invited review

The alcohol breath test—a review

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Hlastala, Michael P. The alcohol breath test—a review. *J. Appl. Physiol.* 84(2): 401–408, 1998.—The alcohol breath test (ABT) is evaluated for variability in response to changes in physiological parameters. The ABT was originally developed in the 1950s, at a time when understanding of pulmonary physiology was quite limited. Over the past decade, physiological studies have shown that alcohol is exchanged entirely within the conducting airways via diffusion from the bronchial circulation. This is in sharp contrast to the old idea that alcohol exchanges in the alveoli in a manner similar to the lower solubility respiratory gases (O_2 and CO_2). The airway alcohol exchange process is diffusion (airway tissue) and perfusion (bronchial circulation) limited. The dynamics of airway alcohol exchange results in a positively sloped exhaled alveolar plateau that contributes to considerable breathing pattern-dependent variation in measured breath alcohol concentration measurements.

airway gas exchange; soluble-gas exchange; forensics; bronchial circulation; diffusion limitation

THE ALCOHOL BREATH TEST (ABT) has been an enigma since it was developed in the 1950s. It has been used for more than 40 years without a clear understanding of the physiological mechanisms involved. A large degree of variability in the measured breath alcohol concentration has led to considerable consternation about the ABT. Substantial effort has gone into justifying the use of the test without regard to the physiological mechanisms involved. Over the past 10 years, this understanding has advanced considerably with an infusion of physiological research related to soluble-gas exchange in the lungs. This review focuses primarily on these recent advances.

The first record of using the breath to estimate blood alcohol concentration (BAC) comes from Bogen (4) in 1927, followed closely by Liljestrand and Linde (35). Development of a practical device for measuring breath alcohol concentration (BrAC) did not occur until the 1950s, through the efforts of Harger et al. (22) and Borkenstein and Smith (5). At that time, it was generally understood that the initial volume of air exhaled from the lungs arose from the conducting airways and had little "alveolar air." Further exhalation would result in exhalation of air from the alveoli containing gas in equilibrium with pulmonary capillary blood. These concepts were derived from the respiratory physiology literature (14, 44) and followed from data obtained with low-solubility gases such as nitrogen.

Without present-day analytical equipment, the profile of exhaled alcohol could not be measured but was expected to be similar to that for nitrogen (after a single breath of oxygen) and to appear as shown in Fig. 1. The first part of the exhaled air, thought to come from the airways, was called the anatomic dead space (phase I). The later part of the exhaled air (with higher gas concentration) was thought to originate solely from the alveolar regions. This later part of the exhaled gas profile was termed "the alveolar plateau" (phase III) (14, 44). It was assumed that end-exhaled alcohol concentration would be independent of exhaled volume after exhalation beyond anatomic dead space volume. It was further assumed that alveolar alcohol concentration was in thermodynamic equilibrium with the arterial BAC and that this physicochemical relationship could be precisely described by the partition coefficient (23). The implicit assumption was that gas-phase alcohol concentration remained unchanged as alveolar air passed through the airways. Viewed through the limited perspective of respiratory physiology of the 1940s, the breath alcohol test seemed to be a reasonable method, in principle, and further development as a noninvasive measure of BAC was justifiable. There is no evidence that any respiratory physiologist had considered the pulmonary exchange of alcohol before Wright et al. (60) in 1975. Their study first identified the possibility of airway alcohol exchange.

Partition Ratio

In the early forensic literature, the partition ratio [PR; equivalent to blood-gas partition coefficient (λ) of ethyl alcohol (EtOH) (λ_{EtOH}) in the physiological litera-

ture] was a common term used to describe the ratio between BAC and BrAC. In recent years, the term "blood-breath ratio" (BBR) has been used to represent the ratio of alcohol concentration in the blood to that in the exhaled breath to avoid any reference to any equilibrium process

