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PAPER

TOXICOLOGY

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Paradigm Shift for the Alcohol Breath Test

ABSTRACT: The alcohol breath test (ABT) has been used for quantification of ethyl alcohol in individuals suspected of driving under the influence for more than 50 years. In this time, there has been little change in the concepts underlying this single breath test. The old model, which assumes that end-exhaled breath alcohol concentration is closely related to alveolar air alcohol concentration, is no longer acceptable. This paper reviews experimental research and mathematical modeling which has evaluated the pulmonary exchange processes for ethyl alcohol. Studies have shown that alcohol exchanges dynamically with the airway tissue both during inspiration and expiration. The airway tissue interaction makes it impossible to deliver air with alveolar alcohol concentration to the mouth. It is concluded that the ABT is dependent on physiological factors that need to be assessed for accurate testing.

KEYWORDS: forensic science, respiratory physiology, airway alcohol exchange, breath alcohol concentration, scientific evolution, airway mucus

Over the years, breath test has become a widely used method for quantitative determination of the level of intoxication of individuals suspected of driving under the influence of alcohol. After recognition of the need for quantitative assessment of intoxication, blood alcohol concentration (BAC) was considered as the single most important variable. However, concern about the invasiveness requirements of drawing a blood sample led to the development of the breath test as a noninvasive means of assessing level of intoxication. The breath test is an indirect test, but has been considered to be a good estimate of the BAC because of the assumption that an end-exhaled breath sample accurately reflects the alveolar (or deep lung) air alcohol concentration which is thought to be in equilibrium with the blood in the pulmonary circulation. In spite of the considerable effort that has gone into the studies attempting to validate the breath test, forensic scientists and toxicologists still have only a very basic understanding of the physiological aspects of the alcohol breath test (ABT) and associated limitations.

Anatomy of the Lungs

The primary function of the lungs is to provide a means for exchanging respiratory gases (oxygen and carbon dioxide) between the blood and the outside environment. This organ allows inspired air to come into proximity with the blood so gases (such as oxygen, carbon dioxide, and ethyl alcohol) can exchange between the air and the blood. The lungs are made up of over 300 million small air sacs called alveoli. Outside air comes to the alveolus from the mouth or nose via the airways. The major airway leading to the lungs from the throat is the trachea. The trachea divides into the left and right "main-stem bronchi" (going to the left and right lungs) which divide further into the "lobar bronchi." This division goes on about 20 times until the alveoli are reached. Actually, some alveoli begin to appear at about the 17th generation airways. Surrounding each alveolus are small blood vessels. The thinness (<0.001 mm) of the membrane separating blood from the air in the lungs allows oxygen and carbon dioxide to exchange readily between the blood and air. Because of the large number of very small alveoli, there is a very large surface area (70 m^2) for this gas exchange process. For more details regarding the basics of lung physiology, see Weibel (1), Hlastala and Berger (2), or any other modern textbook of Respiratory Physiology.

Scientific Evolution

The evolution of scientific understanding depends on the continuous development of new ideas that form the bases for experimentation. This concept has been termed "scientific revolution" (but I prefer the term "evolution") by Kuhn (3), who sees science as the shift from one paradigm to the next. The term, "paradigm" refers to a set of universally recognized scientific achievements that for a time provide a model or conceptual framework for a phenomenon. This paradigm represents the core principles that define the scientific understanding.

A paradigm is established after a number of initial observations are obtained. Experiments are then carried out to test hypotheses related to the paradigm. Usually, these experiments provide data that reinforce the paradigm. Occasionally, these experiments result in anomalies, or results that do not fit within the framework of the original paradigm, and are inconsistent with the predictions of the paradigm.

The accumulation of anomalies leads scientists to develop a new paradigm that provides a new framework for interpreting experimental results that account for the anomalies of the old paradigm as well as new observations. At that point, the new paradigm undergoes scrutiny through newly suggested experiments that provide data to reinforce the new paradigm. The new paradigm must account for the new observations as well as the prior observations. The transition from the old paradigm anomalies to the new paradigm always encounters enormous resistance to change. This resistance is crucial for this scientific progress to occur.

