186	196	191
	94	145	169	181	172	180	177
	107	153	156	160	163	149	156
	129	130	137	134	140	142	141
	143	107	114	124	128	131	137
	166	100	105	109	112	115	116
	175	111	111	106	107	108	106
	190	76	87	88	91	92	94
RG	43	350	358	389	354	376	356
	59	308	300	310	335	319	335
	72	254	281	289	287	281	305
	93	235	242	241	244	255	265
	119	166	176	201	204	202	207
	133	162	164	171	172	186	187

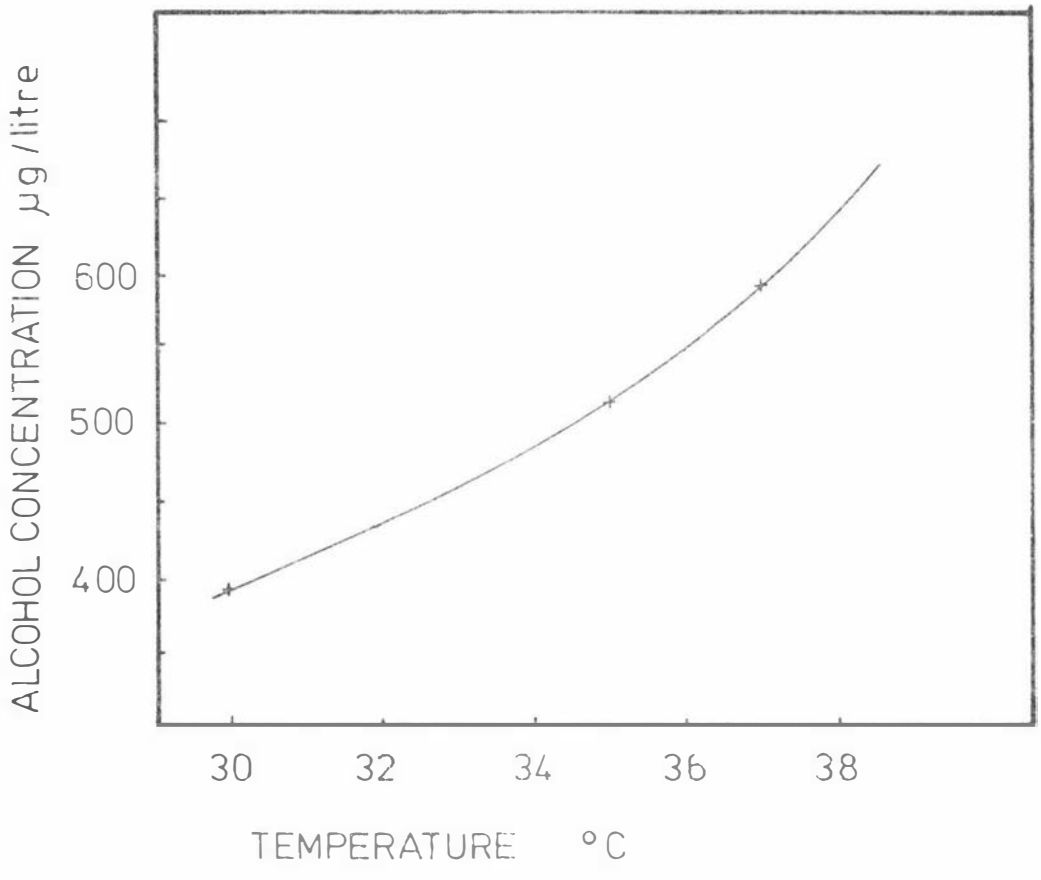


Figure 3.8

The change of alcohol concentration with breath temperature, data taken from Harger et al (1950b).

3.9a to 3.9f. The breath alcohol curves from all subjects showing the effect of temperature correction (upper figure) against the uncorrected values (lower figure). The curves in each figure are generally ranked with the results from the 2 litre expiration at the top and those from the 0.25 litre at the bottom.

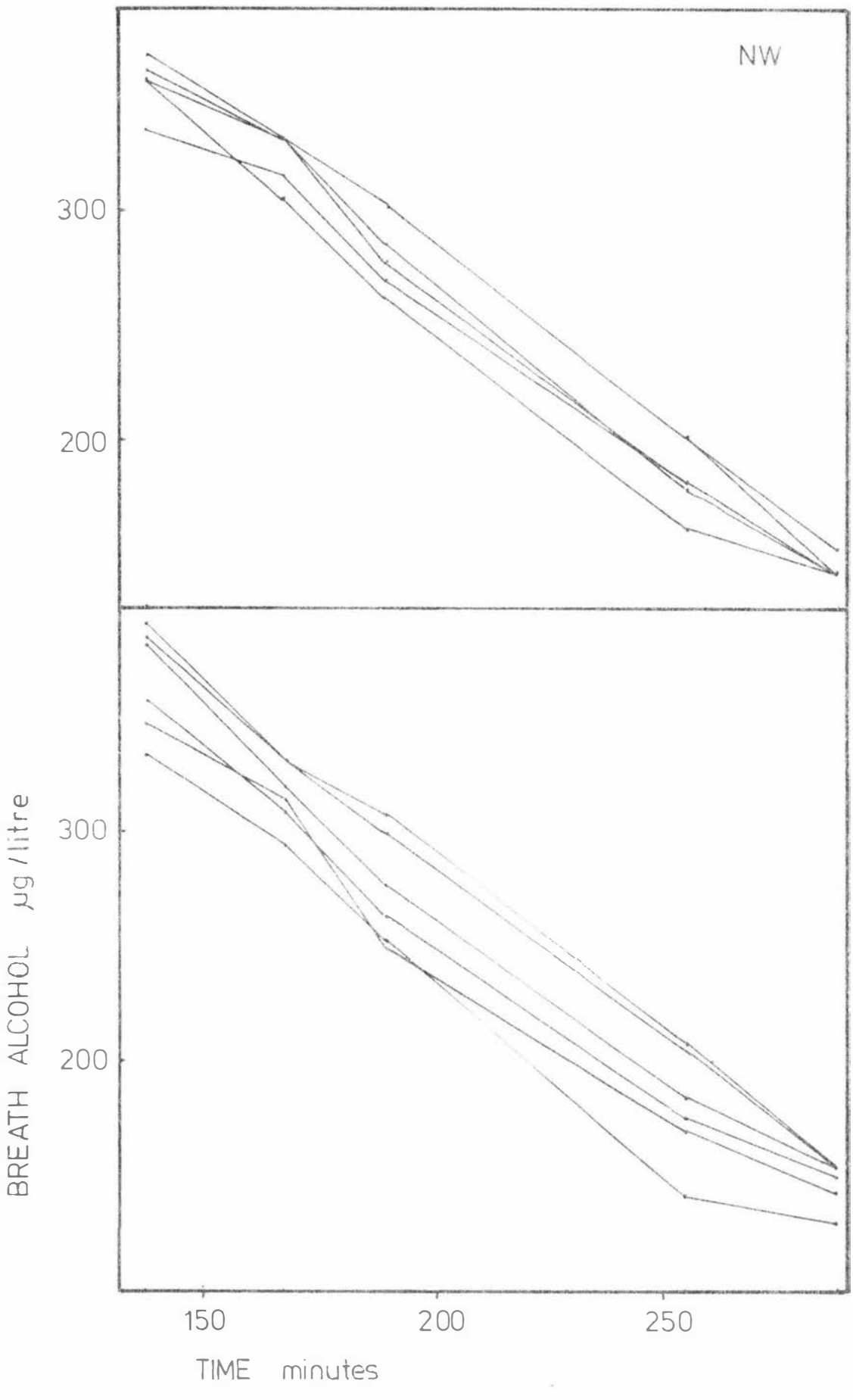

NW
300
200
300
200
BREATH ALCOHOL µg / litre
150
200
250
TIME minutes

Figure 3.9a

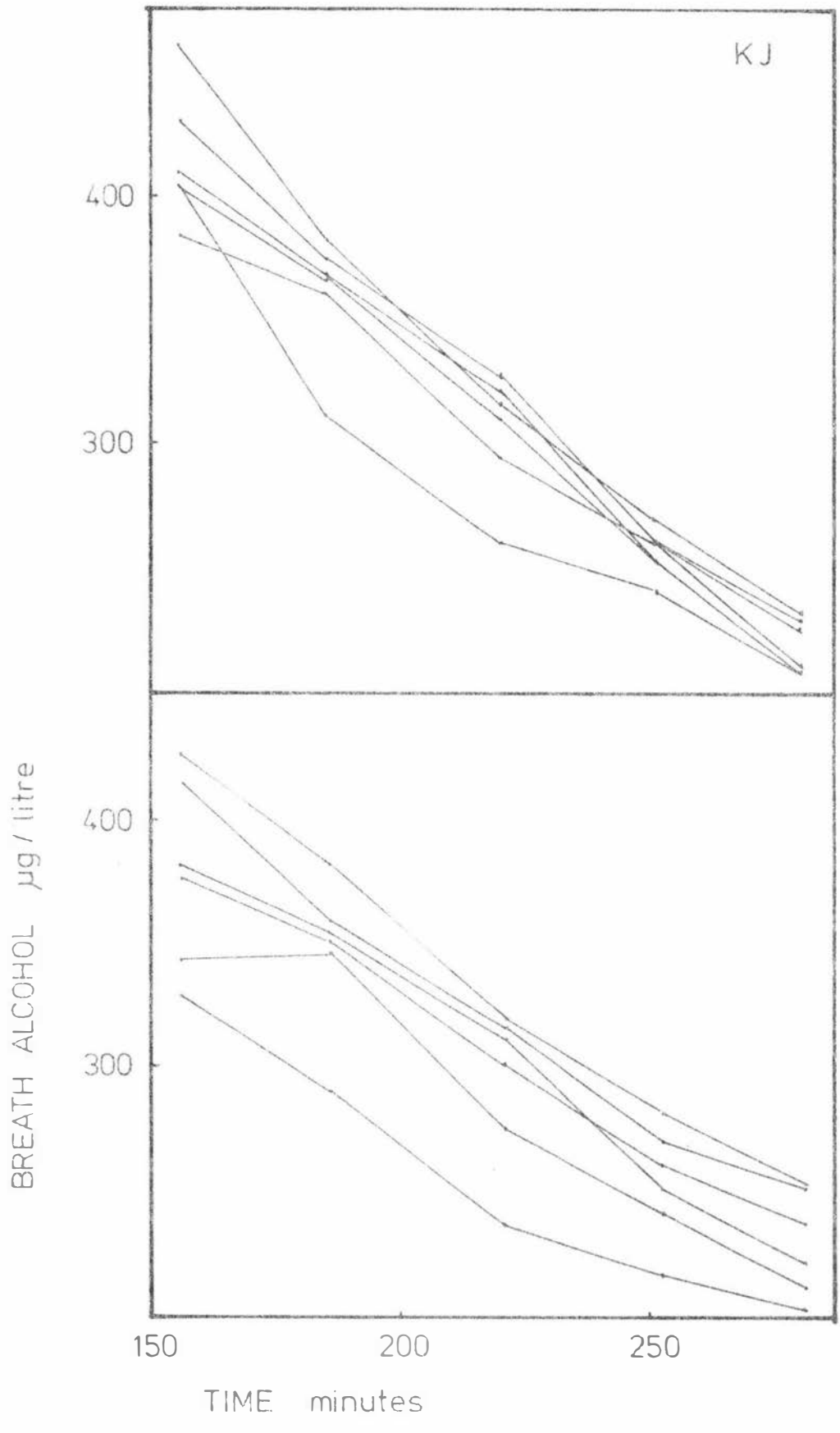

KJ
400
300
400
300
BREATH ALCOHOL µg / litre
150
200
250
TIME minutes

Figure 3.9b

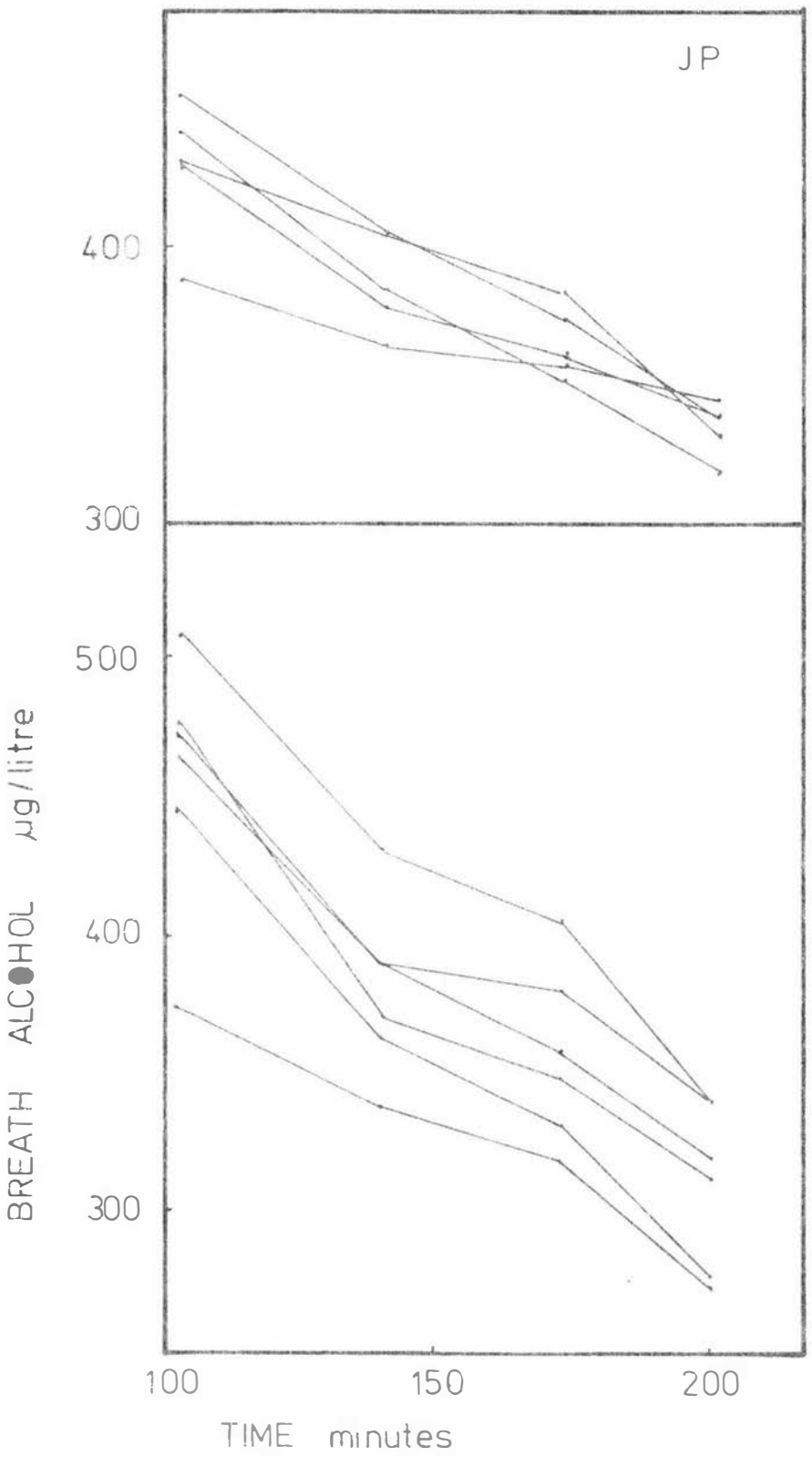

JP
400
300
500
400
300
BREATH ALCOHOL µg/litre
100
150
200
TIME minutes

Figure 3.9c

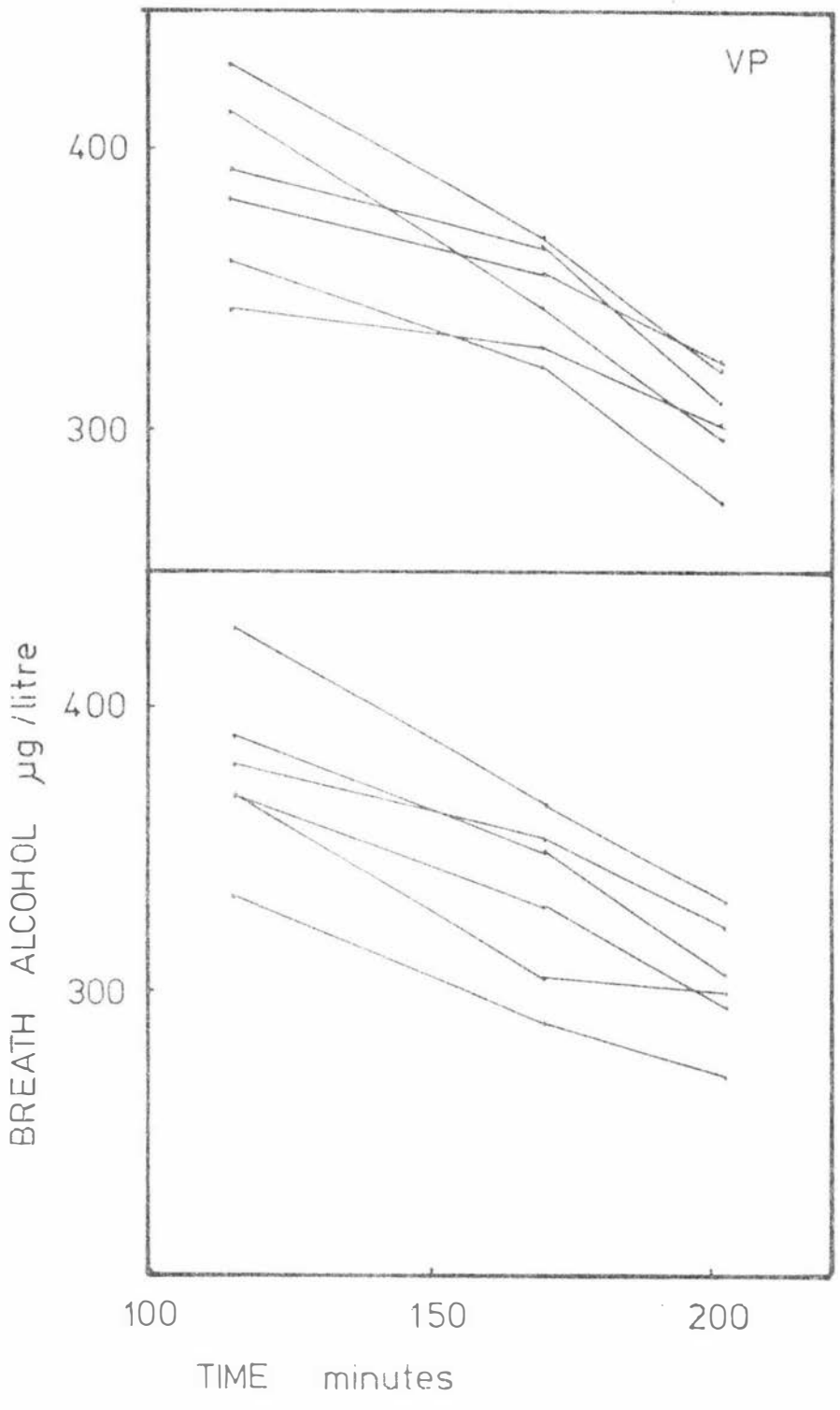

VP
400
300
400
300
BREATH ALCOHOL µg /litre
100
150
200
TIME minutes

Figure 3.9d

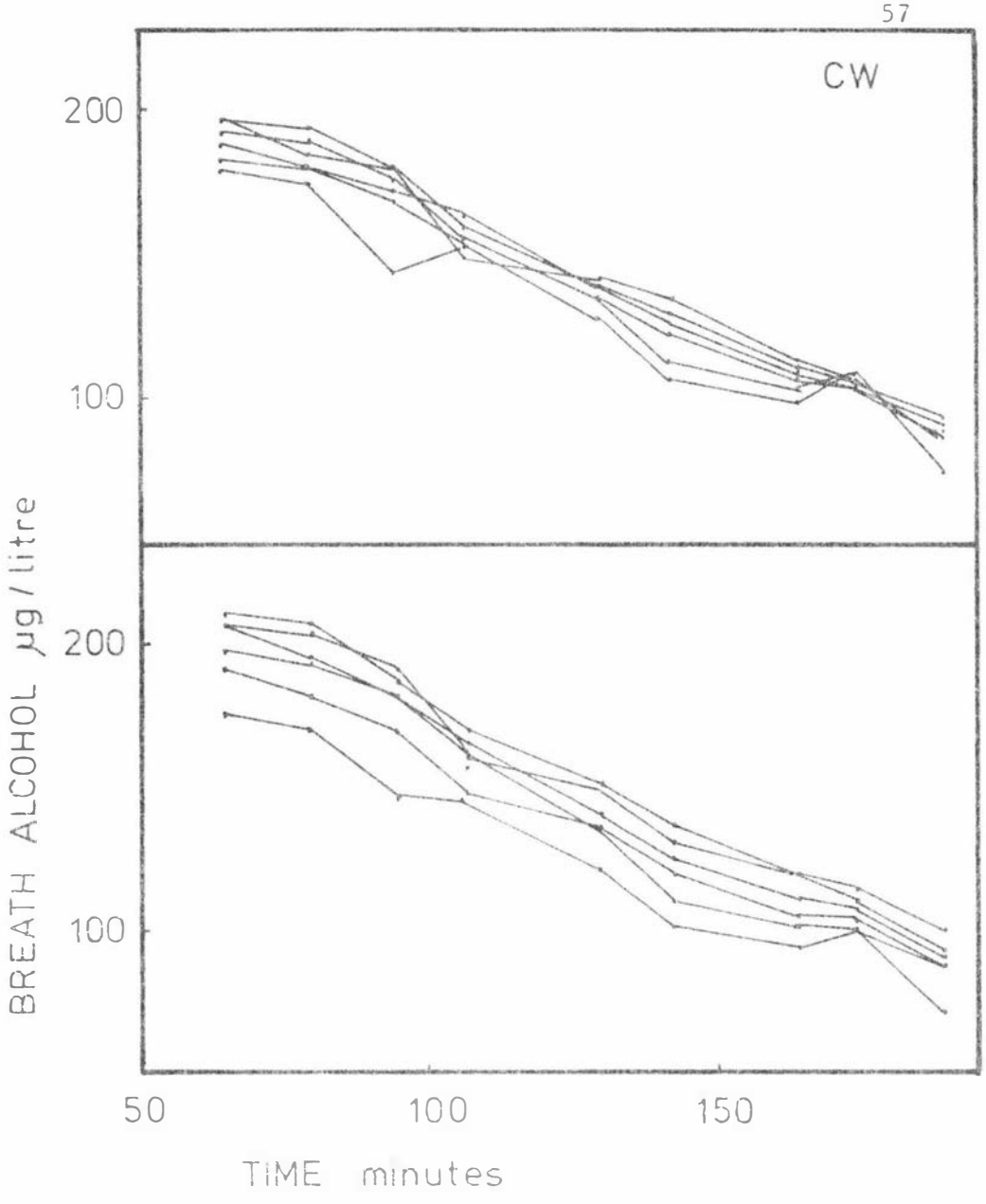

CW
200
100
200
100
BREATH ALCOHOL µg / litre
50
100
150
TIME minutes

Figure 3.9e

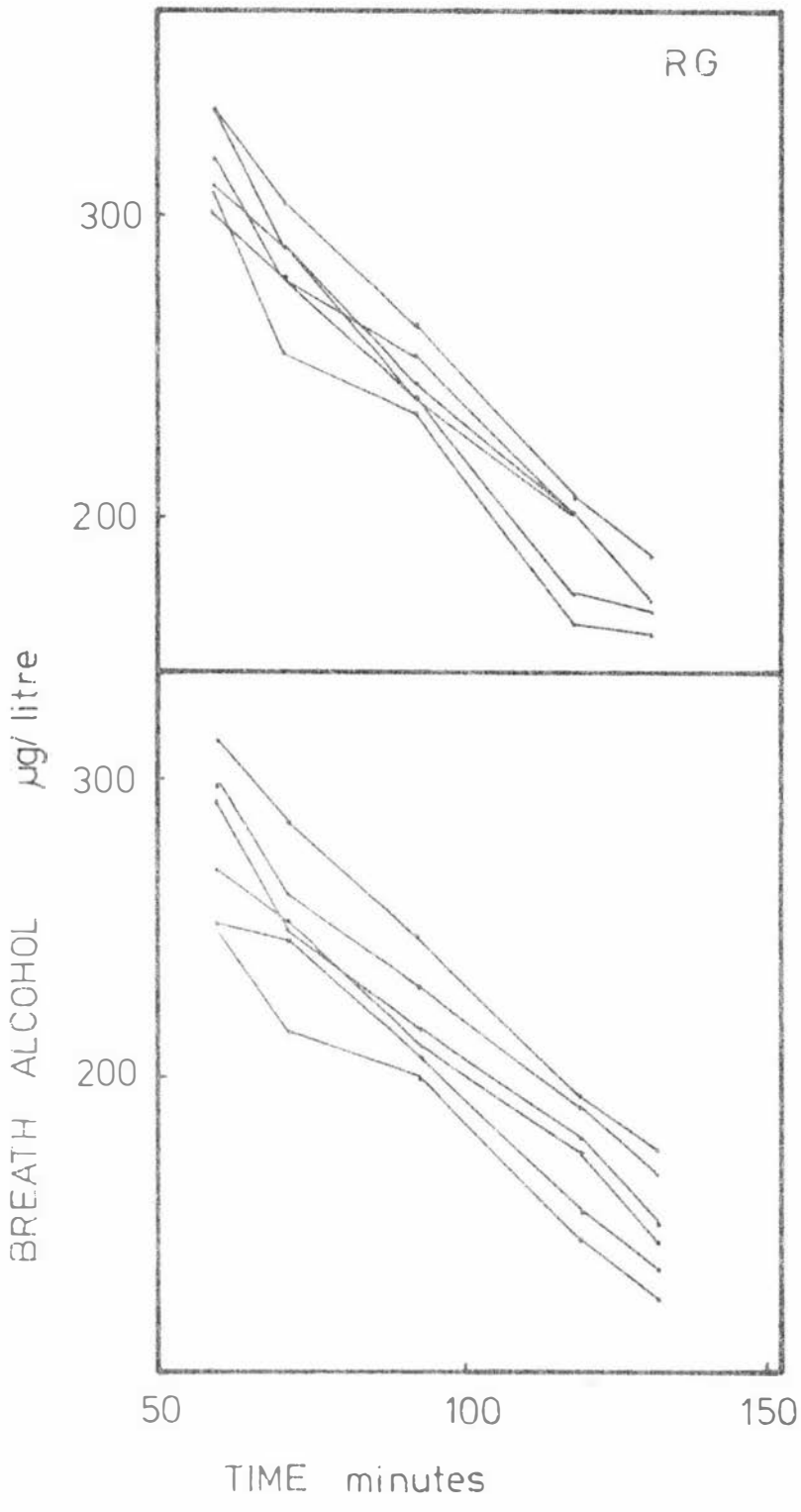

RG
300
200
300
200
BREATH ALCOHOL µg/ litre
50
100
150
TIME minutes

Figure 3.9f

TABLE 3.9 The mean breath alcohol concentrations (µg/l) at each expiration volume, temperature corrected lower and uncorrected (upper) for each subject. Correlation coefficient = r, regression coefficient = b.

Subject	Breath Volume (litres) .25	.5	.75	1.0	1.5	2.0	r	b	Mean µg/l
NW	230	245	251	263	276	277	.961	15	256
	242	246	257	256	265	269	.961	15	256
KJ	271	302	314	326	340	354			
	287	303	305	317	323	332	.962	24	311
JP	326	355	378	386	395	432			
	350	362	372	391	386	403	.929	28	377
VP	297	329	331	349	352	376			
	316	322	349	354	352	371	.906	29	344
RC	171	185	195	198	218	225			
	204	216	226	227	231	241	.937	18	224
CW	124	137	143	146	151	154			
	131	138	142	144	146	146	.858	8	141

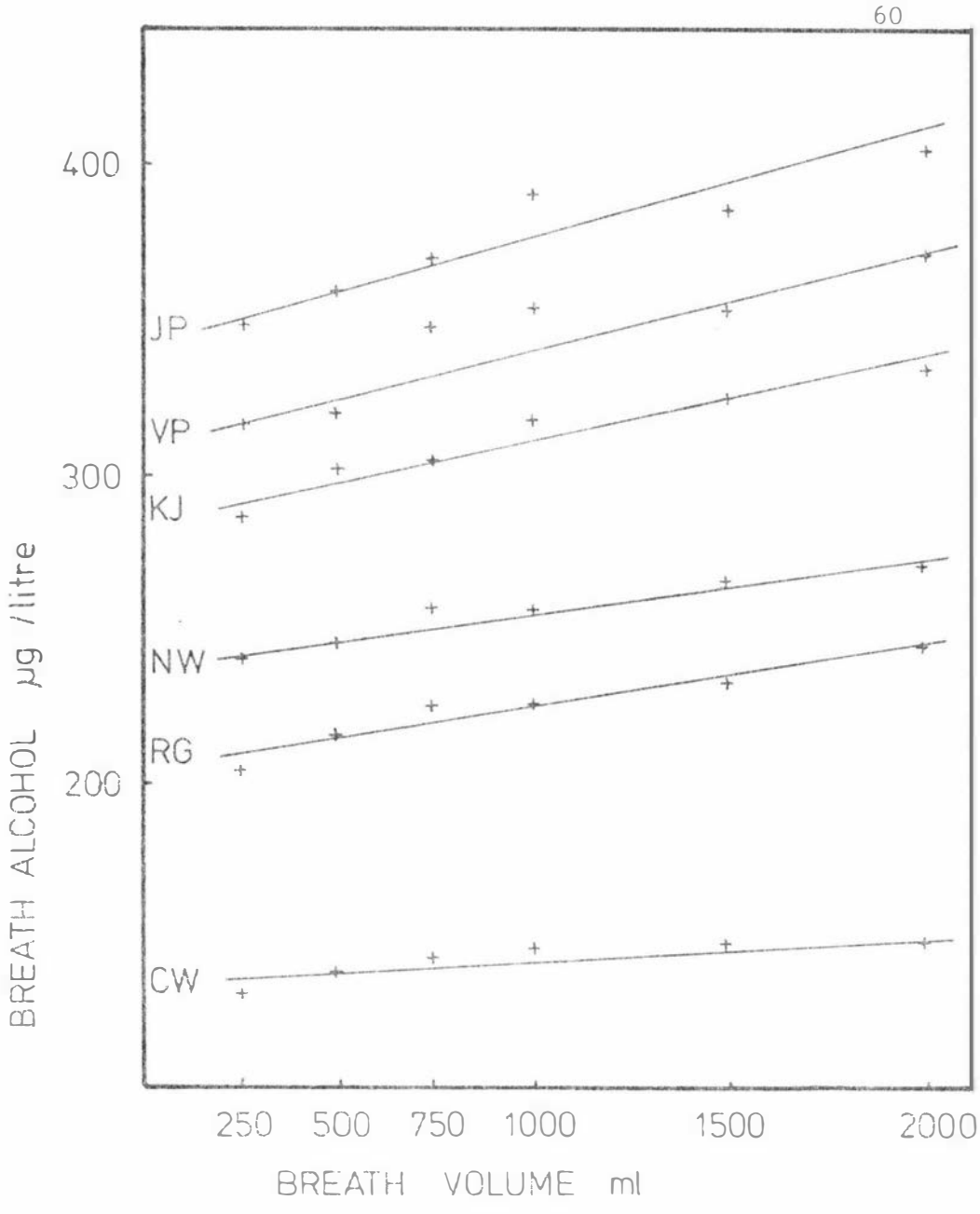


Figure 3.10

The regression of mean corrected breath alcohol concentration against expiration volume for each subject.