$$\text{BrAC} = \frac{\text{BAC}}{\text{BBR}} \qquad (1)$$

After scrutiny of blood-breath correlation data, the PR has been assumed to have an average value of 2,100, and that value has been used for calibration of breath-testing instruments. Some studies (3, 7, 10, 11) found that the average BBR varied between 2,200 and 2,300, resulting in lower average breath readings when a breath-testing instrument calibrated at 2,100 was used. The variability in reported values of BBR in individual subjects is large, with values ranging from ~830 (7) to 9,000 (3). Even recent measurements (33) using modern technology demonstrate a surprisingly large variation with a value of 2,407 ± 213 (SD), with a 95% range of variation between 1,981 and 2,833. This variability of approximately ±20% is a serious concern for ABT readings that are close to the legal limit for driving (a standard that varies from state to state). It is interesting that this variability is not different from a report by Jones (27) 20 years earlier. Little has been done to modify and improve the accuracy of the single-breath ABT.

The term "partition ratio" was incorrectly used when applied to the ABT. The PR (or partition coefficient) defines the distribution at equilibrium of a substance (such as alcohol) between two media (such as blood and air). This distribution depends on temperature (23). It is a physicochemical property of the gas (i.e., alcohol) and the liquid (i.e., blood) at thermodynamic equilibrium of the two phases involved at the interface between the two materials. If the alcohol concentration is altered in any way in either the air or the blood as they are being sampled or analyzed, then the term "partition" cannot be applied. In fact, the true blood-air partition coefficient is 1,756 when measured in vitro (31) at 37°C, >16% smaller than when it is measured by using an exhaled air sample and a blood sample drawn at the same time (36). The thermodynamic aspects of the ABT have been reviewed recently by Thompson (56).

A major complicating factor is the observation that BrAC changes during exhalation (1, 30, 39, 46, 53, 60). The alcohol concentration in the exhaled air at the mouth is lower than it is in alveolar air when measured by rebreathing (see below) (32, 39). Equilibration between breath and blood is never achieved after the breath has departed from the alveolar spaces in the lungs.

Exhaled Alcohol Profile

The BrAC increases as a subject exhales at a constant flow rate. An example of a series of profiles on one subject is shown in Fig. 2. In each of the profiles, the

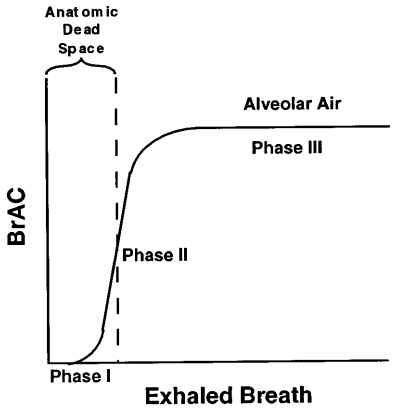

Fig. 1. Assumed exhaled alcohol profile. BrAC, breath alcohol concentration.

BrAC increases continuously as the subject exhales. The phase I and part of phase II is air coming from the dead space (volume between subject's mouth and infrared chamber) of the breath-testing apparatus. As soon as the air from the oropharynx reaches the infrared chamber, BrAC rises in the phase II. Phase I is much smaller for alcohol than it is for nitrogen because of the airway alcohol exchange. Phase II is mixed air coming from both the dead space and the alveoli after some airway alcohol exchange. Most of the breath coming from the alveolar region and passing through the airways shows a gradual (almost linear) rise in BrAC as the subject continues to exhale.

The achievement of a flat slope, or constant BrAC, during exhalation has been presented by breath-test instrument manufacturers and is believed by forensic scientists to be an argument that alveolar air, with its alveolar alcohol concentration, is obtained at the end of an exhalation. However, the notion that a flat slope will always be obtained when expiratory flow rate approaches zero and that this represents alveolar air is incorrect. Figure 3 illustrates a schematic example of exhaled breath alcohol profiles for a normal subject with three different exhalation times. At the end of exhalation, BrAC levels off when flow decreases, irrespective of the exhaled volume. The flat slope does not indicate the presence of air at alveolar concentration