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Eventually, it is likely that another set of anomalies with the new paradigm will lead to yet a third paradigm. This will occur as new technologies reveal new anomalies. These same ideas apply to different fields in very different scales. The concept of the paradigm can also be applied to the ABT.

The Old Paradigm

The first proposal of the single exhalation breath test for alcohol was by Antsie (4). Later development of the breath test for alcohol (5,6) took place in the early 1950s when the field of respiratory physiology was just beginning. At that time, it was generally understood that the first air exhaled from the lungs contained air from the airways and had little "alveolar air." It was thought that further exhalation would result in exhalation of air from the alveoli containing gas in equilibrium with pulmonary capillary blood (Fig. 1). These concepts were held in the respiratory physiology community (7,8) and followed from data obtained with low solubility gases, such as nitrogen. Without the advantage of having present-day analytical equipment, the profile of exhaled alcohol could not be measured in those early days, but was expected to be identical to nitrogen (after a single breath of oxygen) and to appear as shown in Fig. 2. The first part of the exhaled air was thought to come from the airways and was called the anatomic dead space and the later part of the exhaled air (with higher gas concentration) was thought to come from the alveolar regions. This later part of the exhaled gas profile was termed the alveolar plateau (7,8). With a presumed flat exhaled alcohol profile, it was thought 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 precisely related to the arterial BAC by virtue of the physical–chemical relationship known as the partition coefficient (9). The implicit assumption was that the 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 reasonable in principle and further development as a noninvasive measure of BAC was justifiable. So it was reasoned that one could measure the end-exhaled alcohol concentration and correct breath concentration to BAC using a constant term the partition coefficient.

Anomalies

Since 1950, many studies have been performed to quantify the relationship between breath alcohol concentration (BrAC) and BAC with the goal of defining a precise relationship between the two for accurate noninvasive determination of BAC. These studies, undertaken to validate the use of breath tests by comparing BrAC and BAC in normal subjects, have shown a surprising amount of variability (10,11) which has not been improved (12,13) in spite of advances in instrument technology. The physiology of lungs and of the body as a whole remains as the primary explanation for this variability (14,15).

The ABT is a single exhalation maneuver. The subject is asked to inhale (preferably a full inhalation to total lung capacity) and then exhale (preferably a full exhalation to residual volume) into the breath test instrument. Very few restrictions (i.e., exhaled volume, exhaled flow rate, inhaled volume, pretest breathing pattern, air temperature, etc.) are placed on the breathing maneuver. The constraints applied vary among the different breath test instruments and among the operators administering the test, and the level of cooperation varies among subjects, resulting in substantial uncontrolled variation in the precise maneuver used for the breath test (16). This finding is inconsistent with the old paradigm.

The lungs have a relatively simple, but nonuniform, anatomical structure. The airways are a branching, tree-like arrangement of tubes. Inspired air moves through progressively shorter, narrower, and more numerous airways (1). These airways are lined with mucus at a temperature varying between 34°C at the mouth and 37°C in the very smallest airways. However, this temperature range varies depending on the breathing pattern (17). Tissue membranes separate the air in the alveoli and the blood in the capillary walls are so thin that low molecular weight volatiles such as alcohol equilibrate between blood and air very rapidly (18). With exhalation, air within the alveoli is conducted along the airways to the mouth.

During inspiration, air is heated and humidified as it passes through the upper airways (17,19). Some water within the mucous