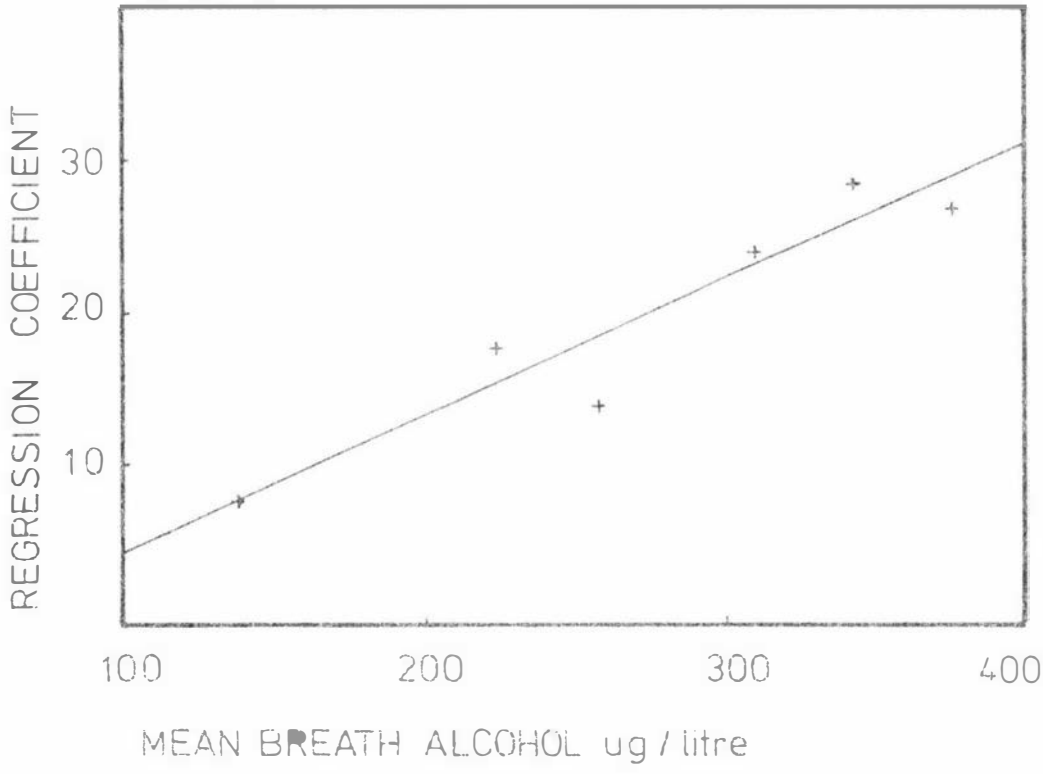


Figure 3.11

A plot of the regression coefficients of breath alcohol concentration on expiration volume against the mean breath alcohol concentration from each subject, (data from Table 3.9).

were the maximum attainable and applying the distribution ratio of 2169 (reciprocal of 461, Table 3.4) at an average haematocrit of 0.45, the mean blood alcohol concentrations were derived. The distribution ratios were then determined which would convert all the other alcohol levels at the various breath volumes to yield the same blood concentration and these are shown in table 3.10. These coefficients showed a considerable variation within each breath volume interval, with standard deviations of 180 µg/litre for low breath volumes decreasing to 106 µg/litre at the 2 litre volume. After temperature correction, these standard deviations were considerably reduced.

In addition to the temperature effects, there are also similar changes in breath alcohol concentration with volume depending on the blood alcohol level. It has been commonly assumed that the alcohol in the breath after the displacement of the tidal air from the 'dead-space' of the upper respiratory tract, is derived from pulmonary arterial blood by equilibration in the alveoli. It is unlikely that equilibration is incomplete in the alveolar space so that the changes in alcohol concentration with breath volume above those compensated by temperature correction are likely to arise in the 'dead-space'.

The rapidity with which alcohol vapours may re-equilibrate in such areas was investigated with an apparatus designed to approximate the upper respiratory tract. A wash bottle head attached to a 100ml glass tube, (Quickfit MF25/3, MF 24/3/8) was immersed in a water-bath at 34^{o}. The inner tube of the head was connected to the gas chromatograph by heated tubing to prevent condensation and breath samples from the simulator were blown through the outer arm. A filter paper cylinder was inserted into the tube and moistened with alcohol solutions of a different concentration to that in the simulator. A standard alcohol vapour was blown through the apparatus at a rate of 6 litres per minute for 6 seconds from the simulator. The results in Table 3.11 show that whatever the initial concentration of alcohol in air, a new value was rapidly attained.

3.3. DISCUSSION

There has been some controversy in recent years over the distribution ratio between blood and breath alcohol concentrations. Some workers would prefer this value to be higher because breath tests frequently underestimate blood levels by 5 - 10%. Examination of Table 3.10 shows

TABLE 3.10 Distribution ratios which convert breath alcohol concentration to the same blood alcohol concentration as determined from the 2.0 litre temperature corrected volume.

Subject	Breath Volume (litres)					
	0.25	0.50	0.75	1.0	1.5	2.0
(a) Uncorrected for breath temperature						
NW	2534	2380	2323	2217	2112	2104
KJ	2657	2384	2293	2209	2117	2033
JP	2680	2462	2312	2264	2212	2066
VP	2710	2484	2432	2306	2286	2140
RG	3058	2827	2682	2641	2399	2324
CW	2554	2311	2215	2169	2097	2056
mean	2699	2475	2376	2301	2204	2121
S.D.	189	183	165	173	120	106
(b) After correcting breath alcohol concentrations for temperature difference from 34°.						
NW	2409	2370	2268	2277	2200	2169
KJ	2508	2376	2360	2271	2229	2169
JP	2497	2414	2349	2235	2264	2169
VP	2547	2500	2306	2274	2286	2169
RG	2563	2421	2314	2303	2264	2169
CW	2417	2295	2230	2199	2169	2169
mean	2490	2396	2304	2260	2235	
S.D.	64	68	49	37	44	

TABLE 3.11 The re-equilibration of alcohol between the aqueous and vapour phases in a simulated upper respiratory tract.

Initial alcohol concentration in the vapour phase µg/litre	465	465	465	465	0
Alcohol concentration on the filter paper µg/litre	Dry	0	380	571	571
Final alcohol concentration in the vapour phase µg/litre	465	248	442	519	452

the considerable variation in distribution ratio with expired breath volume and it is not surprising that agreement cannot be reached over the correct ratio to apply to convert breath to blood levels. There are some advocates of a ratio of 2,300 (Jones, et al, 1974) and this may not be surprising when it is seen from the table that this applies to the 500 - 750 ml breath volume aimed at by many of the breath testing instruments. Harger, (1974) listed the results of 27 studies on the correlations between breath and blood tests with a variety of quantitative breath testing instruments. The variation from -0.3 to -17.5% in twelve different studies with the Breathalyzer probably reflects the differences in expired breath volumes between the studies. Five studies with an Intoximeter were more consistent as might be expected with its closer control on breath volume and the mean percentage differences from the blood tests were -4.9, -4.3, -4.4, -6.6, and -10.2. Only one study was listed with the Alcolmeter and the small mean difference from the blood test of -1.3% might be expected as large breath volumes are readily exhaled with this instrument. Coldwell et al (1959), who made blood to breath comparisons with the Breathalyzer, found that 60 out of 77 tests taken during the elimination phase of the alcohol curve were lower than the blood levels and the average difference for all estimations was - 10mg/100ml ± 12mg/100ml. They explained that this difference was due to the instrument being calibrated for alveolar air and admitted that, in practice, the breath sample was frequently of mixed air, from which statement it can be inferred that the breath volumes were generally low. Enticknap and Wright (1965) measured the discarded air volume at 500ml and found a mean distribution ratio of 2370 in their subjects using two instruments simultaneously to decrease the standard error.

The principal cause of the differences in alcohol concentration appears to be related to breath temperature which is dependent upon expired air volume. The results in the present study were obtained in the laboratory at normal room temperatures. In less ideal conditions, such as breath tests by traffic officers at the roadside, or in subjects who are habitual mouth breathers, the initial breath temperature might be much lower. Further investigations would be required to establish the extent of these variations.

Above the breath temperature effect, is a linear relationship between breath alcohol concentration and expired air volume. It is unlikely that equilibration is incomplete in the lungs which receives its blood supply from the pulmonary artery. This artery conveys most of the output of the right ventricle of the heart to the capillary networks lying in the septa between the alveoli. The networks drain into the pulmonary venules which unite to return the blood to the left atrium of the heart. The cardiac output is 5 - 6 litres per minute and the circulation time between right ventricle and left atrium is about 5 seconds so that only 0.75 seconds is taken to traverse the capillary bed which has a blood volume of 75 - 100 ml spread out into thin walled vessels (Strieder, 1976). Such is the rapidity of exchange, of water at least, that dry air inhaled into the lungs returns fully saturated with water vapour and it has been shown that if the body fluids contain tritiated water, the expired water vapour has the same specific activity. If the transfer is attempted in the reverse direction by inhalation of tritiated water vapour, 85 - 100% absorption is attained during each respiratory cycle (Pinson, 1952). Under these conditions, it is likely that any change in distribution ratio is due to re-equilibration at a site in the upper respiratory tract.

The implications of the re-equilibration experiments are that the so-called respiratory dead space, although 'dead' from the point of view of respiratory gas exchange, is 'live' in alcohol equilibration. In the processes of normal respiration, it is quite likely that the air in this dead space is almost in equilibrium with the alcohol in the surrounding tissues. The experiments show that while an alcohol vapour is passing over a dry surface, alcohol cannot be lost unless condensation takes place. If however, the alcohol vapour is passed over a moist surface, there will be a tendency for re-equilibration between the vapour and the aqueous phases. The extent to which a new equilibrium is reached will depend upon the temperature; the difference in alcohol concentration between the two phases and the rate of flow of the vapour. Harger et al (1950b) found that equilibration of alcohol from aqueous solutions into the air blown through them was very rapid and they were able to modify their original three stage equilibrator for providing standard alcohol vapours, to one stage. Even the diffusing disc used in their studies to break up the air into small bubbles has

been eliminated in the Stephenson simulator with no apparent effect on the alcohol concentrations in the vapour phase. Haggard et al (1941) cited the observations of Liljestrande and Linde in 1930 on the extent to which alcohol diffused into the air of the respiratory dead space, so that mixed expired air contained nearly as much alcohol as alveolar air. Haggard et al also made in vivo equilibration experiments where the mouth of subjects who had been drinking was inflated with air and held for two minutes. The alcohol concentration in this air was 40% of the alveolar air levels.

Alcohol in the breath may be derived from any site in which the surface is covered with an aqueous layer containing alcohol. The most obvious and dramatic effect is that seen in subjects immediately after drinking or rinsing the mouth with alcohol. These subjects show the so-called 'mouth alcohol effect' which is well documented. Begg et al (1966) studied this effect, finding high initial levels which rapidly diminish until they are near the blood levels by 15 minutes after drinking. It seems likely that the deficiency of alcohol in the breath can be explained by a loss of alcohol from the tissue surfaces into the incoming breath in the same way in which heat is also lost, as suggested by Jones et al (1974). This leaves a cooler, alcohol deficient surface because the blood flow through the tissues lining the mouth and the bronchial tree would be relatively low compared to the alveoli. The alveolar expired breath, in equilibrium with the pulmonary blood alcohol and at body core temperature, passes over these surfaces, cools in the process and yields alcohol to the deficient tissue as well as heat. If expiration is prolonged, as in the case of rebreathing, all tissues may come into equilibrium eventually with respect to alcohol concentration.

The total extent of the factors involved in breath alcohol concentration may be seen, for example, in a subject with a blood alcohol level of 100mg/100ml where after the expiration of 500 ml the breath might have a temperature of 31^{o}. If a second test is made after a breath volume of 1.5 litres and a temperature of 34^{o}, the change in breath alcohol concentration would have been equivalent to 21% from the 3^{o} temperature difference and a further 7% from the difference in volume, making a combined total of 28% between the two tests. Such

differences could readily arise where the first test was made with a screening device and the second on an evidential machine.

From a practical point of view, it appears that attempts to sample alveolar air are unnecessary. The linear relationship between alcohol concentration and breath volume after temperature correction suggests that sampling a constant volume, which can even consist of tidal air, will give adequate measurements of blood alcohol concentration, providing there is compensation for breath temperature and the correct distribution ratio for the volume is used. Such corrections could probably be carried out electronically.

In previous studies, many tests have been carried out simultaneously on breath and blood samples (Couchman, 1974). The results were in sufficient agreement that a high degree of confidence was obtained in the ability of a breath alcohol test to reflect the concentrations in the blood. The results of the present study have illustrated points in breath collection which may lead to differences from a blood test. Consequently, it was considered that breath sampling, under defined conditions, could replace blood samples for alcohol estimations.

While there have been many studies on the way in which alcohol is absorbed, distrbuted and eliminated from the body, most have been carried out under laboratory test conditions. In addition, it has been pointed out by Lundquist (1970) that:-

".....some of the problems regarding the pathways of alcohol metabolism might be solved by the accurate measurement of the rate of ethanol removal from the blood at low and high blood alcohol concentrations. Sufficiently accurate experiments of this kind have apparently not been performed."

It seemed appropriate, using the modified gas chromatograph, to make repeated observations on a large number of people, and re-study some of the physiological factors involved in the absorption and elimination of alcohol in subjects under both laboratory and near-normal drinking conditions.

For the investigations to follow in this thesis, either the Intoximeter or the Carle gas chromatographs were used to measure alcohol concentrations. Both were calibrated with aqueous simulator

solutions made up to 1.21 times the concentration of alcohol in the blood, based on the ratio of the partition coefficients air/blood to air/water of 476 : 393, where 476×10^{-6} has been derived from the accepted distribution ratio of 2,100. This commonly accepted ratio was used because it was inconvenient to measure breath temperatures outside of the laboratory and the resulting error would be small where large breath volumes were used. With the Carle instrument, the breath volume was estimated by inflation of a plastic bag on the vent outlet of 1 litre capacity. With the Intoximeter, care was taken that subjects blew into the instrument for at least 6 seconds ensuring that the breath volume exhaled was greater than 600 ml.

Subsequently, all results of breath tests are expressed as blood alcohol concentrations in mg/100ml.

CHAPTER 4 STUDIES ON THE ABSORPTION, DISTRIBUTION AND ELIMINATION OF ALCOHOL IN THE BODY WITH VOLUNTEERS STUDIED UNDER LABORATORY CONDITIONS.

4.1.1 INTRODUCTION

In a previous study, where investigations were initiated to obtain biochemical data on human volunteers who had consumed alcohol (Couchman 1974), it was suggested that the experimental conditions may have a large effect on the nature of the results obtained. A delay in alcohol absorption of up to two hours was observed in the fasted subjects after the rapid consumption of an alcohol dose of 0.4 g/kg body weight. It was considered that further studies on the rates of alcohol absorption and metabolism were clearly warranted, particularly in relation to normal drinking, before further studies were carried out on the effects of alcohol on metabolic pathways or patterns of alcohol metabolism.

For studies from which only blood alcohol levels were required, the previous chapters have shown the advantages of a rapid and accurate breath alcohol test replacing the necessity for obtaining blood samples. Such breath tests may be repeated at frequent intervals over long periods of time without discomfort to the subject under study and the results are immediately available for analysis.

The rate of change in blood alcohol level depends on the equilibrium between the rate of entry from the gut, the rate of elimination mainly by the liver and the rate of equilibration through body water compartments. Total body water is approximately ten times greater than the blood volume and accordingly equilibration through it can potentially affect observed blood alcohol levels significantly.

4.1.2 Body water compartmentation

Blood alcohol levels depend basically upon the amount of alcohol given and the total volume of water in the body through which it will be distributed. There is no reported evidence of any permeability barriers for alcohol through body tissue and organs and it can presumably diffuse through any of the body water compartments.

The basic structures of organs at the cellular level show cells separated by their membranes from a central cylinder of interstitial fluid through which blood capillaries pass (Reeve et al, 1967, p 153).

From this general structure, total body water may be divided into intracellular and extracellular compartments.

Extracellular water is made up in part of interstitial water and, in part, of the water in the blood circulatory system. The capillary compartment is part of the blood circulatory system, but the cell and interstitial compartments are isolated from similar compartments in other tissues except through the circulatory system. There are also compartments where the water has passed from cells into specialised storage areas, such as the bladder, the spinal cord or into the lymphatic ducts. Such water compartments, although part of the extracellular water may be poorly penetrated by molecules used in the measurement of extracellular volume and have been termed transcellular by Edelman (1952). All of these compartments are estimated in the deuterium technique for the determination of total body water and presumably are accessible to alcohol. Some of their relative sizes in a normal 70kg male are indicated in the following data of Edelman:-

Total body water	42 litres
Intracellular	23 litres
Extracellular	19 litres
plasma water	3.5 litres
interstitial	10.5 litres
transcellular	5.0 litres

4.1.3 Measurement of water compartment sizes using alcohol

Compartment sizes or distribution volumes are normally determined by giving a subject a small dose of a tracer compound and following its rate of disappearance from the blood stream. Concentrations in the samples are plotted against time and the intercept on the ordinate of the extrapolated curve estimates the distribution volume (Shipley and Clark, 1972).

If a subject is given a rapid intravenous injection of alcohol, subsequent changes in blood alcohol levels through to complete equilibration might be expected to be influenced by the rates of diffusion between the three main water compartments of the body. Figure 4.1 illustrates a curve of blood alcohol concentration against time

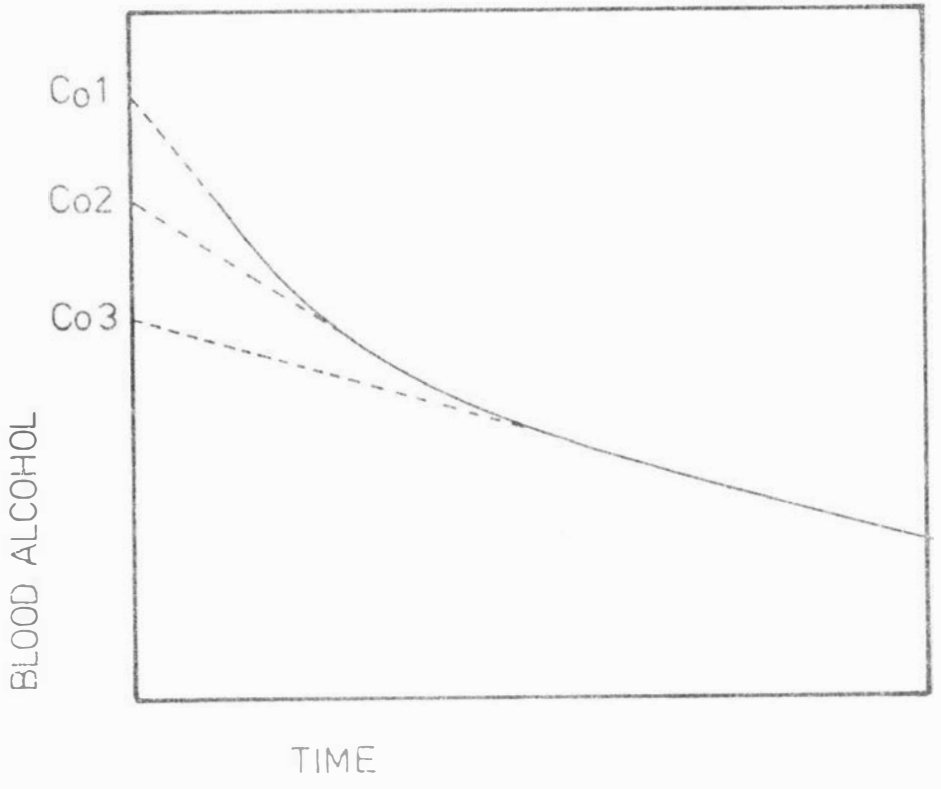


Figure 4.1

The expected blood alcohol curve resulting from a rapid intravenous injection of alcohol. The intercepts Co1, Co2 and Co3 are the results of extrapolating linear portions of the curve.

which might be expected from such an experiment. This curve is composed of three portions, each of which may be linearly extrapolated to the ordinate. The first, giving the highest concentration in the blood, Co1, reflects equilibration with the most accessible pool which is the blood water. The second slope extrapolates to a lower blood concentration reflecting the slower diffusion of alcohol from the bloodstream into the intercellular water compartment (Edelman and Moore, 1951). The last slope extrapolates to Co3, the lowest blood alcohol level when the alcohol has completely equilibrated with all the body water pools.

Such experiments are not usually performed on human subjects although a fairly fast infusion technique has been used to induce alcohol anaesthesia (Dundee et al 1970). For experiments designed to determine rates of alcohol metabolism in man, the infusion of alcohol usually continues up to two hours (Wilkinson et al 1975) so that the resulting blood alcohol distribution curves do not show changes due to the different rates of diffusion into body water compartments. Many experiments have been carried out with oral doses of alcohol and the typical shape of the subsequent alcohol distribution curves have been described by Widmark (1932). There is an absorptive phase, during which blood alcohol levels rise rapidly, followed by an intermediate phase when equilibration between body water compartments is taking place and subsequently an elimination phase which appears to be linear and has been termed the "beta slope" by Widmark. This slope, if extrapolated to the ordinate, can give an estimate of total alcohol distribution volume.

4.1.4. Derivation of the Widmark equation

In 1932, Widmark stated that the total amount of alcohol remaining in the body after a specified time may be calculated from the concentration of alcohol in the blood from the equation:-

$$R = C_t \cdot p \cdot r \qquad (I)$$

where R is the total remaining alcohol in mg; C_t is the concentration of alcohol in the blood in mg/kg at time t ; p is body weight in kg and r is the fraction of the body volume in which alcohol is distributed with the concentration C_t. Values of r were determined experimentally

by extrapolation of beta slopes to the ordinate giving the concentration of alcohol in the blood at zero time, C_o, in mg/kg. The value obtained is a theoretical blood alcohol concentration with an assumption that all the alcohol consumed was absorbed and equilibrated throughout the body water compartments instantaneously at the time at which drinking began. The values for r were calculated by a rearrangement of formula (I):-

$$r = \frac{A}{Co \cdot p} \qquad (II)$$

where R is substituted by A, the amount of alcohol ingested in milligrams. The equation may be derived in the following way. The dose of alcohol given to a subject is:-

$$\frac{A}{p} \quad \text{mg/kg body weight}$$

The concentration of alcohol per kilogram of body weight is obtained by dividing by the decimal fraction (W) of the proportion of water in the body. Alcohol will also be distributed in the blood water, so that by multiplying by the decimal fraction of water in the blood (WB), the concentration of alcohol in whole blood, C, in mg/kg is obtained:-

$$C \text{ mg/kg blood} = \frac{A}{p} \cdot \frac{WB}{W} \qquad (III)$$

This formula can be expressed more simply as:-

$$C \text{ mg/kg blood} = \frac{A}{p} \cdot \frac{1}{r} \qquad (IV)$$

where r is the ratio $\frac{W}{WB}$ or $\frac{\text{the fraction of water in the body}}{\text{the fraction of water in the blood}}$.

This ratio is the same as Widmark's ratio so that r can be calculated from known values of the body water and blood water fractions. These values have been calculated in Table 4.1 from body water contents determined by the deuterium oxide dilution technique (Widdowson and Dickerson 1964) and blood water by the Fischer reagent on bloods donated for transfusion purposes (Davis et al 1953). From this table, a range of 0.65 - 0.84 might be expected for males and 0.59 - 0.67 in females.

Blood alcohol concentrations are usually expressed in mg/100 ml and the beta slope measures the rate of removal of alcohol from the blood in mg/100 ml/1 hour. The rate of alcohol metabolism in the body can be calculated from beta, firstly by converting from a volume to a weight

TABLE 4.1 Widmark ratios (r) calculated from known body water and blood water values.

	Males			Females		
Body water g%	min	mean	max	min	mean	max
	54.5	59.1	62	49.5	51.0	51.9
Blood water g%						
Min extreme 74	.74	.80	.84			
78				.63	.65	.67
Min normal 79	.70	.75	.78			
80	.68	.74	.77	.62	.63	.65
Max normal 82	.66	.72	.76	.60	.62	.63
Max extreme 84	.65	.70	.74	.59	.61	.62

basis:-

$$\frac{10 \ . \ \text{mg/100 ml/hr}}{1.06} \quad \text{mg/kg blood / hour} \qquad (V)$$

where 1.06 is an average density value for blood. Dividing by the decimal fraction of water in the blood (WB) gives the rate of removal from blood water, which is the same as the rate of removal from the body water, providing equilibration between the various compartments is rapid. Multiplication by the fraction of water in the body (W) then gives the rate of removal from the body in mg/kg body weight/hour. This is the same as multiplying formula (V) by the Widmark ratio r.

A simpler method of calculating the rate of metabolism in the body is the extrapolate the beta slope to the abscissa and obtain a time for zero blood alcohol levels. The dose may be divided by time to give an average rate of elimination from the body and divided yet again by body weight to obtain the rate in mg/kg body weight/hour. This method should give identical results to the calculations involving r due to the relationship between the formulae.

4.1.5 The kinetics of alcohol metabolism

The basis of the Widmark calculations depend on the assumption that the elimination of alcohol from the body is linear or a zero order process. In 1958, Lundquist and Wolthers suggested that as alcohol was catabolised in the liver by an enzymic process, the elimination from the body should conform to Michaelis-Menten kinetics. In the Michaelis-Menten formula, the rate of alcohol catabolism V, is calculated from:-

$$V = \frac{Vm \ . \ S}{Km + S}$$

where Vm is the maximal velocity, S is the substrate concentration and Km is the substrate concentration at which the velocity of the reaction is half the maximum rate. Lundquist and Wolthers used this form of analysis on the terminal portions of the blood alcohol curves and found a range of Km values to be between 7 and 14 mg/100 ml with an average at 9.3 mg/100 ml and that Vm varied from 18 to 27 mg/100 ml/hr. The velocities at various substrate concentrations were calculated with a Km of 7 or 14 mg/100 ml and a Vm of 23 mg/100 ml/hr and are presented in Table 4.2. When these rates were plotted from a single point on the

TABLE 4.2 The velocities of alcohol elimination mg/100 ml/hr with a V max of 23 for two values of Km and various substrate (blood alcohol) concentrations.

[S] mg/100 ml	Km = 7	Km = 14
5	9.6	6.1
10	13.5	9.6
20	17.0	13.5
30	18.6	15.7
40	19.6	17.0
50	20.2	18.0
60	20.6	18.6
80	21.1	19.6
100	21.5	20.2
200	22.2	21.5

ordinate, the lower Km curve showed no significant departure from linearity between 20 and 90 mg/100 ml, but at the higher Km value a distinct departure from linearity is observed over the same range (Figure 4.2).

4.1.6. Experimental investigations

Using the modified and accurate methods for determining breath alcohol concentrations, it was decided to re-examine the absorption, equilibration and elimination of alcohol under laboratory conditions with special reference to the kinetics of the *in vivo* removal mechanisms.

4.2 METHODS

4.2.1. Studies on normal volunteers

The results of the breath tests from the previous chapter were included in this study with the addition of a further 9 females and 5 males. The participants were students or staff of the university, none of whom could be classed as heavy drinkers.

An alcohol dose of 1 g/Kg body weight was given diluted *ad libitum* in lemonade, to be consumed in a 20 - 30 minute period, 1 - 2 hours after a light lunch. Breath tests were performed at frequent intervals after drinking was complete using the Carle gas chromatograph.

4.2.2. Studies on alcoholics undergoing detoxication

Alcoholics admitted to hospital for detoxication frequently have high blood alcohol levels on admission. In the majority of these cases, absorption and equilibration would be expected to be complete so that these subjects might well be suitable for the observation of alcohol elimination rates.

Blood samples were obtained by the medical staff of the local hospital from such cases admitted to the detoxication ward. Blood alcohol levels were estimated in the hospital laboratory by a gas chromatographic method. Analyses of breath were made with either an Alcolmeter or the Breathalyzer 1000. In a selected group of patients admitted with blood alcohol levels greater than 250 mg/100 ml, breath tests were made with the Breathalyzer 1000 at hourly intervals

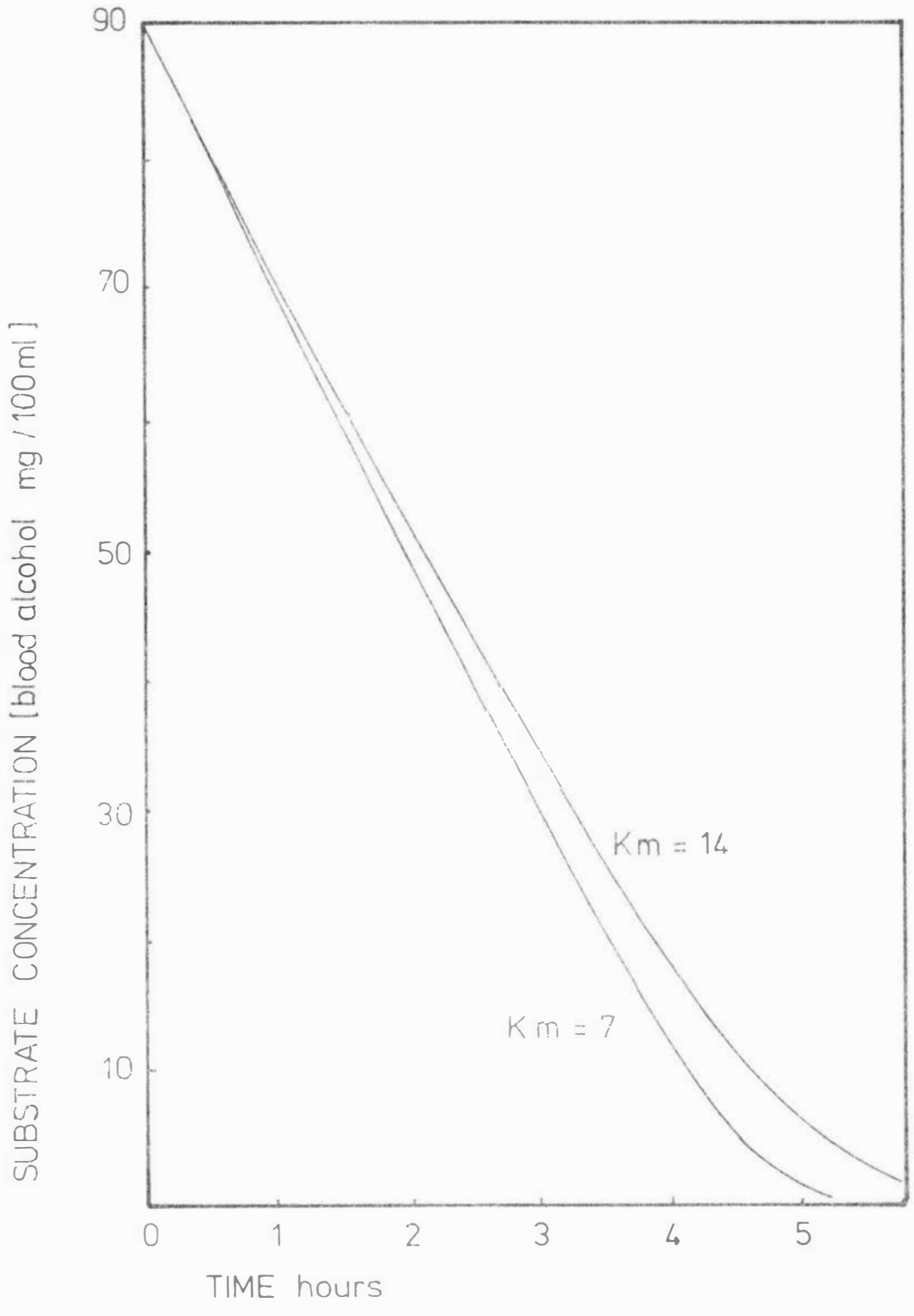


Figure 4.2

Blood alcohol curves generated from the results in table 4.2 illustrating the effect of Michaelis-Menten kinetics.

throughout the entire time course of the alcohol elimination phase, waking the patient up during the night if necessary.

4.3 RESULTS

4.3.1. Normal volunteers

The blood alcohol curves resulting from an alcohol dose of 1.0 g/Kg are shown in Figure 4.3. The absorption phase was taken as the drinking period until the onset of the beta slope. This time averaged two hours (s.d.0.66) and ranged from 1.5 to 3.5 hours, Table 4.3. During the absorption phase, the breath alcohol levels were seen to fluctuate over relatively short periods of time. These phases have been redrawn on a larger scale from representative samples for subjects 5 and 8 in Figures 4.4 a and b respectively to illustrate these fluctuations. During the elimination phase, fluctuations of this magnitude were not seen (Figure 4.5 redrawn from subject 5).

Beta elimination slopes were obtained in all except two female subjects and values for the Widmark ratio, r, was calculated as previously described, extrapolating the linear portion of the curve to the ordinate by linear regression analysis. The results are given in Table 4.3. This ratio was above the calculated range (Table 4.1) in 5 female and 6 male subjects. The mean value for r in the five remaining males was 0.75 (s.d. 0.05).

The rates of elimination of alcohol from the blood as shown by the beta slope averaged 20.4 and 18.8 mg/100 ml/hr for females and males respectively (Table 4.4) with a range from 17 - 20 mg/100 ml/hr in the males. The mean rates of elimination in mg/Kg body weight per hour were 138 (s.d. 32) and 142 (s.d. 15) for females and males respectively.

4.3.2. Alcoholics

Blood samples were taken from 31 alcoholics, but only 20 were suitable for estimating the beta slope due to poorly spaced or missing specimens. These slopes ranged from 8 to 39 mg/100 ml and appeared to be slightly curved in seven subjects. A fit to a logarithmic regression, as suggested by Iber (1971) gave slightly higher correlation coefficients in four of these seven cases (Table 4.5).

Figures 4.3 a - g

Blood alcohol curves from 20 human volunteers given an alcohol dose of 1.0 g/kg body weight. The figure to the right of the intercept on the ordinate is the Widmark ratio, r. The letters m or f denote male or female subject respectively.