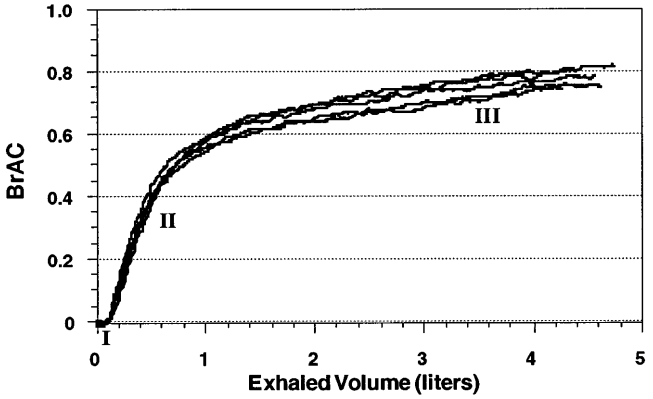

Fig. 2. Exhaled breath alcohol profile in a human subject. Modified from George et al. (17).

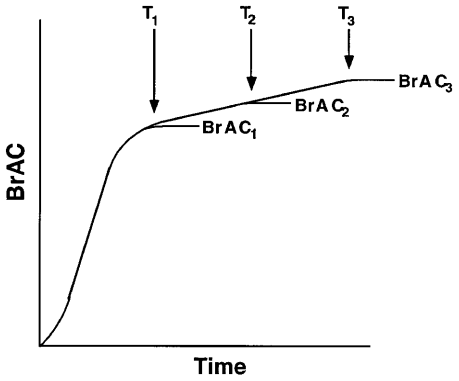

Fig. 3. Actual exhaled alcohol profile. Vertical arrows show 3 separate end-exhalation times (T_1-T_3) with 3 different end-exhalation BrAC values, each with same blood alcohol concentration.

because BrAC is an increasing function with exhaled breath volume.

Sloping Alveolar Plateau

A sloping alveolar plateau is certainly not unique for alcohol. The phase III slope for various low-solubility gases (i.e., N_2) has been explained by several factors, including stratified inhomogeneity (gas phase diffusion limitation) (49), convection-diffusion interaction (41), sequential exhalation from regions with differing ventilation-perfusion ratios ($\dot{V}_A/\dot{Q}$) (49), and continuing gas exchange (20). None of these factors contributes substantially to the slope of the exhaled alcohol profile. Continuing gas exchange will contribute to the slope of the exhaled profile for respiratory gases (CO_2 and O_2) but only slightly for inert gases (20, 25).

According to classic gas-exchange theory (12), the alveolar partial pressure of gas (P_A), normalized to the mixed venous partial pressure ($P\bar{v}$), is related to the blood-gas partition coefficient (λ) and the $\dot{V}_A/\dot{Q}$ of the region

$$\frac{P_A}{P\bar{v}} = \frac{\lambda}{\lambda + \frac{\dot{V}_A}{\dot{Q}}} \qquad (2)$$

For a normal lung with $\dot{V}_A/\dot{Q}$ ratio ranging between 0.1 and 10 (15), $P_A/P\bar{v}$ will range between 0.99433 and 0.99994 for alcohol with a λ_{EtOH} = 1,756 (certainly indistinguishable from one another). Thus sequential emptying can have no contribution for alcohol because the P_A for alcohol will be nearly identical in all alveolar regions of a normal lung. Gas-phase diffusion limitation has little effect on respiratory gas (O_2 and CO_2) exchange (45), particularly for a low-molecular-weight gas like ethyl alcohol (mol wt = 46). Convection-diffusion interaction (41) is an interaction causing a sloping exhaled plateau that is dependent on specific gas physical properties. This occurs in the terminal bronchioles and cannot explain the slope because of alveolar alcohol partial pressure uniformity in regions with differing V_A-to-volume ratio. In addition, convection-diffusion interaction would not be affected by temperature-related factors, which are known to influence the BrAC (18, 28, 31, 32).

Further variation in BrAC can result from changes in the breathing pattern immediately before delivering the sample breath (18, 29, 38, 39). Hyperventilation for 20 s before performing the ABT causes an 11% reduction in BrAC (29). Three deep breaths before the sample breath reduce BrAC by 4% (18). After breath holding for 15 s before exhalation, the BrAC increases by 12% (for a minimum exhalation) and 6% (for a maximum exhalation) (39). A 30-s breath hold before exhalation increases BrAC by 16% (29). These effects are caused by altering the ventilation (hyper- or hypoventilation) passing over the airway mucosa. Such data support the theory of airway surface interaction of alcohol as the mechanism causing BrAC to change during exhalation.

