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Physiological Aspects of Breath-Alcohol Measurement

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ABSTRACT

This paper gives review and opinion about several aspects of quantitative evidential breath-alcohol analysis used in traffic law enforcement. In particular, physiological aspects of breath testing are covered, with emphasis on factors influencing the precision and accuracy of results. The increasing use of punishable limits of blood and/or breath-alcohol concentration makes chemical test evidence a popular target for defense attack and litigation in trials concerned with driving under the influence (DUI). Historical developments in theory and application of breath testing as evidence of intoxication are briefly outlined. The absorption, distribution and elimination of alcohol in the human body are covered as background for understanding the passage of alcohol from blood to breath. Research on the blood/breath alcohol ratio and the factors that influence this relationship including mouth-alcohol, regurgitation, breathing technique, arterio-venous differences, blood hematocrit value, pulmonary disease, body temperature, expired air temperature, and temperature and humidity of ambient air are critically evaluated and discussed. Both blood-alcohol and breath-alcohol measurements are suitable to provide objective evidence of alcohol load in the organism and the associated impairment of driving skills. With per se statutes, the magnitude of sampling and analytical errors inherent in methods of analyzing alcohol for legal purposes must be carefully documented. The final prosecution result can be adjusted to allow for uncertainties in the analytical procedures used.

Introduction

It has been known for more than a century that a small fraction of the alcohol a person drinks is expelled unchanged in the breath (Anstie, 1874). The smell of alcohol on the breath and the individual's general appearance and behavior often arouse the first suspicion of over-indulgence. The simplest alcohol breath-test, using the human nose as sensing device, has its roots in ancient times. Towards the end of the nineteenth century quantitative methods of analyzing alcohol in body fluids began to appear (Benedict and Norris, 1898). Although by modern standards these techniques were fairly crude, they enabled scientists to delineate the fate of alcohol in the body and to establish an approximate relationship between blood-alcohol concentration (BAC) and various stages of alcohol influence (Mellanby, 1919).

The tremendous increase in motor transportation after the First World War brought into sharp focus the role played by alcohol in accidents and deaths on the highway. The call for legislation and sanctions to combat "drunk drivers" created an urgent need to develop and evaluate more reliable ways of testing for alcoholic

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intoxication (Borkenstein, 1985). A clinical examination alone had definite shortcomings as a medicolegal test of whether a driver was under the influence of alcohol. The wide inter-individual variations in signs and symptoms of alcohol influence and the experience of the examining physician tend to discredit the result obtained by ordinary clinical means. This prompted a search for more objective ways of testing whether a driver was impaired and unfit to operate a motor vehicle on the public roads. Close at hand were the chemical-technical methods for measuring alcohol in a biological specimen: blood, breath or urine obtained from the person suspected of DUI. This led to the notion of a criminal justice system based on "chemical tests for intoxication" with punishable limits of alcohol concentration in body fluids as a basis for conviction (Lovell, 1972).

The first person to propose the use of breath-analysis as a test for intoxication was Emil Bogen in 1927 (Bogen, 1927). He collected mixed expired air in a football bladder and passed a known volume of this specimen of breath through a mixture of sulphuric acid and potassium dichromate. This reagent is similar to the liquid contained in Breathalyzer ampoules. The resulting changes in color from yellow to various shades of blue-green-yellow were compared with a series of sealed standard tubes containing the same test reagent to which known amounts of alcohol had been added. Bogen reported a good correlation between the concentration of alcohol in breath (BrAC) and clinical signs and symptoms of intoxication.

Alcohol must reach the brain before it can exert its well known untoward effects on performance and behavior. Because alcohol is transported to the central nervous system by the blood circulation, the concentration of alcohol in a specimen of blood was considered a suitable objective test for alcohol influence and associated deterioration of a person's driving skills. It is important to note that the source of blood in question, whether drawn from artery, capillary, or vein, was initially not defined more precisely. Statutory limits of BAC differ among countries and even within parts of the same country, e.g., states of the USA, Canada, and Australia. The sampling and analysis of breath is a noninvasive technique and efforts were therefore made to develop compact breath-alcohol analyzers suitable for police use. These appeared in the late 1930s with the introduction of the Drunkometer, the Alcolmeter and the Intoximeter (Harger, 1974). The classic Breathalyzer was invented in 1954 by Robert F. Borkenstein (Borkenstein, 1954).

A tricky situation emerged because the drunk driving statutes were defined in terms of BAC although most of the alcohol measurements for legal purposes were made in breath. It was therefore deemed necessary to convert the measured breath concentration into a presumed blood concentration. In practice this meant capturing a sample of expired alveolar air from the test subject and accurately measuring the concentration of alcohol it contained. The raw BrAC reading was then converted into the presumed coexisting BAC by calibrating the breath-analyzer with a constant factor; the blood/breath ratio of alcohol. This is generally stated as one volume of blood containing the same weight of alcohol as 2100 volumes of breath at 34°C. The value chosen for the blood-breath ratio of alcohol is an essential element which determines the accuracy of breath-testing devices when the results are translated into BAC. In forensic science practice, the 2100:1 ratio is assumed to apply for all people under all conditions of testing despite many differences of opinion among early workers in the field (Haggard et al., 1941). Support for use of the 2100:1 blood/breath ratio in law enforcement came from a meeting of experts in 1952 under the auspices of the National Safety Council's committee on tests for intoxication (Muehlberger et al., 1953).

> *The basic principle governing the operation of the three presently used breath alcohol methods (the Drunkometer, the Intoximeter and the Alcolmeter) is the constant ratio existing between the concentration of alcohol in the alveolar air and the blood. Available information indicates that this alveolar air-blood ratio is approximately 1:2100. However, since each method involves different procedures, different empirical factors are involved in the calculation of concentration of alcohol in the blood in each of the methods.*

The above statement was revised by another meeting of experts held at Indiana University, Indianapolis, in 1972. The report of the Ad Hoc Committee on blood/breath alcohol ratio contained the following statement which essentially reaffirmed the 1953 standpoint:

> *The basic principle governing the design of breath alcohol instruments is that a physiological relationship exists between the concentration of alcohol in expired alveolar air and in the blood. Available information indicates that 2.1 liters of expired alveolar air contain approximately the same*

quantity of alcohol as 1 milliliter of blood. Continued use of this ratio in clinical and legal applications is warranted.

Since 1972 great advances have been made in developing new methods and technology for analyzing alcohol in expired breath. A wide range of sophisticated microprocessor-controlled breath-testing instruments are commercially available (Jones 1989a). More and more countries are updating their existing drunk driving statutes to include provisions for evidential breath testing. There are definite practical advantages in using breath-alcohol analyzers for legal purposes compared with traditional methods of forensic blood-alcohol analysis. These include non-invasive sampling techniques, on-the-spot determination of whether an offense has been committed, making immediate sanctions possible, and more effective traffic control and time saving by the police. Last, but not least, one sidesteps the need to handle, transport, and store samples of blood from individuals with AIDS or hepatitis.

In European countries, such as Great Britain (1985), The Netherlands (1987), Austria (1986), France (1985), Norway (1988), and Sweden (1989), the alcohol element of the offense of driving under the influence of alcohol is now defined as a certain concentration present in a sample of end-expiratory breath. A delicate problem concerned the choice of statutory BrAC limits. Because punishable limits of BAC were already well established in these European countries, the existing limits were translated directly into BrAC by the use of an average blood/breath conversion factor. The rationale in choosing the particular blood/breath factors by the legislature of various European countries remains obscure.

Great Britain and Holland opted for 2300:1 blood/breath relationship, which means that their respective earlier BAC limits of 80 mg/100 ml and 0.50 mg/ml now become BrACs of 35 µg/100 ml and 220 µg/liter respectively . In Austria a 2000:1 blood/breath ratio was selected by the legislature so that the BAC limit of 0.80 mg/ml became 0.40 mg/liter of breath. In Norway and Sweden, with BAC limits of 0.50 mg/g (0.525 mg/ml), the blood/breath ratio is 2100:1 to give a breath alcohol limit of 0.25 mg/liter now enforced. The previously existing blood-alcohol statutes operate in parallel with the new breath-alcohol concentration limits. In the USA, Canada and Australia, countries in which quantitative evidential breath-analyzers have been used for decades, the blood to breath conversion factor of 2100 is used. But many states in the USA have now adopted drinking driving statutes that criminalize 0.10 g/210 liters breath or more per se. This means that the 2100:1 blood/breath ratio is incorporated directly into the statute. If, instead of this approach, the legislatures had decided to criminalize BrACs equal to or greater than 0.47 mg/liter [(0.10/2100) x 1000], this would have removed emphasis from the use of 2100:1 conversion factor. The possibility that a DUI suspect might have a concentration of alcohol that was legal in the blood, but illegal in the breath, or vice versa, creates a problem for the legislature and this dilemma has not yet been resolved. The inter-conversion between blood-alcohol (BAC) and breath-alcohol concentration (BrAC) limits is done simply as follows:

$$BAC = BrAC \times \text{blood/breath conversion factor}$$

To set the statutory BrAC limit, the legislature commonly takes the existing BAC limit and divides this by the blood/breath ratio of alcohol deemed appropriate for the particular jurisdiction. Whether milligrams (mg), micrograms (µg), or grams (g) of alcohol present in a breath volume defined in terms of milliliters (ml), deciliters (dl), or liters (L) are selected as the units of concentration seems to be an arbitrary decision.