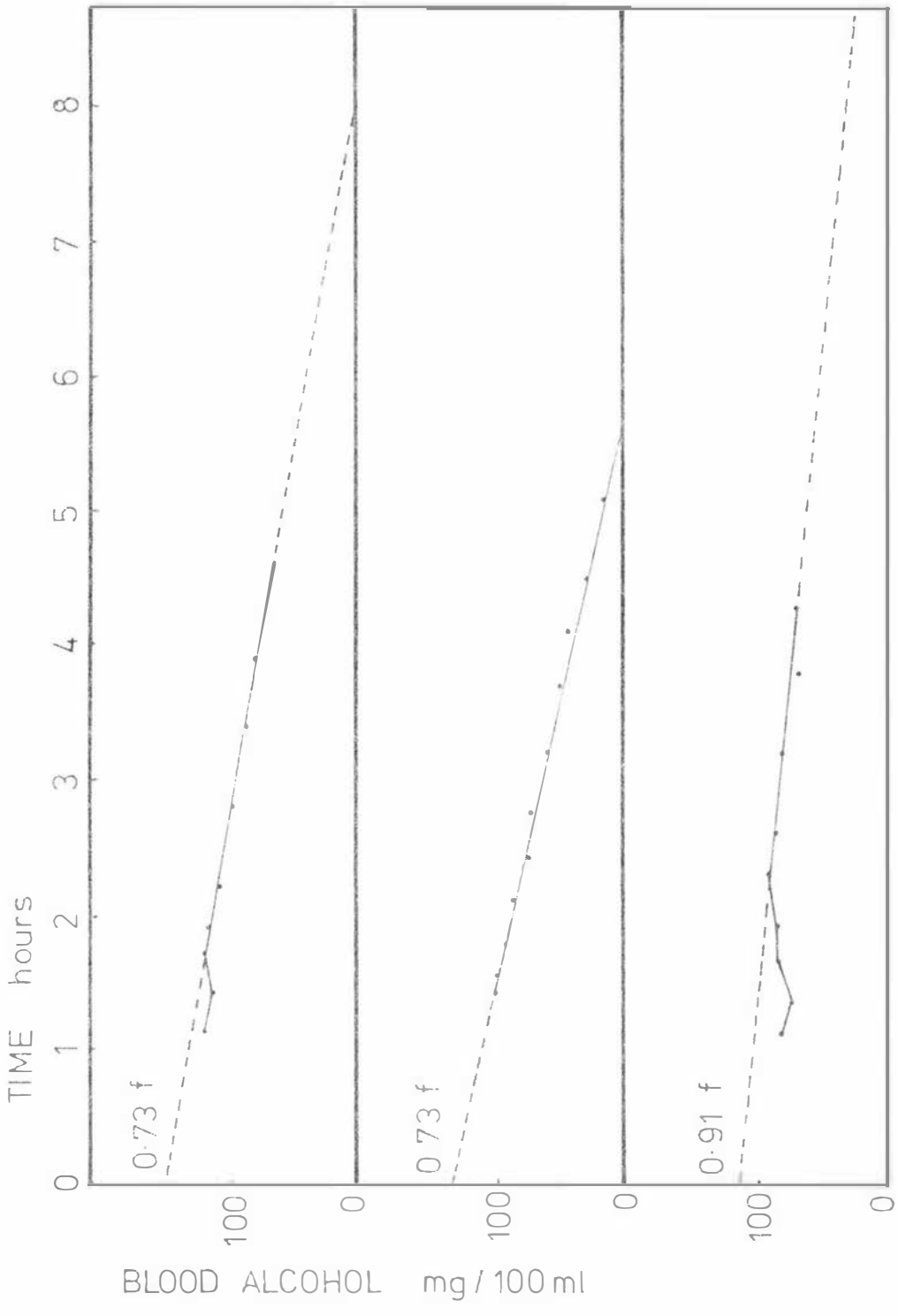
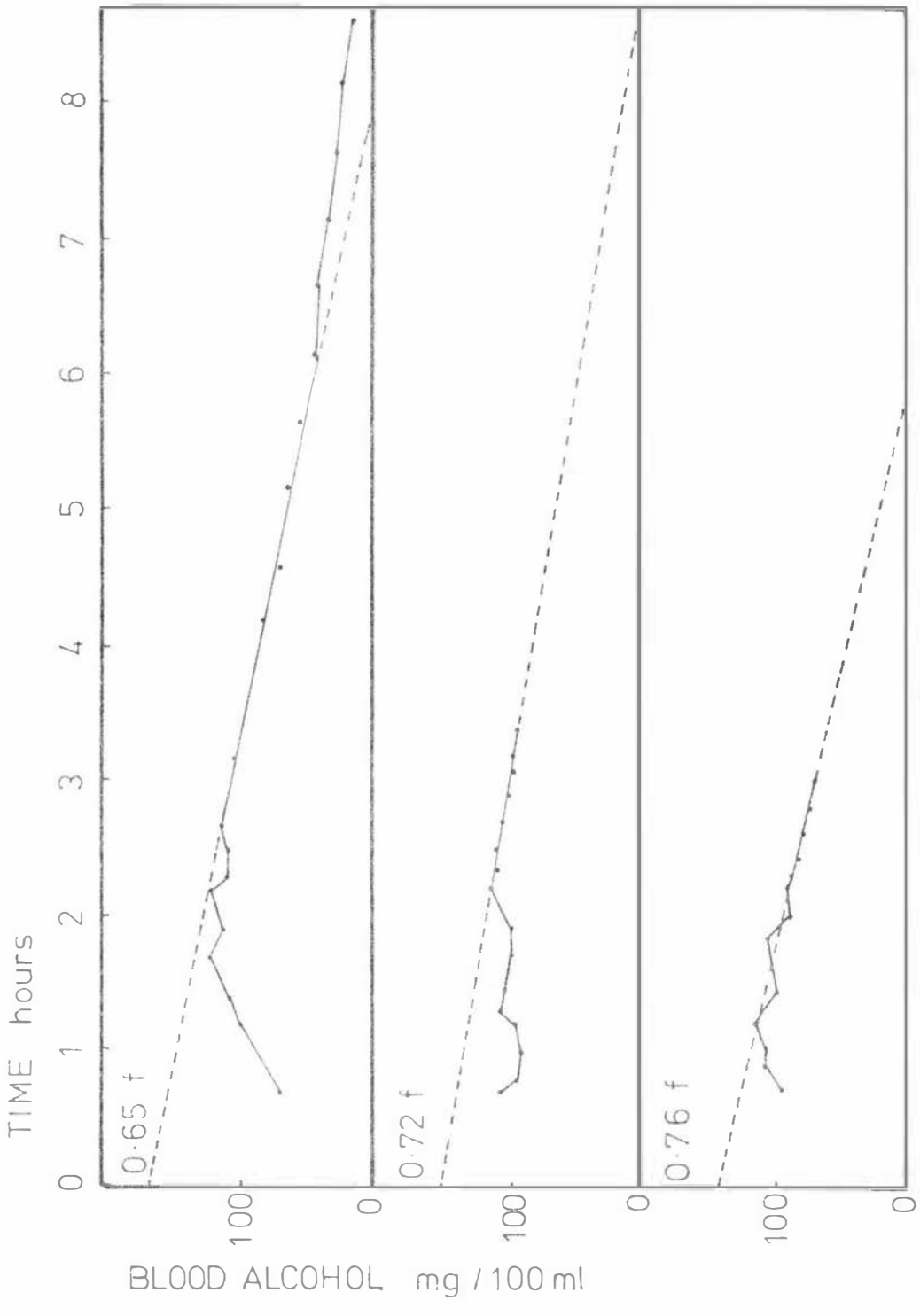


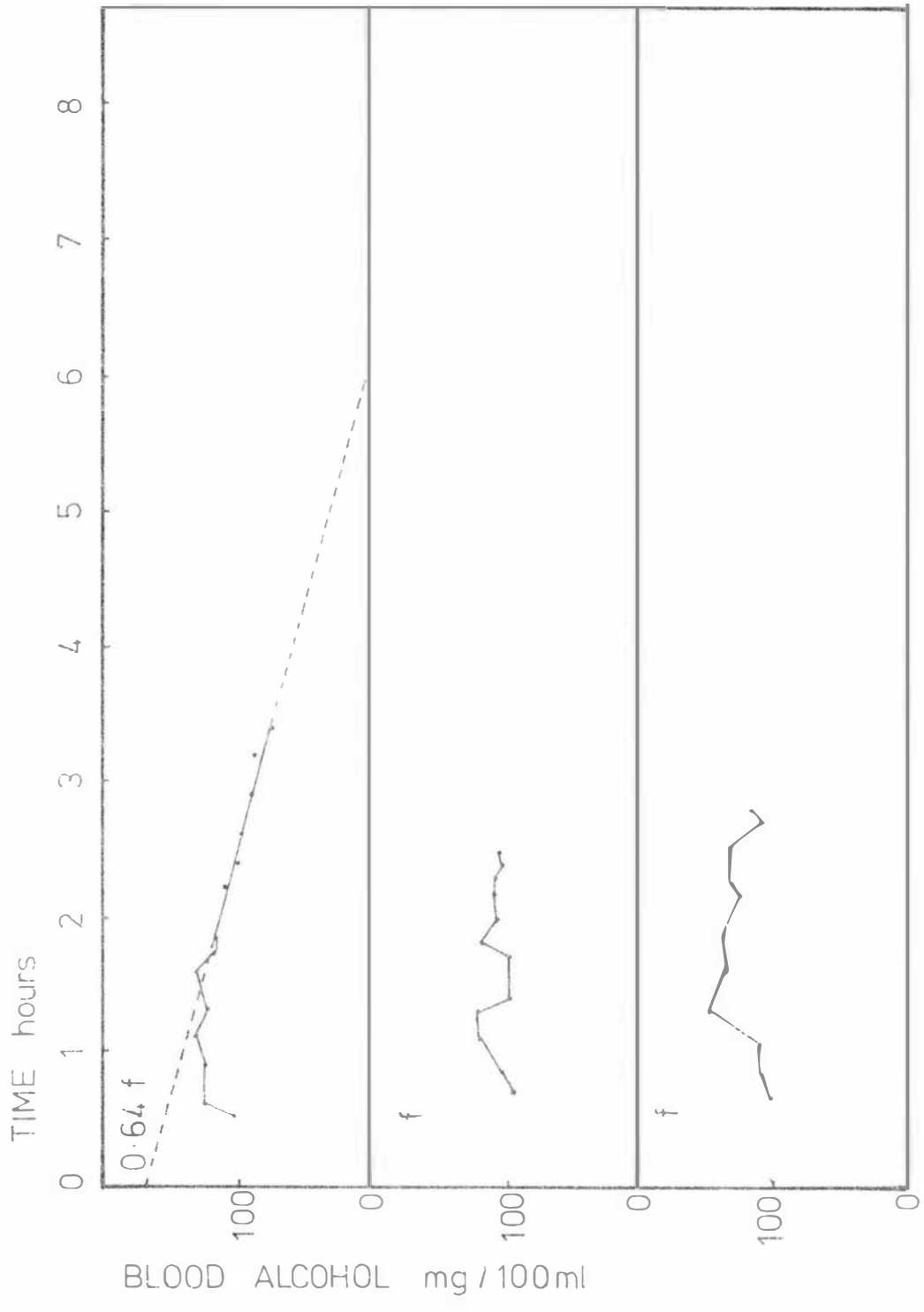
Figure 4.3a

Subject:- 1 2 3



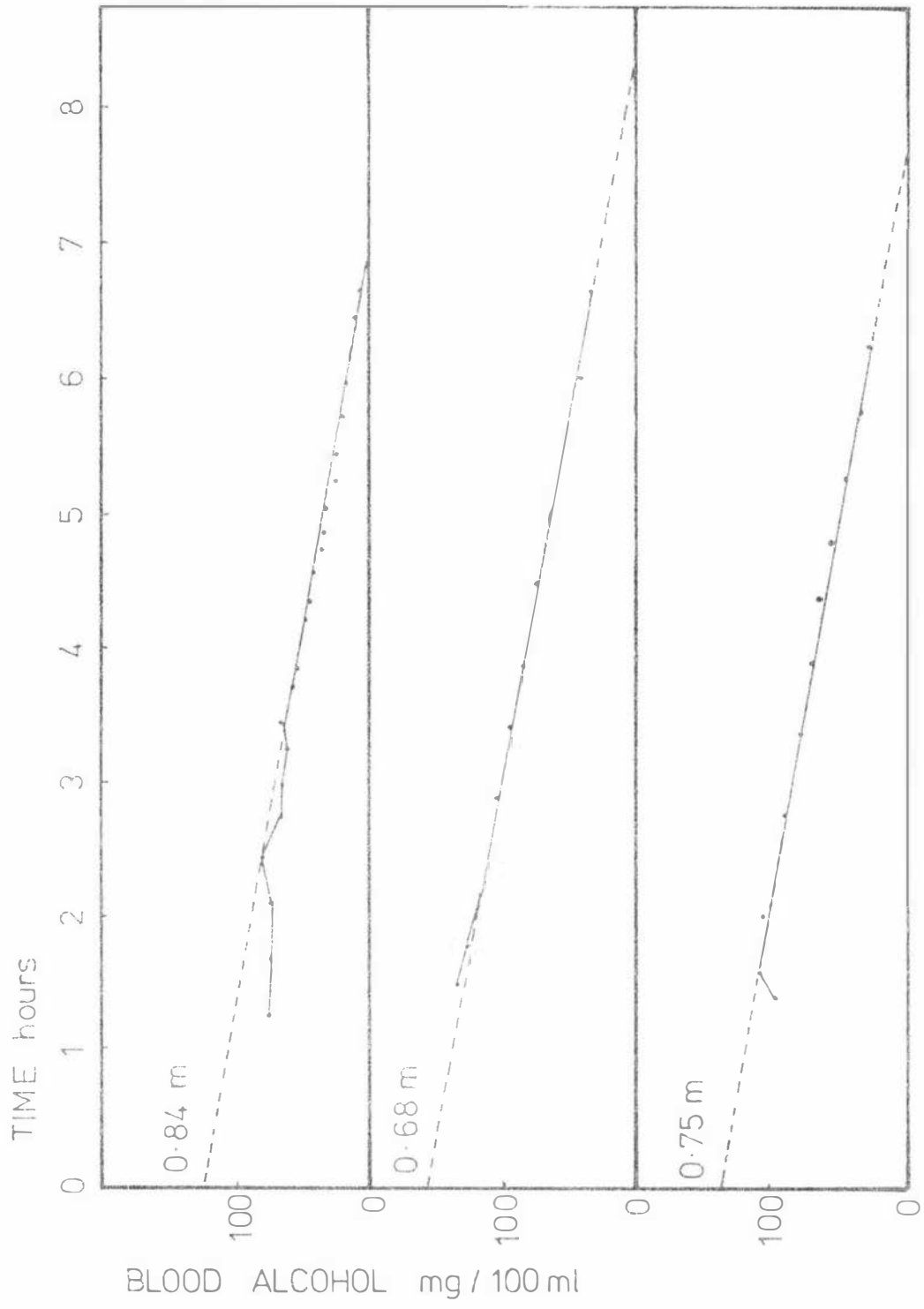
Subject:- 4 5 6

Figure 4.3b



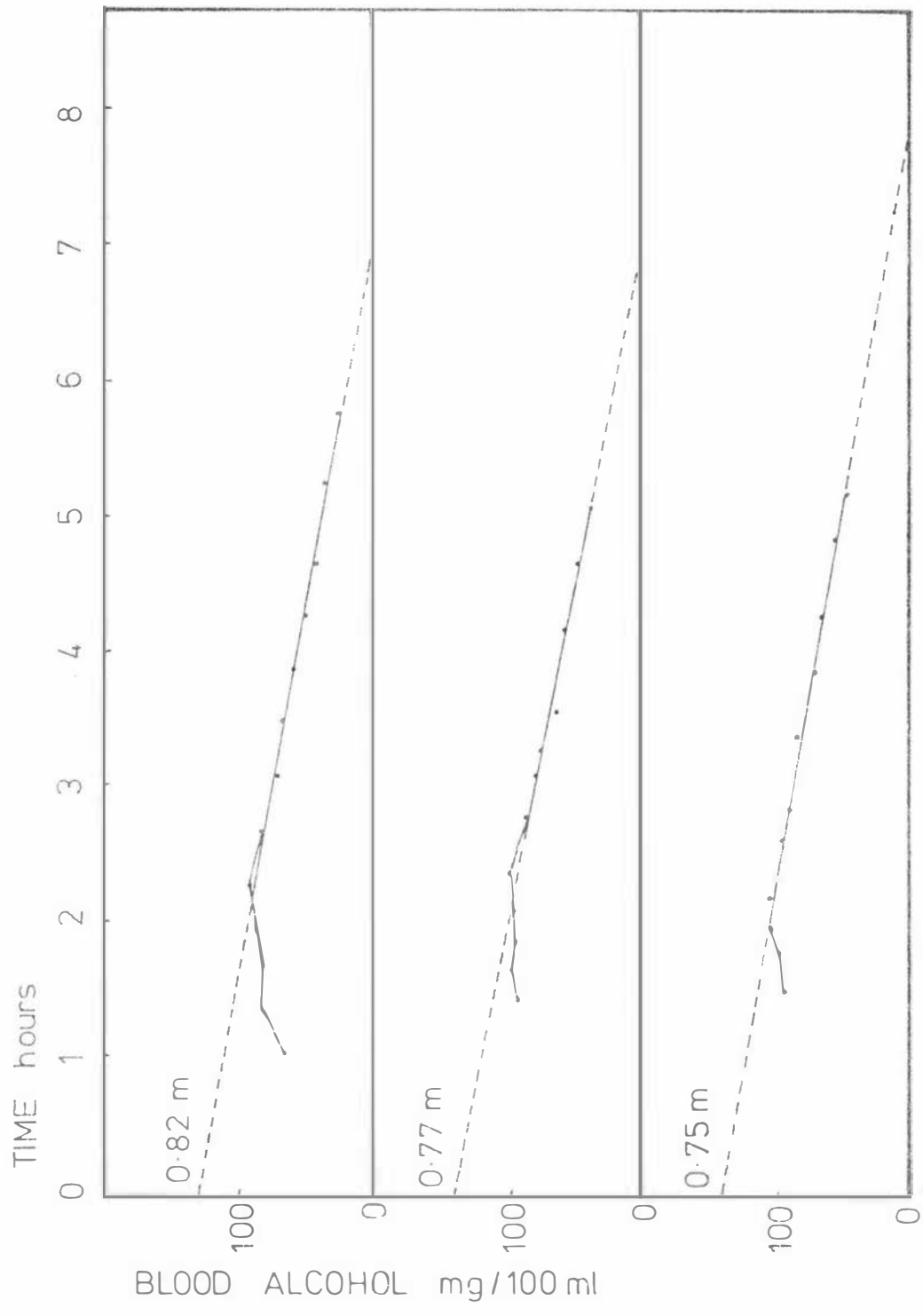
Subject:- 7 8 9

Figure 4.3c



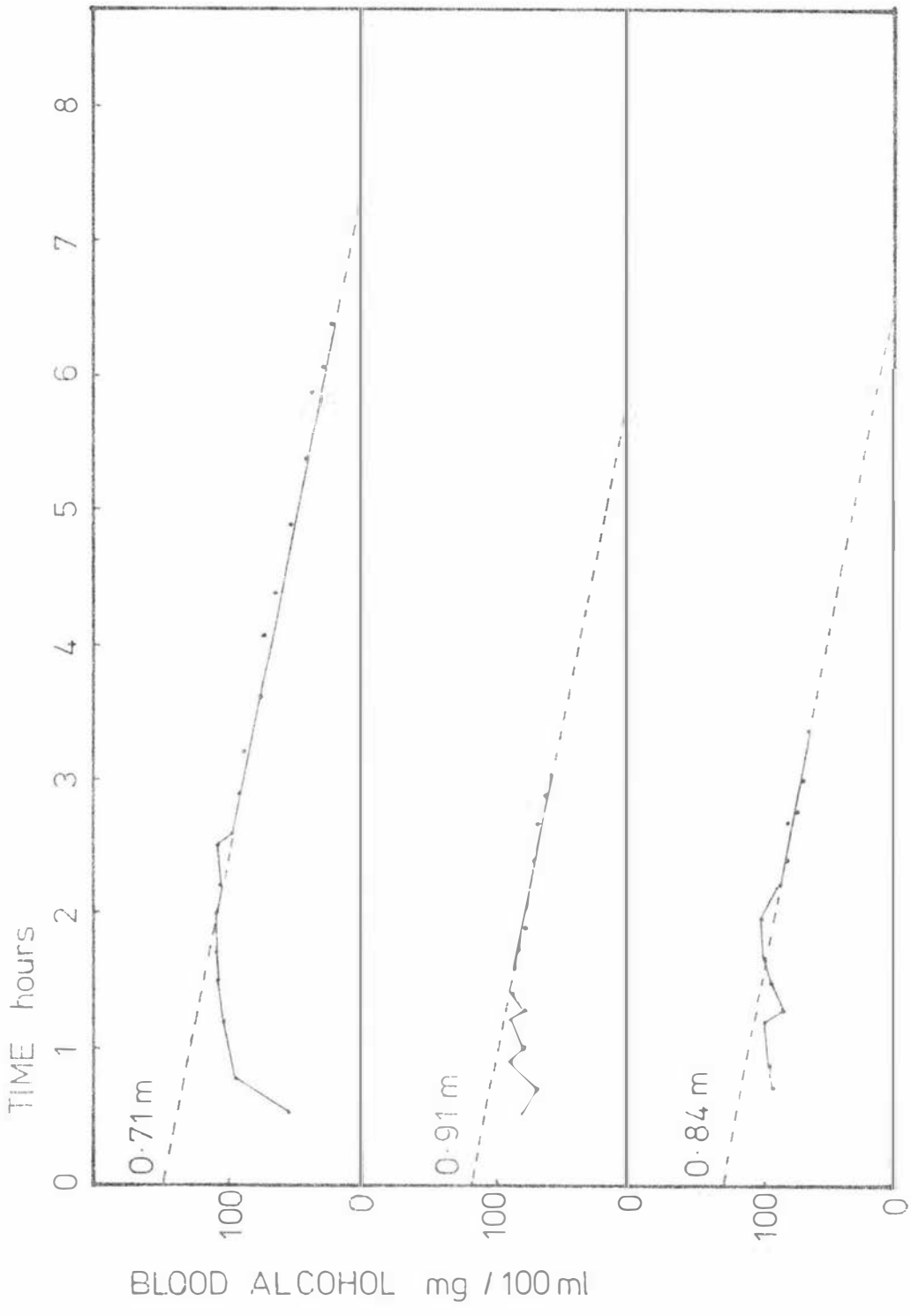
Subject:- 10 11 12

Figure 4.3d



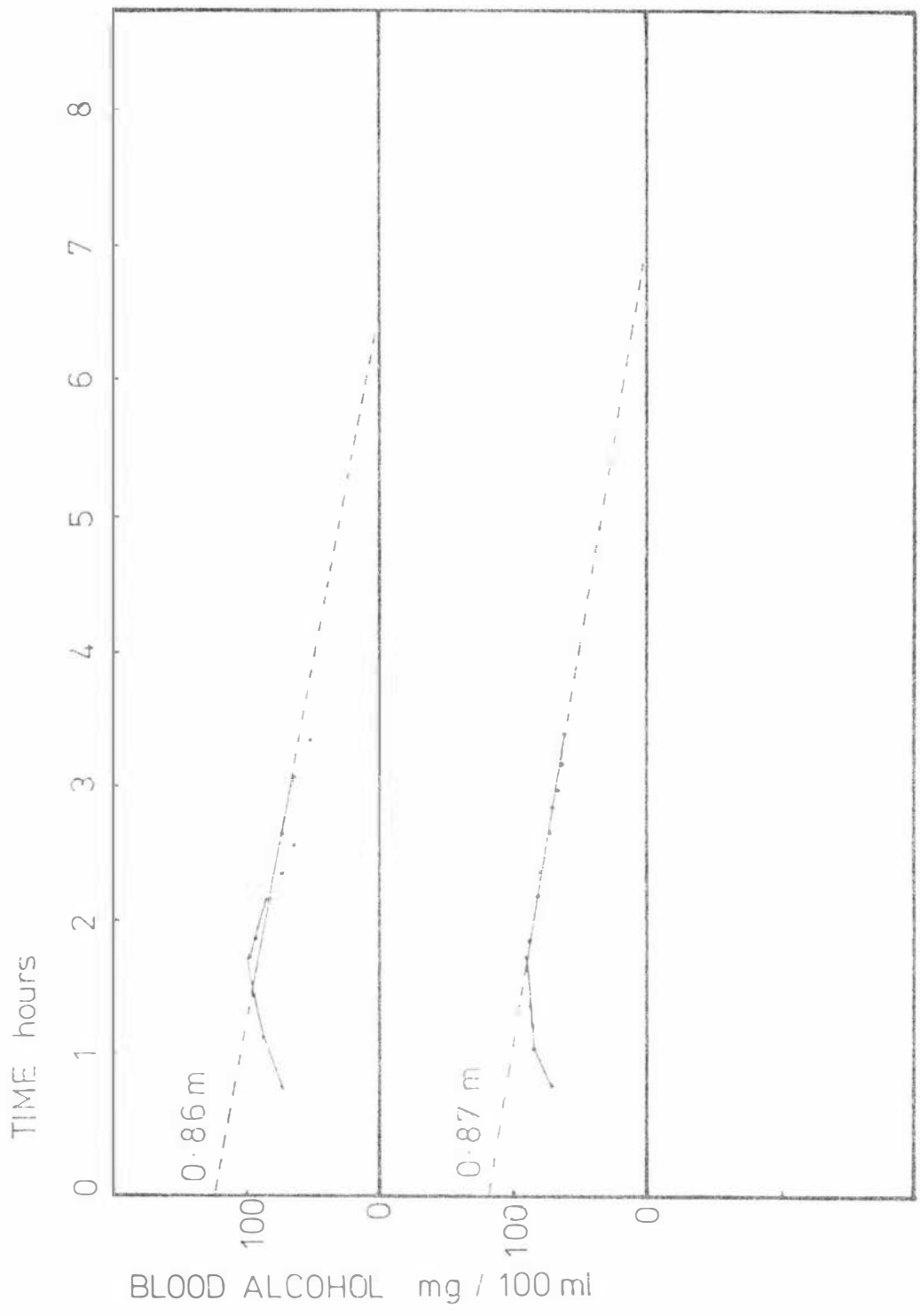
Subject:- 13 14 15

Figure 4.3e



Subject:- 16 17 18

Figure 4.3f



Subject:- 19 20 21

Figure 4.3g

TABLE 4.3 Alcohol distribution concentrations and estimated absorption times for subjects given an alcohol dose of 1.0 g/kg body weight. Females, 1-9; males, 10-20.

Subject	Weight Kg	Co mg/Kg	r	Absorption Time, hrs
1	55	1377	0.73	2.0
2	43	1377	0.73	1.5
3	48	1094	0.91	2.0
4	64	1538	0.65	2.7
5	70	1377	0.72	2.2
6	65	1311	0.76	2.0
7	65	1557	0.64	1.7
8	60	-	-	2.5+
9	60	-	-	2.8+
mean	58.6	1346	0.73	2.0
s.d.	10.0	145	0.09	0.4
10	80	1195	0.84	3.5
11	93	1481	0.68	2.2
12	85	1330	0.75	2.0
13	70	1217	0.82	2.2
14	76	1307	0.77	2.7
15	80	1330	0.75	2.0
16	82	1400	0.71	2.0
17	89	1100	0.91	2.0
18	80	1184	0.84	2.2
19	72	1164	0.86	2.2
20	69	1147	0.87	1.8
mean	79.6	1259	0.80	2.3
s.d.	7.6	118	0.07	0.5

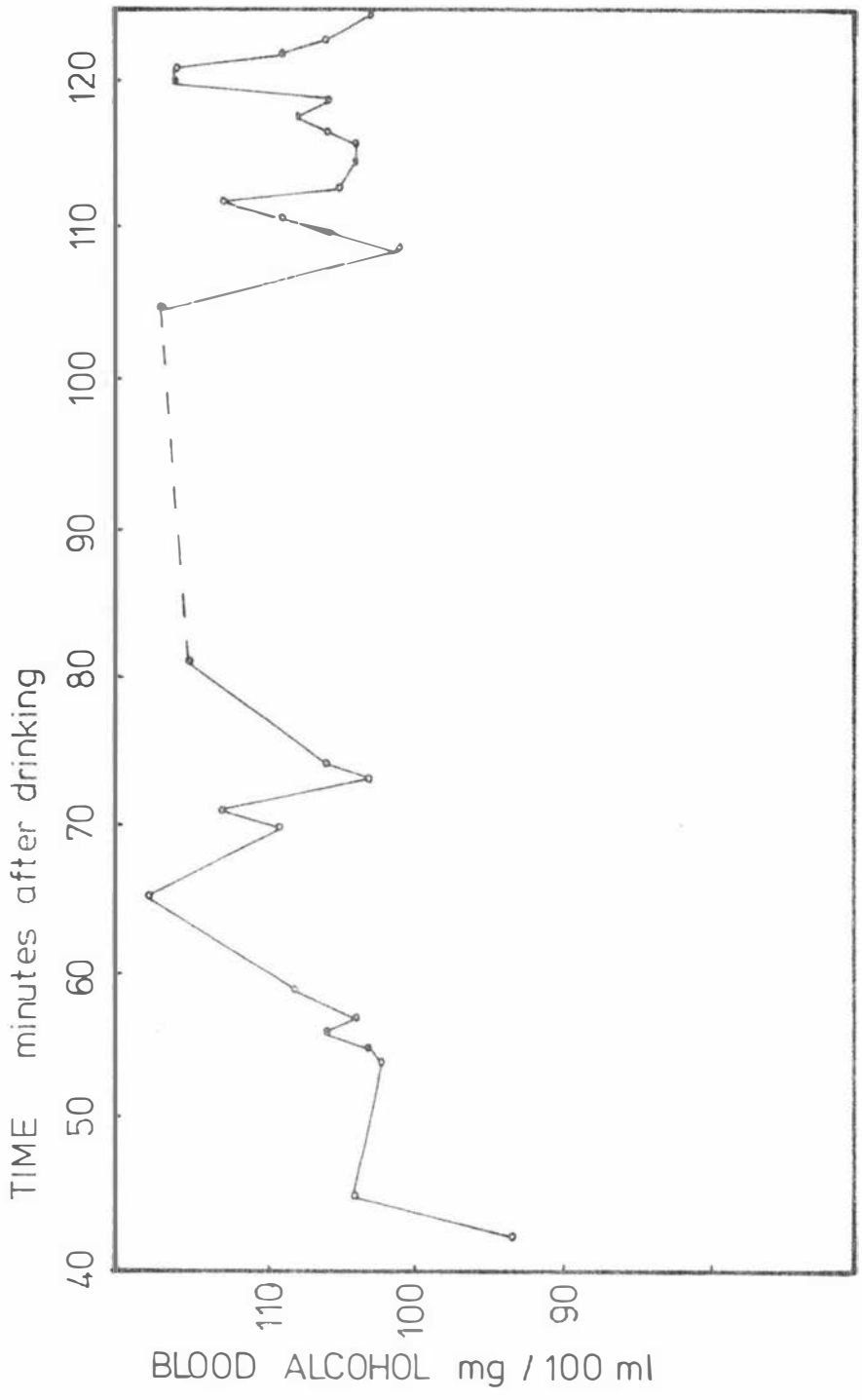


Figure 4.4a

Rapid fluctuations in blood alcohol concentration during the absorptive phase in subject 5.