Rebreathing

Rebreathing has been used to obtain equilibrated alveolar gas samples, as it overcomes problems associated with heterogeneity of exhaled gas concentration from regions with differing $\dot{V}_A/\dot{Q}$ (50). After breathing in and out of a bag for several breaths, the air within the lung and bag system eventually reaches an equilibrium. In the case of alcohol, this would occur after several breaths as the air passes back and forth over the airways, warming the airways to body temperature and equilibrating the airways with the alveoli. After equilibration, the bag-air alcohol concentration should be equal to alveolar air alcohol concentration. However, complete equilibration may not be achieved after a rebreathing maneuver because the rebreathing must be of limited duration (~30 s or less) to obviate the risk of hypoxia. The rebreathing approach has also been used to measure cardiac output because it allows monitoring of alveolar gas concentrations at the mouth of gases such as acetylene or freon-22 ($\lambda \sim 1.0$), which are taken up by blood perfusing the alveoli but not soluble enough to interact significantly with the airways (47). Rebreathing of poorly soluble inert gases (i.e., helium, argon, sulfur hexafluoride) has been used to measure residual volume by dilution. Poorly soluble gases are only minimally taken up by blood or by airway tissue and, thus, mix only in the lung gas.

Early studies with BAC assessment using rebreathing met with limited success (13, 21, 42, 52) because of the use of room-temperature bags. Condensation caused by cooling of the rebreathed air lowered alcohol concentration within the gas phase of the bag. Later studies have used heated rebreathing bags to decrease the influence of temperature and humidity disequilibrium and assist in prevention of airway condensation and subsequent alcohol loss (30, 39). In a test of a heated rebreathing bag, Jones (32) found higher BrAC after rebreathing [BBR = 1,947 ± 110 (SD)] compared with measurements after a single exhalation (BBR = 2,225 ± 111). Ohlsson et al. (39) found BrAC after rebreathing of 2,019 ± 121 compared with single-exhalation BBR of 2,333 ± 163. Because rebreathing produces a breath sample that is closer to the true

mixed alveolar air, the findings of Jones (32) and Ohlsson et al. (39) suggest that alveolar BrAC is greater than end-exhalation BrAC and that there is a normal loss of alcohol to the airway surface during exhalation. Hence, end-exhalation BrAC should be lower than alveolar alcohol concentration.

These rebreathing data are important because they argue strongly against the often-stated idea that the BBR of alcohol in human lungs is 2,100. If the 2,100 ratio were true and correct, then it would be impossible to get an experimental BBR, even with rebreathing, that is lower than 2,100. According to Jones (31) the λ for alcohol (measured in vitro) at 37°C (average core body temperature) is 1,756. It would, therefore, be expected that a rebreathing BBR should be closer to 1,756. The rebreathing BBR of 1,947 obtained by Jones is closer to the theoretical values of 1,756 than the data (rebreathing BBR = 2,019) of Ohlsson et al. (39). The difference may be due to technique and/or a lack of complete equilibrium. Ohlsson et al.'s subjects rebreathed into a heated bag for seven breaths. The sample was then taken from the bag. In Jones' case (31), after rebreathing, subjects held their breath after an inspiration and then exhaled into a breath-testing instruments. The additional breathhold may have resulted in further increase of rebreathed BrAC. Another possible explanation for the difference between the studies may relate to differences in the calibration of the breath-testing instruments used.

