

## **PHYSIOLOGICAL LAWS OF ALCOHOL BREATH TESTING**

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Over the years, breath testing has become a widely used method for quantitative determination of the level of intoxication of individuals suspected of driving while under the influence of alcohol. After recognition of the need for quantitative assessment of intoxication, blood alcohol concentration 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 non-invasive means of assessing level of intoxication.

### **PHYSIOLOGY OF THE LUNGS**

The lungs are located within the chest. The organ allows inspired air to come into close proximity with the blood so gases (such as oxygen and carbon dioxide) can exchange between the air and the blood. The lung is made up of over 300 million small air sacs called alveoli. Outside air comes to the alveoli 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 "mainstem bronchi" (going to the left and right lungs) which divide further into the "lobar bronchi". This division goes on about 23 times until the alveoli are reached. Actually, some alveoli begin to appear at about the seventeenth generation airways. Surrounding each alveolus are small blood vessels. The thinness (less than 0.001 millimeter) 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 square meters) for this gas exchange process. The alveolar region is where alcohol comes from the blood into the air in the lungs. But in order to be tested for alcohol, the breath must first pass from the alveoli along the branching network of airways to the mouth. During this journey through the airways, a great deal happens to the air changing the alcohol concentration.

The lung does not actively participate in the breathing process. The muscles which cause breathing are located outside the lung in the chest wall (intercostal muscles) and the abdomen (diaphragm). There are small muscles in the lung around the blood vessels and airways which assist in controlling the way in which blood flow and air flow are distributed to different alveolar groups (acini). To initiate inspiration, the external intercostal muscles are contracted. This pulls the ribs upward and outward increasing the chest size. In addition, the diaphragm pulls downward, also increasing the chest size. The change in chest size causes a decrease in pressure around the lung which

causes the lung to expand and air to move into the lung. To initiate exhalation, the diaphragm and external intercostal muscles are relaxed. The previously stretched lung and chest wall then relax and shrink down increasing the pressure of the air in the alveoli causing air to flow out of the lung. If a rapid exhalation or an exhalation against a resistance, such as that caused by a breath testing instrument, is required, then the internal intercostal muscles can also be used to pull the ribs down assisting with the exhalation.

The number of molecules that leave the blood and enter the alveolar air is dependent on the blood alcohol concentration and the partition ratio (PR). In order to calculate the BAC from an alveolar sample, the alveolar alcohol concentration and the partition ratio each must be known precisely. However, it is impossible to sample air directly from the alveoli because of the small size of the airways. Therefore, all breath testers attempt to take a sample from the end of the breath for analysis under the assumption that the concentration of alcohol in the end-exhaled breath is the same as the concentration of alcohol in the air within the alveoli. In other words, it is assumed that nothing happens to the alveolar air sample as it is passing through the airways to the breath tester. However, changes do occur to the breath as it is exhaled which serve to alter the breath alcohol concentration.

### Diffusion in the Lung

The process of diffusion governs the exchange of gas between blood and air in the alveolus. As blood enters the capillary in the alveolus, it is exposed to the alveolar air. If alcohol is present in the blood, some of the alcohol will diffuse out through the cells separating the blood from the air and increase the alcohol concentration in the alveolar air. The amount of the decrease of alcohol in the blood is extremely small and is governed by the relative amount of ventilation and blood flow to the alveolus.

The exchange of alcohol across the alveolar-capillary membrane is not limited by diffusion as has sometimes been stated in the alcohol breath testing literature. Blood is in the pulmonary capillary for a long enough time such that the alcohol in the alveolar air is in equilibrium with the alcohol in the blood after it has traversed only a small fraction of the alveolar capillary. This equilibrium is maintained until the end of the capillary. Under such circumstances, the distribution of alcohol is governed by the partition ratio for alcohol in blood at the temperature in the alveolus (normally 37° C). This is true for a very soluble gas like alcohol in a normal alveolus with nearly the same amount of blood flow and air flow.

Gases diffuse very easily within the air of the lung. So the concentration of alcohol is virtually identical throughout the alveolar acinus (containing many alveoli). This addresses another common misconception in the alcohol breath testing literature. The changing alcohol concentration during exhalation is not because the gas near the alveolar surface is in better equilibrium with the blood. Almost all of the gas in the lung (except that in the dead space) is in equilibrium with the blood before exhalation. The

changing alcohol concentration during exhalation is caused by another mechanism related to the changing of temperature of exhaled air (see below).

### True Alcohol Partition Ratio

The scientific relationship governing the solution of gases in liquids is Henry's Law (Henry, 1803) which relates the equilibrium concentration of a dissolved gas in a liquid to its concentration in the air above the liquid. The proportionally constant between the liquid and air concentration in Henry's Law is the partition coefficient (partition ratio). Henry's Law is a general scientific principle which relates to dilute solutions of all ideal gases dissolved in liquids, not just to ethyl alcohol in blood. The partition ratio is different for various gases, various liquids, and is strongly temperature dependent. The partition ratio defines the distribution of molecules between two media, such as gas and liquid.

If the true partition ratio of the blood sample is different from the value assumed by the breath testing instrument, then an error will occur. Halving the partition ratio would cause a doubling of the number of molecules in the air. A breath testing instrument would measure twice as many alcohol molecules and would estimate a BAC which is twice the true value. The error in the breath testing instrument is directly related to the ratio of the actual partition ratio to the assumed value of 2100. Another way of thinking about the effect of changes in partition ratio is to consider the partition ratio as the number of molecules of alcohol in the blood compared to the number of molecules of alcohol in the breath. If the partition ratio is increased, then more molecules will stay in the blood, and fewer will come out in the breath. Thus, the breath test will be too low. If the partition ratio is decreased, then fewer molecules will stay in the blood, a few more will come out in the breath, and the breath test will be too high.