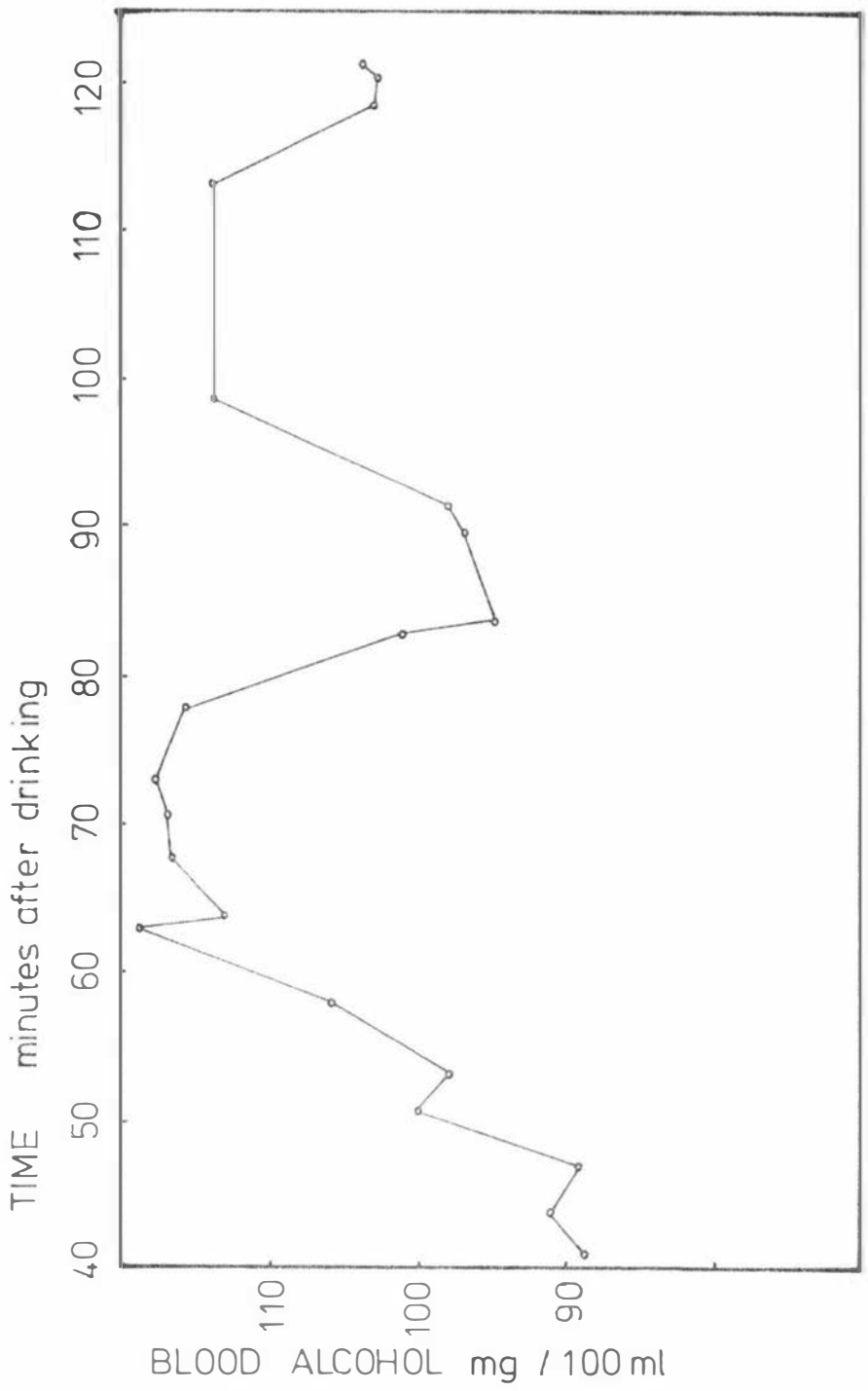


Figure 4.4b

Rapid fluctuations in blood alcohol concentration during the absorptive phase in subject 8.

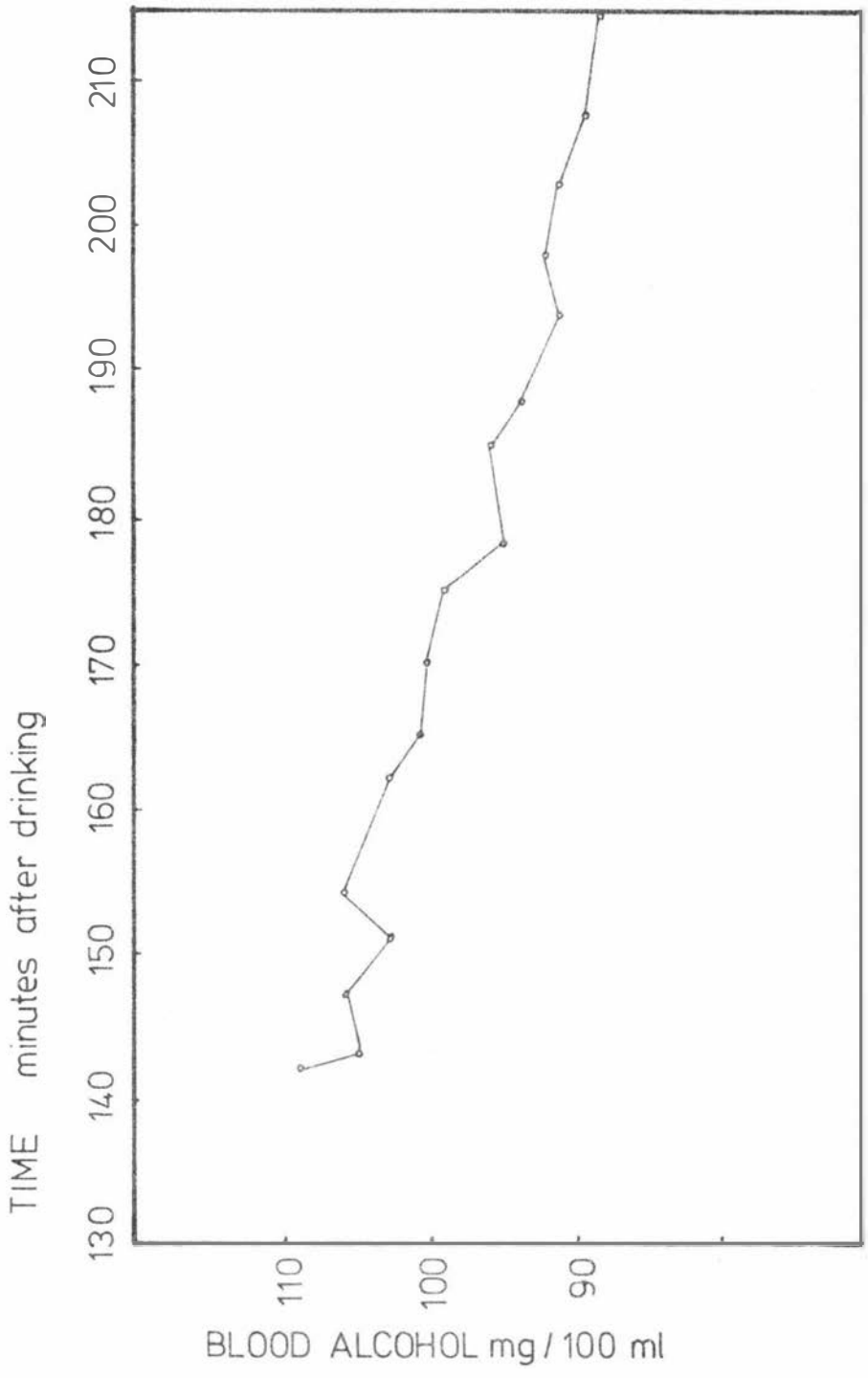


Figure 4.5

A blood alcohol curve in the elimination phase showing the absence of rapid fluctuations, (subject 5).

TABLE 4.4 Alcohol elimination rates in subjects given an alcohol dose of 1.0 g/kg body weight. Females, 1-9; males 10-20. (1) The linear beta slope of the blood alcohol curve; (2) data from (1) converted into mg/kg; (3) Metabolism time obtained from the intercept of linear extrapolation of the beta slope to the abscissa; (4) Alcohol dose divided by metabolism time; (5) data from (4) converted into mg/kg as described in the text.

Subject	(1) mg/100 ml/hr	(2) mg/kg/hr	(3) Total Metabolism Time (hrs)	(5) g/hr	(5) mg/kg/hr
1	18	124	8.0	6.9	125
2	25	172	5.8	7.4	172
3	11	94	10.9	4.4	92
4	20	123	8.0	8.0	125
5	17	115	8.6	8.2	117
6	24	172	5.8	11.2	171
7	28	169	6.0	10.9	167
8	-	-	-	-	-
9	-	-	-	-	-
mean	20.4	138	7.6	8.1	138
s.d.	5.7	32	1.9	2.3	32
10	18	142	6.8	11.8	147
11	19	122	8.4	11.0	118
12	18	127	7.7	11.0	129
13	18	139	7.0	10.0	142
14	20	145	6.9	11.0	144
15	18	127	7.9	10.2	127
16	20	134	7.4	11.0	135
17	20	172	5.8	15.3	172
18	19	151	6.5	12.2	153
19	20	162	6.2	11.6	160
20	17	140	7.0	9.9	143
mean	18.8	142	7.1	11.4	143
s.d.	1.1	15	0.76	1.5	15

TABLE 4.5 Correlation coefficients for regressions of blood alcohol level on time before and after logarithmic transformation.

Case	Linear	Logarithmic
1	.936	.968
3	.934	.974
4	.974	.935
11	.999	.994
16	.979	.990
20	.948	.980
22	.983	.977

Only five subjects were studied with the Breathalyzer 1000 from high blood alcohol levels and in only one was the alcohol curve markedly non-linear (Figure 4.6). A Lineweaver-Burk plot of rates tangent to the slope at various blood alcohol levels suggested a Km of 166 mg/100 ml and a Vm of 71 mg/100 ml at high blood alcohol levels. At low blood alcohol levels, the Km was 14 mg/100 ml and the Vm, 27 mg/100 ml/hr. There was suggestive evidence for a similar curve in one other subject, but the points were spaced too far apart (Figure 4.7). The remaining three subjects showed no evidence of non-linearity, but there were large fluctuations in two which were difficult to explain (Figures 4.8 and 4.9). If there were no experimental or recording errors, these variations may have reflected apparent differences in metabolism, possibly due to poor diffusion of alcohol through water compartments in the peripheral tissues while the subjects were asleep.

4.4 DISCUSSION

Delays in the absorption of an alcohol dose of 1.0 g/kg were marked in many cases and investigations into such delays as well as the fluctuations in observed breath alcohol levels are described in the next chapter.

The pre-beta elimination phase includes a period of equilibration with the total body water. The effects of slow equilibration may be seen where the blood alcohol curve rises temporarily above the maximum attainable for a given distribution volume. Such initial high levels were seen five subjects (1, 6, 14, 18, 19) and suggested that absorption into the blood had been faster than diffusion rates between the blood and body water compartments. The rate at which this diffusion takes place will depend on the concentration gradients between the different compartments, the permeability and surface area of the membranes separating them and the volume of blood flow per mass of tissue. A high proportion of the total equilibration will occur from the capillary beds with the favourable surface area to volume ratios and relatively low blood flow rates. However, from distribution data on blood volumes it has been shown that only a small fraction of the total blood volume is contained in the capillary beds (Reeve et al 1967, p 311). Blood flow through capillaries is also dependent upon the opening and closing of the arterio-venous anastomoses or precapillary sphincters, (vasomotion),

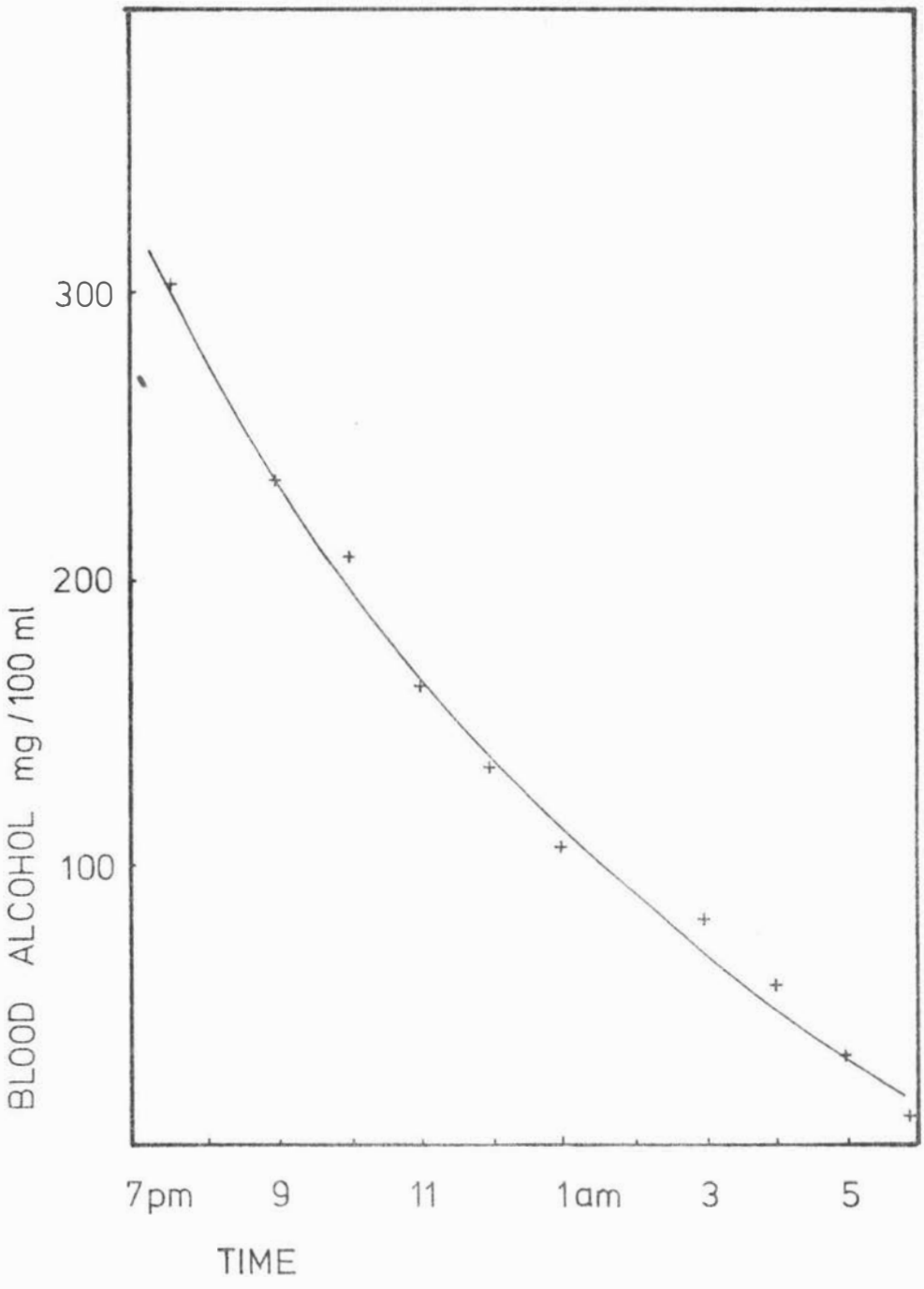


Figure 4.6

A blood alcohol curve from an alcoholic showing marked non-linearity.

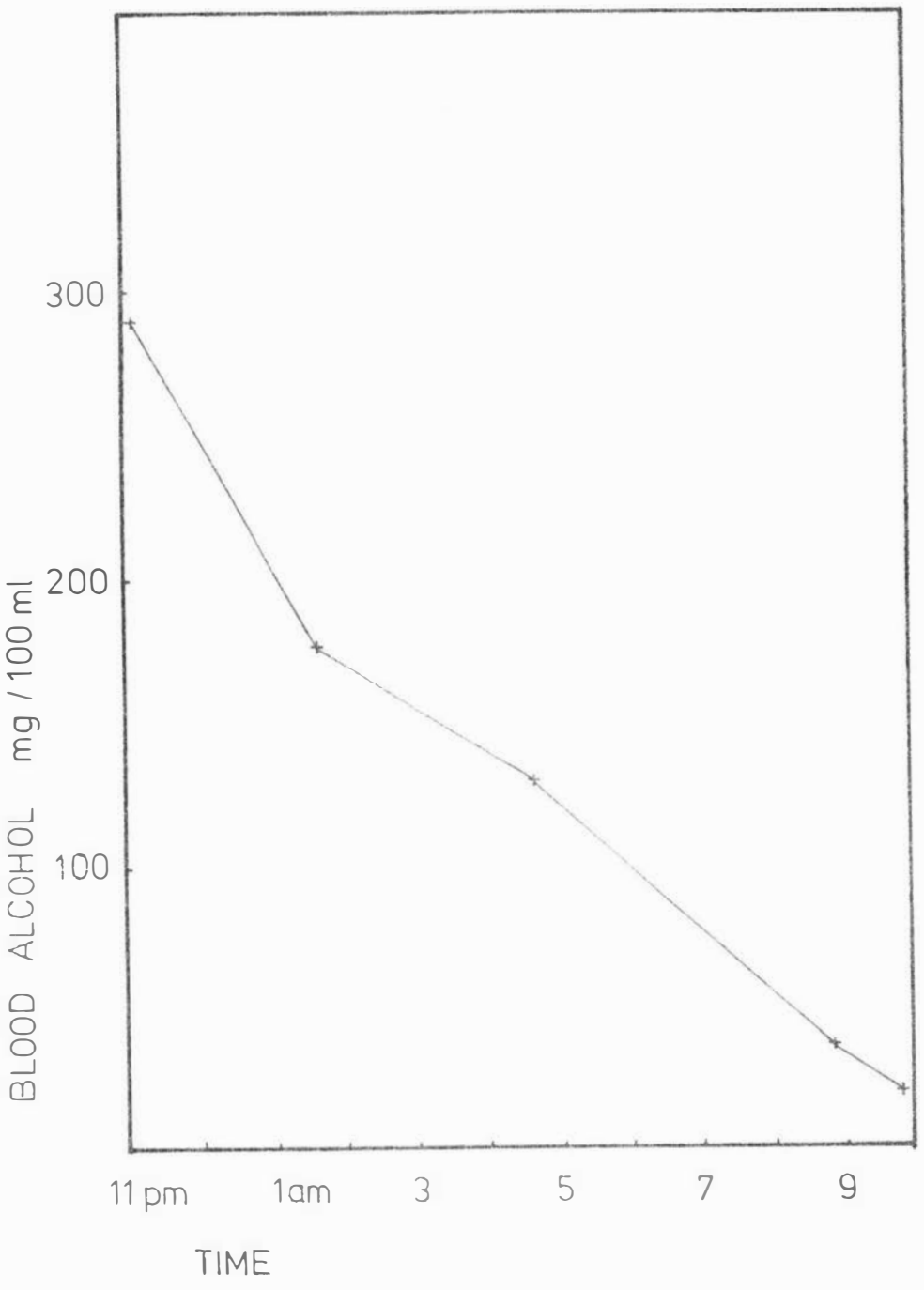


Figure 4.7

A blood alcohol curve from an alcoholic which suggests non-linear elimination.

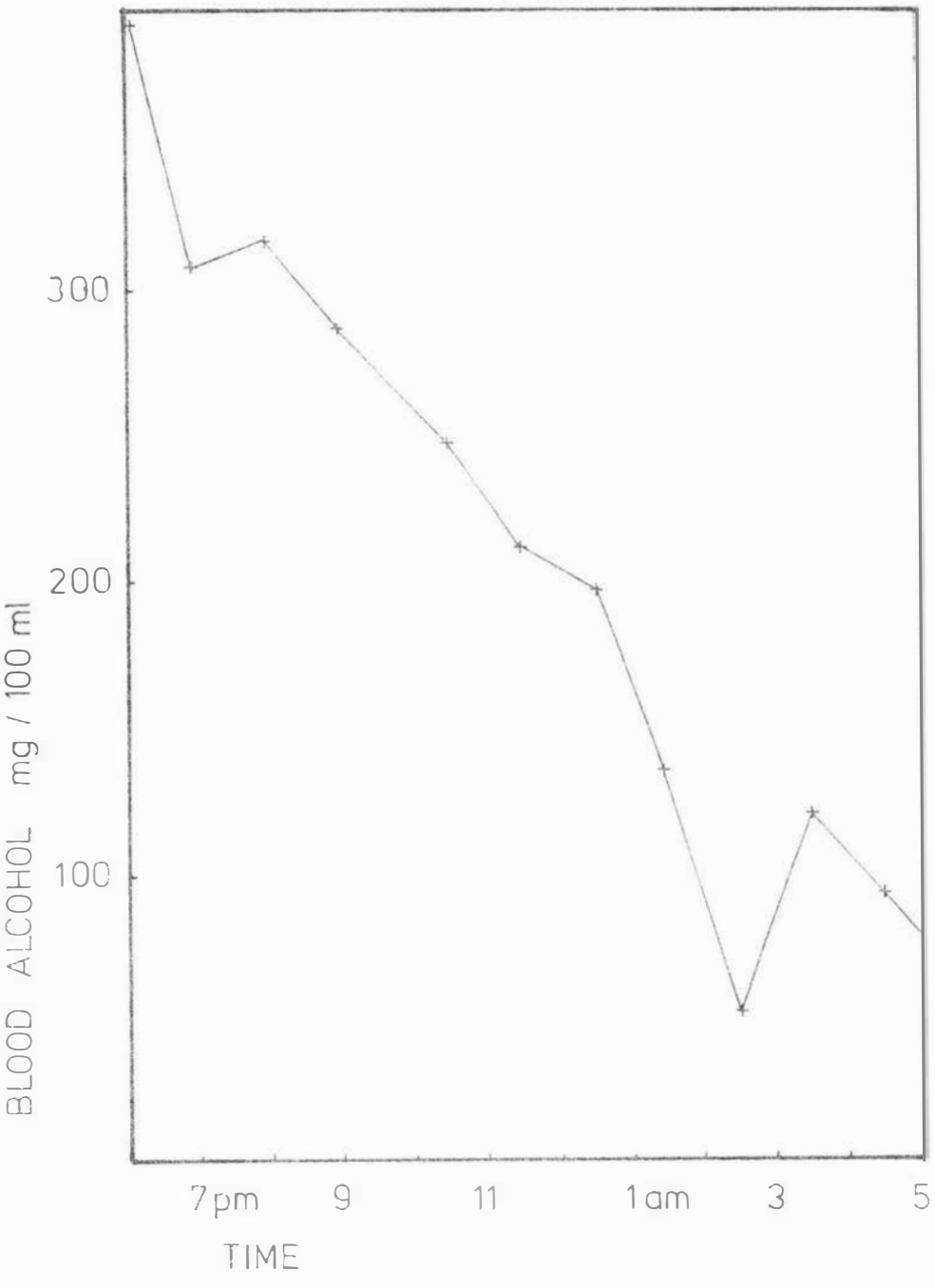


Figure 4.8

Unexplained fluctuations in the blood alcohol curve from an alcoholic.

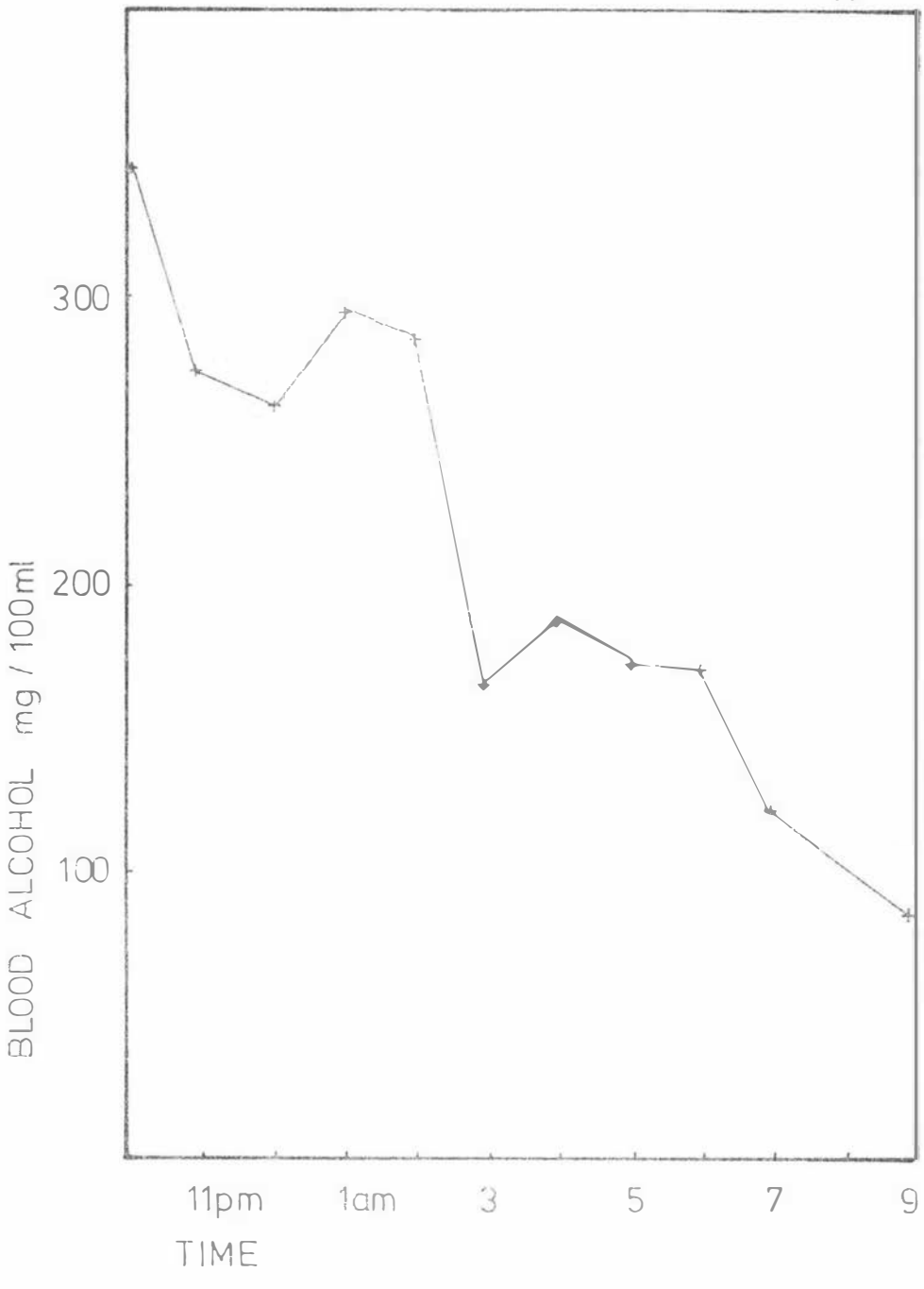


Figure 4.9

Unexplained fluctuations in the blood alcohol curve from an alcoholic.

so that in a particular tissue, the blood flow rate does not necessarily correspond to the perfusion rate and hence the alcohol diffusion rate for the capillary bed. The problem with alcohol is compounded since it can act as either a vasoconstrictor or vasodilator (Dengerink et al 1978).

Experiments with deuterated water have shown that the rate of equilibration into the extracellular water compartments is unexpectedly rapid in 30 seconds (Edelman et al, 1952), but it is much slower with the intracellular water compartments and may take between 20 to 60 minutes after intravenous injection for equilibration to be complete (Pinson 1952). With oral doses of deuterated water, absorption was found to be linear with time, but it took 150 minutes for equilibration after two litres of fluid were ingested and shorter times with small volumes (Pinson 1952). However, the diffusion of water depends on the hydrostatic and colloid osmotic pressures on either side of capillaries (Flexner et al 1948) while the diffusion of alcohol depends upon the concentration gradient.

Alcohol equilibration experiments have been performed on anaesthetised cats by Eggleton (1940). Equilibration with muscle tissue took 30 minutes and a linear decline in blood alcohol levels was not seen until approximately one and a quarter hours after the intravenous injection of alcohol. This suggested that the increased delay was due to the slow equilibration with the transcellular water compartment. It is possible that some organs and particularly muscles, may show different rates of diffusion at various times during the absorption and elimination of alcohol. Because of this, blood alcohol levels may actually rise due to an influx of alcohol from a previously poorly perfused tissue. Such changes due to re-distribution effects were shown by Gruner et al (1958) in subjects who stood motionless for 15 minutes followed by 15 minutes exercise.

While the blood alcohol levels will be higher than expected from a given dose, if diffusion of alcohol from the blood into the body water pools is delayed, the rate of elimination from the blood will appear to be high because of the combined oxidation rate in the liver and the loss due to diffusion into the tissues. Under these circumstances, it is possible that the beta slopes will not be linear throughout the

the elimination phase. Extrapolation of the early portions of such curves would yield high values for the concentration at the ordinate and consequently low values for the total body water. The general tendancy in the experimental results, however, has been to find high values for the Widmark ratio, r, denoting large distribution volumes. This has been a common problem in many alcohol studies (Lundsgaard 1953) and it implies that the fraction of water in the body is greater than normal. For example, a ratio of 0.9 with a normal blood water content of 80% corresponds to a water volume of 72% of body weight. Such figures are well outside physiological variations in normal subjects so that some other factor must have been responsible for the over-estimation of the ratio.

The importance of the Widmark ratio is seen in studies on the rates of alcohol metabolism in the body. It has been shown that there are two methods for calculating these rates of metabolism. The simplest is to extrapolate the beta slope to the abscissa to give the time when zero blood alcohol levels are attained, ignoring the slower rate of removal at low blood alcohol levels. It might be more correct to say, in this case, that this method measures the average rate of removal from the body. The alternative multiplies the rate of elimination of alcohol from the blood by the Widmark ratio. The two methods give identical results if the value of r used is that determined from the results, even though it may be outside physiological bounds. The substitution of a normal and lower r value will result in a disagreement between the two calculations.

A common factor in these calculations is the amount of alcohol ingested and they are only valid if all the alcohol given is absorbed into the blood-stream. If some is metabolised in the gut or excreted in the faeces there would be a deficit in the blood leading to falsely high volume for the body water compartment. Southgate suggested in 1925 that a considerable fraction of the alcohol ingested never enters the bloodstream. His findings showed that alcohol was adsorbed rather than metabolised in faecal suspensions, which suggested that the absence of alcohol in the lower gut does not necessarily imply that absorption is complete. While the removal of alcohol from the blood is mainly by catabolism in the liver and kidneys, the next most active

tissues are those of the stomach and upper intestinal tract. The extent of oxidation at these sites is not known but the enzyme activity of the stomach averages about one twentieth of the liver (Von Wartburg 1971). If the weight of the stomach is one quarter that of the liver, then the approximate rate of oxidation would be 0.0125 of the total rate of alcohol oxidation for the whole body of 7 - 10 grams per hour. It is unlikely that significant amounts of alcohol are metabolised before entry into the bloodstream.

The small amounts of alcohol excreted unchanged in the breath, urine and sweat (Ledermann 1956) originate from the blood. These losses represent only small fractions of the total elimination of alcohol from the body. They make no contribution to losses of alcohol before absorption into the bloodstream.

Lower r values are obtained if the beta slope is increased but such a procedure requires some justification. This may be possible if there was a continual influx of alcohol from the gut during the elimination phase which partially offset the rate of elimination to make it appear that the beta slope was linear. While this may be a possible explanation where the beta slopes were of short duration, it seems unlikely where they would be observed over several hours. This leaves the possibility that the elimination rate is not linear over the entire time course of alcohol metabolism, but that there is an increased rate during the early stages, particularly at the time of the equilibration phase when the blood levels are subject to changes due to influx from the gastro-intestinal tract and equilibration with the body water pools. It is at these times that breath or blood tests are most unreliable for estimating elimination rates.

Marshall and Owens (1955) discussed the problem of an over-estimated r value in male mice and suggested that it could be due to rapid metabolism in the first hour after administration. Nelson et al (1957) were not able to support this concept. However, they had used female mice of a wide weight range and had found that the rate of metabolism was directly related to total body weight. Another factor which had not been considered was the possibility that the homogeneity of mice coming from closed colonies with a considerable degree of inbreeding could result in a loss of variability in the way alcohol was

metabolised. Forney et al (1962) also found an initial rapid rate of alcohol metabolism in mice but suggested that this was confined to the first thirty minutes after the alcohol was given. Support for an intial rapid rate of oxidation cannot be found in work using rat liver slices (Masoro et al 1953), but Thurman et al (1975) found that the rate of metabolism was dependant on the alcohol concentration in perfused rat liver.

Newman et al (1937) have shown that the beta slopes increased with larger doses of alcohol in dogs, but their results depended on fitting straight lines to widely spaced points which could equally well be on curves. Eggleton (1940) in a much more carefully controlled experiment with cats suggested a dose related metabolism, but only at high blood alcohol levels. Her figures show an exponential decay from 300 to 100 mg/100 ml of blood which was apparently linear below a blood level of 100 mg/100 ml. The curve was remarkably similar to that found for one alcoholic in the present study (Figure 4.6). Loomis, (1950) using an intravenous infusion technique, was not able to show any changes in the rate of elimination of alcohol at blood levels between 20 and 250 mg/100 ml in dogs when the rate of infusion was adjusted to maintain a constant blood alcohol levels, but Feinman et al (1977) showed a faster rate at high blood alcohol levels in rats with a similar technique. When the blood levels were in the range 138 - 276 mg/100 ml, the rate of metabolism was 43 mg/litre / hr and below 138 mg/100 ml, the rate was only 34 mg/l/hr.

In studies on humans, Goldberg (1950) found that the beta slopes rose by 50% when the alcohol dose was increased from 0.5 to 1.5 g/kg., while Larsen (1959) showed lower beta slopes with a 0.2 g/kg dose. More recently, Feinman et al (1977) found a 22% faster rate in alcoholics when the blood levels were above 70 mg/100 ml and 11% faster in normal controls.