Another explanation pertains to the peculiarities of the microvasculature in the alveolar region. The in vivo equilibration partition coefficient for alcohol in blood may not be identical to the in vitro whole blood value. The hematocrit of blood in the microcirculation has been shown to be lower than that in the central circulation because of the Fahraeus effect (61). In experimental measurements using positron emission tomography in humans, Brudin et al. (6) have shown not only that the local hematocrit in human lungs is 80–86% of the bulk hematocrit but also that there is a heterogeneity to the distribution of hematocrit in the lungs. In dogs, Presson et al. (43) and Lee et al. (34) have found the pulmonary capillary hematocrit to be ~80% of the bulk hematocrit. Overholser et al. (40) found a ratio of 0.92. Because the solubility of alcohol is greater in plasma than in erythrocytes (31), any decrease in hematocrit in the pulmonary capillaries would cause an increase in λ_{EtOH}. For a normal human bulk hematocrit of 0.45, the corresponding pulmonary hematocrit would be 0.36 (at 80%). When Jones' (31) data showing a whole blood λ_{EtOH} of 1,756 and a plasma λ_{EtOH} of 2,022 are used, the equivalent λ_{EtOH} for blood at 37°C and a hematocrit of 0.36 would be 1,801. The rebreathing data of Ohlsson et al. (39) and Jones (31) are consistent with this hypothesis, showing a rebreathing BBR that is lower than the prolonged single-exhalation value but not as low as the theoretical rebreathing BBR of 1,756. A reduction in pulmonary capillary hematocrit could increase the measured rebreathing BBR to a value greater than the theoretical rebreathing BBR.

Physiological data from the past two decades reveal several observations that are inconsistent with the old model for alcohol exchange demonstrated in Fig. 1. *1*) The BrAC increases with increasing exhaled lung volume; *2*) a flat slope at the end of exhalation does not indicate gas at alveolar concentration; *3*) isothermal rebreathing yields a BrAC higher than a maximum-exhalation BrAC; *4*) BrAC depends on pretest breathing pattern; *5*) some measurements show a BBR <2,100. All of these observations are contrary to the old idea that BrAC is equivalent to alveolar concentration.

Mechanism of Alcohol Exchange by the Lungs

The airways play an important role in the processing of inspired air. During inspiration, air is heated and humidified as it passes through the upper airways (37, 58). Some water within the mucous layer or watery submucous layer will vaporize and heat stored in the airways will be absorbed by the inspired gas (26, 48, 58). During exhalation, the process reverses; fully humidified air at core body temperature is cooled by the airway mucosa, and water vapor condenses on the mucosa. Under normal environmental conditions, exhaled gas has less heat and water than does alveolar air.

The dynamics of soluble-gas exchange are similar to the dynamics of heat and water exchange. The fact that respired air exchanges heat and water with the airways implies similar soluble-gas exchange processes (24). This interaction of soluble gases with airway mucosa is well documented (2, 8, 9, 51). The degree of interaction is directly related to the solubility of the gas in the airways mucosa and mucous lining (2, 51). For alcohol, the first identification of the possibility of airway alcohol exchange was by Wright et al. (60). The very high solubility of alcohol in water implies a strong interaction with airway tissue. Because this interaction depends on temperature and airflow characteristics, variations in tidal volume and frequency can have a substantial effect on the alcohol concentration in the breath sample (29, 57). This variation is affected by the difference in temperature between the outside air and the alveolar air (18, 28).

A schematic illustrating the exchange of gases of varying solubility is shown in Fig. 4. Low- and intermediate-solubility gases with λ <300 exchange primarily in the alveoli. Gases with λ >3 participate in airway gas exchange. Gases with λ >1,000 exchange entirely within the conducting airways.

The above physiological information and data from the literature can be used to formulate a working hypothesis for alcohol exchange by the lungs. As the breath is exhaled, it cools down slightly, and alcohol desorbs from the airstream to the surface of the airways. During the initial phase of exhalation, the airway concentration of alcohol in the mucosa is low, having contributed alcohol to the air during the previous inhalation. Hence, alcohol is desorbed from the airstream, and the amount of alcohol in the breath as it leaves the mouth is lower than it was in the alveolar air. As the later part of the exhaled volume passes