It is important to realize that the partition ratio term is incorrectly used in the breath testing literature. The partition ratio (or partition coefficient, as used in chemistry or physics) defines the distribution at equilibrium of a material (such as alcohol) between two media (such as blood and air). It is a physicochemical property of the substances 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, should not be applied. In fact, the true blood-air partition ratio is quite different when measured directly in an external blood sample than it is when measured from the human breath and a blood sample drawn at the same time (Jones, 1983). In the exhaled breath, the alcohol concentration clearly changes during exhalation (Adrian, 1981; Jones, 1982; Russell and Jones, 1983; Slemeyer, 1981). The alcohol concentration in the breath at the mouth is different from the alcohol concentration in the air within the lungs. Therefore, the term partition ratio does not apply to the relationship between breath and blood after the breath has left the alveolar spaces in the lung. Nevertheless, the partition ratio has been applied before to the measurement of breath and blood. In this chapter, the term blood-breath ratio (BBR) will represent the ratio of alcohol between the blood and a sample of breath. The term partition ratio (PR) is used to represent the equilibrium ratio of alcohol between a liquid and air.

## Body Temperature

Variations in temperature have a profound influence on the partition ratio and the breath alcohol concentration. The partition ratio for alcohol in blood decreases by about 6 1/2% for each 1° C increase in temperature. This implies a 6 1/2% increase in breath alcohol concentration when the body temperature increases by 1° C (equal to 1.8° Fahrenheit).

The average body temperature for humans is 37°C (98.6°F) and varies as much as  $\pm 1^\circ\text{C}$  amongst different individuals. In addition, every person has a normal diurnal (daily) variation of 1°C. Females also have a temperature variation of about 1°C with the menstrual cycle. These temperature variations are normal. In addition, there are factors that can elevate body temperature above the normal range. Many diseases (such as influenza) can cause fever. Physical or emotional trauma can elevate body temperature.

In order to determine the blood alcohol concentration (in a blood "per se" state) or the breath alcohol concentration (in a breath "per se" state) and thus the level of intoxication or driving impairment, it is imperative that the body temperature is known. Breath testing procedures do not require measurement of body temperature. Therefore, any breath test is an inaccurate means of determining level of intoxication.

## Blood Hematocrit

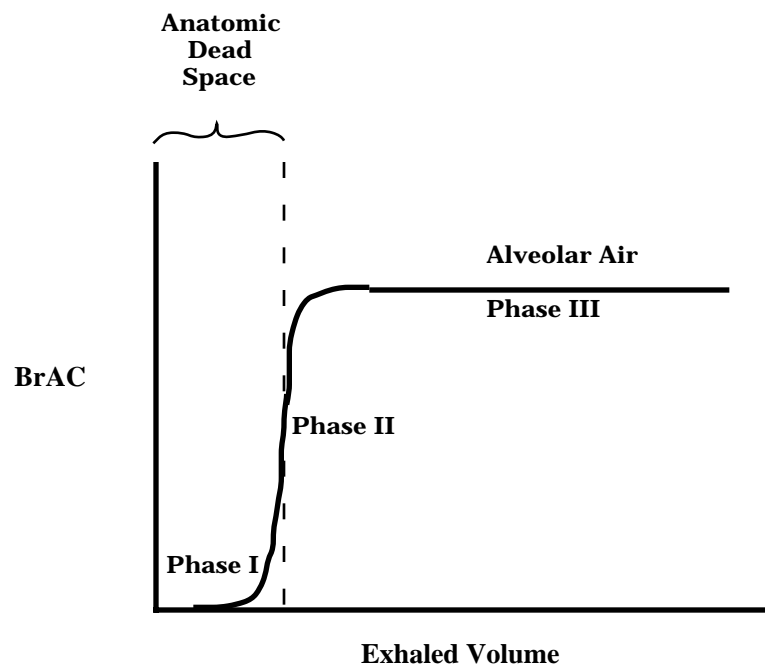
Variations in hematocrit (blood cell concentration) also have a significant influence on the partition ratio and the breath alcohol concentration. Blood is composed of plasma (mostly water) and cells (mostly red cells). The hematocrit is the fraction of blood that is cellular. The male hematocrit normally varies from 0.42 to 0.52 and averages 0.47. The female hematocrit normally varies from 0.37 to 0.47 and averages 0.42. Various types of diseases or other environmental influences can increase or decrease hematocrit beyond the normal range.

When alcohol dissolves in blood, it tends to go into the plasma more than the blood cells. The result is that individuals with a higher hematocrit have a lower partition ratio and a higher breath alcohol concentration.

In order to determine the blood alcohol concentration or the breath alcohol concentration and thus, the level of intoxication or driving impairment, it is imperative that hematocrit is known. Breath testing procedures do not require measurement of hematocrit. Therefore, any breath test is an inaccurate means of determining level of intoxication.

Development of the single breath test for alcohol (Harger et al, 1950; Borkestein and Smith, 1961) took place in the early 1950's 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. These concepts were held in the respiratory physiology community (Rahn et al, 1946; Fowler, 1948) 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, but was expected to be identical to nitrogen (after a single breath of oxygen) and to appear as shown in Figure 1. 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 (Rahn et al, 1946; Fowler, 1948). 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 blood alcohol concentration by virtue of the physical-chemical relationship known as the partition coefficient (Henry, 1803). 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 1940's, the breath alcohol test seemed to be reasonable in principle and further development as a non-invasive measure of blood alcohol concentration was justifiable.



**Figure 1. Assumed exhaled alcohol profile**

Since 1950, many studies have been performed to quantitate the relationship between breath alcohol concentration (BrAC) and blood alcohol concentration (BAC) with the goal of defining a precise relationship between the two for accurate non-invasive 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 (cf; Emerson et al, 1980; Mason and Dubowski, 1976; Jones, 1978) which has not been improved (Simpson, 1987a, 1987b) 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 (Hlastala, 1985; Jones, 1990)

The alcohol breath test is a single exhalation maneuver. The subject is asked to inhale (preferably a full inhalation to total lung capacity, TLC) and then exhale (preferably a full exhalation to residual volume, RV) into the breath testing instrument. Very few restrictions (i.e., exhaled volume, exhaled flow rate, inhaled volume, pre-test breathing pattern, air temperature, etc.) are placed on the breathing maneuver. The constraints applied vary among the different breath testing 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.

In the last decade, there have also been several advances in understanding of the processes which govern pulmonary gas exchange of soluble gases. This new information provides a means for understanding errors associated with the alcohol breath test. This review presents a discussion of pulmonary alcohol exchange from the perspective of a respiratory physiologist using recent data relating to soluble gas exchange.