While the literature appears confused over the rate of alcohol metabolism at relatively high blood alcohol levels, the Michaelis-Menten kinetic effect at low blood alcohol levels has been clearly demonstrated. Wagner et al (1976) showed the dependency of the observed rate of metabolism on dose at low levels, by giving subjects 15, 30, 45, and

60 ml of 95% alcohol and obtaining average beta slopes of 7.4, 12.1, 13.7 and 14.7 mg/100 ml/hr respectively. When non-linear analysis of the alcohol curves was made, the results conformed to enzyme kinetics with a constant Vm and Km for each subject irrespective of the size of the alcohol dose. The low beta slopes found by Larsen (1959) and the studies of Goldberg (1950) which have previously been cited, may be explained in this way. Similarly, an earlier study (Couchman 1974) where an alcohol dose of 0.4 g/kg was given showed beta slopes between 7.3 and 16.0 with an average of 12.0 mg/100 ml/hr. Examination of the alcohol curves from this study showed that linear portions of the beta slope occurred between blood levels of 20 and 40 mg/100 ml. The expected rate of metabolism at the mean substrate level with a Vm of 23 mg/100 ml/hr and a Km of 14 mg/100 ml would be 15.7 mg/100 ml/hr. From the present study, the beta slopes were fitted at an average blood alcohol level of 80 - 100 mg/100 ml and at this substrate concentration the expected rate of metabolism would be 20 mg/100 ml/hr.

The concept of non-linear elimination alters the traditional Widmark analysis as the beta slope need not be extrapolated linearly, but may curve upward, depending on the value of Km. If the Michaelis-Menten kinetic approach to the problem of overestimated body water values is used, then Km must be increased above the previously published results of Lundquist and Wolthers (1958) or Wagner et al (1976). The emphasis of these authors was on the terminal portions of the alcohol curves whereas in the present study, the alcohol dose has been higher, with consequently higher intial blood alcohol levels.

The significance of this approach may be found in the work of Li et al (1977) who have described a second alcohol dehydrogenase (II ADH) with a higher Km value, in some subjects. While there has been some considerable discussion over the induction of a microsomal alcohol oxidising system with a higher Km in subjects drinking excessive amounts of alcohol regularly, (Lieber et al 1973), the possibility exists that a proportion of normal subjects are able to metabolise alcohol at a faster rate if the alcohol dose if high enough. It does not seem possible to give alcohol doses much higher than 1 g/kg to subjects who are not accustomed to drinking large amounts of alcohol regularly, so that a direct confirmation of this point would be difficult to obtain.

An alternative explanation to faster rates of metabolism at high alcohol doses, may be that the alcohol curve is distorted by the rates of absorption and distribution through the total body water. Wallgren and Barry (1970) considered that an elevated value for r in subjects who had not been fasted was due to the increased fluid content of the gastro-intestinal tract with consequent delays in absorption and equilibration. It was considered that investigations into absorption and distribution of alcohol could be made using alcohol labelled with stable isotopes and these studies are described in the next chapter.

5.1 INTRODUCTION

During previous studies with an Alcolimiter, rapid rises and falls in breath alcohol levels were observed which could have amounted to as much as 20 mg/100 ml of blood over a 3 - 5 minute period. At that time, it was not possible to attribute these fluctuations to physiological mechanisms because of uncertainties concerning the accuracy of the instruments used when the tests were repeated after only a very short period of time. Shumate et al (1967), from careful studies using a Breathalyzer, had commented on an unstable period during the first hour or so after the ingestion of alcohol and speculated that it was related to transfer of alcohol from the digestive tract to the bloodstream. In addition, Ponsold (1965), who obtained blood at frequent intervals from an indwelling cannula, noted 'notches' of about 7 mg/100 ml in the blood alcohol curve. He attributed these to either the opening and closing of the pyloric sphincter or to the effect on diffusion of alcohol through the body water compartments from changes in blood flow through peripheral tissues. He showed that when the absorption of alcohol into the body was complete the 'notches' were no longer observed.

It was thought that information concerning these fluctuations in breath alcohol concentrations might be obtained if isotopically-labelled alcohol was given orally during the time when the fluctuations were occurring.

5.2 METHODS

Two subjects were given alcohol at a level of 1.0 g/Kg body weight and then 30 minutes after all the alcohol had been consumed, they were given 1 - 2 ml of deuterated alcohol (C_2D_5OD, 99% atom D, Ciba) diluted in lemonade. A third subject was given an alcohol dose of 0.5 g/Kg body weight in the same manner and with a fourth subject, the isotope was taken with the main alcohol dose of 0.5 g/Kg. Breath alcohol analyses were made using the modified gas chromatograph, while simultaneously alcohol in a portion of the breath was condensed in a glass tube in an ice bath.

The isotope ratio in the condensed breath sample was determined by mass fragmentography using a gas chromatograph coupled to a VG Micromass 12 F mass spectrometer. The main fragments of alcohol had mass to charge ratios (m/e) of 31, 45 and 46 while deuterated alcohol gave m/e values of 33, 49, 50 and 51. The most suitable fragments for determining isotope ratios were 45 and 49. With the accelerating voltage of the mass spectrometer at 4kV, the lower mass was focussed. The higher mass was then focussed by reducing the accelerating voltage while maintaining a constant current through the deflection magnet. The drop in voltage was achieved by a potentiometer which was switched into the circuit by a relay. This relay could be automatically activated at approximately one second intervals and was timed so that the dwell time on each mass was the same. The output from the electron multiplier of the mass spectrometer was fed through an amplifier to relay contacts operating in time with the accelerating voltage relay and then into a twin-pen recorder. In this way, the output at the low m/e was fed to one pen with a 100 mV full scale deflection and the high m/e to the other pen at 1 mV full scale deflection. When the abundance of deuterated alcohol was about 1%, the deflections from both pens were approximately the same.

The condensate was taken up into a capillary from the walls of the tube in which it was collected and then into a 10 µl syringe. The samples were injected into the gas chromatograph of the mass spectrometer containing a 2 meter by 2mm internal diameter glass column filled with Porapak Q. Helium was used as carrier gas at a flow rate of 30 ml/minute and with an oven temperature of 130°. The effluent from the column was passed via a jet separator, which removed most of the carrier gas, into the mass spectrometer at about 3 ml/minute. As the alcohol eluted from the column, a chromatogram was obtained from the mass spectrometer output with peaks corresponding to deuterated and undeuterated alcohol. Recorded peak heights for the m/e 45:49 ratios were converted into isotope ratios using a calibration curve prepared with known standards. Due to slight variations in mass spectrometer sensitivity during each run, a procedure of sample injection followed by a standard was adopted, covering several tests on each sample.

5.3 RESULTS

Abundance of deuterated alcohol in the breath sample was plotted on the same time scale as the blood alcohol level (Figures 5.1 - 5.4). The first two figures show a striking similarity between the isotope abundance and the alcohol concentration in the breath. Fluctuations in breath alcohol levels or isotope abundances were not observed for the subject whose results are shown in Figure 5.3 possibly because of the lower alcohol dose used in this case. In the fourth subject, where the deuterated alcohol was given simultaneously with the main alcohol load, breath alcohol fluctuations were not seen and the isotope abundance increased from 3.3% to 5.5% over a period of three hours (Figure 5.4) suggesting that deuterated alcohol is metabolised at a slower rate than undeuterated alcohol.

5.4 DISCUSSION

Ingested alcohol is absorbed into the body from all tissues through which it passes - the mouth, oesophagous, stomach and small intestines. The main absorption site is the small intestine from which the alcohol is transported to the liver via the portal vein.

A major factor in the rate of alcohol absorption is the speed at which it passes through the stomach. Haggard et al (1941) showed that in rats with a ligature preventing passage of alcohol into the small intestine, alcohol was rapidly absorbed for a short time from the stomach but the rate rapidly decreased even though considerable amounts of alcohol remained. Further absorption depended on the passage of alcohol into the small intestine where absorption was rapid and complete. The transfer of stomach contents to the intestine is controlled by pressure waves within the stomach and the pyloric sphincter which relaxes rhythmically so that in humans, small amounts of stomach contents pass through into the duodenum once in about 20 seconds (Thomas, 1957). Hunt (1954), has suggested that gastric emptying occurs in three phases, (1) an initial phase during which the rate increases with meal volume, (b) a basic or exponential phase where a constant fraction of the stomach contents is emptied per minute and (c) a termination of the exponential phase by a large efflux of contents occurring only after large meals. It has been shown (Hunt et

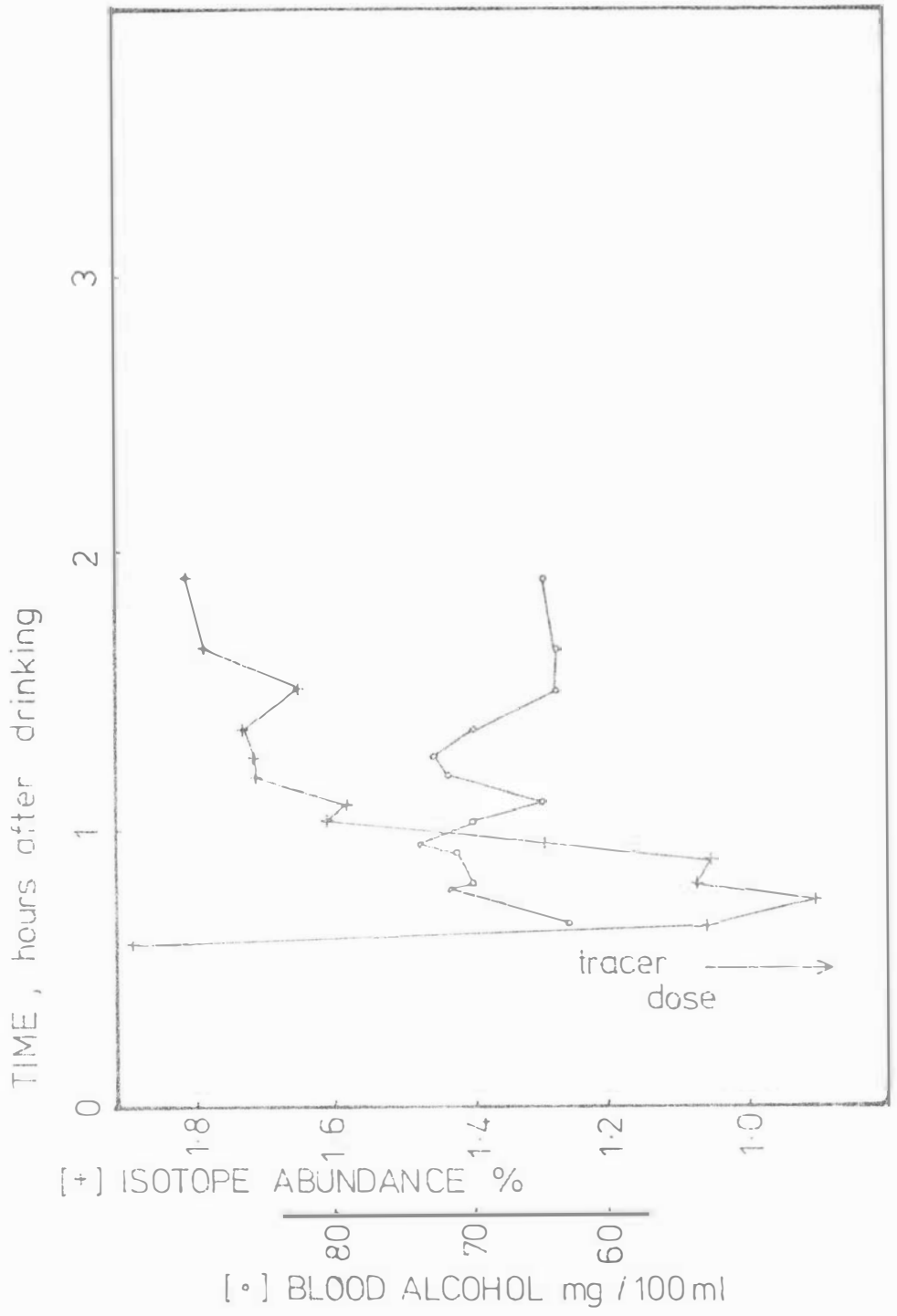


Figure 5.1

Blood alcohol and isotope abundance curve from a subject who had consumed an alcohol dose of 1.0 g/kg followed 30 minutes later by a tracer dose of deuterated alcohol.

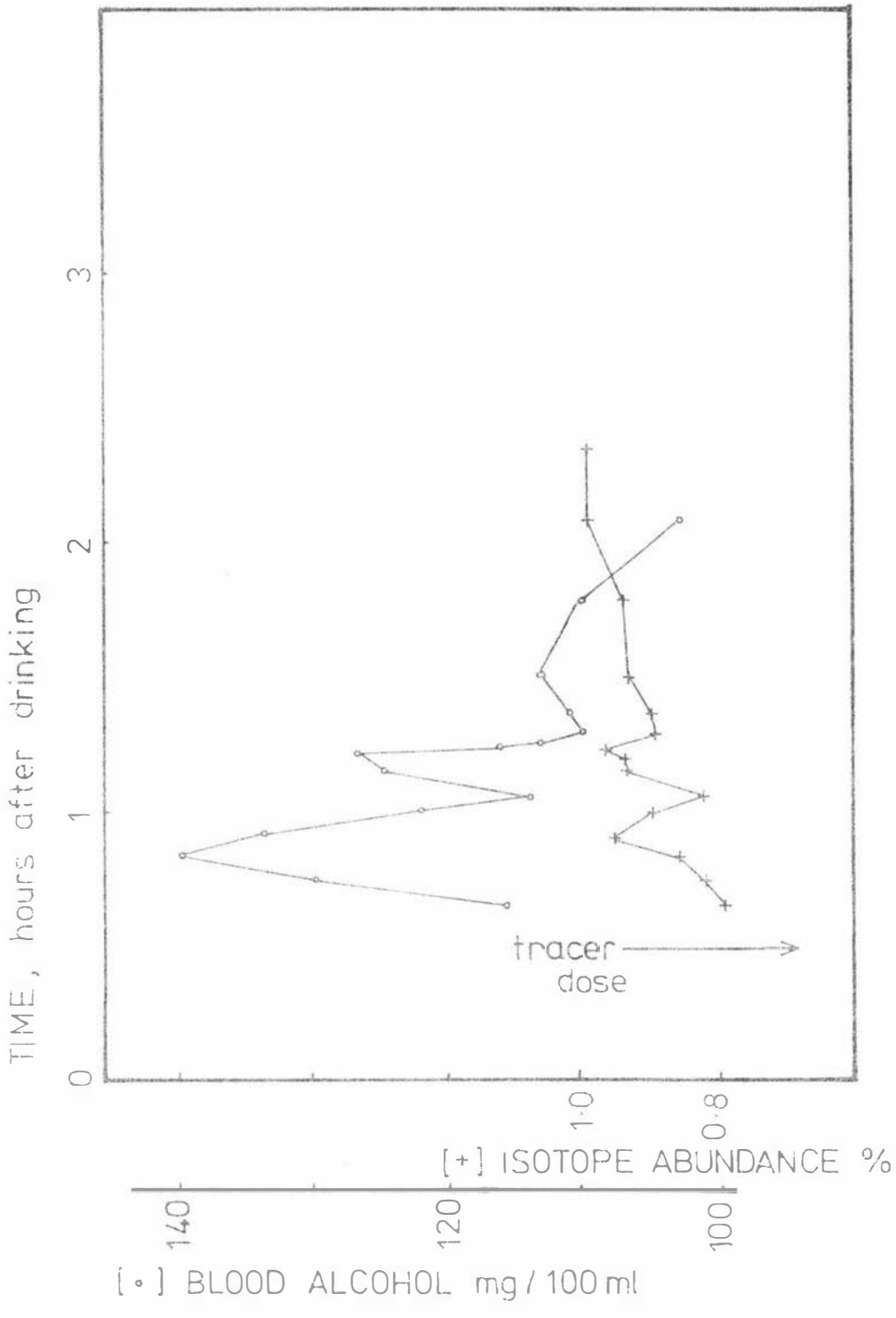


Figure 5.2

Blood alcohol and isotope abundance curve from a subject who had consumed an alcohol dose of 1.0 g/kg followed 30 minutes later by a tracer dose of deuterated alcohol.

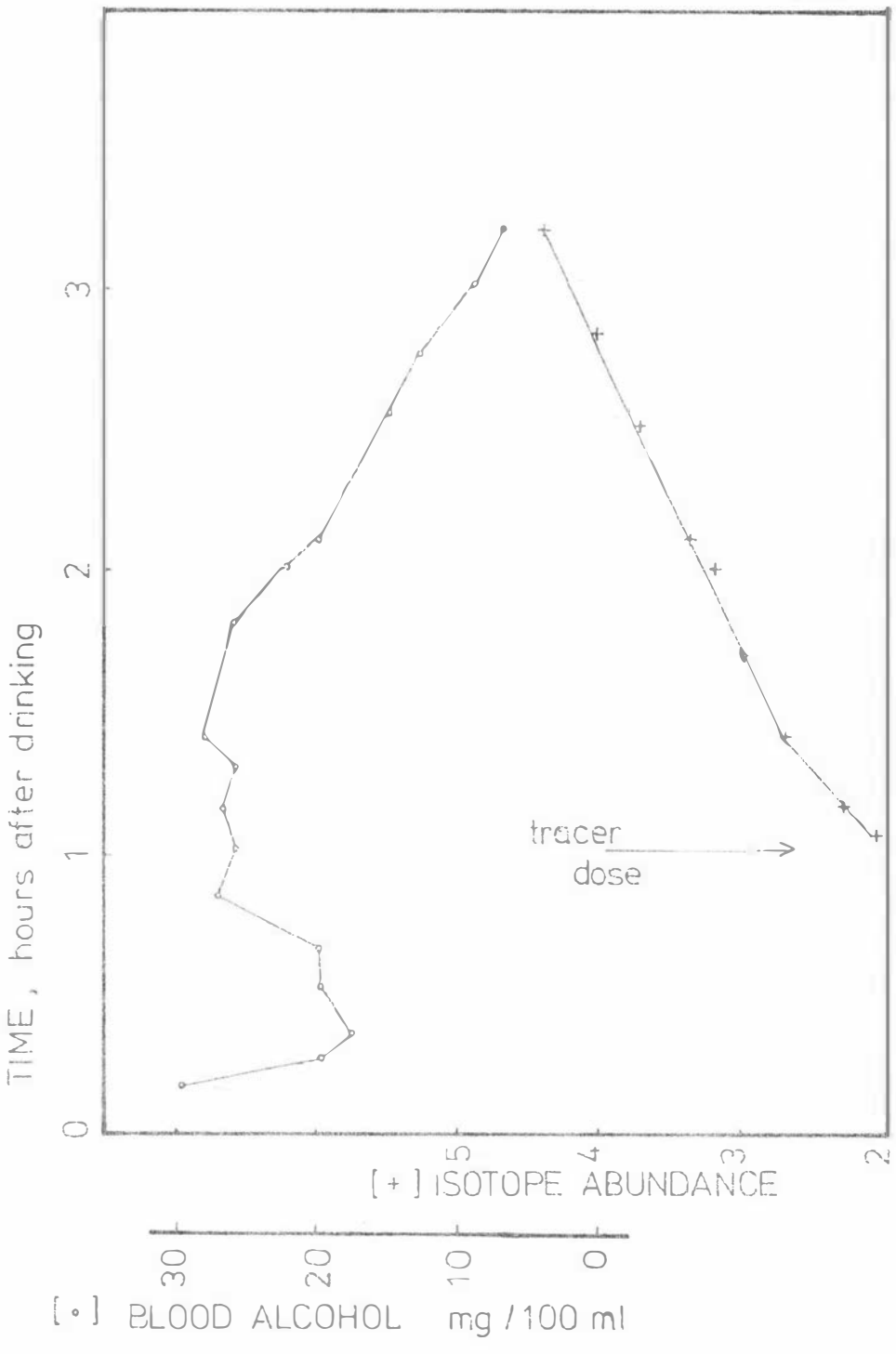


Figure 5.3

Blood alcohol and isotope abundance curve from a subject who had consumed an alcohol dose of 0.5 g/kg followed one hour later by a tracer dose of deuterated alcohol.

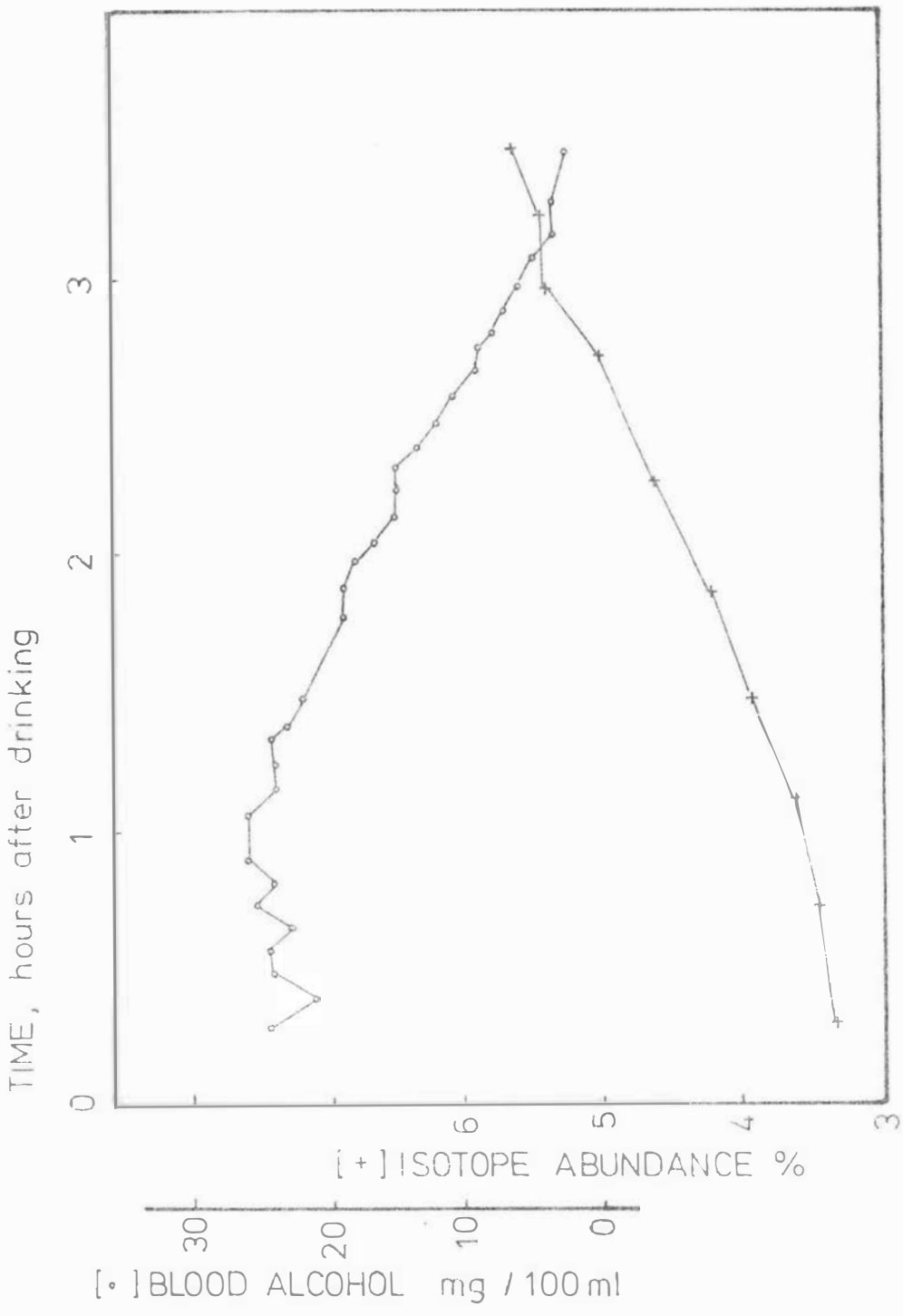


Figure 5.4

Blood alcohol and isotope abundance curve from a subject who had consumed an alcohol dose of 0.5 g/kg together with a tracer dose of deuterated alcohol.

al 1960) that alcohol slows gastric emptying as the concentration increases, in a similar manner to other hypertonic solutions. Redetski et al (1974) had shown that lower blood alcohol levels were observed in rats which had been given potassium chloride in addition to alcohol. It was suggested by Hunt (1960) that the passage through the pylorus is controlled by a feedback mechanism depending upon the osmotic concentration of foodstuffs as they enter the duodenum.

The results with labelled alcohol suggests, that with the rapid consumption of high alcohol doses, the pyloric reactions followed the same pattern which had been observed, using an x-ray technique, by Gershon-Cohen et al (1938). These authors had demonstrated the retention of hypertonic glucose in the stomach and described their findings as follows:-

"Thus when a few cubic centimetres of a 40% sugar solution passes through the pylorus....., the pylorus closes immediately; this closure is maintained not until all the gastric, but only the duodenal contents approaches isotonicity: and this takes place within a relatively short time. In a few minutes, another spurt of glucose is ejected from the pylorus which again closes....."

The substitution of an alcohol solution for a glucose solution in the preceding passage would appear to adequately describe the abnormal functioning of the pylorus after alcohol consumption resulting in rapid rises in blood alcohol levels which equally rapidly fall as the arterial blood equilibrates with the water compartments of the body.

A problem with many alcohol load tests performed in the laboratory is that the subjects are not able to reach high alcohol levels without vomiting. Fox et al (1965) tried to get subjects up to a blood alcohol level of 180 mg/100 ml by giving spirits at a rate of 250 ml each 30 minutes and met such problems with vomiting. This reflex is well known with excessive alcohol consumption and may occur when the blood alcohol level reaches about 120 mg/100 ml irrespective of whether the alcohol is given orally or intravenously, (Harger, 1961). Vomiting is the result of a spasmodic closure of the pyloric sphincter and the unpleasant feelings associated with the nauseous condition are

attributed to high gastric motility (Wolf, 1965). Haggard et al (1941) observed a rigidly closed pylorus in rats given alcohol solutions in large volumes or at strengths above 24 g/100 ml. In these experimental animals the stomachs contained approximately one sixth of the alcohol which had been given 6 hours previously. They reported that with human subjects, the majority of heavy drinkers could tolerate up to 240 ml whisky in 5 - 10 minutes on a empty stomach without vomiting but a considerable number of occasional drinkers could not do this without the development of pylorospasm.

Schedules involving the consumption of large doses of alcohol in short periods of time are typical of the many studies that have been made either for measuring blood alcohol levels, comparing blood with breath alcohols or for measuring the impairment of sensorimotor skills. During such studies, the rates of alcohol absorption may be distorted by its effects on gastric emptying. Such factors are obviously important when comparing blood alcohol levels and rates of elimination of alcohol between different drinking groups or races because they would be variable between subjects and even in the same individual on different occasions.

Distortions of alcohol absorption appear to be a consequence of laboratory investigations with high loading doses of alcohol consumed in short periods of time. Because of this, some workers in recent years have adopted drinking schedules which approximate more nearly to normal social drinking conditions (Kalant et al 1975). The portability of the present breath testing equipment made possible an extension of the present studies into a private bar situation. The findings are described in the next chapter.

CHAPTER 6 ABSORPTION, DISTRIBUTION AND ELIMINATION OF ALCOHOL UNDER NORMAL SOCIAL DRINKING CONDITIONS

6.1 INTRODUCTION

Most laboratory studies on alcohol metabolism are carried out under abnormal drinking conditions with large quantities of alcohol being consumed in a relatively short period of time, often during the morning and normally under fasting conditions. It was shown previously that consuming large quantities of alcohol rapidly may lead to a delay in absorption through the action of alcohol on the normal functioning of the pyloric sphincter leading to a delay in the release of gastric contents into the small intestine (duodenum). With the ability to make rapid, repeated breath tests with portable equipment, it became possible to test large numbers of subjects in private bars under near normal drinking conditions.

6.2 METHODS

An extensive social drinking study has been carried out at the RNZAF base at Ohakea. Studies on alcohol absorption rates were made on members of the Sergeants Mess, representing males over a wide age range. In addition, studies on elimination rates were carried out on members of the Officers Mess, with men who were mainly in a young age group. The bars were opened at 4 pm and the subjects, who had not eaten for 4 hours, purchased and consumed their own alcohol at their own rate mixing freely with other members of the mess who were not involved in the studies. The only restrictions imposed were that each subject be breath-tested at approximately 20 to 40 minute intervals and that before each test, he was to abstain from drinking for at least 10 minutes. In the absorption experiment, some of the participants were asked to stop drinking at 5.30 pm until their breath alcohol levels started to decrease, indicating that they had passed their peak alcohol level. Drinking recommenced as before and continued until 10 pm. To determine elimination rates, the subjects stopped drinking between 6 and 7 pm when breath testing commenced and continued at 20 - 30 minute intervals for at least two hours. Between 6 and 7 pm, the subjects had a meal.

6.3 RESULTS

6.3.1. The "mouth alcohol" effect

To examine the so-called "mouth alcohol" effect, some of the subjects were breath tested at frequent intervals after the first few mouthfuls of drink had been consumed and before any alcohol could be absorbed into the blood. The initial breath alcohol concentrations were greater than 1,500 µg/litre, equivalent to a blood alcohol concentration greater than 300 mg/100 ml. By eight minutes after the first drink, the breath alcohol levels were markedly reduced to about 40 µg/litre and were nearly zero in 10 - 15 minutes.

The tests were then repeated after the subjects had attained a significant blood alcohol level. Breath tests were then carried out immediately after swallowing more alcohol. The breath alcohol level declined in 4 - 5 minutes to a value corresponding to the blood level of the subject before the "mouth effect' rise.

6.3.2. Rate of drinking

A record of the times over which 24 men in the Sergeants Mess consumed either 260 ml glasses of beer or 17 ml nips of spirits showed that the rate of drinking was fairly uniform throughout the period from 3 to 5.30 pm at an average of 4.4 drinks per hour, (range 3.1 - 6.6). A representative sample of drinking rates are shown in Figure 6.1.

6.3.3. Rate of alcohol absorption

The blood alcohol levels increased with continuing consumption (Figure 6.2) but at different rates, no doubt reflecting differences in body weight and rates of metabolism. Between 5.30 and 7.30 pm, the subjects refrained from drinking while maximum blood alcohol levels and rates of elimination were being determined. For those who continued drinking after this time, the average rate of drinking had slowed to 3 drinks per hour and the rate of increase in blood alcohol level was considerably slower (Figure 6.3).

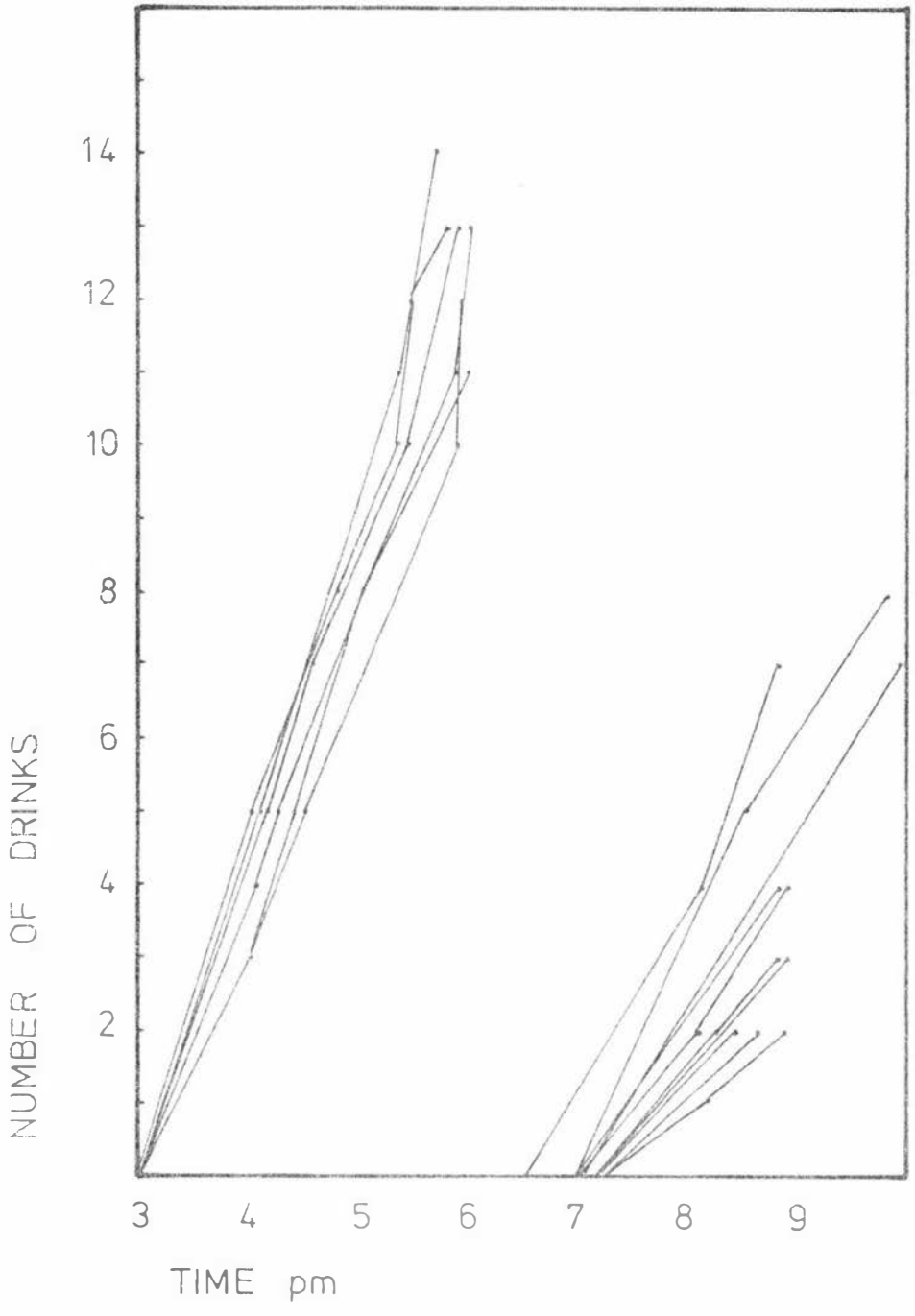


Figure 6.1

A representative sample of the rates of alcohol consumption before and after a meal. A standard drink comprised either 260 ml of beer or 17 ml of spirits.