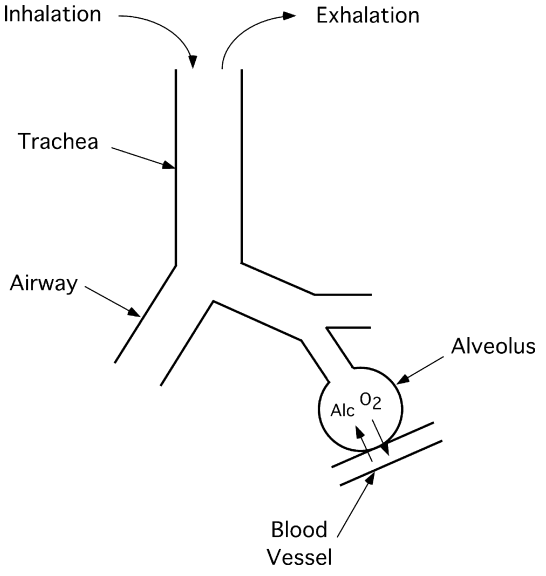

FIG. 1—*Schematic of old paradigm of alcohol exchange in the lungs. All alcohol exchange occurs in the alveolus with no exchange in the airways.*

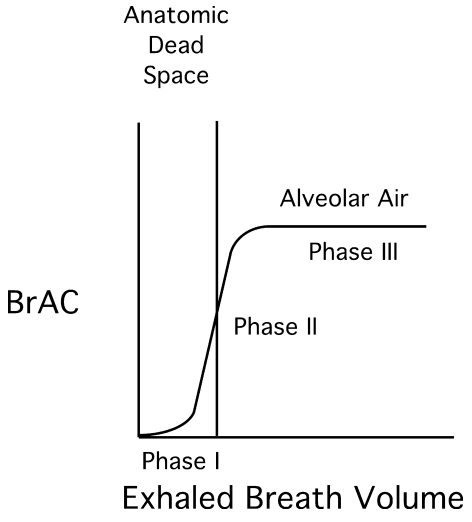

FIG. 2—*Assumed exhaled alcohol profile in the 1950s. BrAC remains constant after exhalation of minimum volume. It was not possible to measure exhaled BrAC profiles before the development of infrared absorption breath test instruments.*

layer or watery submucous layer will vaporize and heat stored in the airways will be picked up by the inspired gas and taken to the alveoli (19–21). During exhalation, the process reverses; fully humidified air at core body temperature is cooled by the cooler airway mucosa and water vapor condenses on the mucosa. This water and heat exchange process is vital because it conditions the inspired air to avoid damaging the delicate alveolar cells while conserving water and heat from major loss in the exhaled air. Under normal environmental conditions, exhaled gas has less heat and less water vapor than does alveolar air. This observation is inconsistent with the old paradigm in that end-exhaled air alcohol concentration is different from alveolar air alcohol concentration.

The dynamics of soluble gas exchange are similar to the dynamics of heat and water exchange. These processes are analyzed using analogous equations (22). The fact that respired air exchanges heat and water with the airways implies similar soluble gas exchange processes (23). This interaction of ethyl alcohol with airway mucosa was first suggested by Wright et al. (24) and is now well documented (25–28). In 1975, Wright et al. first recognized the importance of air alcohol interaction with airway tissue both during inspiration and expiration. The degree of interaction is directly related to the solubility of the gas in the airway mucosa and mucous lining (25,28). The very high solubility of alcohol in water guarantees its 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 (29,30). This variation is affected by the difference in temperature between the outside air and the alveolar air (31). These findings are inconsistent with the old paradigm.

The exchanges of heat and gas with the airways are complex and interactive processes. The relative significance of this exchange depends on the effective solubility of the gas in the mucosa that is dependent on the tissue temperature. 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. 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. (30) and further refined by George et al. (32) and Anderson et al. (33) which shows that during normal breathing, the inspired air is equilibrated with alcohol, picking it up from the airways, before reaching the seventeenth generation airways (start of the alveolar region). Zhang et al. (34) have shown that during inspiration of ethyl alcohol vapors, complete uptake occurs entirely within the upper airways. With exhalation, alcohol is rapidly lost to the airways primarily within the fifth to fifteenth generations. Along the airway, more alcohol is lost to the airways. The alcohol that arrives at the mouth comes essentially from the airways and not from the alveoli. This is also the case for water vapor. The humidification of inspired air is performed by the airways.