## **BLOOD-BREATH RATIO**

The partition ratio is a common term used to describe the ratio between blood alcohol concentration and breath alcohol concentration. After scrutiny of blood-breath correlation data, the partition ratio has been assumed to have a value of 2100 and that value has been used for calibration of breath testing instruments. Some studies find that the average blood-breath ratio is actually 2200-2300 resulting in lower average breath readings when using a breath testing instrument calibrated at 2100.

The partition ratio term is incorrectly used when applied to the alcohol breath test. The partition ratio (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. It is a physicochemical property of the substances 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 quite different when measured *in vitro* (Jones, 1983) than it is when measured using an exhaled air sample and a blood sample drawn at the same time (Mason and Dubowski, 1976; Ohlsson, et al, 1990). In the exhaled breath, the alcohol concentration changes during exhalation (Ohlsson, et al, 1990; Adrian, 1981; Russell and Jones, 1983; Jones, 1982; Slemeyer, 1981; Gullberg, 1991). The alcohol concentration in the exhaled air at the mouth is lower than the alcohol concentration in alveolar air when measured by rebreathing (see below)(Ohlsson, et al, 1990; Jones, 1983). Therefore, the term "partition ratio" does not apply to the relationship between breath and blood after the

breath has left the alveolar spaces in the lungs. Nevertheless, the partition ratio has been applied before to the measurement of breath and blood. In this paper, the term blood-breath ratio (BBR) will represent the ratio of alcohol concentration between the blood and breath. The term partition ratio (PR) is used to represent the equilibrium ratio of alcohol between blood and air in the alveoli or in an *in vitro* sample.

Use of the term, PR, for the BBR has led to the unfortunate perpetuation of misconceptions regarding the equilibrium of alcohol. In most of the breath testing literature, it has been represented that the partition of alcohol between alveolar air and blood at 37°C is with a ratio of 2100. It is thought that any loss of alcohol to the airways during exhalation would result in an erroneously low breath test (when compared to blood). In most cases, when breath and blood are compared, the ratio is greater than 2100 implying that the alcohol concentration has been reduced with exhalation. However, the magnitude of the alcohol loss has not been measured directly because it is impossible to measure alveolar alcohol concentration directly with methods that are currently available. Attempts have been made using rebreathing into a heated bag. This indirect method finds average ratios of blood to alveolar air less than 2100 (see below), an indication that alveolar alcohol concentration is higher than end-exhaled alcohol concentration. In addition, *in vitro* measurements (Jones, 1983) indicate that the true blood alcohol PR at 37°C is closer to 1756 (over 20% different from the average BBR measurements presented in the literature). If the theoretical basis of the breath test that end-exhaled alcohol is correct, then full exhalation should result in a BBR of about 1756. But such values are seen only on very rare occasions.

## **ALCOHOL-AIRWAY MUCOSA INTERACTION**

The lungs have a relatively simple, but non-uniform, anatomical structure. The airways are a branching, tree-like arrangement of tubes. Inspired air moves through progressively shorter, narrower and more numerous airways (Weibel, 1963). These airways are lined with mucus at a temperature varying between approximately 34°C at the mouth and 37°C in the very smallest airways. However, this temperature range varies depending on the breathing pattern (McFadden, Jr., 1983). The airways bifurcate up to 23 times and eventually reach alveoli. The membranes separating the air in the alveoli and the blood in the capillaries are so thin that inert gases such as alcohol equilibrate between blood and air very rapidly (Wagner, 1977). 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 (McFadden, Jr., 1983; Tsu et al, 1988). Some water within the mucous layer or watery sub-mucous layer will vaporize and heat stored in the airways will be picked up by the inspired gas and taken to the alveoli (Tsu et al, 1988; Ingenito et al, 1986; Saidel et al, 1983). 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.

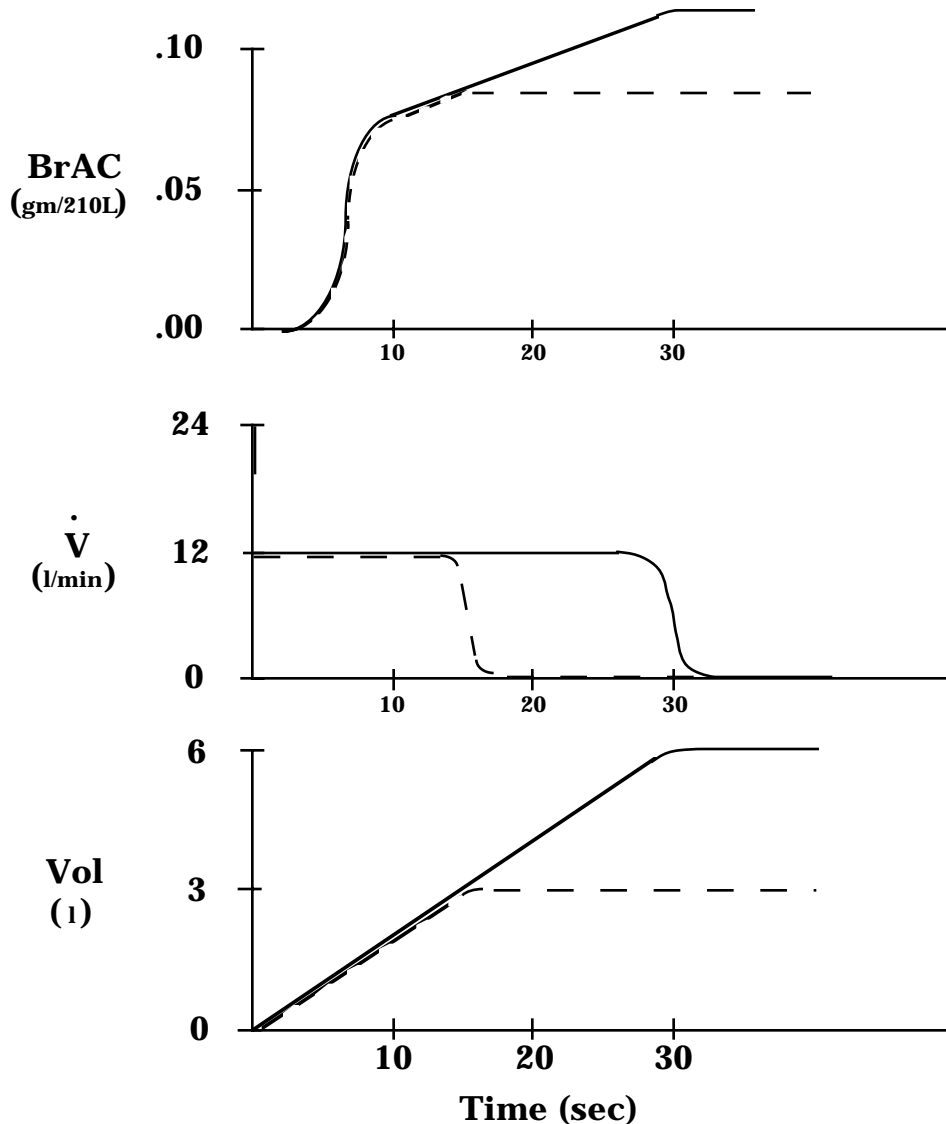
The dynamics of soluble gas exchange are similar to the dynamics of heat and water exchange. These processes are analyzed using analogous equations (Bird et al, 1960). The fact that respired air exchanges heat and water with the airways implies similar soluble gas exchange processes (Hlastala and Swenson, 1992). This interaction of soluble gases with airway mucosa is well documented (Aharonson et al, 1974; Cander and Forster, 1959; Davies, 1985; Schrikker et al, 1985). The degree of interaction is directly related to the solubility of the gas in the airway mucosa and mucous lining (Aharonson et al, 1974; Schrikker et al, 1985). 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 (Jones, 1982; Tsu et al, 1991). This variation is affected by the difference in temperature between the outside air and the alveolar air (Jones, 1982).