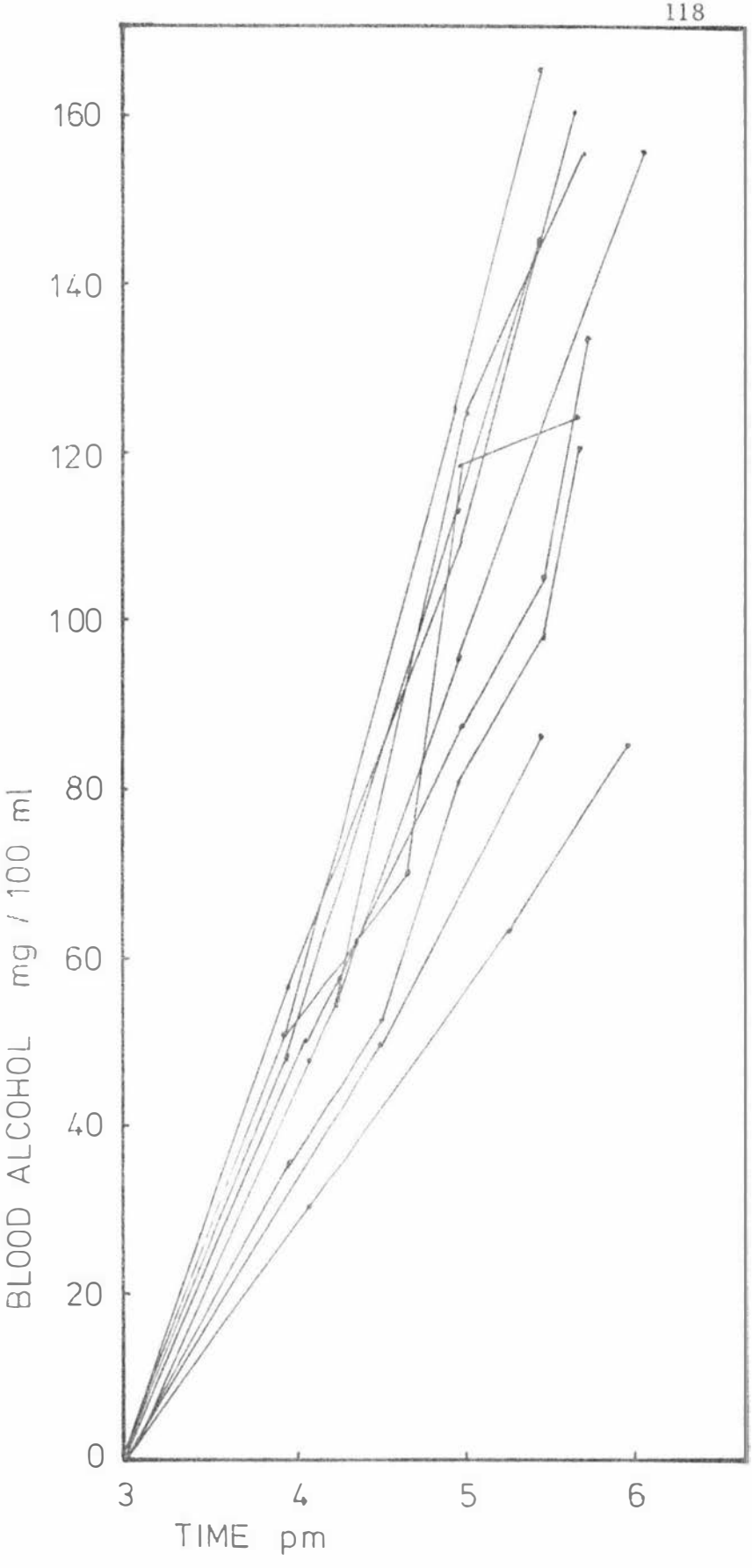


Figure 6.2a

The rate of increase in blood alcohol level during the drinking session before a meal

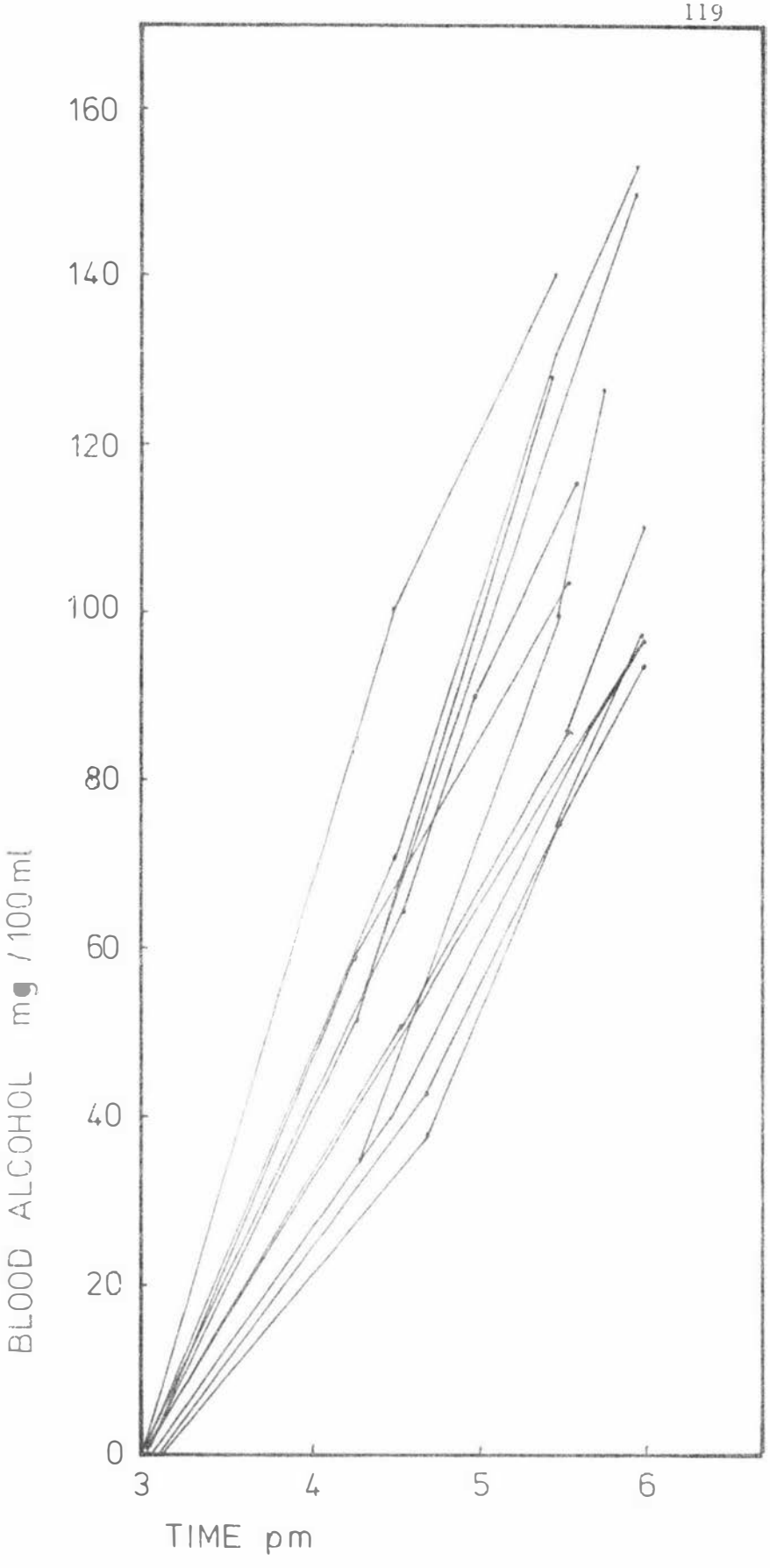


Figure 6.2b

The rate of increase in blood alcohol level during the drinking session before a meal.

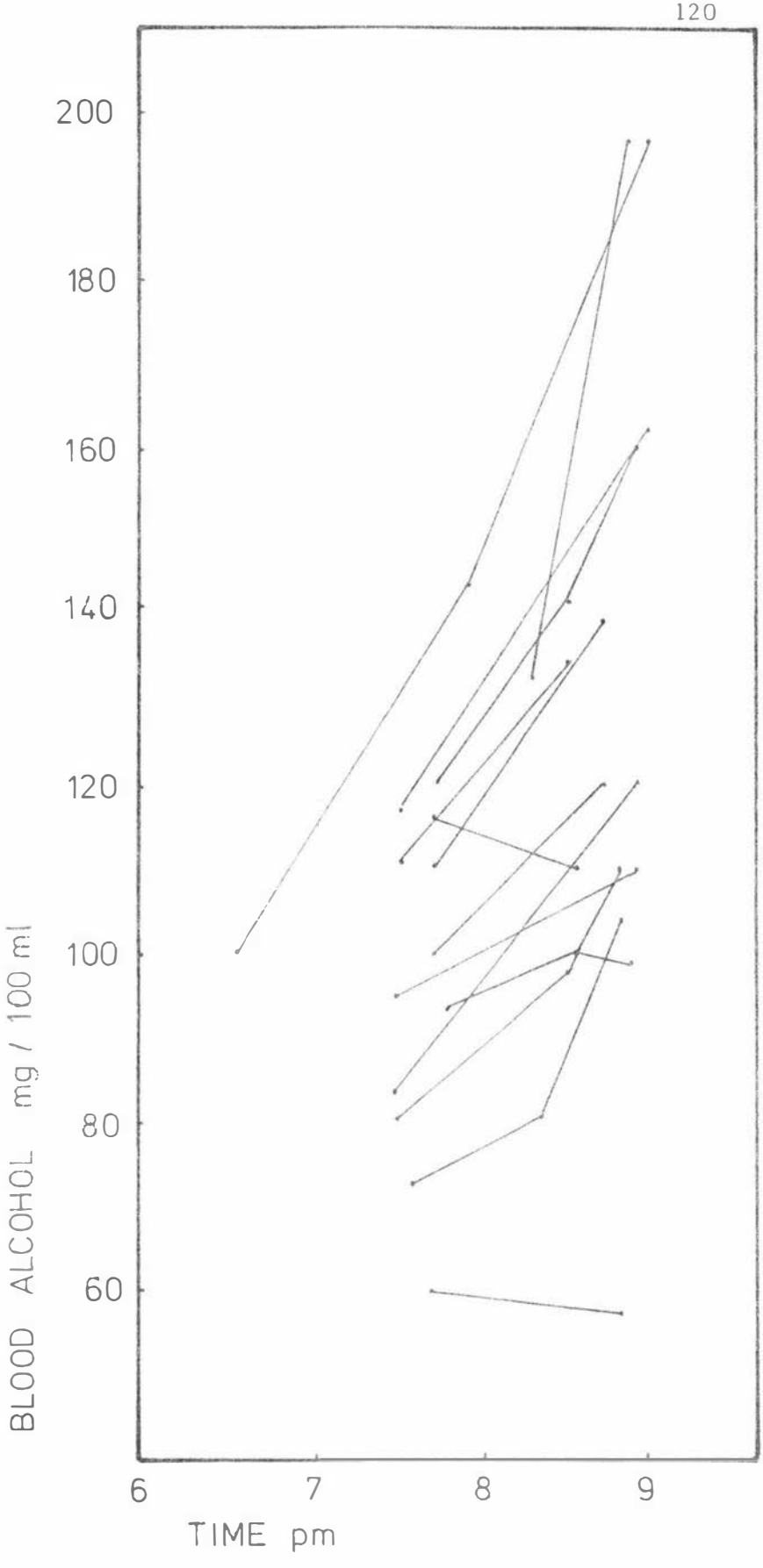


Figure 6.3

The rate of increase in blood alcohol levels during the drinking session after a meal.

6.3.4. Rate of alcohol elimination

When the first drinking period ended between 5.30 and 6.30 pm the majority of subjects showed declining blood alcohol levels, (Figure 6.4) at an average rate of 20 mg/100 ml/hr. Three subjects increased their blood alcohol level during this period.

In the Officers Mess, alcohol consumption for 31 beer drinkers ranged from 0.6 to 1.6 g/kg body weight and for 11 spirit drinkers, from 0.5 to 1.1 g/kg. The beta slopes obtained from linear regression analysis of blood alcohol concentration on time varied from 11.2 to 28.9 mg/100 ml/hr with a mean of 18 mg/100 ml/hr for both drinking groups. The rates of alcohol elimination determined from the total metabolism time and dose averaged 10.7 (s.d. 1.7) grams per hour for both beer and spirit drinkers. When calculated as a rate of elimination in milligrams per kilogram body weight, beer drinkers showed 143 (s.d. 18) and spirit drinkers 156 (s.d. 30) mg/kg/hr (Tables 6.1 and 6.2).

6.3.5. Widmark ratios

The Widmark ratios of the Officers ranged from 0.61 - 1.27 with a mean value of 0.82 (s.d. 0.1) for beer drinkers and 0.95 (s.d. 0.2) for spirit drinkers (Tables 6.1 and 6.2). The frequency diagram (Figure 6.5) shows the general tendency for over estimation of this ratio, particularly in the spirit drinkers.

In 18 subjects, only the first 3 - 4 blood alcohol levels, which included those within 30 minutes of drinking, were analysed (Table 6.3). The mean value of the Widmark ratio was reduced to 0.74 with a range from 0.56 to 0.90 and the beta slopes showed an overall increase with a mean of 23.5 and a range of 17.5 to 32.2 mg/100 ml/hr.

A significant correlation between the values for 'r' and the beta slopes was found with a correlation coefficient of -0.744. This correlation diminished to -0.463 when the first 3 - 4 points only were analysed.

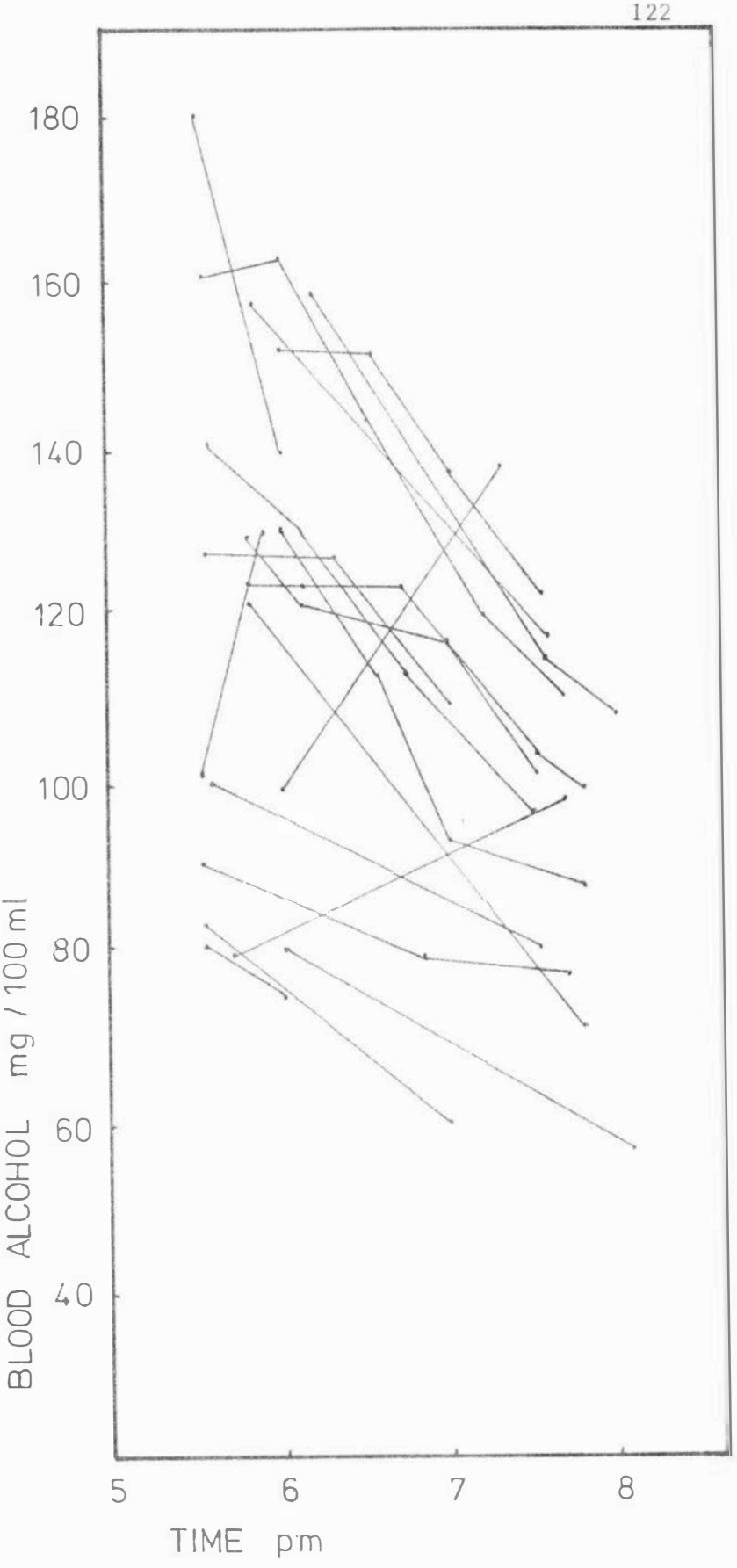


Figure 6.4

The rate of decrease in blood alcohol levels. The first breath tests were made 10 minutes after drinking had finished.

TABLE 6.1 Alcohol distribution concentrations and elimination rates for beer drinkers (Officers Mess).

Subject	Wt Kg	Dose g/Kg	Co mg/Kg	r	B mg/100 ml/hr	mg/Kg/hr	Total Time hrs	g/hr
1	81	0.70	1094	0.64	21.0	127	5.5	10.4
2	72	1.60	2605	0.61	25.5	147	10.8	10.6
3	71	1.21	1481	0.82	21.2	164	7.0	12.3
4	72	1.10	1212	0.91	18.2	156	7.4	10.7
5	61	1.64	1700	0.96	14.4	130	12.5	8.0
6	83	0.95	1256	0.76	19.4	139	6.9	11.4
7	78	1.10	1377	0.80	20.4	154	7.2	11.9
8	68	1.26	1599	0.79	21.5	160	7.9	10.9
9	74	1.16	1266	0.92	17.0	148	7.9	10.9
10	79	1.00	1077	0.93	18.1	159	6.3	12.5
11	70	0.71	797	0.90	15.3	130	5.6	8.9
12	81	0.80	1098	0.73	20.4	140	5.7	11.4
13	73	0.59	770	0.76	19.3	138	4.2	10.2
14	78	0.73	888	0.82	16.8	130	5.6	10.2
15	65	0.88	1065	0.82	20.2	156	5.6	10.2
16	75	0.76	866	0.88	19.9	165	4.6	12.4
17	85	0.85	1067	0.79	20.0	149	5.8	12.4
18	64	0.89	863	1.00	12.5	118	7.3	7.8
19	88	1.15	1786	0.64	28.9	174	6.5	15.5
20	77	1.03	1300	0.79	16.3	121	8.4	9.4
21	79	1.65	1879	0.87	17.0	140	11.8	11.0
22	56	1.29	1746	0.74	22.5	157	8.3	8.7
23	77	0.84	915	0.92	16.2	141	5.9	11.0
24	80	1.35	1807	0.75	23.1	163	8.3	13.0
25	63	1.49	1607	0.92	20.6	179	8.3	11.3
26	82	0.79	1005	0.79	17.9	133	5.9	11.0
27	76	1.04	1129	0.92	14.1	122	8.5	9.3
28	77	0.66	1011	0.65	18.4	113	5.8	8.8
29	79	1.28	1412	0.91	15.9	137	9.5	10.6
30	73	1.29	1446	0.89	12.3	103	12.4	7.5
31	70	1.03	1089	0.94	17.1	152	6.7	10.7
x		1.06		0.82	18.8	143		10.7
s.d.		0.05		0.10	3.6	18		1.7

TABLE 6.2 Alcohol distribution concentrations and elimination rates for spirit drinkers (Officers Mess).

Subject	Wt Kg	Dose g/Kg	Co mg/Kg	r	B mg/100 ml/hr	mg/Kg/hr	Total Time hrs	g/hr
1	76	1.13	1086	1.04	12.9	127	9.0	9.6
2	75	0.57	452	1.27	11.2	134	4.3	10.0
3	65	0.66	625	1.06	14.0	140	4.8	9.0
4	68	0.91	1360	0.67	16.6	105	8.7	7.1
5	57	0.86	731	1.18	14.7	164	5.3	9.2
6	65	0.57	485	1.17	15.2	168	3.4	10.9
7	77	0.71	896	0.78	23.7	174	4.0	13.8
8	72	0.51	585	0.89	16.1	135	3.3	11.2
9	61	1.03	1098	0.94	23.4	208	5.0	12.6
10	67	1.04	1668	0.63	29.5	175	6.5	10.8
11	72	0.97	1174	0.83	23.4	183	5.2	13.5
x		0.81		0.95	18.2	156		10.7
s.d.		0.20		0.21	5.8	30		2.0

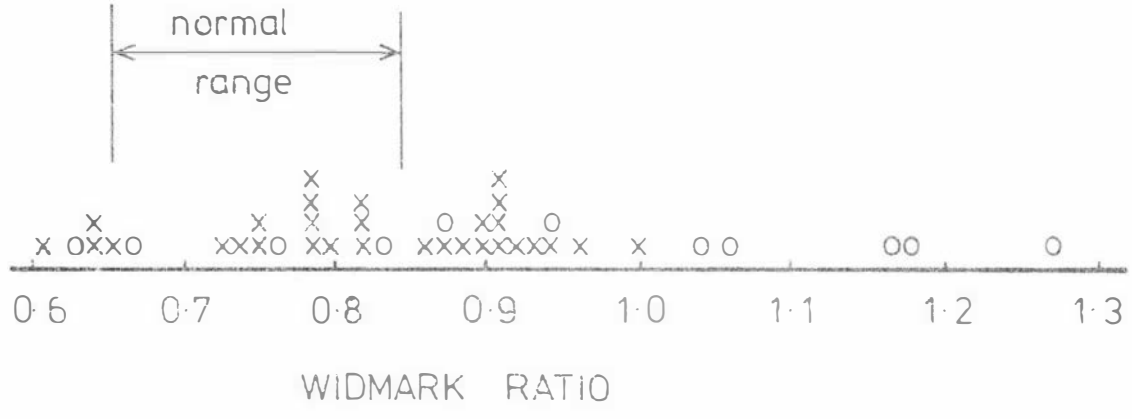


Figure 6.5

A frequency diagram of calculated Widmark ratios for spirit drinkers (O) and beer drinkers (X).

TABLE 6.3 A comparison of the beta slopes and Widmark ratios obtained by analysing the blood alcohol levels obtained, (a) from all points; (b) the first three to four points and (c) the terminal points of the alcohol curve.

Subject	(a)			(b)			(c)		
	Co	B	r	Co	B	r	Co	B	r
6	1256	19.4	0.76	1396	25.1	0.68	1155	16.7	0.82
7	1377	20.4	0.8	1518	24.9	0.73	1160	15.7	0.95
9	1266	17.0	0.92	1368	19.8	0.85	1235	14.1	0.94
10	1077	18.1	0.93	1245	18.7	0.80	962	15.6	1.04
12	1098	20.4	0.73	1330	28.0	0.60	990	15.2	0.81
14	888	16.8	0.82	934	19.1	0.78	754	13.3	0.97
15	1065	20.2	0.82	1245	27.0	0.70	990	17.2	0.88
16	866	19.9	0.88	896	21.6	0.85	858	19.8	0.88
17	1067	20.0	0.79	1264	29.2	0.67	811	12.4	1.04
22	1746	22.5	0.74	1830	25.0	0.70	1792	20.1	0.72
23			0.92						
24	1807	23.1	0.75	1821	23.3	0.74	1745	21.7	0.77
27	1129	14.1	0.92	1245	17.5	0.83	1075	12.9	0.97
28	1011	18.4	0.65	1179	25.1	0.56	886	14.5	0.74
30	1412	15.9	0.91	1858	32.2	0.69	1141	9.7	1.11
15	1086	12.9	1.04	1415	22.0	0.80	1075	12.6	1.05
45	1360	13.6	0.67	1415	18.2	0.64	1226	13.6	0.74
85	585	16.1	0.89	698	22.4	0.74	367	8.9	1.4
95		23.4	0.94		25.4	0.90	1471	24.0	0.71
105							1471	24.0	0.71

6.4 DISCUSSION

The significance of the results obtained depended, in part, on the absence of a "mouth alcohol" effect. Results from drinkers with relatively high blood alcohol levels showed an apparent return to equivalent blood levels in about 4 - 6 minutes. Dubowski (1975), had shown that elimination of residual mouth alcohol was exponential and near zero levels occurred 11 minutes after rinsing the mouth with alcohol. This time was reducible to 7 minutes if the mouth was rinsed with water at room temperature. A point which may be overlooked when water-rinsing is adopted prior to breath tests, is that the mouth temperature may be lowered by this procedure with a consequent fall in breath temperature and corresponding apparent alcohol concentration. Dramatic decreases in alcohol concentrations have been demonstrated in cases where cubes of ice where held in the mouth for five minutes before breath testing (Monnier 1956).

Payne et al (1966) found a prolonged "mouth alcohol effect" in one of four subjects tested where the instrument readings were off-scale for 40 minutes after drinking. It is difficult to explain this finding. Six further references were quoted in an editorial in the same journal on the mouth alcohol effect with the comment that there had been no record of a prolonged alcohol retention. A temporary elevation in breath alcohol may arise from either regurgitation of stomach contents or eructation. In the former case, the soft tissues above the larynx would become saturated with alcohol from the stomach contents and high breath readings might be obtained. Alcoholic beverages frequently contain dissolved carbon dioxide which comes out of solution in the stomach. Air may also be swallowed during drinking. In either case, the distension of the stomach may be followed by eructation with gas released which will contain alcohol vapour at concentrations related to the alcohol concentration in the stomach contents and may give false high breath values. Denture wearers may conceivably have a longer mouth alcohol clearance time but this was not demonstrated in the study of Begg et al (1966). The "mouth alcohol" effect is an important factor if breath alcohol tests are to be performed on subjects who would not voluntarily wait for 15 - 20 minutes without drinking prior to the test. The results of this study suggest

that where the blood alcohol levels are already high, the waiting period may be shortened to 5 minutes. In cases where a "mouth alcohol" effect is suspected, a test repeated only minutes after the first would show a much lower alcohol concentration.

In the studies described in the sergeants mess, three subjects drank only spirits, but at the same rate of alcohol consumption as the beer drinkers and their rates of increase in blood alcohol level were similar. A further three subjects supplemented their beer intake with spirits and again there was no effect on the rate of alcohol consumption or rate of increase in blood alcohol levels. The majority of subjects appeared to have reached a maximum blood alcohol level within 10 - 30 minutes after they had ceased drinking, which is in marked contrast to the findings in the laboratory studies. Significant differences from the laboratory studies would be in the volumes of alcoholic liquor consumed, the concentrations of alcohol in the drinks and the longer drinking period at a slower rate of consumption under social drinking conditions.

In spite of the absence of any apparent anomalies in alcohol absorption, the Widmark ratios were for some subjects, still outside a physiologically acceptable range. However, a correlation could be shown between the values for 'r' and the beta slope; where the beta slopes were high, the value of 'r' tended to be low and vice versa. A similar negative correlation coefficient was noted by Lundsgaard (1953) citing earlier work of Widmark and Schmidt. A low beta slope and a high 'r' value has been shown to occur when alcohol is consumed after food and this has been ascribed to a slow absorption of alcohol from the gut (Yi-Jong et al 1976). It seems that the portion of the beta slope examined in these studies was at the terminal end where elimination is slower than maximum. In the present study, there is some evidence for a changing rate of elimination, in that, where initial blood alcohol levels were analysed separately, the dependence of 'r' on the beta slope diminished. Under ideal conditions, these two factors should be completely independent. If a fixed dose of alcohol is given to non-obese subjects, the resulting alcohol curves would radiate from a narrow area on the ordinate and reflect ranges of values for individual distribution volumes and the rate of elimination.

It is commonly believed that the steeper initial portion of the beta slope immediately after drinking reflects a rapid absorption from the gut into the blood leading to high levels until the alcohol has equilibrated with the extracellular water pool. These findings suggest that this can also reflect a faster rate of alcohol metabolism during the early stages of drinking while the blood alcohol levels are high. On the other hand, support for a physiological absorption and distribution effect comes from the observed difference between spirit and beer drinkers, with the former group showing higher values for 'r'. It is unlikely that such differences are due to faster rates of metabolism which depend on the type of alcohol consumed and it is more likely to be related to the volume of fluid and the rate of absorption or equilibration of alcohol between body water pools. At present, it is not possible to state with certainty which of a number of possibilities is correct.

The findings of this study are important when considering the possibility of increased rate of alcohol metabolism in alcoholics over normal controls, (review by Lelbach, 1974). It has long been known that alcoholics are able to absorb alcohol from the gut and attain higher blood alcohol levels than inexperienced drinkers. Consequently, it might be expected that such subjects would show faster rates of alcohol elimination at an earlier time after drinking because the distortion in absorption and equilibration due to a high dosage are not apparent. There may, in fact, be no real differences in the rates of alcohol metabolism between alcoholic and normal drinkers.

The results in this chapter indicate that under normal social drinking conditions, the increase in blood alcohol concentration parallels the rate of drinking. Data has been obtained on the maximum blood alcohol levels for given quantities of alcohol consumed. In the next chapter, the ability to predict such blood alcohol concentrations from known consumptions will be examined.

CHAPTER 7 ESTIMATIONS OF BLOOD ALCOHOL LEVELS AFTER DRINKING

7.1 INTRODUCTION

Objectives for many of the studies on alcohol metabolism have been to (a) predict the blood alcohol levels after drinking alcoholic beverages; (b) measure the rate of alcohol oxidation or (c) determine whether there are differences between so-called normal drinkers and alcoholics.

In alcohol studies related to forensic medicine, attention has been directed specifically to making estimates of blood alcohol levels of a subject at the time of an accident or death. There are two main approaches to this type of problem. Firstly, where the amount of alcohol consumed is known, the concentration in the blood can be calculated after allowing for the amount metabolised. In the second, back calculations are made from known blood alcohol levels at a particular time, using average rates for the disappearance of alcohol from the blood.

The information obtained during the course of the preceding studies was used to test the accuracy of such predictions.

7.2 CALCULATIONS

The usual method of calculating blood alcohol levels from consumption figures is to rearrange the Widmark formula, obtaining the blood alcohol level at the time drinking began:-

$$\text{Concentration at zero time, Co mg/kg blood} = \frac{A}{p \cdot r}$$

Insertion of the average specific gravity of blood divided by ten will give the blood alcohol concentration in more familiar terms:-

$$\text{Co mg/100 ml blood} = \frac{0.106\ A}{p \cdot r}$$

If the mean values for r of 0.74 for males and 0.63 for females are inserted, these formulae become:-

$\frac{0.143\ A}{p}$ and $\frac{0.168\ A}{p}$ mg/100 ml for males and females respectively,

where A is the dose of alcohol in milligrams and p is the body weight in kilograms. Blood alcohol levels are required at some time after drinking, so that Co must be modified by subtracting the average rate of disappearance from the blood for the time period from when drinking

began until the estimate of blood alcohol level.

It has been shown in the previous chapters that values for 'r' inserted into the Widmark equation are frequently overestimated in drinking studies. Such an overestimate will lead to errors in the calculation of blood alcohol levels. Am empirical approach to this problem may be made by inserting the average values for 'r' found from actual drinking experiments.

A simpler approach was suggested by Harger et al (1956). A common factor is derived from the formula:-

$$\text{Factor} = \frac{\text{blood alcohol level mg/100 ml x body weight kg}}{\text{alcohol dose in grams}}$$

so that the blood alcohol levels may be calculated by rearrangement:-

$$\text{Blood alcohol mg/100 ml} = \frac{\text{Factor x alcohol dose}}{\text{body weight}}$$

or more simply as Factor x dose in g/kg

Harger used this formula to calculate the peak blood alcohols but obviously, factors can be calculated for a blood alcohol level at any time after drinking by the use of the appropriate data.