Table 1 shows the relationship among various units used to report the concentrations of alcohol in blood for clinical and forensic purposes. This is important information because blood samples for alcohol analysis are sometimes sent to hospital clinical chemistry laboratories and the results afterwards presented in the law courts. Defense and prosecution attorneys should therefore be aware of these different ways of expressing BAC results.

Table 2 gives examples of the currently used statutory limits of blood and breath-alcohol concentrations in those countries where both kinds of biological specimen are approved for forensic purposes and the results afterwards used for prosecution of drinking drivers.

Fate of Alcohol in the Body

Ethanol (CH_3CH_2OH), generally called alcohol, is the second member of a family of monohydric (one hydroxyl [-OH] group) aliphatic alcohols; the first member being methanol (CH_3OH) and the third member 1-propanol or n-propanol ($CH_3CH_2CH_2OH$). Ethanol has a molecular weight of 46.06, boils at 78°C and mixes

TABLE 1

Different ways of reporting blood-alcohol concentration (BAC) which appear in the reports from clinical and forensic laboratories.

BAC concentration units	BAC units in the United States 0.05 g%	0.08 g%	0.10 g%
Percent alcohol in blood (w/v; g/100 ml)	0.05	0.08	0.10
Milligrams per deciliter (mg/dl; mg/100 ml)	50	80	100
Milligrams per milliliter (w/v; mg/ml)	0.50	0.80	1.00
Milligrams per gram (w/w; mg/g)[a]	0.47	0.76	0.95
Grams per liter (g/L)	0.50	0.80	1.00
Millimoles per liter (mM; mmol/L)[b]	10.8	17.3	21.7

[a] The specific gravity of whole blood is taken as 1.05; 1 ml = 1.05 g.
[b] The molecular weight of ethanol is taken as 46

TABLE 2

Concentration units currently used to express blood-alcohol and breath-alcohol concentration and the statutory blood/breath alcohol relationships chosen by the legislature in various countries.

Country	Effective ratio blood/breath	Statutory concentration threshold Breath alcohol	Blood alcohol
USA	2100:1	0.10 g/210 L	0.10 g/100 ml
Great Britain	2300:1	35 µg/100 ml	80 mg/100 ml
The Netherlands	2300:1	220 µg/L	0.50 mg/ml
Austria	2000:1	0.40 mg/L	0.80 mg/ml
Norway	2100:1	0.25 mg/L	0.50 mg/g[a]
Sweden	2100:1	0.25 mg/L	0.50 mg/g[a]

[a] Note: 0.50 mg/g is equivalent to 0.525 mg/ml; specific weight of blood is 1.05

with water in all proportions. These physicochemical properties combined with the relatively low reactivity of the neutral hydroxyl group mean that alcohol can easily pass through biological membranes, interstitial spaces, and the blood-brain barrier. Absorbed alcohol is distributed by the blood into all body fluids and tissue according to the amount of water they contain. Ethanol does not combine with plasma proteins and other endogenous molecules and therefore the equilibrium concentrations reached in body fluids such as urine and saliva, which are roughly 99% w/w water, will be higher than in the same volume of whole blood which contains only 80% w/w water. Major developments in methods of alcohol analysis in body fluids were recently the subject of a comprehensive review (Dubowski, 1986) and this topic will not be covered in the present article. Besides the determination of alcohol in blood and breath for legal purposes, other biological specimens are available from living subjects for analysis of alcohol. The materials listed below have been used at one time or another as the biological matrix for alcohol analysis in clinical medicine, research or medicolegal practice:

Plasma and serum (Winek and Carlanga, 1987)
Erythrocytes (red-blood cells) (Payne et al., 1968)
Tears (Lund, 1984)

Saliva: mixed secretion (Jones, 1979), parotid (DiGregorio et al., 1978)
Urine (Biasotti and Valentine, 1985)
Cerebrospinal fluid (Mehrtens and Newman, 1933)
Sweat and perspiration (Brown, 1985)
Breast milk (Kesäniemi, 1974)

The fate of alcohol in the body after drinking can be followed through three different physiological processes: absorption, distribution, and elimination (Kalant, 1971). The relative influence of absorption of alcohol compared with the speed of reaching diffusion equilibrium leads to a situation whereby the shape of the blood-concentration versus time profile can be completely different for the same quantity (dose) administered

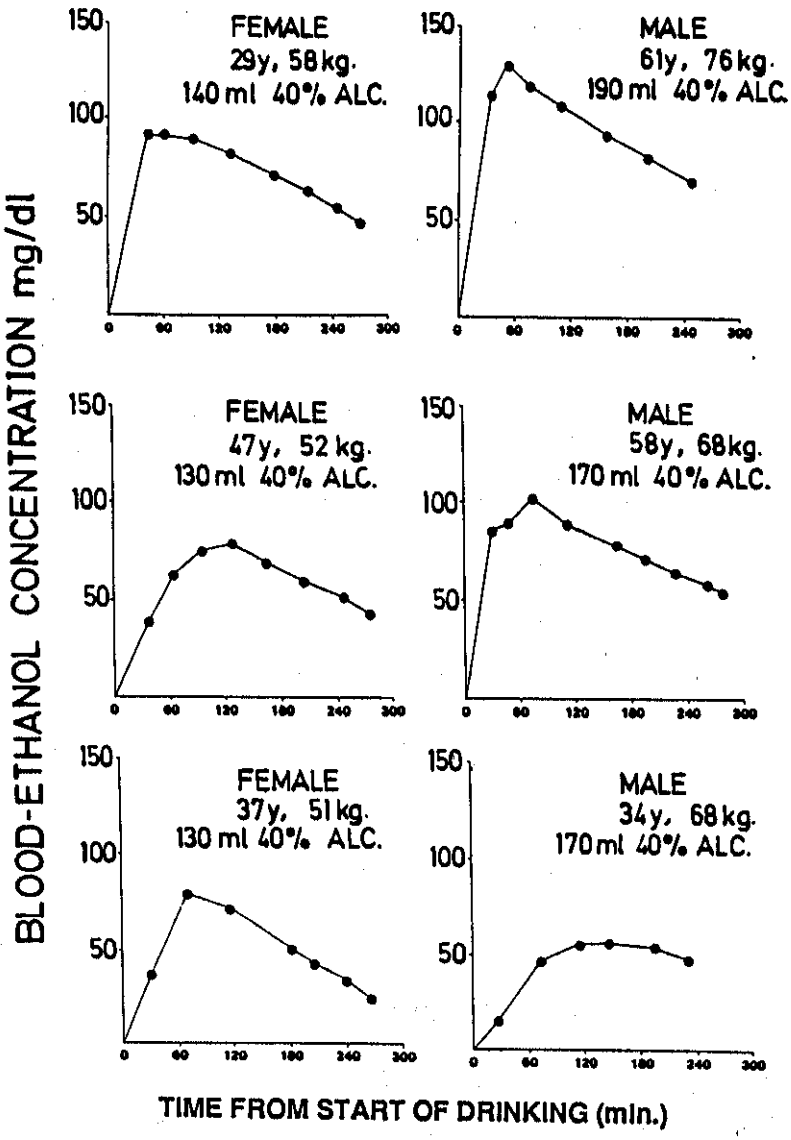

FIGURE 1

Concentration-time profiles of ethanol in specimens of venous blood of healthy men and women. The test subjects drank 0.8 g ethanol/kg body weight in 30 min after food deprivation for 2–3 hours. The drink was made from 95% v/v ethanol diluted to about 25% v/v with orange juice to give a cocktail. The sex, age, body weight, and volume of alcohol consumed by each subject is shown on the figure. The volume is given as 40% v/v alcohol, being about the same strength as vodka.

per kilogram body weight and for the same pattern of drinking. Actual examples of the unpredictable nature of alcohol absorption from the stomach and the wide variation in the peak BAC reached are illustrated in Figure 1. This depicts the venous BAC profiles obtained when six volunteers (3 men and 3 women) drank 0.80 g alcohol per kg body weight in 30 minutes. The alcohol was given as a 25% v/v orange juice cocktail at about 2–3 hours after their last meal. The concentration–time profiles and the peak BAC reached showed wide inter-subject variation from 57–130 mg/dl. The time of occurrence of the peak after end of drinking ranged from 10–110 minutes.

Absorption Process

The absorption of alcohol begins to occur immediately after drinking. The rate of absorption of alcohol depends to a large extent on the nature and volume of the stomach contents before subjects start to drink. The amount and composition of any food present, whether carbohydrate, protein, or fat seem to play an important role because of the delaying influence these have on the emptying time of the stomach (Sedman et al., 1976a). The amount or dose of alcohol taken, the frequency of intake, and the kind of alcoholic beverage consumed also influence the rate of absorption and peak BAC reached. The alcohol contained in liquor such as whisky and vodka (40% v/v, 31.6 g/100 ml) is thought to be absorbed faster than for beer (3.6 g/100 ml) or wine 10 g/100 ml), but there is a lack of well-designed studies addressing this issue. The dilution and buffer capacity of the beverages taken also seems to influence absorption rate (Newman and Abramson, 1942).