The early basic assumption of the breath alcohol test was that the breath alcohol concentration was the same irrespective of the exhaled volume as long as the dead space volume is exhaled. However, Jones, and others (*vide supra*) have shown that the breath alcohol concentration depends on exhaled volume. The breath testing 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 breath alcohol concentration depends on the volume of air delivered to the breath testing 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 is dependent on air temperature (Ralph et al, 1985). If the subject exhales only a small volume (beyond dead space), then the estimated BAC will likely be substantially lower than the true BAC (Ohlsson et al, 1990; Jones, 1983).

The achievement of a flat slope during exhalation has been presented as a demonstration that "alveolar air" with its alveolar alcohol concentration is obtained at the end of an exhalation. However, this hypothesis is incorrect in that a flat slope will always be obtained when expiratory flow rate approaches zero whether alveolar air is reached or not. Figure 2 illustrates a schematic example of an individual with a vital capacity of 6 liters who exhales into an alcohol breath testing instrument at a rate of 12 liters per second for a period of 30 seconds. The exhaled alcohol concentration rises until a plateau is reached after the end of exhalation (solid curve). If the same subject exhales for only 15 seconds, then a plateau in alcohol concentration will also be achieved at the end of exhalation (dashed curve). But in this case the plateau value is lower. A plateau is reached in both cases, but neither represents a true alveolar sample. If it were possible for the subject to continue to exhale beyond his residual volume (minimum lung volume), then the exhaled alcohol concentration would continue to rise until alveolar alcohol concentration (as represented by rebreathing, see below) were reached. As further evidence to this issue, alterations in pre-test breath breathing pattern should not effect the end exhalation value if it is true alveolar air. However, hyperventilation



decreases breath alcohol concentration while a breathhold increases breath alcohol concentration (Jones, 1982; Ohlsson, 1990). End-exhalation air cannot be in equilibrium with respect to alveolar alcohol concentration because the conditions of the airways affects the breath alcohol concentration.



A sloping alveolar plateau for various low solubility gases has been explained by several factors including stratified inhomogeneity (gas phase diffusion limitation) (Scheid and Piiper, 1981), convection-diffusion interaction (Paiva and Engel, 1981), sequential exhalation from regions with differing  $V_A/Q$  (Scheid and Piiper, 1981) and continuing gas exchange (Grønlund et al, 1987). None of these factors contribute substantially to the slope of the exhaled alcohol profile. Continuing gas exchange will contribute to the slope of the exhaled profile for respiratory gases ( $\text{CO}_2$  and  $\text{O}_2$ ), but not inert gases (Scheid and Piiper, 1981; Grønlund et al, 1987; Hlastala, 1972). Sequential emptying can have no contribution for alcohol because the alveolar partial pressure for alcohol will be nearly identical in all alveolar regions of a normal lung. According to classical gas exchange theory (Hlastala, 1984), the alveolar partial pressure of gas, normalized to the mixed

venous partial pressure, is related to the blood-gas partition ratio (PR) and the ventilation to perfusion ratio ( $V_A/Q$ ) of the region:

$$\frac{P_A}{P_V} = \frac{PR}{PR + V_A/Q}$$

For a normal lung with  $V_A/Q$  ratio ranging between 0.1 and 10 (Farhi, 1967),  $P_A/P_V$  will range between 0.99433 and 0.99994 (certainly indistinguishable from one another). Gas-phase diffusion limitation has little affect in normal gas exchange (Robertson et al, 1986), particularly for a low molecular weight gas like alcohol (MW=46). Convection-diffusion interaction cannot explain the slope because of alveolar alcohol partial pressure uniformity in regions with differing  $V_A/Vol$  ratio. In addition, convection-diffusion interaction would not be affected by temperature-related factors (which are known to affect the breath alcohol concentration (Ohlsson, 1990; Jones, 1983; Jones, 1983; Jones 1982). For alcohol, diffusion disequilibrium (thought to explain the changing exhaled BrAC by some forensic scientists) is not the explanation for a sloping exhaled alcohol profile because of the minimal role of gas-phase diffusion limitation in the normal lung (Robertson et al, 1986; Hlastala, 1987).

Further variation in BrAC will result from changing the breathing pattern immediately before delivering the sample breath. Hyperventilation for 20 seconds prior to delivering a sample breath to the breath tester causes an 11% reduction in BrAC (33). Three deep breaths prior to the sample breath reduces BrAC by 4% (14). After breath-holding for 15 seconds prior to exhalation, the BrAC increases by 12% (for a minimum exhalation) and 6% (for a maximum exhalation) (Ohlsson, 1990). A 30 second breathhold prior to exhalation increases BrAC by 16% (Jones, 1982). These effects are caused by the respective cooling or warming of the airways and the data further support the airway surface interaction of alcohol as the mechanism causing the changing alcohol concentration during exhalation.