Alternatively, the dependance of blood alcohol levels on dose may be statistically analysed to give regression formulae which will predict likely blood alcohol levels under similar circumstances. However, drinking circumstances may differ substantially from the conditions under which the data for the regression was obtained. It is more generally applicable to use such regressions to calculate the theoretical blood alcohol levels at zero time, or the time at which drinking began, assuming that all the alcohol consumed in the subsequent period was absorbed and equilibrated throughout the body at this time. Blood alcohol levels at any later time may be found by subtracting the mean rate of elimination of alcohol from the blood per hour.

7.3 RESULTS

Using the Widmark formula with the calculated mean value for 'r' the expected blood alcohol levels for an alcohol dose of 0.4 g/kg are 57 and 67 mg/100 ml for males and females respectively. Taking the average rate of elimination of 15 mg/100 ml/hr, the expected blood

alcohol level one hour after drinking would be 42 and 52 mg/100 ml respectively. Similarly, with an alcohol dose of 1.0 g/kg and an elimination rate of 15 mg/100 ml/hr over two hours, the expected blood alcohol levels would be 113 and 138 mg/100 ml for males and females respectively. The mean observed blood alcohol levels in the 0.4 and 1.0 g/kg studies were high by 10% and 35% respectively (Table 7.1). Harger factors calculated from the mean blood alcohol level and the dose from each group are also shown in Table 7.1 and correct the one-way bias of the Widmark calculations.

In the social drinking study (Chapter 6), the alcohol dose varied from person to person. The blood alcohol levels were calculated for each dose in g/kg from the Widmark formula, subtracting the amount metabolised at an average rate of 18 mg/100 ml/hr for the time between the start of drinking and 30 minutes after drinking had stopped. This calculated value was compared with the test result obtained by interpolation or linear extrapolation of the actual blood alcohol levels. The calculated result consistently overestimated the actual level by an average of 23% with a standard deviation of 17% for the beer drinkers, and 75% (s.d. 59%) in the spirit drinkers. The use of the Harger factors of 82 and 62 for the beer and spirit drinkers respectively, corrected the bias as before with a small improvement in standard deviation of 12 and 52%.

The regression coefficient of blood alcohol level on dose for this data was 125 with an intercept of 2. Blood alcohol levels for three hours after drinking began were determined from the formula:-

$$(125 \times \text{dose g/kg}) + 2 - (\text{average B} \times \text{time})$$

Blood alcohol levels were obtained by linear interpolation of the actual levels and compared to the calculated values (Figure 7.1) and ninety percent of the results fell within -25 and +20 mg/100 ml of the regression line. For the 0.4 g/kg dose and one hour after drinking, the formula predicted a blood alcohol level of 37 mg/100 ml and for the 1.0 g/kg dose and two hours after drinking, a blood alcohol level of 91 mg/100 ml for male subjects. When the formula was applied to the drinking study detailed in appendix 1 (RYLA project) for a mean time after drinking began of 150 minutes, the results from 33 out of 43

TABLE 7.1 Calculated and observed blood alcohol levels in subjects one hour after consuming an alcohol dose of 0.4 g/kg body weight or two hours after consuming 1.0 g/kg. The Harger factors were calculated from the mean observed blood alcohol levels and the dose.

Alcohol dose	g/kg	Calculated blood alcohol mg/100 ml	Observed blood alcohol		Harger Factors
			mean	range	
0.4 g/kg	male	42	50	32 - 76	124
	female	52	56	46 - 64	139
1.0 g/kg	male	113	89	66 - 120	113
	female	138	98	77 - 115	138

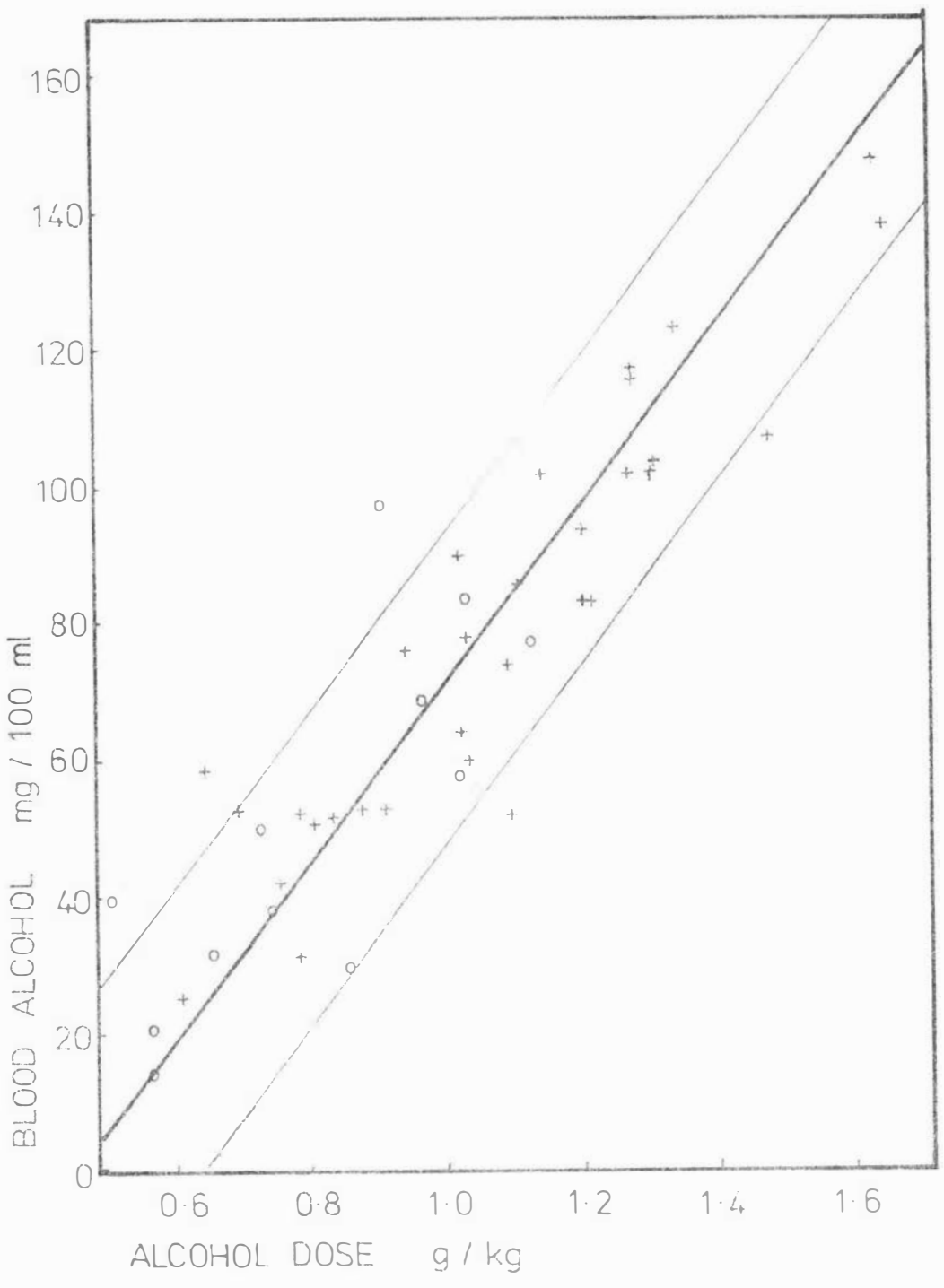


Figure 7.1

Observed blood alcohol levels 3 hours after drinking began against alcohol consumption. The mean regression line is shown with ± 20 mg/100 ml bounds.

subjects lay within a ±20 mg/100 ml spread of calculated blood alcohol levels.

7.4 DISCUSSION

These calculations show that even where many of the variables associated with drinking such as prior eating, quantity, time of consumption and time of tests are strictly controlled, the errors in estimating blood levels from consumption figures can be considerable. The use of the Widmark formula can lead, in the majority of cases, to an overestimation of the actual blood alcohol levels which is probably caused by incomplete alcohol absorption from the gut and non-linear alcohol elimination kinetics.

The use of Harger factors avoids the bias of the Widmark method, but these factors are only applicable to similar periods of drinking and time of test. This limitation also applies to the regression formula. The more generally applicable formula is that which calculates the concentration at the ordinate, subsequently subtracting the amount of alcohol eliminated in the blood during the drinking period. This method underestimated the expected blood alcohol levels when the alcohol dose was low, probably because of the slower elimination from the blood at low alcohol levels. With the 1.0 g/kg study, the formula predicted the mean blood alcohol level with remarkable accuracy. When applied to the RYLA study, the worst predictions were with those subjects who had consumed large doses of alcohol and it is likely that absorption from the gut was not complete in these subjects. A tendancy to underestimate blood levels at low alcohol doses was also seen in this group, but there are bound to be some discrepancies due to the variable time of test in this group. The testing period covered a 90 minute interval so that some results were obtained only one hour after drinking had started and others at two and a half hours.

The general applicability of the formula can be seen by comparison with reported data in the literature. Dubowski (1976) published an identical regression coefficient and value for the intercept to estimate maximum blood alcohol levels. Coldwell et al (1959), published the results of blood alcohol levels in 50 subjects, 1 - 2 hours after the consumption of varying doses of alcohol, one hour after a light meal.

The results followed the regression lines for one or two hours after drinking when a regression coefficient of 125 was used. A regression coefficient of 143 obtained from the Widmark formula led to a progressive overestimate of blood alcohol level as the alcohol dose increased. This point may be seen as further evidence in favour of a faster rate of metabolism at high alcohol doses.

In conclusion, the calculation of likely blood alcohol levels from a known dose of alcohol is best made from a regression model, calculating the alcohol level at the intercept and then subtracting the amount of elimination from the blood over the requisite time interval. If a regression coefficient of 125 is used and the average rate of elimination from the blood of 18 mg/100 ml/hr, then the majority of estimates are within ±20 mg/100 ml. Back calculations from a known blood alcohol level may be made using this rate of elimination, but if extended too far, the errors may be considerable as the range of beta elimination has been shown to be from 11 - 29 mg/100 ml/hour.

The ability to predict blood alcohol levels after the consumption of known quantities of alcohol brings with it an important corollary, that consumption may be estimated from a known blood alcohol level. The feasibility of rapid breath tests to estimate blood alcohol levels has been demonstrated and it is now possible to use this method as a tool in sociological research. The practicability of such experiments are demonstrated in appendix 1 and 2 where such studies have been made. The first was on a captive group of young people drinking in a party situation and the second was extended to cover the drinking habits of patrons of the bars of hotels or taverns.

CHAPTER 8 GENERAL DISCUSSION

Comparitive studies on breath-alcohol testing devices have shown the magnitude of some deficiences in this area of technology. Ideally, such devices should be portable, require a minimum number of re-calibrations and provide accurate results. Fuel cell instruments are being developed to a stage which approaches this ideal situation, but there is still uncertainty with frequent calibrations and they are unsuitable for mass-screening programmes. It seems that improvements in recovery times after a breath analysis has been carried out could be achieved if the fuel cell temperature was raised. At the present time, the whole sampling head is maintained at approximately 60^{o} which is at the upper limit for operator comfort in handling the device. It would be logical to localise the heating element at the catalytic surface where much higher temperatures could be attained with lower power consumption. However, it is still not known whether such an increase in temperature would produce substantial gains in reproducibility and speed of instrument recovery between estimations.

Wet chemical methods, such as that used in the Breathalyzer, offer advantages in avoiding the need for calibrations. However, the use of a sulphuric acid-containing mixture presents problems and can be hazardous. Even if a non-corrosive reactant for alcohol was found, there could still be problems in using glass ampoules. Many, laboratory instruments operate on a basis of continuous flow analysis and it is possible that a modification of this system could be made with either a completely enclosed apparatus or encapsulated reagents for discrete analysis. Gas chromatographs at present require operating temperatures of near 100^{o} usually with flame ionisation detection. Separations might be obtained at lower column temperatures with different packings and more compact detection systems. Thermal conductivity monitoring is unsuitable for breath analysis because of its high sensitivity to water vapour. However, breath contains few other components in quantities equivalent to alcohol concentrations in subjects who have been drinking and this situation may provide advantages in adapting simple fuel cells or gas sensitive semiconductors for the detection of alcohol. Such detectors offer advantages of low

cost and low power consumption. A rewarding area for development could be the adaptation of a portable gas chromatograph using such a detector at an oven temperature of 40-50°, i.e., just sufficient to prevent condensation of water vapour and with air as the carrier gas. At present, semiconductor devices are only useful in programmes where relatively large numbers of people are screened with a fairly low level of accuracy in breath alcohol analysis. Apart from improvements to the detection systems, some standardisation of breath volume and also partition coefficient for blood to air is desirable. The Breathalyzer 1000 has been developed some way towards this end with its twin breath containers. An automatic cut-off of breath flow once the second container is full would lead to further improvements in reproducibility. The design concept of all instruments appears to assume that the breath alcohol concentration is constant after the expiration of tidal air and this is clearly not so. Further work on breath temperatures is required, particularly where a breath test may be required at the roadside. It seems highly probable that, at the present time, roadside breath tests would underestimate the blood alcohol level in a subject quite considerably, especially in the wintertime.

With increasing accuracy of breath testing and the elimination of factors leading to variations in alcohol estimations not of physiological origin, the breath can be regarded as a sample in its own right. The analysis of breath alone can give an accurate measure of the amount of alcohol in the body. Increasingly, behavioural scientists are becoming interested in brain alcohol levels. Such levels may be quite different from those found in the venous blood taken from a vein in the cubital fossa. By contrast, breath levels could be more relevant in reflecting concentrations in arterial blood as it leaves the lungs. At the present time, impairment of performance is usually related to a blood alcohol levels. However, there is no important reason why it could not be related to the concentration of alcohol in the breath. In part, this is accepted in recent drinking-driving legislation where it is an offence to drive a motor vehicle with a breath alcohol concentration greater than 500 µg/litre (Act of New Zealand Parliament, 1978).

From studies on the absorption, equilibration and elimination of alcohol in human volunteers, it is clear that there are difficulties in the measurement of rates of elimination of alcohol. If the alcohol dose for a subject is low, the distribution volume can be measured with reasonable accuracy, but elimination rates are in such cases, also low. As the alcohol dose is increased, the observed elimination rates are higher but the accuracy of measurements for distribution volumes decreases. Observed rates of alcohol elimination will correspond to the true oxidation rates of alcohol in the body, if the alcohol has become fully equilibrated in all of the body water. Such equilibration is especially important if differences in alcohol elimination between various racial groups or between alcohol and normal subjects are to be measured.

Alternative methods of measuring the alcohol oxidation rates are required which avoid, or at least detect anomalies caused by delayed absorption and equilibration. Preliminary studies have been made on the use of stable isotopes as tracers to study such rates of absorption and equilibration. In the experiments described in chapter 5, some insight has been gained into the role of the pyloric sphincter in controlling the passage of stomach contents into the duodenum. This work should be extended and repeated on many more subjects. Compounds in which deuterium atoms have replaced hydrogen are readily identified by mass fragmentograph and can be used in higher doses with less risk than compounds labelled with radioactive isotopes. If a small intravenous dose of labelled alcohol is give to a subject already primed with a larger, unlabelled oral dose, the rate of decline in abundance of the label in the blood may give information of the rates of equilibration with body water pools and perhaps the rate of oxidation of alcohol by the liver. Although it does not seem likely that the rates of incorporation of label into the acetaldehyde pool can be measured, due to the very small quantities and fast turnover in peripheral blood of this substance, it may be possible to make significant measurements of acetate. The acetate pool size and turnover rates may be measured giving independent estimates of the rates of alcohol catabolism. In such applications, stable isotopes provide an exciting new tool with which to probe metabolic pathways in human

subjects. Information from studies in which only concentrations are measured is limited because although a metabolite in the blood may be at a low concentration, its turnover rate may be very high and vice versa. While it is expected that alcohol clearance rates measured by isotope dilution should be the same as the disappearance of alcohol from the blood, this would not be so if some of the alcohol was adsorbed in the gut or converted by a condensation reaction to some intermediate metabolite other than acetaldehyde. The existance of such mechanisms are, at the present time, largely speculative. The application of mass spectrometry combined with gas chromatography and the use of stable isotope probes into human metabolic pathways may well open up a new era in alcohol research both in terms of the kinetics of alcohol metabolism and disturbances produced by alcohol in other metabolic pathways.

Much of the research on alcohol metabolism has involved studies in which alcohol consumption has been observed and followed under rigidly controlled conditions. While such studies have been justified, the effects of distortions in absorption and equilibration have frequently been overlooked and it is now recognised that the rates of alcohol consumption under normal social conditions may differ markedly from those observed under laboratory conditions. There have been many studies in the past on drinking patterns in which rates and amounts of drinking have been measured. However, few studies have measured the blood alcohol levels repeatedly during consumption and elimination because of the difficulties in obtaining blood samples or uncertainties associated with breath testing. Such studies can now be readily carried out by following with breath analyses the rates of increase of alcohol in the blood and ultimate blood alcohol levels. The possibilities now exist for the application of new breath testing instrumentation in the field of behavioural research as well as for law enforcement.

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APPENDIX 1

A REPORT PREPARED FOR A ROTARY YOUTH LEADERSHIP COURSE

MASSEY UNIVERSITY

JOINT PROJECT

DEPARTMENT OF BIOCHEMISTRY AND DEPARTMENT OF SOCIOLOGY

MASSEY UNIVERSITY

BLOOD ALCOHOL LEVELS IN YOUNG ADULTS AFTER FREE DRINKING

The aim of this project was to teach 60 young adults the effects of alcohol on themselves and others; to provide information on blood alcohol levels and to collect information on the drinking patterns of this selected group under the condition of test.

METHODS

The 60 young adults, aged 18 to 24 were selected by Rotary Clubs throughout the lower half of the North Island, New Zealand, to attend a 5 day residential leadership course at Massey University. The present study was one of the projects undertaken.

The session commenced immediately after an evening meal when the participants were given a brief introduction and then divided into two groups:

One of 15 subjects (8 female and 7 male) who were teetotall or did not wish to drink that evening.

The other group consisting of 45 subjects (9 female and 36 male) who were divided again on a random basis into those to drink either beer or spirits, but not both.

A free bar was opened and the drinkers were able to obtain as much as they wished of their designated drink by recording this with the bar attendant. The bar was manned by three workers from the alcohol research group who dispensed either 17ml of spirits (Whisky, gin, rum or vodka) in a standard measure of either lemonade or coca cola, or beer by the 200ml glass or 750ml bottle. Drinking was allowed for one hour only after which the bar was closed and there was no possibility of further alcohol being obtained.

The non drinkers were asked to observe three each of the drinkers; record their behaviour and check performance on simple tasks and at allotted times present the subjects for a breath alcohol test. These tasks were scheduled to start 45 minutes after drinking had stopped. Between the time the bar closed and commencing tests, a short talk on alcohol use and abuse was given and this enabled the allotment of subjects to each observer on the basis of alcohol consumption and type of beverage so that no one group was loaded with high or low alcohol consumers.

Breath tests were performed either on an "Intoximeter", a commercial gas chromatograph specially designed for breath alcohol measurement or on a portable gas chromatograph that had been adapted for the purpose. Both instruments were calibrated with the same standard simulator solution at a temperature of 34 C equivalent to a blood alcohol level of 100mg% and a partition ratio of water to air of 1:2,100.

RESULTS OF THE ALCOHOL EDUCATION SESSION

I. ALCOHOL CONSUMPTION

Twenty three subjects drank between them 48.3 litres of beer (64 bottles) or 1.44 Kg of pure alcohol. A breakdown of consumption is shown in Fig. 1a and is summarised as follows:

3	persons	(13%)	drank	5%	of the total	at a cost of	$1.08 or 36 cents per head
15	"	(65%)	"	59%	"	"	$12.75 or 85 cents per head
5	"	(22%)	"	36%	"	"	$7.78 or $1.56

The remaining 22 subjects drank between them 4.35 litres of spirits or 1.38 Kg of pure alcohol. This can be broken down into 1.6 litres of whisky, 1.17 of vodka, 0.87 of gin and 0.71 of rum. The consumption of individuals is shown in Figure 1b and is summarised as follows:

9	persons	(41%)	drank	16%	of the total	at a cost of	45 cents per head
10	"	(45%)	"	47%	"	"	$1.54 per head
3	"	(14%)	"	37%	"	"	$3.89 per head

These analyses were based on wholesale prices but did not include the cost of the soft drinks. Consumption in monetary terms are given in Figure 1c. The cost of the spirits was $31.11 and the beer $21.62.

II. BLOOD ALCOHOL LEVELS

The blood alcohol estimates from breath tests were obtained on 44 subjects and ranged from 1 to 120 mg/100 ml. Two of these figures were rejected for subsequent analysis because the subjects were known to have vomited a portion of their high alcohol intake. The remaining subjects gave results which were proportional to the amount of alcohol consumed and corresponded to a blood level of 1 mg of alcohol per 100ml for every gram of alcohol consumed. This can be expressed more simply in the following manner: one glass containing 200ml (7oz) of beer or one nip (NZ 17ml) of spirits contains 6 grams of alcohol which would cause a rise in blood alcohol level of 6 mg% under the conditions of the test, that is the blood level one hour after drinking has finished where the alcohol was consumed shortly after a meal and over a period of one hour. The blood alcohol level could be estimated over the range from 0 to 120 mg% with an accuracy of plus or minus 10 mg% for the majority of subjects.

III. THE EFFECT OF ALCOHOL ON THE PERFORMANCE OF SIMPLE TASKS

Attitude

In general, there was little change in attitude from normal when the alcohol levels were below 50mg%. Above this level, the frequency of talkativeness, excitability and hilarity increased.

Performance; alcohol less than 25mg% (12 subjects)

Only two showed slight impairment in balance and turning. One subject felt unfit to drive but passed all tests.

alcohol between 26 and 55mg% (13 subjects)

Ten of these subjects showed some impairment as assessed by the observer. The most common test failed was that of finger to nose (6/13 failed). The observers considered two of these subjects sufficiently impaired to be unable to drive and a further two considered themselves unfit.

alcohol between 56 and 80mg% (8 subjects)

Only two were able to pass all tests. Three expressed the opinion that they were unfit to drive which was in agreement with the observer.

alcohol greater than 80mg% (11 subjects)

Two passed all tests but considered themselves unfit to drive; their observers were not able to detect more than slight impairment. All the remaining subjects showed some impairment, six of them failing in balance, walking, turning and the finger to nose test. A total of 9 were unfit to drive either on their own assessment or on that of the observer but 4 of these all with alcohol levels above 100mg% considered themselves fit to drive.

CONCLUSIONS

The total cost of alcohol for this hour long party for 60 persons was only $53 or less than one dollar per head. This insignificant expenditure enabled 25 of the participants to exceed blood alcohol levels of 50mg% (the legal limit in Victoria, Australia) and 5 of these to exceed 100mg%, the legal limit for driving in New Zealand. Undoubtedly, if the party had been extended in time, the average consumption would have increased with resulting higher blood alcohol levels and a greater proportion of persons over 50mg%.

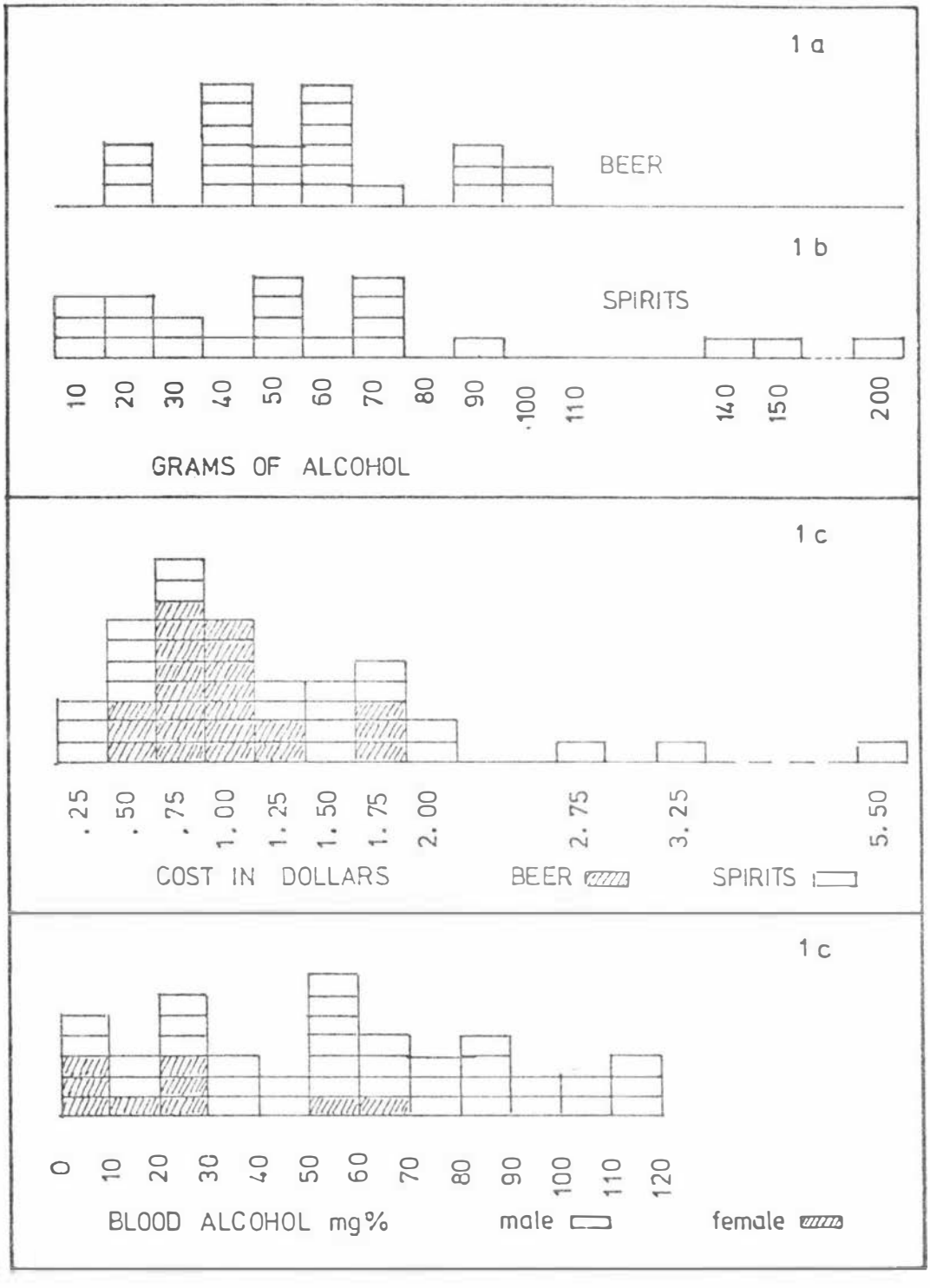
The blood alcohol levels are significantly lower than those based on theoretical calculations. The reason for this is that under laboratory conditions, the subjects were given alcohol after a 12 hour fast so that their stomachs were empty. This resulted in a very rapid absorption of alcohol from the intestinal tract and the blood levels were nearly double those seen in the present study which approximates the normal drinking patterns. There is considerable evidence from other studies done in this laboratory, that drinking after a meal results in a slow absorption from the gut and the blood levels reach a plateau which persists for 1-2 hours after drinking has stopped.

Some of the subjects were re-tested after an hour and the results substantiate the general assumption that all subjects maintained their blood alcohol at a constant level during the 1½ hour testing period. A time analysis of the data suggested that the results fell no more than 6mg% from the beginning to the end of this period. There was no difference in the results whether the alcohol was consumed as beer or spirits. Although there were few females in the study and most of these has low alcohol levels, there was no evidence of a difference in blood alcohols from males when the dose in grams per kilogram of body weight

was taken into consideration.

The impaired performance at simple tasks by those with the higher blood levels amply bears out the relevance of the statutory limit for driving. These tasks may have seemed mundane to the participants but all measure aspects related to driving performance. Balance and stumbling whilst turning both have their counterparts in the sensing of position of a car being driven around a bend. The finger to nose test and that of picking up coins demonstrates the impaired ability to manipulate the controls of a car. There is no truth that these performances improve under stress, in fact, recent research demonstrated the reverse and that the drunken driver is not able to cope with the potential accident situation.

Of considerable importance is the small group with high alcohol levels who were obviously impaired, yet maintained their ability to drive. It must not be forgotten that alcohol impairs judgement so that the inebriate overestimates his/her ability to perform at a variety of tasks.


1 a
BEER
1 b
SPIRITS
10 20 30 40 50 60 70 80 90 100 110 140 150 200
GRAMS OF ALCOHOL
1 c
.25 .50 .75 1.00 1.25 1.50 1.75 2.00 2.75 3.25 5.50
COST IN DOLLARS
BEER
SPIRITS
1 c
0 10 20 30 40 50 60 70 80 90 100 110 120
BLOOD ALCOHOL mg%
male
female

ALCOHOLIC INFLUENCE REPORT FORM

NAME: NAME OF OBSERVER:

AGE: SEX: APPROX. WEIGHT:

Breath:	Odour of alcoholic beverage:		strong	moderate	faint	none
Attitude:	excited combative	hilarious indifferent	talkative insulting	carefree cocky	sleepy co-operative	profanity polite
Unusual actions:	hiccough	belching	vomiting	fighting	crying	laughing
Speech:	not understandable	mumbled	slurred	confused		
	thick tongued	stuttered	accented	fair	good	

PERFORMANCE CHECKS

Balance:	falling	needed support	wobbling	swaying	unsure	sure
Walking:	falling	staggering	stumbling	swaying	unsure	sure
Turning:	falling	staggering	hesitant	swaying	unsure	sure
Finger to nose:	Right:-	missed	hesitant	sure		
	Left:-	missed	hesitant	sure		
Coins:	unable	fumbling	dropped	slow	sure	
Ability to understand instrucs.:		poor	fair	good		
Observers opinion:	Effect of Alcohol		extreme	obvious	slight	none
	Ability to Drive		unfit	fit		
Subjects opinion:	Ability to Drive		unfit	fit		

PERFORMANCE TESTS

Balance:	(a)	stand erect, feet together, eyes closed; maintain 15 seconds
	(b)	arms forward, bend at waist; maintain 15 seconds (eyes closed)
Walking:	(a)	10 - 12 steps one foot directly in front of the other.
Turning:	(b)	Give surprise instruction to turn and come back.
Finger to nose:		Stand erect, eyes closed; touch tip of nose with each index finger. Repeat left and right 3 times.
Coins:		A number of coins (5) on floor. Subject asked to pick them up and arrange in denomination.

A REPORT PREPARED FOR THE ALCOHOLIC LIQUOR ADVISORY COUNCIL

BREATH-TESTING FOR ALCOHOL WITH HOTEL PATRONS

K. G. Couchman and R. D. Batt

Alcohol Research Group,
Massey University,
Palmerston North.

3rd July, 1978.

INDEX

ACKNOWLEDGEMENTS

The project was financed, in part, by a grant from the Alcoholic Liquor Advisory Council and carried out by skilled instrument operators, two of whom were employed under a research grant from the Medical Research Council of New Zealand.

Appreciation is expressed for the co-operation of the Managers of the two hotels and the approval of the Hotel Association of New Zealand to carry out the study.

To provide the large number of tests and collect the substantial quantity of information, required the help of a large number of efficient and enthusiastic colleagues. Without this help, the project could not have led to the significant conclusions of the study. Special mention is made of the capable and willing assistance of Mrs. C. Veale in testing and the subsequent detailed analysis of the data collected.

SUMMARY

Breath-testing instruments, manned by experienced operators, were made available in two Palmerston North hotels to enable patrons to have free breath alcohol tests carried out from 6.0 p.m. to closing time during a week at each hotel. Patrons were required to wait 10 minutes after consuming their last drink and were asked to complete a questionnaire while waiting. No names of patrons were recorded. Individuals could have as many tests carried out as they wished.

The total number of patrons tested at least once during the two weeks was 841. There was great interest in the tests and, on occasions, queues of up to 10 patrons were waiting for a breath analysis. Of the two instruments used, one had been specially modified to give a result in 30 seconds. However, despite this speed of operation, the facilities could not always handle the demand without a waiting time, particularly on the Thursday, Friday and Saturday nights.

The results showed clearly that the breath-testing facilities were highly acceptable and generated remarkable interest amongst a high proportion of the clients.

An analysis of the information obtained from completed questionnaires and a general assessment of recorded breath alcohol levels are included in the attached report. Following are some comments on observations and findings from the project.

At the time of testing nearly one third of the patrons had blood alcohol levels above 100 mg per 100 ml of blood and it seemed likely that this proportion would have increased if all individuals who had been tested were retested some time later.

Although the two hotels were chosen for marked differences in the clientele (one attracted young people and the other older age groups), the ranges of blood alcohol levels were not significantly different between the two hotels. A small group of patrons tested had not eaten for at least 12 hours before the test and had considerably higher blood alcohol levels than the average for all patrons tested.

As a general observation, the higher the blood alcohol level recorded the less surprise the patron showed at the result. Further, the younger the patron the more surprise shown if the level was not over 100 mg%.