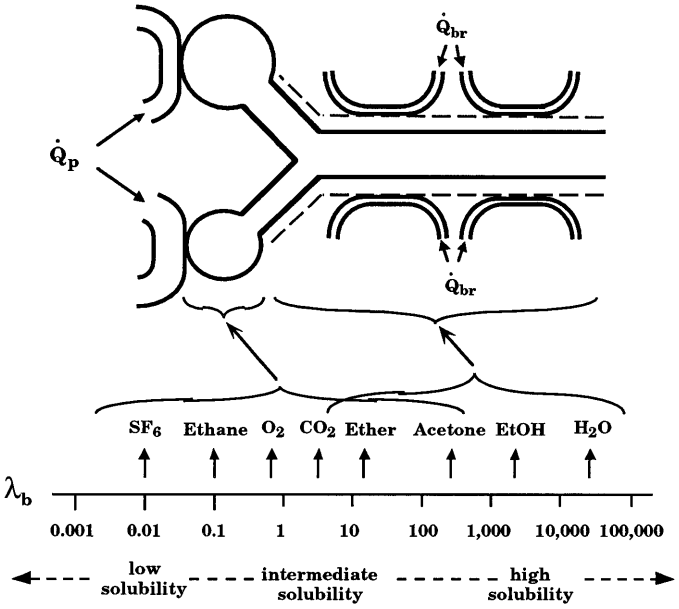

Fig. 4. Schematic diagram of lung demonstrating location of gas exchange for gases of varying blood-gas partition coefficient (λ_b). Airways are shown with surrounding airway tissue and bronchial circulation. Pulmonary perfusion ($\dot{Q}_p$) to alveoli is also shown. $\dot{Q}_{br}$, bronchial blood flow; SF_6, sulfur hexafluoride; EtOH, ethyl alcohol.

through the airways, less alcohol is desorbed to the airways because some alcohol has already been desorbed from the earlier part of the breath. In addition, the temperature of the mucosa near the mouth increases during exhalation as it is warmed by the warmer exhaled air. The increased temperature decreases mucosal alcohol solubility, decreasing the tendency toward alcohol deposition later in the exhalation. The later part of the breath coming from the mouth has a higher alcohol concentration, but it is not the same as the alveolar air. If a sample of alveolar air is taken (impossible when using a single breath but possible with rebreathing), the measured BBR should be equal to the in vivo PR for alcohol in pulmonary capillary blood at 37°C. If a sample of air is taken from the earlier part of the breath (the subject only exhales approximately one-third of the vital capacity), then the breath alcohol will be lower than average, and the measured BBR would be higher than 2,100 (~2,500 in the early breath example shown in Fig. 5). If a sample of air is taken from the later part of the breath (the subject exhales the entire amount possible), then breath alcohol sample will be higher than the average breath alcohol, and the measured BBR would be lower. Depending on the conditions, the alcohol concentration could be high enough to result in a BBR <2,100 (~1,900 in the later breath sample shown in Fig. 5).

Airway Alcohol Exchange

The exchange of heat and of gas with the airways is a complex and interactive process. The relative significance of this exchange depends on the effective solubility of the gas in the mucosa. For the respiratory gases, oxygen and carbon dioxide, airway tissue solubility is small. For both water and alcohol, airway solubility is quite large. Moreover, the exchange processes are interactive (24). During inspiration, heat, water, and alcohol are transported from the mucosa to the air. The exchange of heat cools the mucosa, causing an increase in its alcohol solubility and, hence, a decrease in the partial pressure of alcohol in the mucosa and a reduction in alcohol flux into the airway lumen. These various processes have been integrated into a mathematical model developed by Tsu et al. (57) and further refined by George et al. (17), which has been used to evaluate the dynamics of airway alcohol exchange. The model provides an explanation of the unusual behavior of alcohol exchange in the lungs. The model was based on physiological, physical, and engineering principles and is used to predict the observations of alcohol exchange within the framework of airway alcohol exchange with the bronchial circulation.