The exchanges of heat and of 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. 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* (1991) and further refined by George et al (1993) 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). Upon reaching the alveoli an additional 20% alcohol is picked up because the solubility of alcohol in blood is 20% lower than the solubility of alcohol in water (Jones,

1982). The equilibrium partial pressure of alcohol in vapor above blood is greater than in vapor above water at the same temperature. With exhalation, the excess 20% alcohol picked up in the alveoli is immediately lost to the airways within the sixteenth or fifteenth generation. 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.

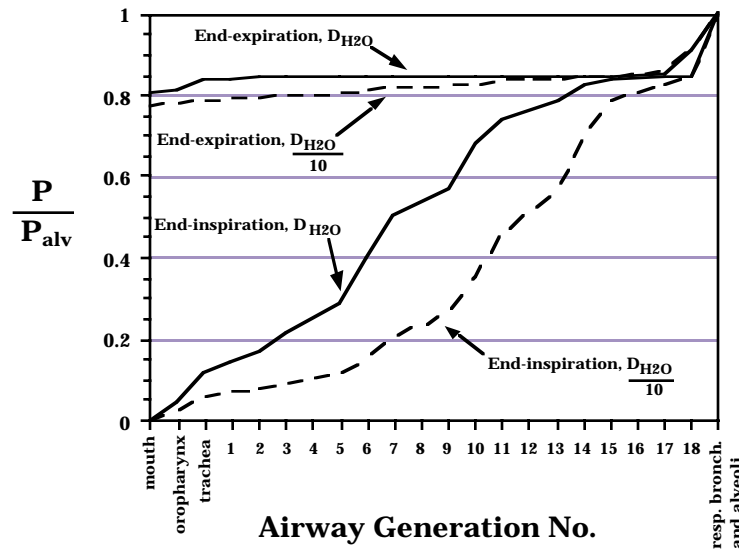


Figure 3. Amount of alcohol in breath at different positions in the airways.

Figure 3 comes from George et al (1993) and shows the calculated alcohol concentration at various positions along the airways at end-exhalation and at end-inspiration for both oral and nasal breathing. Two curves are shown for conditions where alcohol diffuses through airway tissue as easily as it does through water (solid lines) and where alcohol diffuses through airway tissue at one tenth the rate that it does through water (dashed lines). The important conclusion from work such as this is that most of the alcohol that comes out of the mouth in the breath comes from the airway surfaces rather than from the alveolar region.

The use of the mathematical model is that the airway concentrations can be calculated from exhaled alcohol profiles as shown in Figure 4. When the diffusivity of alcohol through airway tissue is assumed to be equal to that through water, the mathematical model predicts an exhaled alcohol profile as shown by the dashed line, a curve that clearly does not match the experimental data points shown as dots. When the diffusivity of alcohol through tissue is reduced to about one tenth of the diffusivity of alcohol through water, the model predicts a profile as shown by the solid curve which nearly exactly fits the experimental data.

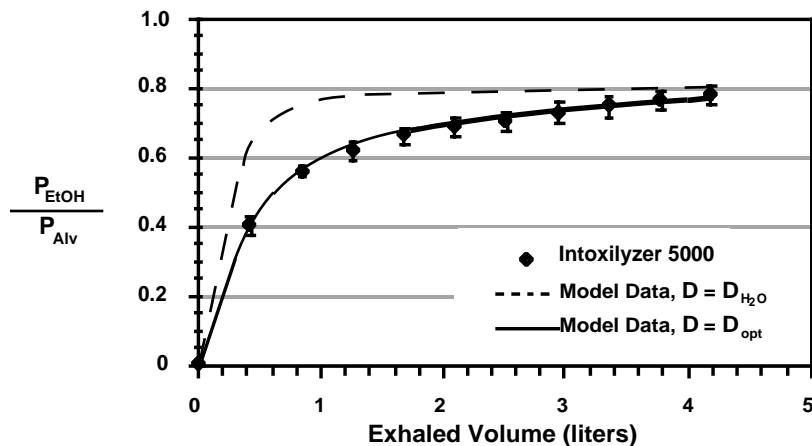


Figure 4. Exhaled breath alcohol profile. Dashed curve shows model prediction for rapid diffusion through tissue. Solid curve shows model prediction for reduced diffusion.

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. An additional 20% of the alcohol is picked up in the alveoli, coming from the pulmonary circulation. On exhalation, some of the alcohol is redeposited on the airway surfaces. The fact that alcohol comes primarily from the airways is why the breath alcohol concentration can be so easily changed by changing the breathing pattern. This contributes to the very large variation in the alcohol breath test readings obtained from actual subjects.

## REBREATHING

Rebreathing has been used to obtain equilibrated alveolar gas samples because of the advantage of overcoming problems associated with heterogeneity of exhaled gas concentration coming from regions with differing ventilation/perfusion ratio (Piiper and Scheid, 1981). After breathing in and out of a bag for several breaths, the air within the lung and bag system eventually should reach an equilibrium. 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 alcohol. 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 (about 30 seconds 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 (PR \_ 1) which are taken up by bloodperfusing the alveoli, but not soluble enough to interact significantly with the airways. 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 not 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 (Forney et al, 1964; Pinkwart et al, 1981; Harger et al, 1956; Schwartz et al, 1982) because of the use of room temperature bags. Condensation caused by cooling of the rebreathed air lowered alcohol concentration because of solution of alcohol in the water condensate. 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 (Ohlsson et al, 1990; Jones, 1982). In a test of a heated rebreathing bag, Jones (1982) found higher BrAC after rebreathing (blood-breath ratio of  $1947 \pm 110$ , mean  $\pm$  SD) compared to measurements after a single exhalation (blood-breath ratio of  $2225 \pm 111$ , mean  $\pm$  SD). Ohlsson et al (1990) found rebreathing BBR values of  $2019 \pm 121$  (mean  $\pm$  SD) compared to single exhalation BBR of  $2333 \pm 163$  (mean  $\pm$  SD). Since rebreathing produces a breath sample which is closer to the true mixed alveolar air, the findings of Jones and Ohlsson et al suggest that there is a normal loss of alcohol to the airway surface during exhalation and that end exhalation alcohol concentration is always lower than alveolar alcohol concentration.