The early basic assumption of the breath alcohol test was that the BrAC was the same irrespective of the exhaled volume as long as the dead space volume is exhaled (as shown in Fig. 2). However, Jones (29), and others (19,35) have shown that the BrAC depends on exhaled volume. The breath test instrument takes a sample of air from the end of the breath whenever the subject stops but the volume of breath exhaled is neither controlled nor measured. Therefore, the apparent BrAC depends on the volume of air delivered to the breath test instrument. The last part of the breath can be well above the average single breath alcohol level because the alveolar plateau has a positive slope that depends on air temperature (36). This finding is inconsistent to the old paradigm.

A sloping alveolar plateau for various low solubility gases has been explained by several factors including stratified inhomogeneity (gas phase diffusion limitation) (37), convection–diffusion interaction (38), sequential exhalation from regions with differing $\dot{V}_A/\dot{Q}$ ventilation to perfusion ratio (37) and continuing gas exchange (39). None of these factors contribute substantially to the slope of the exhaled alcohol profile because the alcohol concentration is nearly identical in all regions of the lung (40). Continuing gas exchange will contribute to the slope of the exhaled profile for respiratory gases (CO_2 and O_2), but not low blood solubility inert gases (37,39,41). The observation that the exhalation profile does not reach a level plateau is contrary to the old paradigm.

Further variation in BrAC will result from changing the breathing pattern just prior to delivering the sample breath. Hyperventilation for 20 sec prior to delivering a sample breath to the breath tester causes an 11% reduction in BrAC (42). Three deep breaths prior to the sample breath reduces BrAC by 4% (35). After breath-holding for 15 sec prior to exhalation, the BrAC increases by 12% (for a minimum exhalation) and 6% (for a maximum exhalation) (35). A 30-sec breath hold prior to exhalation increases BrAC by 16% (42). These effects are caused partially by the respective cooling or warming of the airways, but mostly by altered diffusive exchange of alcohol between the respired air and the airway mucosa with altered ventilation. The data further support the airway surface interaction of alcohol as the mechanism causing the changing alcohol concentration during exhalation. This observation is inconsistent to the old paradigm.

The New Paradigm

The conclusions of the above studies are that alcohol leaves the lungs by diffusing from the bronchial circulation through the airway tissue where it is picked up by the inspired air (Fig. 3). By the time it reaches the alveoli, the air has picked up as much alcohol

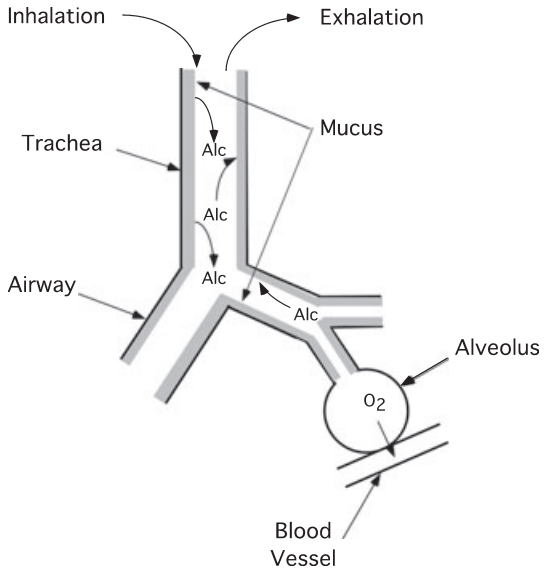

FIG. 3—*New paradigm of alcohol exchange. During inhalation, alcohol is picked up from the airway tissue. During exhalation, alcohol is redeposited on the airway tissue.*

as is possible. Therefore, no additional alcohol can be picked up in the alveoli (43). On exhalation, some of the alcohol is redeposited on the airway surfaces. All of the alcohol exhaled at the mouth comes from the airway surface via the bronchial circulation. Very little, if any, alcohol originates from the pulmonary circulation surrounding the alveoli. The fact that alcohol comes primarily from the airways is the reason why the BrAC depends on the breathing pattern. This contributes to the very large variation in the ABT readings obtained from actual subjects.