Mixed drinks or cocktails are sometimes more rapidly absorbed than neat spirits. Intake of spirits in an undiluted form with an empty stomach might cause irritation of the gastric surfaces. In some people this leads to a delayed absorption mediated through a tight closure of the pylorus valve and this condition is commonly called pyloric spasm. This is associated with a slow absorption profile and peak times lasting 2–3 hours are not uncommon in these special circumstances. The much larger surface area available in the small intestine makes it certain that uptake of alcohol into the blood is very fast when the stomach empties its contents into the duodenum. The opening of the pylorus valve, which controls gastric emptying, therefore plays a key role in regulating the rate of absorption of alcohol. Moreover, the speed of absorption relative to distribution might influence the magnitude of any alcohol concentration gradients operating in the arterial (A) and the venous (V) blood circulation. As discussed later in this review, the existence of A–V differences is important to consider when a constant blood/breath ratio is used to estimate venous BAC indirectly from the analysis of breath.

In DUI trials only general guidelines can be given about the rate of alcohol absorption for a random subject from the population of drivers because so many unknown factors must be considered. An actual experiment designed to replicate the drinking pattern just prior to the offense might provide the most clearcut evidence. Uncertainties surrounding the absorption kinetics of alcohol make it very difficult for a forensic expert witness to state unequivocally whether the BAC was rising or falling at the time of the road-traffic incident. A relatively short time interval between consumption of alcohol on the one hand and driving the vehicle on the other hand lead to DUI suspects pleading the so-called "rising blood-alcohol defense". If evidence can be mustered to suggest that the peak BAC was reached after the incident, the driver might have been below the statutory limit at the time of driving and an acquittal is therefore a possible outcome.

Distribution Process

Alcohol is absorbed from the gastrointestinal tract into the blood capillaries that drain the stomach and small intestine. These form the portal circulation which leads to the liver. The hepatic vein carries the blood away from the liver and any alcohol present becomes diluted with mixed venous blood returning to the right side of the heart. The blood is then immediately pumped via the pulmonary artery into the lungs where an exchange of gases takes place. The oxygenated blood returns to the left side of the heart via the pulmonary vein. Thereafter blood is circulated throughout the body. During its passage to all body organs and tissue some of the alcohol is removed from the arterial blood. All body fluids and tissues which are initially alcohol-free are supplied with alcohol from the arterial blood until the whole system reaches a state of equilibrium. This loss of alcohol from arterial blood and uptake by tissue occurs progressively as absorption from the gut continues. The time taken to achieve equilibrium for alcohol depends on the rate of blood flow to the various organs and tissue, their water contents, and the alcohol concentration gradients present (Kalant, 1971).

Organs with a rich blood supply, such as the lungs, the kidneys, and the brain, receive a proportionally higher concentration of alcohol during the early stages of absorption when the BAC curve is rising. The concentration of alcohol in arterial blood is therefore higher than that in the venous return from an anticubital (elbow) or femoral (leg) vein. This phenomenon is known as the arterio-venous alcohol difference. It follows that the concentration of alcohol in the breath is a better reflection of brain exposure to alcohol than the venous BAC during the absorption stage of the concentration-time profile. The concentration of alcohol in capillary blood during this time is closer to the arterial blood (Forney et al., 1964). When the concentration of alcohol in all body fluids and tissue equilibrates with the arterial blood, which occurs after drinking when absorption ends, the distribution of alcohol is complete. This A–V crossover point for alcohol might serve as one index of the time of onset of the "post-absorptive" stage of alcohol kinetics. But, in forensic practice, the time after the peak BAC is generally used to denote the start of the post-absorptive period. The venous BAC will now be slightly higher than the capillary and arterial BAC and remains so for the rest of the time alcohol is elevated in blood (Martin et al., 1984; Jones et al., 1989). Differences in alcohol concentration may also exist between left-right arm veins, and between the arms and legs (Forney et al., 1964; Jones et al., 1989).

Elimination Process

Alcohol is removed from the body in two fundamentally different ways. The bulk of the total amount of alcohol absorbed and distributed into the water compartment of the body is broken down or metabolized in organs and tissue (liver, kidney and gut) or wherever alcohol-metabolizing enzymes exist. The primary product of ethanol metabolism by all known pathways is a substance called acetaldehyde (CH_3CHO), which is itself rapidly oxidized into acetate. The end products of alcohol metabolism are carbon dioxide and water generated from acetate through the normal metabolic pathways. These metabolic events are controlled by the enzymes alcohol dehydrogenase (EC 1.1.1.1, ADH), which oxidizes alcohol into acetaldehyde, and aldehyde dehydrogenase (EC 1.2.1.3, ALDH), which converts acetaldehyde into acetate (Crabb et al., 1987). Both these biological oxidation reactions require the coenzyme nicotinamide adenine dinucleotide (NAD^+) which is converted into its reduced form NADH. Many of the untoward effects of ethanol on the body's normal metabolic functions and intermediary metabolism can be explained by the excess NADH generated in the liver cell during combustion of alcohol (Lieber, 1982). These alcohol oxidation reactions are usually depicted in chemical symbols as follows:

$$CH_3CH_2OH + NAD^+ \leftrightarrow CH_3CHO + NADH + H^+$$
$$CH_3CHO + NAD^+ = CH_3COOH + NADH + H^+$$
$$CH_3COOH = CO_2 + H_2O$$

The principal alcohol metabolizing enzyme ADH is mainly located in the liver, but some activity exists also in the gastrointestinal tract and in the kidney (Lieber, 1988). About 95–98% of a moderate dose of alcohol is removed from the body by enzymatic oxidation, predominantly taking place in the liver. The remaining 2–5% of the dose is excreted unchanged in urine, sweat and expired air (Holford, 1987). The rate of disappearance of alcohol from blood is normally calculated from the slope of the rectilinear elimination phase of the BAC time-profile. By tradition, this is denoted as Widmark's beta (β) factor (Widmark, 1932). Beta factors vary among individuals, depending in part on genetic and racial differences, the maximum BAC reached after drinking and the person's drinking habits. Values of β ranging from 0.01 to 0.025 g% per hour are easy to find in the literature and higher rates of elimination may occur in alcoholics on a drinking binge (Holzbecher and Wells, 1984). An alcohol-tolerant individual will tend to "burn-off" alcohol faster than an occasional drinker. The liver is equipped with another metabolic pathway for removal of alcohol from the blood known as the microsomal ethanol oxidizing system (MEOS). This is located in a sub-cellular structure of the liver cells called the endoplasmic reticulum (Teschke and Gellert, 1986). MEOS has the property of becoming more active in the course of chronic alcohol exposure, a process known as enzyme induction. But, after a short period of abstinence (2–3 days), the rate of ethanol metabolism returns to near normal limits (Keiding et al., 1983). Moreover, the MEOS enzymes exert their maximum effect when the BAC exceeds about 0.05 g/100 ml; that is, after moderate drinking.

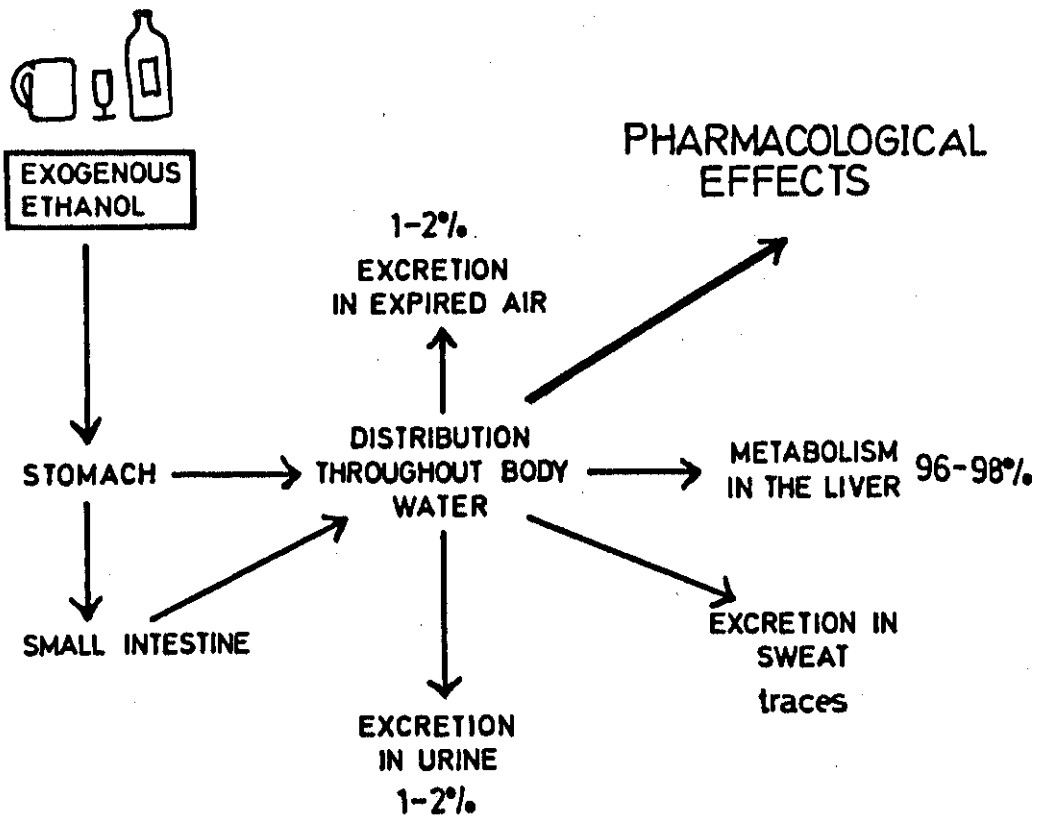

FIGURE 2

Schematic diagram depicting the fate of alcohol in the body after drinking. About 96–98% of the dose administered is removed by enzymatic oxidation occurring mainly in the liver. The remaining 2–4% is excreted unchanged in urine, expired air and sweat. Alcohol must cross the blood-brain-barrier (BBB) before it exerts its well-known pharmacological effects on performance and behavior.