These rebreathing data are important because they argue against the often stated idea that the true partition ratio of alcohol in human lungs is 2100. If the 2100 ratio were true and correct, then it would be impossible to get an experimental BBR, even with rebreathing, that is lower than 2100. According to Jones (1982) the partition coefficient for blood (measured *in vitro*) at 37°C (average core body temperature) is 1755. It would therefore be expected that a rebreathing BBR should be closer to 1756. The rebreathing BBR of 1947 obtained by Jones (1983) is closer to the theoretical values of 1756 than the data (rebreathing BBR = 2019) of Ohlsson (1990). The difference may be due to differences in technique and/or a lack of complete equilibrium. Ohlsson's subjects rebreathed into a heated bag for seven breaths. The sample was then taken from the bag. In Jones case, after rebreathing, subjects held their breath after an inspiration and then exhaled into a breath testing instrument. The additional breathhold may have resulted in further increase of BrAC.

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 generally been thought to be lower than that in the central circulation due to the Fahraeus effect (Yen and Fung, 1977). In experimental measurements using positron emission tomography in humans, Brudin et al (Brudin et al, 1986) have shown not only that the local hematocrit in human lungs is lower than the bulk hematocrit, but also that there is a heterogeneity to the distribution of hematocrit in the lungs. Because the solubility of alcohol is greater in plasma than in erythrocytes (Jones, 1982), any decrease in hematocrit in the pulmonary capillaries would cause an increase in PR. The rebreathing data of Ohlsson and Jones are consistent with this hypothesis, showing a BBR that is lower than the prolonged single exhalation value, but not as low as the theoretical rebreathing BBR of 1755. A reduction in pulmonary capillary hematocrit could increase the measured rebreathing BBR to a value greater than the theoretical rebreathing BBR.

## MECHANISM OF ALCOHOL EXCHANGE BY THE LUNGS

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 is deposited on the surface of the airways. During the initial phase of exhalation, the airway mucosa is low in alcohol having contributed alcohol to the inspired fresh air. So 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 through the airways, less alcohol is lost to the airways because some alcohol has already been deposited 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 using a single breath but possible with rebreathing), the measured BBR should equal to the *in vivo* partition ratio for alcohol in pulmonary capillary blood at 37°C. Theoretically, this should be 1755 if pulmonary capillary blood has a hematocrit equal to that in large vessels and if the temperature is 37°C. If a sample of air is taken from the earlier part of the breath (the subject only exhales about 1/3 of the amount possible), then the breath alcohol will be lower than average and the measured BBR would be higher than 2100 (about 2500 in the early breath example shown in Figure 5). If a sample of air is taken from the later part of the breath (the subject exhales the entire amount possible), then the 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 lower than 2100 (about 1900 in the late breath example shown in Figure 5).

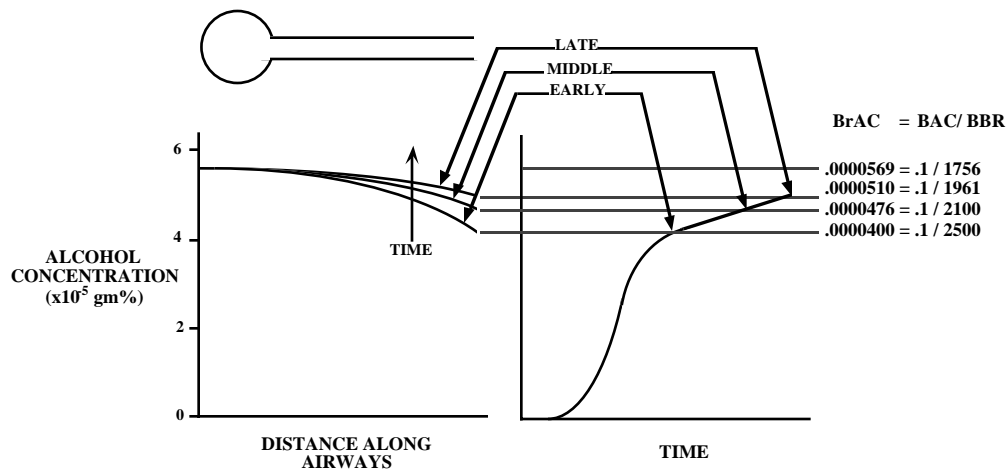


Figure 5. Left graph shows alcohol concentration along the airways during exhalation for early, middle and late breath samples. Right graph shows the exhaled alcohol profile as breath is leaving the mouth during exhalation.

The proposed theoretical construct would predict that, on the average, an exhalation results in the loss of about 20% of the alveolar alcohol. Breath testing instruments are calibrated with a ratio of 2100, in effect, assuming an average 20% loss. The 2100 ratio was inferred from actual experimental data in human subjects. If a particular subject exhales in a manner resulting in a 30% loss, then correction of the breath test with a 2100 "partition ratio" results in a 10% underestimate of BAC. If a particular subject exhales in a manner resulting in a 10% loss, then correction of the breath test with a 2100 "partition ratio" results in a 10% overestimate of BAC.

## **SLOPE DETECTOR**

Slope detectors currently used on breath testing machines have two primary functions. One is to detect the presence of mouth alcohol by identifying a declining slope as the subject is exhaling. The other is to identify the presence of "alveolar air" so that an alveolar sample is guaranteed. Unfortunately, neither of these features works as intended.

The detection of mouth alcohol does work as intended under most conditions. If an individual takes alcohol into the mouth, swishes it around and spits it out without swallowing, some alcohol will remain dissolved in the mucosal lining of the mouth. Then as he/she is blowing out into a breath testing machine, alcohol will be picked up as breath is passing through the mouth and an erroneously high breath test reading will be seen. Under normal conditions, during such a prolonged exhalation, the alcohol concentration first increases and then decreases. The detection of a decreasing slope by the breath testing machine is sufficient to register as an invalid sample due to the presumed presence of mouth alcohol. However, if the individual stops exhaling at just the point where the alcohol concentration reaches a maximum (before it starts decreasing), then the machine cannot distinguish this pattern from the normal exhalation profile and will not identify the presence of mouth alcohol.

There is another circumstance when the slope detector will not distinguish a contribution of mouth alcohol. If mouth alcohol is present in small quantity, it will add to the normal exhaled profile of alcohol coming from the blood and alveoli. The result is that a small amount of alcohol (and its decreasing concentration) will be added to the normal exhaled profile (and its increasing concentration) with a net effect of producing a constant (or slightly increasing) alcohol concentration. The slope detector will not work correctly when alcohol is present both in the blood and the mouth. The measured BrAC will be higher than it should be. However, the slope detector will not detect the contribution of mouth alcohol.