A section in the questionnaire on attitudes to the drinking-driving legislation showed that a high proportion of the patrons tested were (a) not in favour of breath-testing being a basis for prosecution and (b) opposed to proposals for random testing.

A comparison of alcohol consumption, recorded by individual patrons, and the observed blood alcohol level gave average figures of 6-7 mg of alcohol/100 ml of blood for each standard drink. Studies on volunteers by the Research Group, where amounts of alcohol consumed could be accurately determined, gave average results of 10 mg of alcohol/100 ml of blood for each standard drink, when the volunteers had not eaten within several hours of drinking. With subjects who had eaten shortly before drinking, the average increase in blood alcohol level was only 3 mg/100 ml for each standard drink.

General conclusions from the project are that (a) hotel patrons are interested in being breath-tested and in the results, (b) some patrons very quickly acquire the basic principles which enable them to predict what their blood alcohol level will be in relation to the amount of alcohol consumed, (c) there was little evidence of patrons using the availability of breath-testing facilities to drink competitively, (d) there was complete acceptance of the facilities and instrument operators as being part of the hotel operation with no suggestion that there were any links with law enforcement agencies, and (e) while a small number of patrons indicated that they were using the breath-test information to decide who in their groups would drive their cars, it would seem that a high proportion of hotel patrons would have driven their cars away knowing that their blood alcohol levels were well above the legal limit.

INTRODUCTION

In the 1977 Annual Report of the Parliamentary Select Committee on Road Safety, a proposal that breath-testing devices be made available to the general public was discussed and, after listing some objections, reported that "there was no good reason to prohibit coin operated or other devices being set up in bars. We did feel however that before actively encouraging their use a trial should be conducted using reliable equipment and experienced operators. The operating technician would be able to answer questions and comment on the significance of breath alcohol readings. Such an approach would be essentially educational and should be accompanied by appropriate evaluation, and only after this should any further action be initiated".

The Committee then made the two following recommendations:

"That the Ministry of Transport encourage an experimental trial of educational breath testing devices and that an evaluation of any such trial be reported to the committee".

"That the Alcoholic Liquor Advisory Council be asked to provide financial assistance for the project".

Late in 1977, discussions took place with Dr. P. M. Hurst, Senior Research Officer of the Road Transport Division, Ministry of Transport, on the way in which such a trial might be conducted. The present project was planned, basically, to determine the acceptability of alcohol breath-testing devices to hotel patrons and obtain evidence on the accuracy of the instruments under the testing conditions. The educational aspects and requirement for an evaluation of the trial, referred to by the Select Committee on Road Safety, were considered to be met, in part, by (a) providing some printed information on the effect of alcohol on the body, and (b) requesting individuals who were tested to complete a questionnaire which provided data for subsequent analysis.

A sum of $2,000 was granted by the Alcoholic Liquor Advisory Council, primarily to provide some additional casual labour to the Alcohol Research Group for help with the testing and processing of results. Members of the research group operated selected instruments, which were chosen for their speed of analysis and known reliability.

Testing was carried out in two hotels in Palmerston North. Although it was planned to return to one hotel several months later to assess the reaction of the patrons at a second opportunity to be breath-tested, this part of the planned project was abandoned through lack of staff.

It was considered to be important to avoid the Christmas and summer holiday months for the trials because drinking patterns could then become abnormal and the patrons may not have been a representative sample of the regular clientele. The testing was completed in two weeks during November, 1977. If it had been possible to complete the original plan, testing would have resumed in April, 1978.

METHODS

A Mark IV Intoximeter breath-alcohol gas-chromatograph (Intoximeter Inc., St. Louis, U.S.A.) was installed in a hotel bar for testing, free of charge, any hotel patrons who were interested, between 6 p.m. and closing time. The instrument was operated by members of the staff of the Alcohol Research Group with assistance from graduate students who had been trained to use such machines. During the first evening of the trial, the demand for tests was so great that queues of up to 10 people were waiting for a breath analysis, despite the fact that the instrument was giving individual results at 2 minute intervals.

For subsequent evenings an alternative instrument (a modified standard gas-chromatograph) with an analysis time of 30 seconds was used.

The results from the Intoximeter were displayed in digital form while those from the standard gas-chromatograph appeared as peaks on a chart recorder. Although digital display is an impressive way of presenting results, the recordings on chart paper read by comparison with a calibrated scale were readily understood by patrons.

The questionnaire (Appendix 1) was designed to assess the understanding of individuals on blood alcohol levels and alcohol consumption. It also included questions suggested by Dr. Hurst on attitudes to the drinking-driving laws. These are given in Appendix 2.

The project began in a privately-owned hotel on a Thursday night and continued through to include the following Wednesday. From the experience gained during this week it was decided to modify the

questionnaire, mainly to make the questions easier to understand and answer. The modified questionnaire, which is attached (Appendix 3), was used during a second week when testing took place in a brewery-owned tavern.

For the analysis of answers on alcohol consumption, a standard drink was considered to be 1 200 ml glass of beer or 1 single nip of spirits (0.62 oz). In the second questionnaire, other quantities of drink could be given (Question 2). These were converted into standard drinks by the following factors:

	Number of standard drinks
1 jug of beer	5
1 handle of beer	2.5
1 5 oz glass of beer	0.75
1 7 oz glass of beer	1
1 can or small bottle of beer (300 ml)	2
1 750 ml bottle of beer	4
1 bottle of wine	13
1 single nip of spirits	1

RESULTS

1. Access to equipment

During the first week of testing in a privately-owned hotel, the breath-testing equipment was sited at one end of the saloon bar adjacent and opening into a lounge bar which formed one arm of a total U-shaped area. There was ready access from the public bar through a connecting corridor.

In the second week, testing was carried out in a brewery-owned tavern where the equipment was set up in a small foyer between the lounge bar, a dining-room and an exit. Access from the public bar was difficult; patrons from this bar either had to go outside the tavern and re-enter the lounge bar or walk through the bottle store and then along the full length of the lounge bar. The site was chosen to permit conversation with patrons. A band played each night in the tavern and the sound volume precluded conversation in the lounge itself. Although

the siting was not ideal in that it was out of view from the patrons, it was the best compromise which could be made.

2. Numbers and ages of patrons tested

In the hotel, 429 individuals were tested at least once during the week with very few people declining to complete the questionnaire. Some forms were completed only in part.

The number of patrons tested in the tavern was 412 with a larger number than for the hotel who did not complete the questionnaire, mainly because of restrictions imposed by the siting of the equipment. However, the number was still small.

The number of tests carried out each day are given in Table 1 and the ages of people tested are summarised in Figure 1 and Figure 2. In the hotel, 24.4% of the patrons tested were under the age of 25 while in the tavern, 73.5% were younger than 25. These different percentages reflect the different types of drinking environment attracting different clienteles.

The response from the patrons was at the maximum level which the operators could handle on the busiest nights of the week.

Table 1: Number of patrons breath-tested each day

Location	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	TOTAL
Hotel	25	40	38	80	122	124	429
Tavern	-	-	45	102	97	168	412

3. Attitudes to the drinking-driving laws

Replies to the question on whether the legal blood alcohol limit is too high, too low or about right are summarised in Table 2. An analysis by age of the responses did not show any significant age differences from the attitudes for all of the respondents.

Table 2: Legal blood alcohol level

	Hotel %	Tavern %	Total Replies
"Too high"	22.4	24.3	746
"Too low"	17.7	26.1	
"About right"	55.0	38.8	
No answer	4.9	10.8	

4. Breath versus blood tests

Replies to the question concerning the acceptability of breath analyses as legal evidence in place of blood tests are summarised in Table 3.

Table 3: Acceptability of a breath test as legal evidence

	Hotel %	Tavern %
Yes	36.2	39.8
No	48.5	41.1
Not sure	15.3	19.1
Total replies	774	

5. Random testing

Attitudes to random testing are summarised in Table 4 into categories of approval, disapproval or for research purposes only.

Table 4: Random testing

	Hotel %	Tavern %
Approve	37	46
Research only	37	32
Disapprove	26	22

6. Estimates of number of drinks to reach the legal limit

The answers to the question on how many drinks would need to be consumed over a three hour period to reach the legal limit are shown diagrammatically in Figure 3.

The mode is at 10 drinks which is about right for an average person.

Before the project commenced, leaflets were made available to patrons at the two testing sites (Appendix 4). The leaflet included a figure of 5 for the number of drinks to give a blood alcohol of 100 mg/100 ml blood which is a minimum quantity for alcohol consumed very rapidly under fasting conditions. This figure and the wide publicity given to the "rule of three" could have influenced the number of replies for figures less than 10. The number of patrons who did not know or

who estimated more than 12 drinks represented 44% of the total which suggests that there is a large educational area on alcohol consumption which needs attention.

7. Blood alcohol levels

The results of the first breath test on each subject were adjusted to the nearest 10 mg% and frequency histograms plotted for each location (Figure 4). At the hotel, 38% were over the legal limit of 100 mg/100 ml blood and 54% over 80 mg/100 ml blood. For the tavern, the figures were 28% over 100 mg/100 ml and 43% over 80 mg/100 ml.

The results for patrons who had a second breath test after consuming more alcohol showed (for 121 individuals) 28% had a blood alcohol level greater than 100 mg/100 ml at the first test increasing to 61% at the last test.

8. Blood alcohol levels related to age

Correlations between age and blood alcohol levels which were over 100 mg/100 ml are given in Table 5. The different percentages for the "over 40" group were probably related to the fact that many of the older people tested at the tavern had been in the dining-room for dinner.

Table 5: Relationship between age and blood alcohol levels over the legal limit

Age	20	21	22-25	26-29	30-39	Over 40
Hotel (%)	13	26	33	41	34	49
Tavern (%)	22	28	28	36	35	20

9. Average blood alcohol levels by age

The numbers of patrons tested in different age groups with their average blood alcohol levels are given in Table 6. As noted previously, there was a difference in the results for older patrons at the tavern who came mainly from the dining-room and would be expected to have lower blood alcohol levels if they had been drinking with their meal.

Table 6: Average blood alcohol levels in different age groups

Age	Hotel		Tavern	
	Number	BAL*	Number	BAL*
20	31	52	143	66
21	19	58	53	75
22-23	32	72	48	86
24-25	23	95	37	66
26-29	59	90	44	77
30-39	96	81	43	79
40-49	74	89	10	71
Over 50	66	102	10	75

*BAL : Average blood alcohol level : mg alcohol/100 ml blood

10. Blood alcohol levels in relation to the last meal

Table 7 shows the number and percentage of patrons with blood alcohol levels above 100 mg/100 ml in relation to the time at which they had last eaten.

Table 7: Blood alcohol levels in relation to the last meal

	Hotel		Tavern	
	Number	%	Number	%
A Had eaten an evening meal prior to drinking	40	27	44	18
B Nothing to eat since lunch	83	42	43	38
C Nothing to eat since breakfast or earlier	37	54	16	50

11. Self-estimates of blood alcohol levels

Of the patrons tested, 39% estimated their blood alcohol levels to within 20 mg/100 ml of the recorded value, while 18% overestimated and 43% underestimated the level by more than 20 mg/100 ml.

12. Self-estimates of fitness to drive

Eighty per cent of the patrons tested with blood alcohol levels below 100 mg/100 ml thought they were fit to drive while 68% with blood alcohol levels above 100 mg/100 ml blood also considered they were fit to drive.

13. Alcohol consumed related to blood alcohol levels

Quantities of alcohol said to have been consumed by individuals prior to testing ranged from 1 to over 35 standard drinks per person. The mean consumption for all persons tested was approximately 13 standard drinks.

When the blood alcohol levels were plotted against the quantity of alcohol consumed per person an average increase in blood alcohol level per drink could be estimated.

For individuals who had had an evening meal before drinking, a standard drink raised the blood alcohol level by 3-4 mg/100 ml. For individuals who were in the equivalent of a fasting state, a standard drink raised the blood alcohol level by 6-7 mg/100 ml.

DISCUSSION

When breath-testing for alcohol was made available, free of charge, to bar patrons there was an immediate acceptance of the facility and the requests for tests fully extended the instruments to the maximum throughput of analyses.

The most popular drinking evenings at both testing locations were Thursday, Friday and Saturday, with bars very well patronised from 7 p.m. onwards, and each catering for about 300 people. On the busiest nights only about one third of the customers were tested.

For the first breath test, one third of all subjects were over 100 mg alcohol/100 ml blood. It is reasonable to assume that many of the people who had levels below 100 mg/100 ml of blood would go above this level if they continued drinking after the test.

It has been argued that the availability of breath tests could encourage patrons to drink up to the legal limit. The operators obtained no evidence that this happened. However, a counter argument

can be claimed, that the legal limit should be at such a level that drinking up to it is not thought to be undesirable.

It has also been claimed that breath-tests may be used by clients for competitive drinking. There was no definite evidence that this happened. If it had occurred, only a very small number of people would have been involved.

A remarkable finding from the study was the ability of many patrons to estimate their blood alcohol levels very accurately after one test and with the information sheets provided.

Although a small number of people wanted to be tested to decide who should drive their cars, a high proportion of the patrons with blood alcohol levels above 100 mg/100 ml presumably drove their cars even although they knew they were breaking the law. In this sense, breath-testing as an educational exercise is basically ineffective.

The large number of people leaving hotels at closing time with blood alcohol levels above 100 mg/100 ml, makes it likely that the proposed breath alcohol legislation will be unsatisfactory unless provision is made for breath-testing of drivers to be completed at the place where they are stopped, including issuing a "ticket" and taking car keys if a drinking-driving offence has been committed. If drivers have to be taken to a police-station, only one person can be checked while perhaps another 50 drive away illegally from the hotel or tavern car park.

Although it may have been expected, it is of considerable interest to have indications that at least 50% of all patrons leaving the hotels and taverns have blood alcohol levels over the legal limit for driving.

AGE DISTRIBUTION OF PATRONS TESTED : *HOTEL*

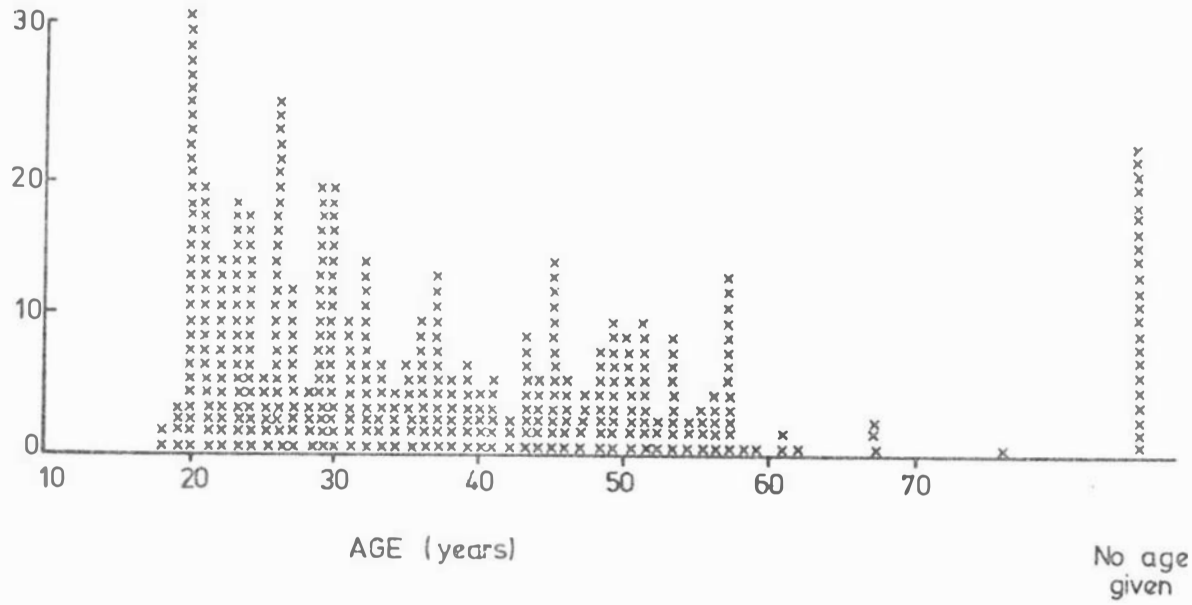
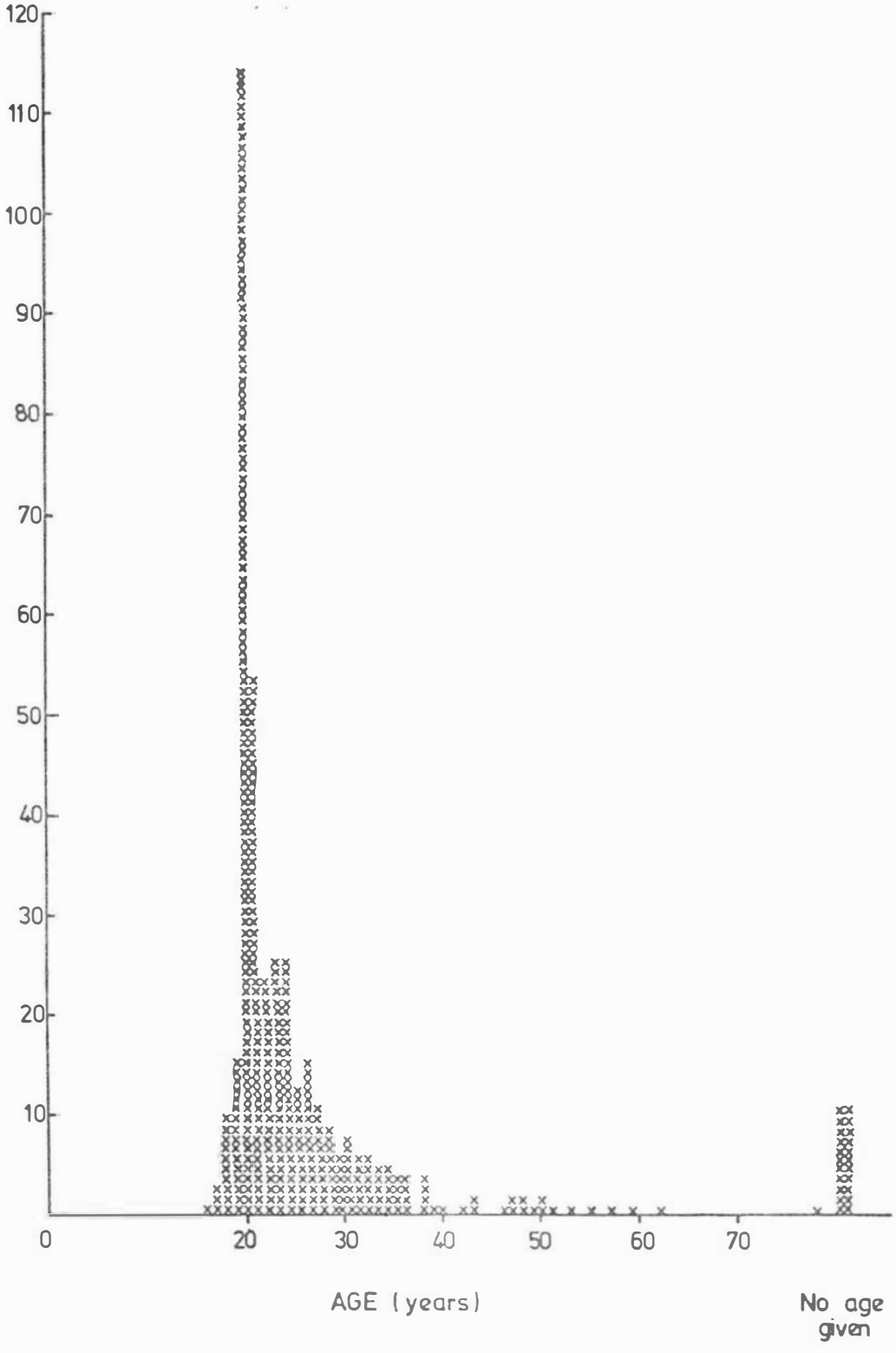


Figure 1

AGE DISTRIBUTION OF PATRONS TESTED : *TAVERN*.

Figure 2



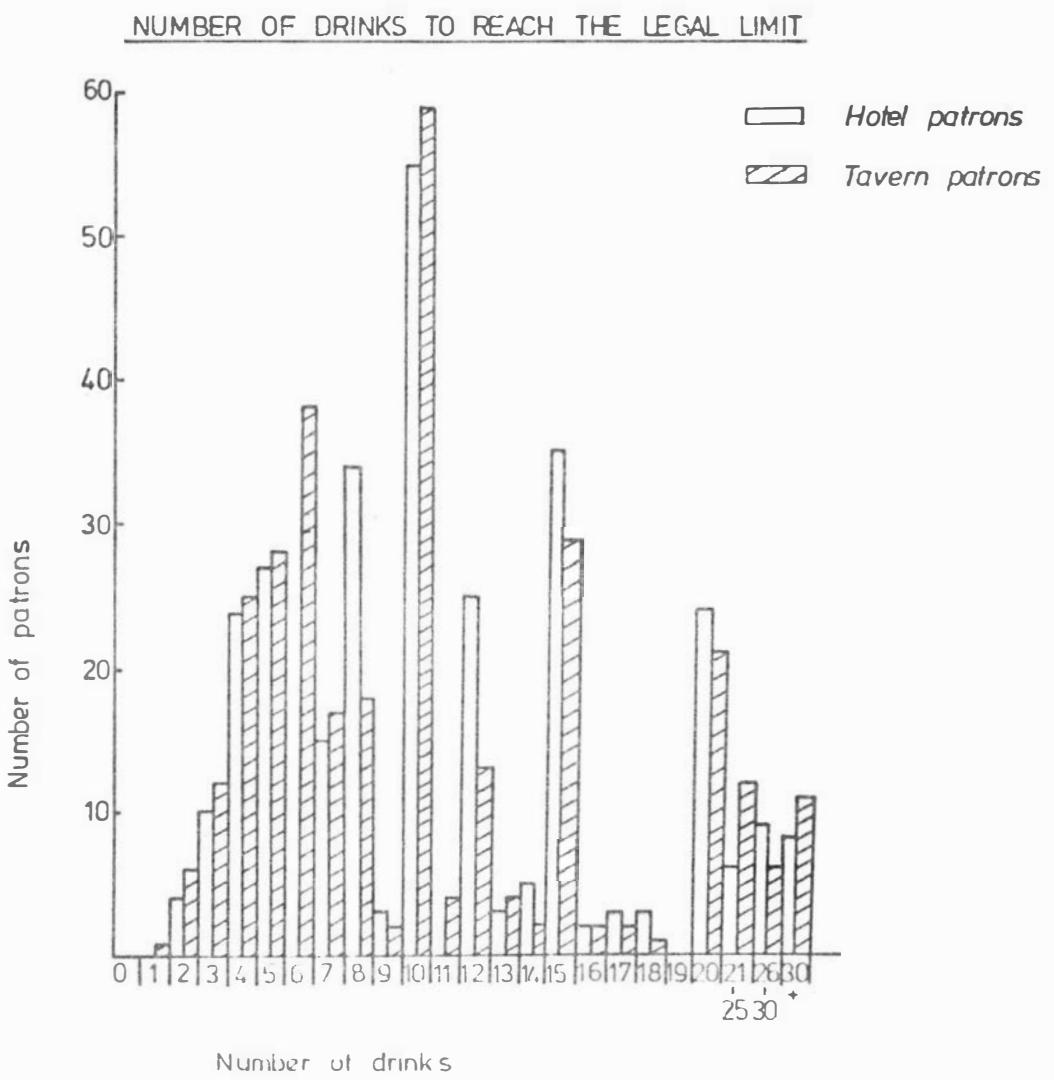

NUMBER OF DRINKS TO REACH THE LEGAL LIMIT
Hotel patrons
Tavern patrons
Number of patrons
60
50
40
30
20
10
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 26 30
25 30 +
Number of drinks

Figure 3

BLOOD ALCOHOL LEVELS : FIRST TEST

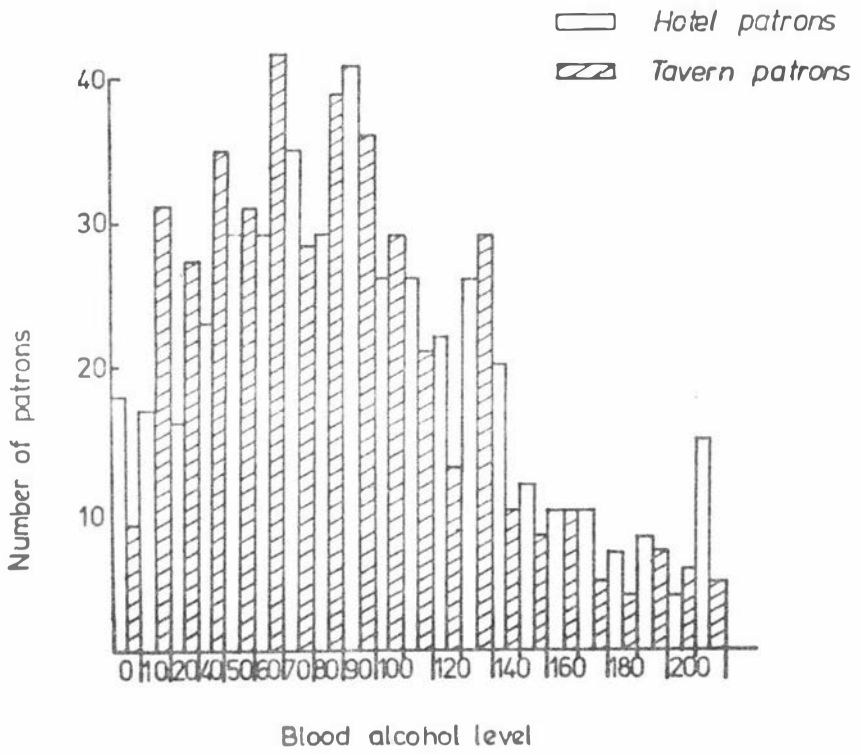


Figure 4

MASSEY UNIVERSITY

ALCOHOL RESEARCH GROUP

THE FOLLOWING QUESTIONNAIRE IS ENTIRELY VOLUNTARY. OUR ASSISTANTS WILL ANSWER ANY OF YOUR QUERIES IF YOU WISH.

AGE: SEX: HEIGHT: WEIGHT:

1. About what blood alcohol level do you think you are at: (CIRCLE)

   0 20 40 60 80 100 120 140 160 180 200 over 200

2. How many drinks have you had? (1 drink = 1 glass beer or 1 nip spirits) _____

3. What time did you start drinking today? _____

4. When did you last have a meal? _____

5. Is the legal limit for driving: (CIRCLE)

   Too high Too low About right

6. How many drinks do you think it takes to reach the legal limit? _____

7. Do you consider yourself fit to drive? (CIRCLE)

   Yes No Not sure

8. What is your attitude toward random (roadblock) breath testing? (TICK)

   I would approve of it, either for research or for prosecution.

   I would approve only of voluntary random testing for research purposes, with results being kept confidential.

   I would approve only compulsory random testing, for purposes of prosecution.

   I am opposed to random testing in any form.

9. Do you believe that the results of quantitative breath analysis should be acceptable as legal evidence, in place of blood tests? (TICK)

   Yes No Not sure

24th November, 1977.

DO NOT COMPLETE THIS SIDE

POST TEST QUESTIONNAIRE

(TO BE FILLED IN BY THE UNIVERSITY STAFF IN ATTENDANCE)

Time of Test _____

Machine Reading _____

Subject Tested: 1st time 2nd 3rd 4th 5th

Did the subject change his/her mind about Q.3? Yes No ?

Any surprise at the result? Yes No ?

Was it expected to be: Higher Lower

Has the breath test been of any value to the subject? Yes No ?

BREATHTEST QUESTIONNAIRE

Date

(a) The legal blood alcohol limit is:

too high
too low
about right.

(b) On the average, how many drinks does it take over a three hour period to reach the legal limit? (One drink = single nip or 7oz beer).

(c) Do you believe that the results of quantitative breath analysis should be acceptable as legal evidence, in place of blood tests?

yes
no
not sure.

(d) What is your attitude toward random (roadblock) breath testing?

I would approve of it, either for research or for prosecution.

I would approve only of voluntary random testing for research purposes, with results being kept confidential.

I would approve only compulsory random testing, for purposes of prosecution.

I am opposed to random testing in any form.

MASSEY UNIVERSITY

ALCOHOL RESEARCH GROUP

THE FOLLOWING QUESTIONNAIRE IS ENTIRELY VOLUNTARY. OUR ASSISTANTS WILL ANSWER ANY OF YOUR QUERIES IF YOU WISH.

AGE: SEX: HEIGHT: WEIGHT:

1. About what blood alcohol level do you think you are at: (CIRCLE)

   0 20 40 60 80 100 120 140 160 180 200 over 200

2. How many drinks have you had?

Jugs	Handles	5 oz Glass	7 oz Glass	Small Bottles	Large Bottles	Bottles Wine	Nips of Spirits

3. What time did you start drinking today? _____

4. When did you last have a meal? _____

5. How many drinks do you think it takes to reach the legal limit? _____

6. Do you consider yourself fit to drive? (CIRCLE)

   Yes No Not sure

7. The legal blood alcohol limit for driving is 100. Indicate what you think it should be: (CIRCLE)

   0 50 80 100 120 150 Don't know

8. Should breath tests replace blood tests? (CIRCLE)

   Yes No Not sure

9. What is your attitude to random breath testing: (CIRCLE)

   Approve For research only Disapprove

DO NOT COMPLETE THIS SIDE

POST TEST QUESTIONNAIRE

(TO BE FILLED IN BY THE UNIVERSITY STAFF IN ATTENDANCE)

Tested on earlier occasion: Day _____ Result _____

Time of Test: _____

Machine Reading: _____

Subject Tested:	1st time	2nd	3rd	4th	5th
Previous Result:	_____	_____	_____	_____	_____

Any surprise at the result? Yes No ?

Was it expected to be: Higher Lower

Do you think the legal limit for driving should be:

0 50 80 100 120 150 Not sure

MASSEY UNIVERSITY

ALCOHOL RESEARCH GROUP

In collaboration with the Hotel Association of New Zealand
and supported by the Alcoholic Liquor Advisory Council

The group will be present in this bar with breath testing equipment in a few days time and members of the group will invite you to check your own blood alcohol level by simply providing a breath sample.

It is now widely recognised around the world that the amount of alcohol in the blood can be estimated from breath samples. The alcohol research group of Massey University has been investigating the accuracy of breath alcohol tests for several years and has been trying out various breath testing instruments on individuals in the laboratory and at various private functions. During these studies, it has become increasingly apparent that most people in the community have little idea of what amounts of liquor consumed could take a person over the legal limit for driving.

There are many misconceptions surrounding drinking. For example, alcohol is not eliminated in the urine to any significant degree, but is "burnt up" very slowly by the liver. One of the effects of alcohol is to increase the urine volume above normal, but at the same time it becomes considerably diluted so that it is almost pure water. It is also not possible to sober-up quickly; while coffee, a breath of fresh air or other changes in circumstances may lead a person to believe that the effect of alcohol has worn off, the amount of alcohol in the blood affecting the brain remains virtually unchanged. Blood alcohol levels decline slowly at a constant rate of 15-20 mg/100 ml for most people, so that it would take at least 5 hours to reach zero from the legal limit of 100 mg/100 ml. The average level in intoxicated drivers apprehended by traffic officers is about 170 mg/100 ml so that it would be at least 3 hours before such a person got down to the legal limit and a further 5 hours to completely use up the remaining alcohol in the body. It is probable that many people start the day with alcohol in their blood, remaining from a party or a heavy drinking session the night before. Similarly, after a "fortified" lunch, the 5 o'clock drinker may have a head start in the blood alcohol stakes.

What are your blood alcohol levels during and after your normal drinking session? Are you within the legal limit and safe to drive? How quickly do the blood levels go down when drinking has finished?

In the next few days we will be bringing our breath testing equipment to this bar so that you may see for yourself the answer to some of these questions and our staff will be in attendance to test you if you wish. We ask that before taking a breath test, you refrain from drinking any alcoholic liquor for at least 10 minutes. This is because the alcohol content, even of beer, is much higher than blood levels and consequently the concentration in the mouth remains very much higher for up to 10 minutes after drinking.

Below are some guidelines derived from our research work where drinking was under normal social conditions in a bar.

GUIDELINES TO BLOOD ALCOHOL LEVELS FROM DRINKING OVER A 2-3 HOUR PERIOD

Body Weight		Number of drinks (lower limits)											
Kg.	Stones	1	2	3	4	5	6	7	8	9	10	11	12+
50	8												
70	11												
90	14												
Blood alcohol level mg/100 ml		50					80			100			
Legal implications		Legally sober					Possibly illegal			Illegal			
		Drive cautiously					Should not drive			Do not drive Allow one hour for every drink over the legal limit			
N.B. 1 Drink is 1 glass of beer (7 oz or 200 ml) or 1 nip of spirits (17 ml) or 1 glass of wine													

Normally a person's body can use up about one drink per hour. If you have no more than one per hour you can remain legally sober. However, even one drink can affect driving for some people.

(Modified from an Orange County, U.S.A. card)