Another aspect of ethanol metabolism which is starting to generate research interest is the "first pass effect" (DiPadova et al., 1987). This implies that a part of the dose of alcohol a person drinks is removed from the body before it reaches the general circulation. This phenomenon might have implications in forensic science practice when an expert witness is asked to make theoretical calculations of expected BAC based on amounts consumed. Interestingly, first-pass metabolism of alcohol is less pronounced in alcoholics compared with moderate drinkers and also less evident in women compared with men. The first-pass effect is maximum when alcohol is consumed together with or after food and is least under fasting conditions (DiPadova et al., 1989). The magnitude of this phenomenon is dose-dependent and seems to be greater when small quantities of alcohol are taken (0.15–0.30 g/kg). For the same dose of alcohol, the peak BAC reached is lower and alcohol remains in the blood for shorter periods of time in those individuals displaying a measurable "first-pass effect". The proposed mechanism of first-pass removal is the oxidation by isozymes of alcohol dehydrogenase in the stomach mucous lining (Caballeria et al., 1989). A part of the alcohol consumed is therefore oxidized before it reaches the liver. This gut-ADH is less active in women and heavy drinkers and these groups accordingly show a smaller first-pass effect. The proportion of the population that exhibits a first-pass metabolism is unknown and the results obtained so far are confined to low doses of alcohol (0.15–0.30 g/kg) administered in the morning about 60 min after a normal breakfast (Palmer, 1989).

Figure 2 is a schematic representation of what happens to alcohol in the body after drinking. This background on the fate of alcohol in the human body is important for a proper understanding of breath-alcohol analysis and the scientific basis of chemical testing for intoxication.

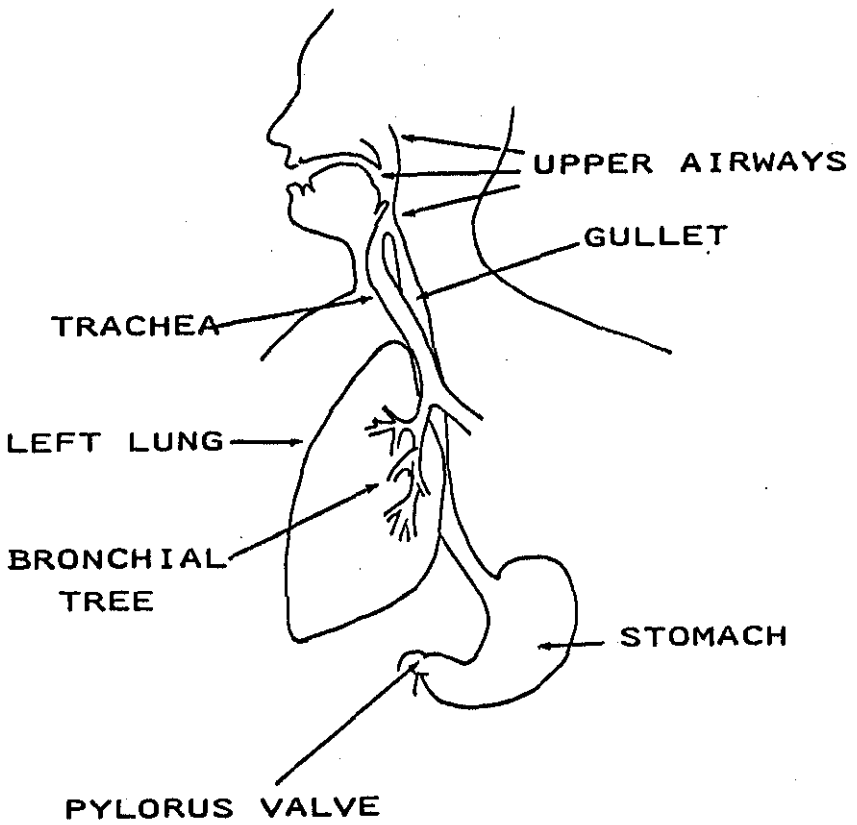

FIGURE 3

Schematic diagram showing the relationship between lungs and stomach. The trachea (windpipe) connects the upper airway, nose, mouth, and throat, all carpeted with a watery mucous membrane, to the two bronchi. Each bronchus undergoes repeated and continuous subdivision terminating in the microscopic alveolar sacs where gas exchange between blood and breath takes place. The gullet (esophagus) connects the throat and mouth to the stomach. The pylorus valve controls the emptying of stomach contents into the upper part of the small intestine (duodenum).

The Passage of Alcohol from Blood to Breath

After its passage through the liver, the blood containing alcohol is pumped from the right side of the heart and enters the lungs via the pulmonary artery at a flow rate of about 5–6 liters/min. This massive blood flow is distributed over a large surface area of about 60 square meters (Comroe, 1962). The volume of blood in the lung capillaries at any given time varies from 60–140 ml which means that there is a thin film spread over an enormous surface area. The human respiratory tract can be considered, for simplicity, to exist in two parts, each serving a different function. The upper part, or upper respiratory tract (URT), comprises the nose, the mouth, the pharynx (throat), the trachea (windpipe) and the two bronchi before they undergo subdivision within the lungs. The main function of the URT is to remove foreign particles and dust from the inhaled air and also to modify the condition of the air with respect to its temperature and water content (humidity) (Proctor and Andersen, 1982). The inhaled air is warmed to body temperature and saturated with water vapor by the time it reaches the microscopic gas exchange surfaces in the alveoli. This conditioning process is controlled by the mucus which lines the walls of the URT (Proctor, 1977). The mucus provides heat and moisture to warm inspired air during breathing in cold climates. This results in a cooling of the mucous surface. During the following normal exhalation the alveolar air, which is now at body temperature (37°C) and saturated with water vapor, returns heat and moisture to the mucus. When expired air leaves the mouth the air temperature has dropped to about 34.5°C during its passage through the respiratory tract (Jones, 1982a). It must be obvious that water soluble agents like acetone and alcohol, if these are present in the expired air, will interact with the airway

mucous membranes during breathing. The equilibration of alcohol vapor between respired air and the mucus occurs during normal breathing and is exaggerated by any abnormal change in a subject's pattern of breathing or by extreme alterations in the temperature and humidity of the ambient air breathed. A failure in the past to monitor carefully the way in which breath specimens are provided for analysis, because of the high solubility of alcohol in the airway mucus, explains to a large extent the wide range of blood-breath ratios of alcohol reported in the literature. Figure 3 gives a much simplified anatomical scheme of the stomach and the lungs in humans.

Exchange of Gases in the Lungs

The second part of the respiratory system begins at the point where the trachea divides into the two bronchi, the left and right sides of the lung, to form the bronchial tree. Each bronchus then undergoes repeated and continuous subdivision 23 times before terminating in the bronchioles which open into fine microscopic tubes called the respiratory bronchioles (Davson and Eggleton, 1968). These branch into the alveolar ducts. The lungs of an adult person with average body build contain approximately 300 million alveoli. The interalveolar septa are covered with a rich capillary network which facilitates effective gas exchanges between blood and alveolar air. The total surface area available for gas exchange is between 50–90 square meters, being about 70 square meters on average. This is roughly equal to the floor area of a room 34 feet long by 25 feet wide. The blood and air in the lungs are separated by the alveolar-capillary membrane which is only 0.001 mm thick (Ganong, 1979). Oxygen is taken up from the inspired air and combines with hemoglobin, a protein within the red blood cells. This is the mode of transport of oxygen throughout the body. Excess carbon dioxide present in the pulmonary blood is removed to maintain the proper acid-base balance and CO_2 is therefore a waste product excreted in the breath. The exchange of gases across the alveolar-capillary membrane is a diffusion process and whether uptake or excretion occurs depends on the concentration gradients existing. A list of respiratory parameters relevant to gas exchange in the lungs is given in Table 3.

TABLE 3

Respiratory parameters of the adult lung important in connection with gas exchange and physiology of breath-alcohol measurements. All values are taken from standard works in respiration physiology except for end-respiratory temperatures which were reported by Dubowski and Essary (1985).