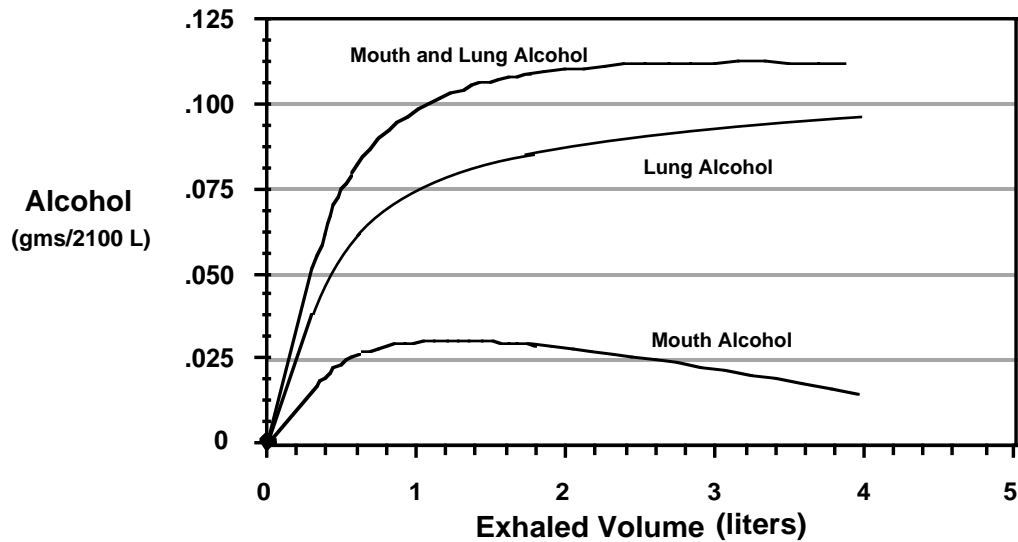


Figure 6. Exhaled breath alcohol profiles. The lower curve is obtained with alcohol dissolved in the oral mucosa with no alcohol in the blood. The middle curve is obtained with alcohol in the blood with no alcohol in the mouth. The top curve is the sum of the two other curves obtained with alcohol in the blood and alcohol dissolved in the oral mucosa.

The other intended feature of the slope detector is to identify the so-called "alveolar plateau" or the point on the exhaled alcohol curve when a constant value is reached. The plateau has been thought to indicate air coming from the so-called "deep alveolar" region. However, it is now known that pure alveolar air with alcohol can never be obtained with a single exhalation. The breath alcohol concentration always changes during exhalation.

At the end of exhalation, when the subject stops exhaling, no new air is delivered to the sample chamber, so the alcohol concentration will not change. The instrument perceives a plateau whenever the subject stops exhaling, even though the "deep alveolar air" is not yet reached. The dilemma is that the slope detector cannot distinguish a voluntary stop in exhalation from an end of exhalation limited by lung volume.

## CONTAMINANTS

The newer breath testing instruments use an analytical process called infrared absorption spectroscopy. Alcohol in the vapor form absorbs light of a particular color and this principal has been used to provide a quantitative means of measuring breath alcohol concentration.



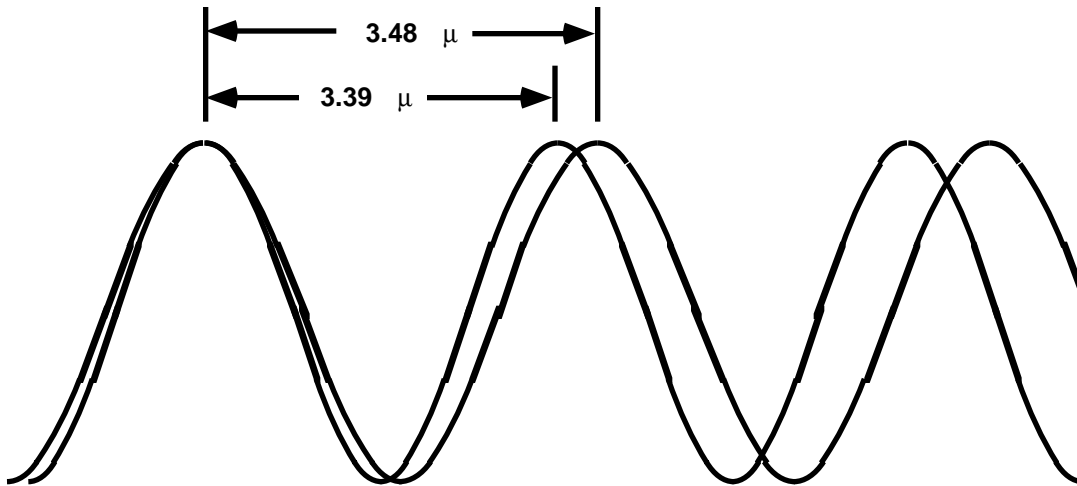


Figure 7. Two light waves with wavelengths of 3.39  $\mu$  and 3.48  $\mu$ .

Light is a wave of electromagnetic radiation called a photon. Figure 7 shows two such waves. The distance that light goes in one vibration is the wavelength. The frequency is the number of times per second that the light vibrates. If the wavelength ( $\lambda$ ) is multiplied by the frequency ( $\nu$ ) of the light, we get the distance that the light travels in a unit of time (second) which is the speed of light ( $c$ , about 186,000 miles/sec):

$$\lambda\nu = c$$

Light that we can see is composed of photons of many different wavelengths (or colors). In fact, electromagnetic waves encompass many wavelengths ranging from radio waves to X-rays. The visible light takes up only a very small part of this range.

The energy ( $E$ ) of a photon is directly related to its frequency by a constant  $h$  (Planck's constant):

$$E = h\nu$$

So X-rays and  $\gamma$ -rays, because of their high frequency and energy, have the potential to do much greater damage than radio waves. It also follows that infrared radiation is of lower energy than visible light. Infrared light is used for alcohol measurement because light in that range is absorbed by the alcohol molecules.