The flux of alcohol from the mucous surface into the air (positive values) during inspiration and the flux of alcohol from the air to the mucus surface (negative values) during expiration are demonstrated in Fig. 4. The data shown in this figure were calculated using a mathematical model of the human airway structure (32). During inspiration, alcohol is taken up into the inspired air immediately at the mouth. The greatest alcohol uptake occurs in the trachea and generations 6 through 13. During expiration, the redeposition of alcohol occurs primarily at these same airway generations. The important conclusion from this work is that all of the alcohol that comes out of the mouth in the breath comes from the airway surfaces rather than from the alveolar regions. Airway alcohol exchange during both inspiration and expiration is inconsistent with the old paradigm.

As air is exhaled from the mouth, alcohol concentration continues to rise, never reaching alveolar alcohol concentration. When the subject stops exhaling, the alcohol concentration levels off when plotting against time. An example of an exhaled alcohol profile is shown plotted against exhaled volume (Fig. 5, left) and against time (Fig. 5, right). The subject is exhaling at a constant exhaled flow rate. Figure 5 (left) shows the pattern if exhalation is stopped with volumes of 2, 4, and 6 L. Figure 5 (right) shows the same exhalations plotted against time. When the subject stops exhaling (either 2, 4, or 6 L) the BrAC continues at a constant level. The end exhalation BrAC depends on the amount of volume exhaled by the subject. The flat exhaled profile when plotted against time has been assumed to indicate that alveolar air is obtained. However, the observation changes when BrAC is plotted against time. The leveling off of the exhaled profile against time shows that end-exhaled BrAC varies when altering exhaled volume.

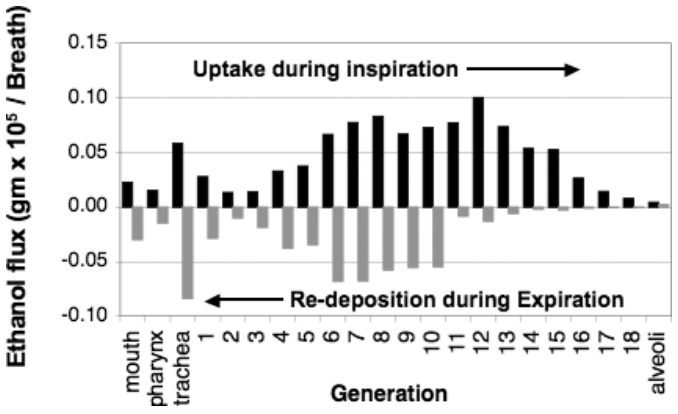

FIG. 4—*Alcohol exchange occurs within the airways. The relative alcohol flux within each airway generation is shown (modified from [30]). These data argue that very little alcohol exchanges in the alveoli. The alcohol exchanges with the airway tissue.*

Respired air alcohol concentration continues to rise during inspiration as inspired air (containing no alcohol) passes through the airways taking up from the surface of the airway mucosa. Alveolar air alcohol concentration when compared with BAC has a ratio of 1756 (not 2100) at 37°C (normal body temperature) (44). End-exhaled alcohol concentration varies depending on factors such as exhaled volume (32,45), pretest breathing pattern (35,46), body temperature (47,48), and inspired volume (16). These observations are inconsistent with the old paradigm.

The concentration of alcohol in the breath sample has been thought to be related to the venous (pulmonary arterial) BAC as the venous circulation perfuses the alveoli in the lungs. Under the old paradigm, it had been assumed that the end-exhaled alcohol concentration was related to the mixed venous blood as the systemic venous blood that perfuses alveoli in the lungs providing the source of alcohol for the breath. Recent modeling and experimental observations have shown the presence of a substantial difference in alcohol between arterial and venous blood during both the absorptive and postabsorptive phases of alcohol pharmacokinetics. During the absorptive phase while alcohol is being delivered to the body tissues, arterial alcohol concentration exceeds venous alcohol concentration (49–51). In a recent study using a new breath test instrument that accepts free exhalation (not through a tube), Lindberg et al. (52) have shown a strong correlation between BrAC and arterial alcohol concentration. This unique observation is consistent with the new paradigm in that exhaled breath alcohol is closely related to the alcohol originating from the bronchial (systemic arterial) circulation perfusing the pulmonary airways.