Parameter	Average values for healthy males	
Pulmonary blood flow	5 liters per minute	
Alveolar ventilation	4 liters per minute	
Surface area for gas exchange	70 square meters	
Number of alveoli	300 million	
Thickness of alveolar membrane	0.001–0.002 millimeters	
Tidal volume at rest	500 ml	
Respiratory frequency	10–13 breaths per minute	
Ventilation/perfusion ratio	0.8 average	
Forced vital capacity	Men	4.5 liters
	Women	3.2 liters
Anatomical deadspace	150 ml	
End-expiratory temperature	Men	34.65°C (range 32.41–36.32)
	Women	34.67°C (range 33.53–35.77)

The passage of alcohol from blood to breath follows the same basic process as for the respiratory gases. The main difference is that alcohol is much more soluble in water and, therefore, in blood, which contains 80% w/w water. Alcohol diffuses from the pulmonary blood into the alveolar air until an equilibrium is established at the prevailing body temperature of about 37°C. The ratio of the concentrations of alcohol in blood and alveolar air at equilibrium is called the blood/breath partition coefficient or the Ostwald solubility coefficient (Eger and Larson, 1964). In fact, this has never actually been measured at the alveolar-capillary membrane in humans because of technical difficulties and ethical issues. The anatomy and physiology of the lung is well

suited for gas-exchange and, therefore, it can be generally assumed that a complete and virtually instantaneous equilibrium of alcohol occurs between the pulmonary blood and the alveolar air. The temperature of blood flowing through the pulmonary bed can be considered the same as normal core body temperature (Edwards et al., 1963).

Ventilation-Perfusion Relationship

An important aspect of the uptake and/or elimination of gases in the alveolar regions of the lung is the relationship between ventilation (V) and blood flow or perfusion (Q). V/Q is the ratio between the volume of fresh air reaching an alveolus per minute to the volume of blood perfusing the same alveolus per minute (Klocke, 1977). Lung ventilation is the product of two factors: the tidal volume, which is the amount of air moved with each breath per minute, and the respiratory rate, which at rest is about 10–13 breaths per minute. In a person with a tidal volume of 500 ml, only about 350 ml of fresh air is available for effective gas exchange. The remaining 150 ml stays in the first part of the upper airway, which is called the dead-space region of the lung. With an average pulmonary blood-flow of 5.0 liters/minute and a ventilation of 4.0 liters/minute the V/Q is simply calculated as 4/5 and therefore equals 0.8. This represents an average V/Q for the lung as a whole and this varies between and within individuals from about 0.7 to 1.0. In certain situations, an alveolus might be ventilated, but not perfused, and vice versa. Accordingly, V/Q is different for different regions of the lung. Values of V/Q might range from 0.5 for alveoli at the base of the lung to 3.0 for those at the apex (Davson and Eggleton, 1968).

TABLE 4

Values of blood/air partition coefficients for ethanol compared with other gases and vapors encountered in respiration physiology. There will be 1800 parts ethanol present in blood with only 1 part present in the alveolar air. The interaction between gas solubility (k) and the ventilation–perfusion relationship (V/Q), according to Farhi and Yokoyama (1967), is given by the following equation:

$$\% \text{ Retention} = \frac{P_a}{P_v} = \frac{k}{\left[k + \frac{V}{Q}\right]}$$

Where P_a and P_v are the partial pressures of the gas or vapor in arterial and venous blood respectively. This equation estimates the retention of the vapor in blood as it flows through an alveolus. Clearly, retention of highly soluble vapors such as ethanol is negligibly influenced by large variations in V/Q.

Substance	Average blood/air partition coefficient at 37°C	Reference
Ethylene	0.140	Eger and Larson (1964)
Nitrous oxide	0.468	Eger and Larson (1964)
Toluene	7.0	Wallén (1986)
Chloroform	10.3	Eger and Larson (1964)
Diethyl ether	15.2	Eger and Larson (1964)
Acetaldehyde	189	Stowell et al. (1980)
Acetone	275	Wigaeus et al. (1981)
n-butanol	1200	Åstrand et al. (1976)
Ethanol	1800	Jones (1983a)

For the respiratory and anaesthetic gases extreme variations in V/Q for a particular alveolus can dramatically impair the uptake or washout of these agents through the lung (Kelman, 1982). But, for gases and vapors with high volubility in water, such as alcohol, one might expect that variations in V/Q throughout the lungs has a marginal effect on the concentration entering the alveolar air (Farhi and Yokoyama, 1967). Even a poorly perfused alveolus will have a certain vapor tension of alcohol derived from alcohol dissolved in the

watery liquid membrane at the pulmonary blood/alveolar air interface. Table 4 gives the values of blood/air partition coefficients for ethanol compared with other gases and vapors equilibrated in vitro at 37°C. The equation which defines the relationship between solubility of the agent and ventilation-perfusion ratio in the lung is also given.

Pathological conditions that cause a thickening of the alveolar walls or disturbances in V/Q ratio are of minor importance for gases with blood/air solubility coefficients as high as ethanol, 1800 at 37°C (Jones, 1983a). Respiratory physiologists consider that the general anaesthetic vapor diethyl ether is a very soluble gas in terms of its blood/air partition coefficient, which is 15 compared with ethanol's 1800. The excretion of very soluble gases and vapors through the human lung, such as acetone with a blood/air partition ratio of 275 at 37°C (Wigaeus et al., 1981), should be marginally influenced by gross abnormalities of the ventilation/perfusion relationships within the alveoli (Farhi and Yokoyama, 1967). Instead, these highly water soluble agents behave abnormally in the lung because of the vapor/liquid exchanges taking place with the airway mucus during breathing. The concentration of alcohol in expired air is less than in alveolar air but how much less depends on a host of physiological factors. Key variables are the heating and cooling processes in the airway and the dynamic equilibration of alcohol with the mucous membranes. This offers one possible explanation for the wide range of blood/air ratios of ethanol reported in the literature derived from in vivo studies. It seems likely that the status of equilibrium at the alveolar-capillary membrane plays a subordinate role.

Application of Henry's Law of Gas Solubility

Early proponents of breath alcohol analysis for legal purposes often cited Henry's law as the scientific basis for the use of this technique. Henry was a British chemist who studied, among other things, the physical properties of solutions of various gases and volatile substances in water. In 1803 he published his work which became accepted as a scientific law or principle pertaining to the solubility of gases in liquids and the effects of pressure, volume, and temperature thereon (Henry, 1803). Henry never mentioned testing alcohol in his experiments and certainly not solutions of it in blood. Moreover, breath analysis in vivo is a dynamic gas exchange process not only involving a diffusion across the alveolar membrane, but also air/liquid exchanges throughout the respiratory tract during breathing. To compare breath-alcohol measurements in law enforcement practice with Henry's law of gas solubility is therefore an over-simplification of the process. Nevertheless, this reference to Henry's law gave the early techniques of breath analysis a kind of scientific credibility and, indeed, this law certainly applies when an equilibrator or simulator device is used to produce a known concentration of alcohol in air. These devices are used extensively to produce air-alcohol-vapor standards to check the accuracy of breath-alcohol analyzers before and after a subject is tested (Dubowski, 1979).

Henry's law is stated in text books in different ways, one of which is "the quantity of a gas which dissolves in a liquid is directly proportional to the partial pressure of the gas and when an equilibrium is reached, the partial pressure in the gaseous phase will equal the partial pressure in the liquid phase." It therefore follows that when a gas or volatile agent equilibrates between two phases, for example air and water, the ratio of the concentration of the substance in one phase to its concentration in the other phase is a constant. When equilibrium is reached at a fixed temperature the liquid/air solubility coefficient is given by:

$$\text{Solubility coefficient} = \frac{\text{Concentration in the liquid phase}}{\text{Concentration in the vapor phase}}$$

The value of the solubility coefficient or partition ratio for distribution of alcohol between air and various liquid phases (water, blood, urine, and plasma) can be determined in vitro in a number of ways. The classic study of Harger et al. (1950a) is often cited in connection with the use of breath-alcohol analysis for law enforcement purposes. Results of my own work concerned with in vitro equilibration of ethanol using blood samples taken from healthy men and women are presented in Table 5 (Jones, 1983a). The differences observed for blood samples taken from men and women after adding alcohol were statistically significant. The lower mean hematocrit value of female blood suggests more water per unit volume of whole blood. Thus, with the same concentration of alcohol in whole blood, those specimens with low hematocrit value (such as female blood) will have a lower concentration of alcohol in the available water fraction and therefore a lower concentration in an air or vapor phase equilibrated with it. This leads to slightly higher blood/air ratios of ethanol at equilibrium for bloods with low hematocrit value (Jones, 1983a).

TABLE 5

Blood/air partition ratios for dilute solutions of ethanol in specimens of whole blood obtained from healthy men and women. Specimens were held at equilibrium temperatures of 34°C and 37°C in vitro. Values given are mean ± standard error (Jones, 1983a).