The basis of the model (19) is demonstrated schematically in Fig. 6. Each control volume represents portions of the human airway tree. The volume is arranged into four regions: capillary sheet, nonperfused tissue, mucus, and airway lumen. The control volumes are arranged in series starting with nasopharynx and ending with the respiratory bronchioles. Evaluation of airway gas exchange for gases of varying blood solubility demonstrates a significant role for perfusion (bronchial blood flow) and diffusion (across the airway tissue)

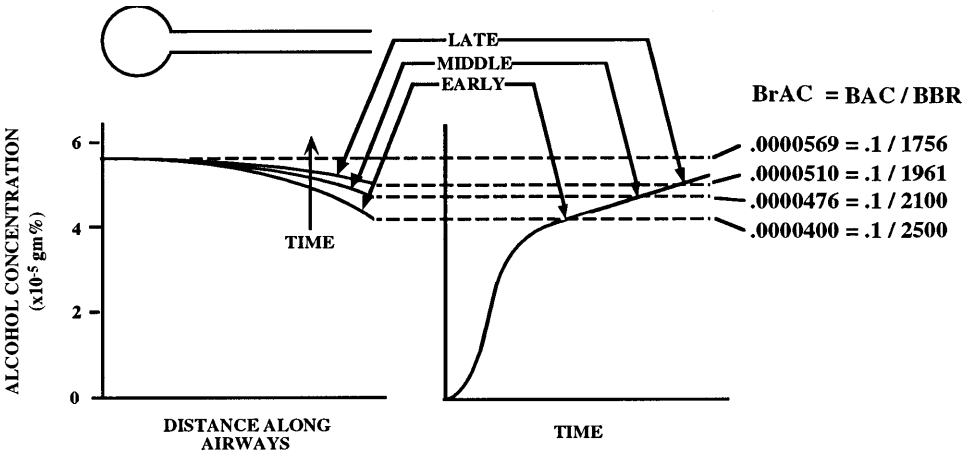

Fig. 5. On *left*, alcohol concentration along airways during exhalation for early, middle, and late breath samples. On *right*, exhaled alcohol profile as breath is exhaled from the mouth. Increase in exhaled volume beyond minimum required by breath-test instrument (usually 4–6 s) results in an increased BrAC and decreased blood-breath ratio (BBR). BAC, blood alcohol concentration.

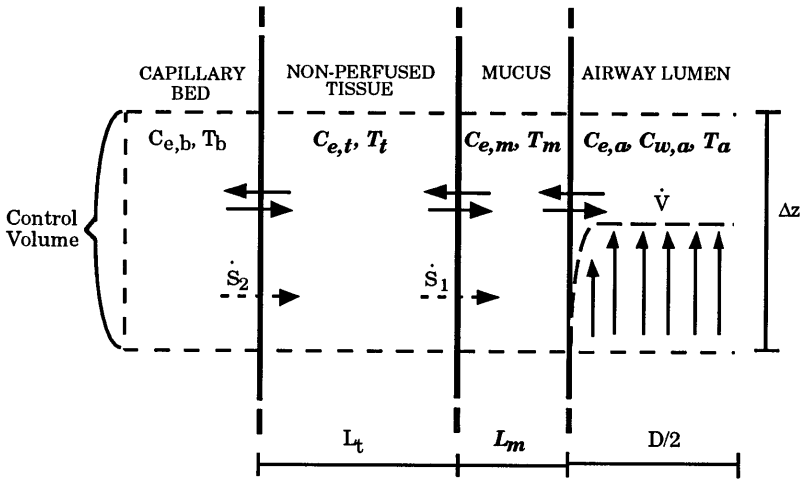

Fig. 6. Control volume for mathematical model of airway alcohol exchange. $C_{e,b}$, concentration of alcohol in blood; $C_{e,t}$, concentration of alcohol in tissue; $C_{e,m}$, concentration of alcohol in mucus; $C_{e,a}$, concentration of alcohol in air; $C_{w,a}$, concentration of water in air; T_b, temperature of blood; T_t, temperature of tissue; T_m, temperature of mucus; T_a, temperature of air; $\dot{S}$, flux; L_t, thickness of tissue layer; L_m, thickness of mucus layer; D, diameter; $\dot{V}$, flow rate of air; Δz, change in axial distance into the airway from the mouth. [From George et al. (18).]

limitation (54, 55). Ventilation limitation becomes important for higher solubility gases such as acetone or alcohol.