The ethyl alcohol molecule is composed of two carbon, one oxygen and six hydrogen atoms arranged as shown in Figure 8. In the vapor phase, the atoms act like balls connected to each other by springs. The springs are continually oscillating and rotating. Because of the mass of the atoms and the strength of the bond between the atoms, each "spring" absorbs light of a particular energy level. In the case of infrared

alcohol breath testing instruments, light with a wavelength of about  $3.39\mu$  is used because it is absorbed by the bond between the two carbon atoms. In reality, the instruments are measuring the vibration of the methyl tail of the alcohol molecule. There is a strong absorption and therefore it is easy to measure alcohol in such low concentrations as that present in human breath.

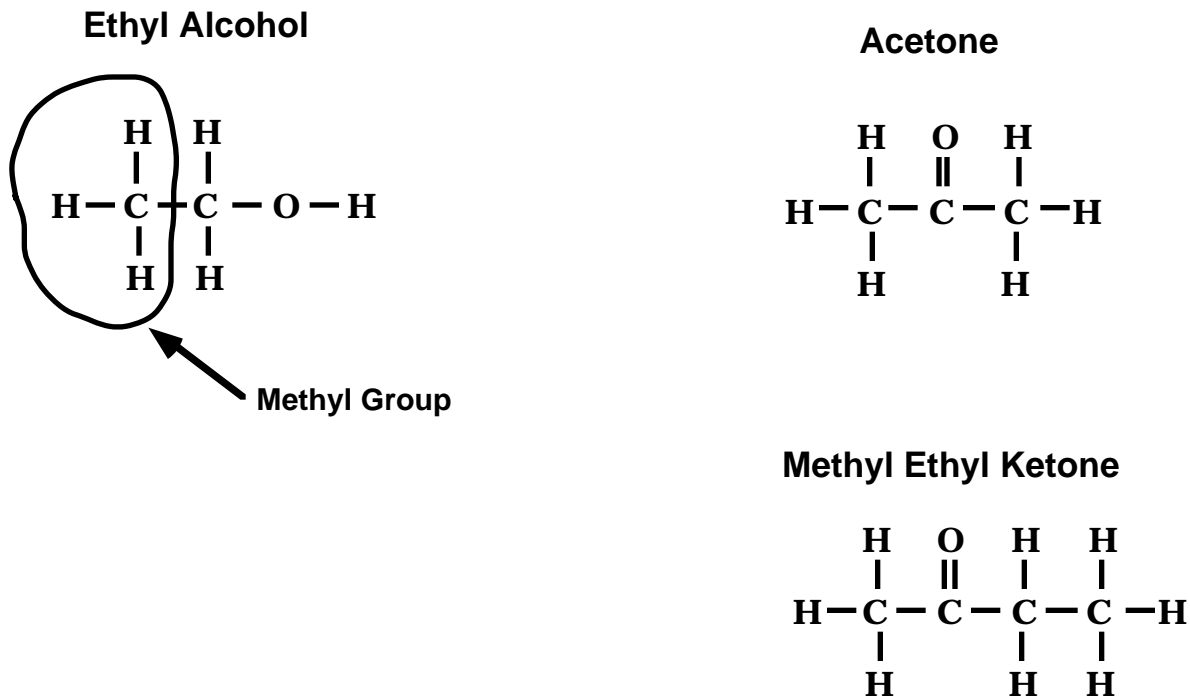


Figure 8. Molecular structure of Ethyl Alcohol, Acetone and Methyl Ethyl Ketone.

A significant problem in measuring ethyl alcohol with infrared absorption is the presence of many substances on the human breath that have methyl tails. Examples shown in Figure 8 are acetone and methyl ethyl ketone. Acetone is present in the breath as a break-down product of fat metabolism in the body. Each of these molecules have methyl tails and absorb light in the methyl stretch region and thus can potentially cause a false positive or erroneously high breath alcohol reading.

Breath test instrument designers have recognized this problem with respect to acetone. Most instruments have a second light with a slightly different wavelength. An example is the BAC Verifier which uses  $3.37\mu$  and  $3.44\mu$ . Both of the lights are absorbed by both alcohol and acetone. However, they are absorbed in different ratios. If light is absorbed in the ratio suitable for alcohol, then the instrument recognizes the unknown as alcohol. If light is absorbed in the ratio suitable for acetone, then the instrument recognizes the unknown as acetone.

The dual wavelength breath testing instruments are incapable of identifying other contaminating substances such as MEK or toluene because they only have two lights. An instrument can only identify an unknown substance as alcohol, acetone, or some combination of the two. A potential solution to the problem could be to include several lights of differing wavelength. Such an approach is used in the diode array spectrophotometers. However, a problem is that the more wavelengths one adds, the greater the error. This is a general problem with infrared spectroscopy.

MEK can be present in individuals who are exposed to MEK in the work environment. In fact, Krotoszynski et al (1977) and Conkle et al (1975) have identified a large number of substances that are present on the breath and may interfere with an accurate reading on an infrared breath testing instrument. These substances are absorbed into the body through the inspiration of air with vapors or through diffusion through the skin after physical contact with the liquids. These are absorbed into the blood and distributed throughout the body, a process that takes time. Longer exposures imply a greater likelihood of breath test contamination. In addition, it takes time to eliminate the substances, each of which washes out at a different rate. Several studies have been performed on body uptake and elimination of industrial contaminants. A few are listed in the reference section of this paper: Bøelum, 1991; Brugnone, et al, 1976; Brugnone, et al, 1980; Cooper, 1981; Couchman, et al, 1980; Cowan, Jr, 1989; Cowan, Jr, et al, 1990; Dubowski, et al, 1984; Eriksson, 1983; Freund and O'Hallaren, 1965; Garriott, et al, 1981; Gill et al, 1991a; Gill et al, 1991b; Gill, et al, 1991c; Jones, 1986; Jones, 1987; Jones, 1988; Konietzko et al, 1980; Lindros, et al, 1980; Perbellini et al, 1984.

Contamination can happen! Two brief studies published in the *Journal of Analytical Toxicology* are relevant here. Edwards et al (1986) and Giguiere et al (1988) took individuals who were painting and studied them with Intoxilyzers. They found high breath alcohol readings with no alcohol in their blood. This is a clear indication that contamination can happen and should be a serious concern when an individual testing positive on an infrared breath testing instrument was working in an environment of paints or solvents.

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