Equilibrium temperature	Males (N = 20) Hematocrit value 44.3 ± 0.72%	Females (N = 15) Hematocrit value 40.0 ± 0.77%
34°C	2157 ± 9.6	2195 ± 10.9
37°C	1783 ± 8.1	1830 ± 7.8

Breath-Analysis and the Blood/Breath Alcohol Relationship

In 1910 a British pharmacologist, A.R. Cushny, investigated the excretion of various volatile agents such as acetone, chloroform, and alcohol through the lungs of cats (Cushny, 1910). Although he gave only scant attention to the behavior of alcohol, his conclusions are often cited by those who review the history of breath-alcohol analysis:

> *The exhalation of volatile substances from the lungs is exactly analogous to their evaporation from solutions in water and the pulmonary cells seem to be purely passive in this process.*

This statement implies that Henry's law operates for volatile agents like alcohol even under in vivo conditions and therefore during the transfer of gases and vapors from blood to breath. But, when alveolar air passes over the mucous membrane of the upper respiratory tract, re-equilibration occurs and the temperature of the system drops from 37°C to about 34.5°C in the course of a full exhalation (Jones, 1982a). The measured blood/expired-air ratio of ethanol is composed of blood/alveolar air equilibrium at the pulmonary membrane of the lungs as well as airway fluid/expired air equilibrium at lower temperatures in the upper respiratory tract (Jones, 1983b). It seems that the nearest one comes to the general application of Henry's law as stated in text books of physical chemistry is that concentrations of alcohol in expired breath increase as a direct function of the coexisting BAC. The proportionality constant between the two is the "apparent" blood/expired-breath partition ratio, which is taken as 2100:1 for traffic law enforcement purposes in the USA. Note that this is higher than the value of 1800:1 which applies to blood/air equilibration of ethanol at 37°C according to experiments in vitro. The alcohol content of expired air is accordingly less than in alveolar air even though there is an apparent rise in BrAC during a prolonged exhalation (Jones, 1982a).

A pioneer work concerned with the physiological principles of breath-alcohol measurement was done by two Swedish scientists, Liljestrand and Linde (1930). They studied the distribution of alcohol between blood and air at various equilibrium temperatures by putting small volumes of blood into large glass flasks and then analyzing the concentration of alcohol entering the blood and the air phases after a few hours at constant temperature. From these in vitro experiments they estimated the blood/air partition coefficient for ethanol. In a second part of the same study, human volunteers drank moderate amounts of ethanol and the concentrations were determined in samples of end-expired breath and arterialized venous blood. The blood samples were obtained by warming a subject's hand in hot water before puncturing a superficial vein. They reported that BAC after drinking followed a time course similar to BrAC x 2000. This implies the following relationship between blood and breath alcohol concentrations:

Arterial BAC = End-expired BrAC x 2000

The problems associated with "mouth-alcohol" and the possibility of stomach gases erupting into the mouth as well as the influence of arterio-venous differences in the concentration of alcohol were well recognized by Liljestrand and Linde (1930). This seminal work was continued by Rolla N. Harger and his collaborators who devoted much effort to getting breath-alcohol analysis accepted for use in traffic law enforcement as an indirect

way of measuring BAC (Harger et al, 1950b, 1956). During his long scientific career Harger became the main supporter and outspoken advocate of the use of breath-alcohol analysis as a test for intoxication (Harger, 1975).

Obviously, there cannot exist a universal fixed blood/breath ratio of ethanol which applies for all subjects under all conditions of testing. The values derived empirically show inter- and intra-individual variations depending on, among other things, the nature of the blood sample analyzed, whether from artery, vein, or capillary, and the technique of sampling breath before analysis, such as end-expiratory, mixed-expiratory, or rebreathed air. Furthermore, the precision, accuracy and specificity of the methods of analysis used to determine alcohol in blood and breath will contribute to the variations and the reported range of values of the ratios. It is pointless and misleading to compute apparent blood/breath ratios when the concentration of alcohol in the specimens is less than about 0.03 g% w/v. At these low BACs, relatively small absolute differences in concentration tend to enlarge the calculated ratio. The current use of a 2100:1 blood/breath ratio for law enforcement purposes can be considered a compromise that survives from the 1950s. Many recent blood/breath correlation studies appearing in the literature point to a partition ratio higher than 2100:1 and, indeed, 2300:1–2400:1 seems to give better agreement between post-absorptive venous blood and end-expiratory breath (Dubowski, 1985; Wright et al., 1975; Alobaidi et al., 1976; Dubowski and O'Neill, 1979; Emerson et al., 1980). The theoretical range of blood/breath ratios could be from 1800:1, corresponding to the blood/air ratio of alcohol at 37°C, to 2586:1, which represents the water/air partition coefficient at 34°C. This latter value might apply if alcohol in expired air equilibrates with watery mucus or saliva before the breath leaves the mouth. Table 6 presents capillary-blood/end-expired breath ratios of ethanol for healthy men and women when tested with two different breath-alcohol analyzers (Jones, 1989b). If venous blood had been used for analysis in these experiments, the corresponding post-absorptive blood/breath ratios would have averaged somewhat higher (Jones et al., 1989).

TABLE 6

Blood/breath ratios of ethanol determined in tests with healthy men and women after they drank a bolus dose of 0.8 g/kg body weight as pure ethanol diluted with tonic water 50:50. Capillary fingertip blood was analyzed in triplicate and end-expiratory air in duplicate. the mean BAC and BrAC results were then used to calculate apparent blood/breath ratios. Intoxilyzer 4011 is a single wavelength infra-red analyzer and Alcolmeter AE-D1 makes use of an electrochemical oxidation principle for analysis of ethanol (Jones, 1989b). N = number of blood-breath pairs. All values below BAC of 0.02 g/100 ml were omitted.

	Men			Women		
Breath-analyzer	N	Mean ± SD	Range	N	Mean ± SD	Range
Intoxilyzer 4011	97	2094 ± 243	1789–2922	86	2144 ± 217	1864–2683
Alcolmeter AE-D1	115	2148 ± 196	1669–2676	106	2174 ± 197	1621–2558

Physiological Variables Influencing Breath-Alcohol Measurement

A host of physiological factors must be considered when breath-alcohol instruments are used for clinical and legal purposes (Hlastala, 1985). Table 7 lists the main physiological sources of variation that might arise during practical use of breath-tests for intoxication. To a large extent these potential physiological errors can be minimized and therefore controlled for if standardized procedures are followed during the day-to-day routine use of breath-alcohol analyzers (Wilson, 1986). Moreover, some of the latest generation of evidential breath-testing instruments incorporate sensing devices that can monitor the changes in temperature, volume and concentration of alcohol in a subject's breath during a prolonged exhalation.

TABLE 7

List of physiological variables potentially important in connection with breath-alcohol measurement for legal purposes. Failure to adequately control these biological factors will contribute to the variations in the blood/breath alcohol relationship reported in the literature.

- Phase of ethanol metabolism
- Arterio-venous differences
- Source of blood analyzed; arterial, venous, capillary
- Blood hematology; hematocrit value, salt, fat, and protein content
- Intra-pulmonary gas pressure
- Ambient temperature and humidity
- Expired-breath temperature
- Breathing pattern; hypo- and hyper-ventilation
- Bronchopulmonary disease
- Presence of mouth alcohol
- Regurgitation of stomach fluids
- Phase of exhalation; end expiratory or top-lung air
- Breath specimen; rebreathed, end-expired, mixed expired
- Body temperature; hyperthermia–hypothermia

Blood Composition and Hematocrit

Whole blood is a complex fluid containing about 80% w/w water, small amounts of lipid (fats), glucose, proteins, urea, inorganic salts as well as a constellation of other substances in trace amounts (Lentner, 1982). The composition of whole blood varies from person to person and is exaggerated in various disease states. If a test tube containing whole blood is centrifuged at several thousand revolutions per minutes, the red cells or erythrocytes separate at the bottom of the tube and the clear liquid above them is the plasma fraction. The volume of packed cells in relation to the volume of whole blood is called the hematocrit value. The water content of plasma is 92% w/w, being greater than for red cells (68% w/w water). This means that a blood specimen with an abnormally low hematocrit value will have more water per unit volume than a blood with high hematocrit value. Healthy adult men have a mean hematocrit value of 46.2% (range 43.2–49.2) and healthy adult women a mean of 40.6% (range 35.8–45.4) (Lentner, 1982). For two individuals with the same concentration of alcohol in whole blood, the person with the higher hematocrit value will have a slightly higher concentration of alcohol in the water fraction of whole blood and likewise in the air phase (or breath) equilibrated with it. Accordingly, high hematocrit values (male blood) are associated with a lower blood/air ratio of ethanol when equilibrated in vitro (Jones, 1983a). It might therefore be argued, but has never been demonstrated experimentally, that a similar situation applies when breath-alcohol measurements are made for legal purposes. Two individuals with the same BAC might have different BrAC simply because of the different hematocrit values of blood and therefore total blood-water content. In practice, however, it seems that there are so many other physiological factors and biological variations inherent in the quantitative measurement of BrAC that this hematocrit effect is completely submerged (Jones, 1989b).