A major concern about the ABT has developed after the observation by Hlastala and Anderson (16) that the BrAC (relative to the BAC) depends on lung volume. This observation is caused by the fact that alcohol concentration continues to increase during

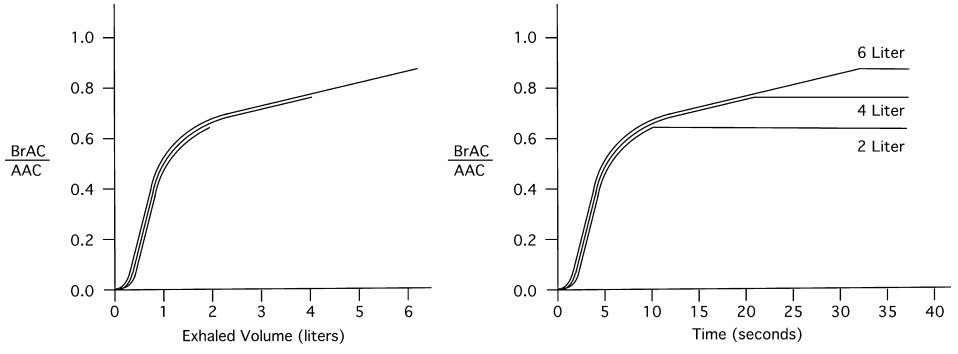

FIG. 5—*Left: Alcohol concentration versus exhaled volume with a constant exhalation flow rate for three exhalations with a volume of 2, 4, and 6 L. Right: Alcohol concentration versus time with a constant exhalation flow rate for three exhalations with a volume of 2, 4, and 6 L. For ease of visualization, the three separate exhaled profiles are slightly offset on the volume scale.*

exhalation. Most alcohol breath testers require a minimum exhalation volume (normally between 1.1 and 1.5 L) before the breath sample can be obtained. A smaller subject with a smaller lung volume must exhale a greater fraction of their available lung volume compared with a larger subject with a larger lung volume before a breath sample is obtained. For details on the quantitative aspects of this problem, see 16. These observations are consistent with the data of Skåle et al. (53) and Jones and Andersson (54).

It is time for forensic scientists to reexamine the ABT to consider the importance of alcohol interaction with the airway tissue during both inspiration and expiration. The result of this interaction is that the breath test is fairer for some subjects than others. Another consequence is that the BrAC continues to increase as the subject continues to exhale. The resulting end-exhaled breath concentration is only partially related to the BAC. And therefore, the ABT exhibits much more variability than previously recognized. Future research should focus on understanding the mechanisms causing this variation and development of modified protocols to enhance the accuracy of the ABT.

What should be done about these new paradigm considerations for the breath test? The BrAC depends on factors such as inhaled volume, exhaled volume, prebreath hypoventilation or hyperventilation, rate of exhalation, arterial blood concentration, and lung volume. End-exhaled alcohol concentration can never reach alveolar (deep lung) alcohol concentration. A possible solution is to use isothermal rebreathing (exhaling into and inhaling out of a temperature-controlled bag) (35,46). However, the rebreathing maneuver can be difficult for subjects to cope with particularly at high BACs. Another possible solution is to control all variables that influence the BrAC. This would place undue constraints on the ABT and could be difficult for the average operator to easily control.

Given the variation in the breath alcohol test, it might be appropriate to consider decreasing the importance of threshold levels for penalties. After further experimentation, it might be possible to define the variation due to breathing-related variables and to allow for a magnitude of error in the breath test. Penalties could be graded with a sliding scale that allows for error in the breath test and a continuously graded scale of penalties as the BrAC increases. In any case, this new recognition of the limitations of accuracy of the ABT warrants reconsideration of the breath test protocols used.

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