Alcohol flux across the tracheal mucosa strip has been measured directly by George et al. (16). An Ussing-type chamber was used to measure directly the flux of alcohol in the presence or absence of the epithelial tight junction. The diffusivity of EtOH through the airway tissue was found to be 34% that of water. EtOH diffusivity increased by 11.7% after opening the epithelial tight junction. The diffusion limitation for alcohol between the bronchial capillaries and respired air is the major cause of the positively sloped phase III of the exhaled alcohol profile (see Fig. 2).

It is not possible to measure directly the alcohol flux at each airway generation. Hence, the model was used to predict the airway flux during both inspiration and expiration. Figure 7 shows model-predicted alcohol flux values. During inspiration, the alcohol absorption (positive flux) from the mucosa is greatest for the mouth, trachea, and airway *generations 6* through *12*. By the time inspired air reaches the seventeenth generation, airstream absorption of alcohol reaches zero, indicating local equilibrium with blood alcohol. On exhalation, alcohol is desorbed (negative flux) to the airway mucosa, particularly in *generations 10–6* and in the trachea. Thus pulmonary alcohol exchange takes place entirely within the oropharynx and conducting airways.

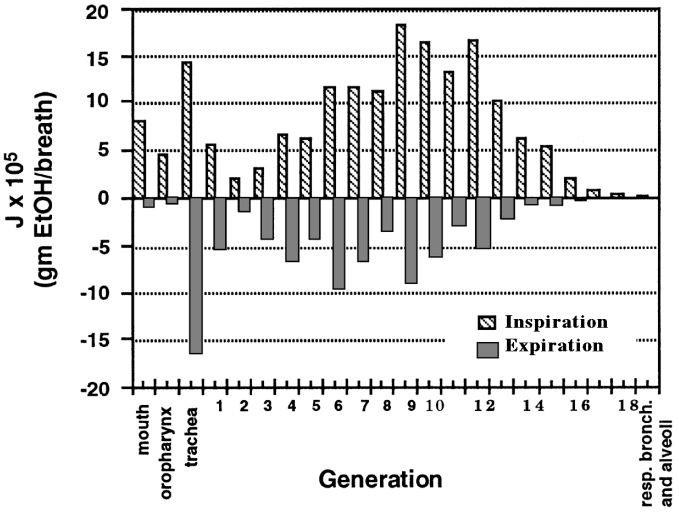

Fig. 7. Calculated alcohol flux vs. airway generation. Both inspiration and expiration are shown. Resp, respiration; bronch, bronchia. [From George et al. (18).]

The conclusions of the above studies are that alcohol excretion by the lungs is via diffusion from the bronchial circulation through the airway tissue, where it is absorbed by the inspired air. By the time air reaches the alveoli, the airstream is in equilibrium with airway tissue and BAC. Therefore, no additional alcohol can be absorbed or desorbed in the alveoli. During inhalation, the alcohol absorbed by the air from the mucosa is partially replaced by alcohol diffusing from the bronchial capillaries (16, 24). On exhalation, some of the alcohol is desorbed back to the airway surfaces. All of the alcohol exhaled at the mouth comes from the airway surface via the bronchial circulation. No exhaled alcohol originates from the pulmonary circulation in the alveoli. The fact that alcohol is derived from the airways explains why the BrAC can be so easily altered by the breathing pattern. This contributes to the very large variation in the ABT readings obtained from actual subjects.

Implications for the ABT

For years, forensic scientists have struggled to explain the variability in BrAC. The problem followed directly from the tenaciously held belief that the last part of the exhaled BrAC was equal to the alveolar alcohol concentration. Recent experimental and theoretical studies dealing with the gas exchange of highly soluble gases have led to a new model for pulmonary alcohol exchange. This new model is based on the airway exchange of alcohol and can be used to explain the large observed variability in BrAC.

The theory of the ABT is old and outdated. In principle, the ABT, as currently used, is based on the respiratory physiology of the 1940s and 1950s. The physiological understanding of pulmonary alcohol exchange has gone through a tremendous evolution in the

past 50 years, revealing that physiological variability has a great impact on the ABT. It is now clear that most of the variability is due to physiological parameters that may change from one ABT to the next. Recognition that alcohol exchanges in the airways, rather than the alveoli, opens up the ABT for a new wave of research to improve the accuracy of BrAC measurement.

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