"Mouth-Alcohol" Effect

When breath-test results are intended for quantitative evidential purposes, the measurements must not be made less than 15–20 minutes after the subject has finished drinking. This time delay is necessary to allow for dispersion of high concentrations of alcohol mixed with saliva and mucous secretions in the mouth. The concentrations of alcohol in beer, wine, and spirits are hundreds of times greater than those in the blood and breath so there is a risk of contaminating expired air with beverage alcohol if tests are made too soon after the end of drinking (Bogen, 1927). This could invalidate results of evidential breath-tests and lead to false high readings. Controlled studies have shown that 20 minutes is ample time to eliminate the mouth-alcohol effect (Caddy et al., 1978). In one study the presence of dentures in the mouth did not prolong the wash-out time for

mouth alcohol (Begg et al., 1964). A simple way to control for the existence of a mouth-alcohol effect is always to make duplicate determinations on separate breaths 3–5 minutes apart (Dubowski and Essary, 1987). Immediately after drinking, the concentrations of alcohol in the saliva and mucus of the mouth drops rapidly in an exponential manner (Dubowski, 1975). If the individual assays of each duplicate determination show good agreement or if the second result is higher than the first, this speaks against the existence of significant mouth alcohol. But, if the first exhalation is significantly higher than the second by more than about 0.025 g/210 liters, a mouth alcohol effect might be present and further control tests should be made. Some of the latest state-of-the-art quantitative evidential breath analyzers are able to monitor the rate of change of breath-alcohol during a single exhalation. If the BrAC up-slope is above the pre-set tolerance limit, or rapidly declines after an initial rise, the instrument warns of a possible influence from mouth-alcohol or, otherwise, the breath-test is aborted.

Regurgitation or Vomiting of Stomach Fluid Contents

Two recent studies addressed the question of regurgitation of stomach contents into the mouth and the influence this might have on breath instrument readings (Denney and Williams, 1987; Penners and Bilzer, 1987). Although higher breath instrument response was obtained immediately after subjects regurgitated, this was a transient effect and the results returned to normal within a few minutes. The interval of time after drinking to the point when subjects regurgitate was an important variable to consider. The concentration of alcohol in the stomach decreases after drinking, owing to a possible dilution with stomach contents and through a continuous diffusion of alcohol into the blood. Any attempt to invalidate results of breath-alcohol analysis for legal purposes by alleged belching or burping immediately before supplying a sample of breath for analysis must be considered seriously. The breath-instrument operator should make careful observations of the subject and record any body movements or unusual behavior just prior to testing. Some people suffer from a complaint known as gastro-esophageal reflux and these individuals might spontaneously bring up stomach contents into the throat and mouth. Indeed, alcohol consumption itself might provoke this gastro-esophageal reflux action (Kaufman and Kaye, 1978). An alleged eruption of alcohol from the stomach into the mouth was documented in a successful defense challenge in a British DUI case (Duffus and Dunbar, 1984). It was reported and commented upon in the medical literature and the testimony from a consultant gastroenterologist got the suspect acquitted (Wright, 1984).

Arterio-Venous Differences in Concentration of Alcohol

The concentration of alcohol in different segments of the vascular system, such as the arterial, the venous, or the capillary circulation, are not the same and the magnitude of the difference depends to a large extent on the phase of ethanol metabolism when specimens of blood were obtained (Forney et al., 1964; Martin et al., 1984; Jones et al., 1989). During absorption of alcohol from the gut arterial BAC > capillary BAC > venous BAC, whereas during the post-absorptive phase this concentration gradient is reversed. This provides one explanation for the observed variability in blood-breath ratios of alcohol measured as a function of time after drinking (Jones, 1978). Because breath-alcohol concentrations mirror the concentration of alcohol in arterial blood in the lungs, systematic difference in the time course of arterial BAC and BrAC should be small or negligible regardless of the phase of metabolism when comparisons were made. The widely used 2100:1 blood/breath ratio of ethanol was originally established by analyzing end-expired breath and presumed post-absorptive venous or capillary blood. The practical importance of arterio-venous differences in situations when venous BAC is estimated from BrAC during the absorption state is often speculated upon by defense experts. Expired air gives a better indication of exposure of the brain to alcohol and therefore of the severity of alcohol-induced impairment compared with venous blood during rapid absorption of alcohol from the gut (Jones, 1988).

The distribution of alcohol into various segments of the vascular system, including expired air, was investigated in detail by Forney et al. (1964). They observed that venous BAC lagged behind arterial BAC during the absorption phase and was about equal at the plateau of the BAC curve when equilibrium of alcohol is reached in the total body water. Unfortunately, the experiments were terminated too soon after subjects finished drinking alcohol and it became generally accepted that during the post-absorptive state the concentration of alcohol was the same in all parts of the vascular system. This was not confirmed when venous and capillary BAC were measured at 15 minute intervals for the entire BAC time frame (Sedman et al., 1976b; Jones et al., 1989). The phenomenon of marked dependence of drug concentration on blood sampling site and the

implications this might have in pharmacokinetics and toxicology was recently the subject of a comprehensive review (Chiou, 1989a, b).

Most quantitative evidential breath-alcohol analyzers are calibrated to read directly in terms of BAC based on a 2100 breath to blood conversion factor. This makes it impossible to get perfect agreement between near simultaneous venous blood and breath alcohol concentrations throughout absorption, distribution and elimination stages of metabolism. The actual venous BAC and the values estimated indirectly by analysis of breath will show deviations depending on the phase of metabolism when samples were taken. During the absorption phase and around the peak BAC, breath analysis tends to overestimate venous BAC and the differences will depend on the actual blood/breath ratio for the person tested in comparison with the 2100 calibration factor and the magnitude of arterio-venous difference. The best agreement between blood- and breath-alcohol over the entire concentration-time frame would be expected if arterial blood were compared with BrAC. This assumes that the arterial-blood/breath ratio was calculated empirically and this result used to calibrate the breath analyzer to give direct readings in terms of presumed arterial BAC.

Several careful studies indicate that a blood-breath conversion factor of 2300 or 2400 is more appropriate to give unbiased estimates and closest agreement between post-absorptive venous BAC and end-expiratory breath in laboratory tests and in the field (Cobb and Dabbs, 1985). Accordingly, breath-test results obtained with an instrument calibrated with a 2300 conversion factor will tend to exaggerate differences during the absorption period if venous BAC and breath are compared. It therefore follows that the 2100 conversion factor, which is used extensively in the USA, works to the suspect's advantage (typically 9% less than venous BAC) if comparisons are made when subjects are post-absorptive. Furthermore, if comparisons are made during the rising portion of the BAC profile (absorption phase), the differences between venous BAC and breath-test results will be less for a 2100 conversion factor compared with 2300.

Drink-driving statutes rarely if ever specify the source of blood required for analysis. This suggests that arterial, venous or capillary (fingertip) blood suffice. But the concentrations of alcohol in these samples are not the same, as discussed above, and any future speculation about the most correct value of the blood/breath ratio should consider the source of blood being used for alcohol analysis.

Body Temperature and Breath Temperature

The temperature coefficient of ethanol solubility for solutions in water and biological media is 6.5% for each degree Celsius change in the equilibrium temperature (Harger et al., 1950a; Jones, 1983a). The temperature in the lungs and upper airway is therefore an important respiratory parameter influencing the measured breath-alcohol concentration. The temperature of breath as it leaves the mouth rises from about 33.3 to 34.4°C as the volume of breath exhaled rises from 500 to 4500 ml (Jones, 1982a). Dubowski and Essary (1985) made extensive measurements of expired air temperature for a large number of healthy male and female subjects. The results are given in Table 3. Mason and Dubowski (1974) suggest that breath-alcohol analyzers should be equipped with a fast-responding thermistor device and in this way monitor the temperature of expired breath and, if necessary, adjust the breath-alcohol reading to a constant temperature, such as 34°C, for all subjects. Factors that elevate body temperature such as a fever might be expected to cause a rise in breath temperature and therefore in the expired breath-alcohol concentration.

An in vivo study showed that the blood/expired-air ratio of alcohol increased on average by 5.7% per 1°C rise in breath temperature (Jones, 1983b). Fox and Hayward (1987) let volunteer subjects stand in cold water up to their necks and in this way lower the core body temperature. This brought about the expected lowering of BrAC. On leaving the water, the subject's BrAC increased again in parallel with normalization of core body temperature. A drop in core temperature works to the advantage of the suspect when breath test results are reported for legal purposes. The conclusion that Breathalyzer results were invalid in subjects with low body temperature was therefore disputed (Hodgson, 1988). Fox and Hayward (1989) also looked at the influence of hyperthermia on BrAC determined with a Breathalyzer 900. Subjects stood immersed in hot water up to their necks and their body temperature (mouth and rectum) was monitored before, during and after the immersion. Venous BAC and Breathalyzer results were compared during the experiment. Venous BAC profiles were unchanged by hot water immersion whereas the BrAC measurements were distorted and the concentration of alcohol in breath increased. These workers reported average increases in BrAC over BAC by 8.6% for each

degree Celsius increase in deep-core body temperature. These findings support the notion of making some kind of temperature control in connection with evidential breath testing and if necessary a correction to the results.

Temperature and Humidity of Ambient Air Breathed

The temperature and humidity of the ambient air a person breathes is an important consideration when quantitative evidential breath-alcohol measurements are made. The heating and cooling process within the airway during breathing are tightly linked with observed variations in breath-alcohol concentration. Whenever possible, breath-alcohol instruments used for evidential purposes should be placed in an air conditioned room maintained at constant temperature and humidity. I studied the influence of extreme change in the temperature and humidity of the inhaled air on the BrAC during exhalation (Jones, 1982b). On breathing cold-dry-air, cold-wet-air, warm-dry-air or warm-wet-air, the overall effect was a decrease in the concentration of alcohol in expired air by as much as 10%. This finding was attributed to cooling of the airway surfaces because of the evaporation of water needed to moisten the dry inhaled air. The expired alveolar air, which is initially at body temperature, therefore has to return heat and water to the mucus. The expired air on leaving the mouth is now cooled below its normal temperature and the alcohol concentration it contains is accordingly lowered. Breathing air saturated with moisture at higher temperatures than 37°C dilutes the mucous surfaces with excess water through condensation and this leads to a greater removal of alcohol from expired alveolar air when it moves back over the airway surfaces during exhalation. The mechanism of heat and water exchanges in the respiratory tract is a complex biophysical process (Walker et al., 1961). Somewhat similar effects on breath alcohol were noted when subjects held ice cold water in their mouths immediately before breath was provided for analysis (Gaylarde et al., 1987). This finding is probably related to a cooling of the mucous surfaces that equilibrate with expired alcohol during exhalation. The temperature of expired air at the point of analysis was unfortunately not reported in the study. However, a marked lowering can be predicted. In addition, some alcohol from the expired alveolar air might be removed by dissolving in the excess water present in the mouth.

Breathing Technique

The subject's manner and mode of breathing just prior to providing breath for analysis can significantly alter the concentration of alcohol in the resulting exhalation (Jones, 1982c; Schoknecht et al., 1989). The effect of hyperventilation, high frequency deep inhalations and exhalations of room air, immediately before blowing into the breath analyzer has now been well studied (Mulder and Neuteboom, 1987; Normann et al., 1988). This breathing maneuver lowers the breath-alcohol concentration by as much as 20% compared with a single moderate inhalation and forced exhalation used as control tests (Jones, 1982c). Holding the breath for a short time (20 seconds) before exhalation increases the alcohol concentration in exhaled air by 15%. The overall change in the concentration of alcohol from hyper- to hypoventilation can therefore be much greater than 20%. This might explain, at least in part, some of the large differences (>0.02 g% w/v BAC equivalent) between the results of duplicate determinations made within 2–3 minutes under field conditions. In Great Britain, for example, the statutory regulations for evidential breath testing permit use of the lowest of two separate breath-test results as the prosecution evidence (Walls and Brownlie, 1985). This has become common knowledge and has encouraged drunk drivers to hyperventilate intentionally in attempts to get as big a difference as possible between the two consecutive readings. The observed rise or fall in breath-alcohol can be partly attributed to the drop in expired-breath temperature induced by hyperventilation and concomitant altered interaction of alcohol at the airway surfaces (Jones, 1982c).

Pulmonary Disease

Diseases of the lungs will certainly influence the magnitude and variation of some of the respiratory parameters listed in Table 3. Obstructive pulmonary disease, for example, is associated with smaller vital capacity and forced expiratory volumes are also lower than normal values. Whether these pathological changes influence breath-alcohol concentration and the blood/breath ratio must be tested experimentally. Several studies have addressed this issue because of the high prevalence of chronic obstructive pulmonary disease among smokers who might also be heavy drinkers and therefore potential DUI suspects. If a person suffers from bronchopulmonary disease and this can be proved to influence his apparent blood/breath ratio of alcohol then this might conceivably influence the outcome of the DUI trial when results are translated into presumed BAC.

In one study, arterial BAC was compared with BrAC determined with a Breathalyzer 900 device (Haas and Morris, 1972). Twenty-four patients suffering from chronic bronchopulmonary disease were evaluated, but, unfortunately, there were no tests made with a control group of subjects with a normal lung function. The Breathalyzer results averaged 15% less than the arterial BAC measurements. It is a well known fact that this kind of breath-analyzer always reads low compared with near simultaneous measurements of venous BAC in part because of the 2100:1 blood/breath ratio used for calibration (Begg et al., 1964). The practical importance of pulmonary disease in accounting for this observed blood-breath alcohol difference is therefore hard to interpret. Another study (Russell and Jones, 1983) recorded breath-alcohol profiles during a single continuous exhalation in subjects with normal lung function and in those with obstructive pulmonary disease. There were differences in the alcohol-concentration expired volume profiles for the two groups of subjects, but, according to a correlation and regression analysis of the results, the blood-breath scatter diagrams were not significantly different. A third study (Wilson et al., 1987) attempted to establish a relationship between the age and a person's blood/breath ratio of alcohol for individuals with and without chronic pulmonary disease. The average blood/breath ratio was 3760 for subjects with lung disease and 3051 for an age-matched (65 y) control group. The reason for these high apparent ratios compared with the 2100:1 calibration value requires explanation. Indeed, for a group of younger healthy subjects (33 y) tested with the Breathalyzer 900 on a different occasion, the blood/breath ratios were on average much less, being 2283. There was a positive association between blood/breath ratio of alcohol and increasing age of the subject tested, although the data presented were not very convincing. The Breathalyzer results underestimated coexisting venous BAC for the individuals with pulmonary disease more than for the healthy control subjects. This discrepancy gives an advantage to the suspect and can be tolerated in forensic practice.

Concluding Remarks

Whatever else, the analysis of end-expiratory breath provides an excellent way to monitor the presence of gases and volatile substances circulating in the blood (Manolis, 1983). In the case of alcohol, even if the samples of breath analyzed come from the upper airway and therefore represent air residing in the dead-space region of the lungs, the concentration of alcohol is at least 65% of the concentration in end-expired alveolar air (Jones, 1982a). This observation is not generally recognized, but follows as a consequence of the high solubility of alcohol in the mucous surfaces of the mouth and upper airway. Some alcohol always tends to diffuse from the mucus into the dead-space air. As a screening test for alcohol influence even the worst possible technique of breath sampling gives a good indication of the alcohol load in the body. Thus, even a qualitative breath-alcohol test gives useful information to challenge or support clinical signs and symptoms of intoxication derived from the use of various field sobriety tests.

One drawback with the present use of breath-alcohol analyzers in law enforcement is that quality assurance and proficiency testing programs under operational conditions in the field are less well developed compared with methods of forensic blood-alcohol analysis. In law enforcement practice, quantitative evidential breath-analyzer units replace the technician at blood-alcohol laboratories. More research is therefore needed on the subject of analytical quality control and the day-to-day performance of breath-alcohol analyzers under field conditions. The recent introduction of computer networks and telephone modem communications linking individual breath-analyzer units to a central agency is a step in the right direction. It might prove a shrewd tactic to have the quality assurance tests and all necessary statistical evaluation supervised by scientists who are independent of the police department. Moreover, all the breath-test records should be stored on-line in the internal memory of the analyzer and this material periodically down-loaded by those experienced with principles of quality control. All stored information about the individual test results and the subject tested should be resistant to manipulation by unauthorized police personnel. These changes in breath testing procedures might help to reduce the frequency of litigation in DUI trials.

It is gratifying to note increasing use of duplicate determinations of BrAC as a mandatory requirement when breath-analyzers are used for evidential purposes (Cobb and Dabbs, 1985; Gullberg, 1988). But this makes it important to point out that the spread of the differences in concentration between duplicate readings, which is a measure of analytical precision, contains components of variation for both sampling of breath and the analysis of ethanol. By contrast, the differences between duplicate determinations of the concentration of alcohol in a specimen of blood sent to a forensic laboratory reflect only the analytical sources of variation unless, of course, two tubes are drawn a few minutes apart and aliquots taken for analysis from each tube

separately. This basic difference between BAC and BrAC measurements must be considered when precision, accuracy and reliability of breath-testing is compared and commented upon in the medicolegal literature.

As suggested by many workers, the concept of using a presumed blood/breath partition ratio should be abandoned and driving under the influence statutes should be written in terms of the concentration of alcohol present in the breath specimens analyzed (Mason and Dubowski, 1974). In addition to this, a wise move would be to make a deduction from the mean result of at least duplicate determinations on two separate breaths (Dubowski and Essary, 1987). The size of the subtraction term is open to discussion, but it must be calculated by conventional methods of statistics according to the size and structure of the random errors inherent in the techniques of breath analysis used. The allowance should include components for both the sampling breath-to-breath and the analytical errors inherent in the instrument. As a suggestion, if the deduction term is calculated so that the final prosecution result is not more than the true value with 99.9% confidence this gives the defendant an acceptable margin of safety. This high level of probability can be achieved by subtracting about 0.015 g/210 liters from the mean of a duplicate determination on separate breaths according to tests with some of the latest generation of quantitative evidential breath-analyzers. This leaves a 1 in 1000 chance that the prosecution figure is higher than the true value. But this will only have any relevance at concentrations of alcohol exactly at a critical legal limit. Nonetheless, if 99.9% probability is sufficient to meet the "beyond a reasonable doubt" standard normally demanded in criminal justice proceedings then I am confident that both the tested individual and society would develop a greater respect and understanding for the use of chemical tests of intoxication involving analysis of breath.

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