

Diffusion-dependence of pulmonary gas mixing at 5.5 and 9.5 ATA

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Van Liew, H. D., E. D. Thalmann, and D. K. Sponholtz. 1979. Diffusion-dependence of pulmonary gas mixing at 5.5 and 9.5 ATA. Undersea Biomed. Res. 6(3):251-258.—Gas-phase diffusivity is inversely proportional to pressure, so mixing of inspired gas in the lung can be expected to be poor in hyperbaric environments. Subjects performed multiple-breath wash-in of a mixture (4% each of SF₆, Ar, Ne, and He; 21% O₂, 63% N₂) at 1.5, 5.5, and 9.5 ATA. At the higher pressures there were marked differences of concentrations between the indicator gases, measured by mass spectrometer at the mouth during a single expiration. Compared to heavier gases, light gases fell from dead space concentration to the "alveolar" level sooner, had a flatter plateau, and had a lower average expired concentration, indicating that more of the light gases were retained in the Functional Residual Capacity (FRC) after the breath. However, wash-in rates for the indicators were about the same; a rapid initial rate for He diminished so that it was about the same as the SF₆ rate, because in later breaths a back pressure developed for He. The findings illustrate the basic principle that the amount of gas that diffuses from one location to another in a container depends not only on diffusivity, but also in an interdependent manner on concentration gradient, time for diffusion, and configuration of the container.

diffusivity
gas-phase diffusion
respiratory gas exchange

hyperbaric air
pulmonary gas mixing

Poor diffusive mixing of inspired gas with residual gas in the lung may be a handicap in hyperbaric environments, over and above the handicap of increased mechanical work of breathing (Maio and Farhi 1967; Wood and Bryan 1978). In this paper we present data on the effect of diffusivity obtained when men breathing *ad libitum* changed from air to an air-like mixture containing four inert indicator gases that spanned a 6-fold range of diffusivity. For a number of breaths, the indicators washed into the lungs; then the men changed back to air and the indicators washed out. The pattern of indicators relative to each other in expired air of one breath provides information on diffusive processes that took place in the lung; the wash-in and wash-out rates provide information on the overall impact of effects seen in the individual breaths.

Using the same methods in another study (Van Liew 1978), we found that when time for diffusion was curtailed, as in exercise hyperpnea, mixing per breath was noticeably less complete, but the effect on multiple-breath equilibration was small. In the present work we show that the decreased diffusivity in hyperbaric environments gives essentially the same result; low diffusivity resembles short diffusion time.

METHODS

All experiments were done in the hyperbaric chamber at SUNY at Buffalo. High pressure measurements were at 5.5 or 9.5 ATA. Control measurements were run at 1.5 ATA, slightly above normal pressure, to permit use of exactly the same sampling and analysis system for control and high pressure measurements. Subjects were compressed at 60 to 75 ft per minute and the measurements were begun within 5 min after reaching depth.

Subjects were male laboratory personnel, experienced in diving procedures, who had been examined 6 months previously for health and fitness, especially with regard to the cardiopulmonary system. Ranges of their characteristics are: weight 77–127 kg, height 182–183 cm, vital capacity 5.5–6.4 liters, residual volume 1.1–1.4 liters, and FRC 3.2–3.9 liters.

Our method was very simple. The seated subject turned a large-bore stopcock so that he could inspire the breathing mixture from a large bag via a Rudolph valve and mouthpiece and exhale to the chamber. The breathing mixture, essentially the same density and viscosity as air because indicator gases were present in low concentrations, consisted of approximately 4% each of SF_6 , Ar, Ne, and He in 21% O_2 and 63% N_2 . A continuous sample for mass spectrometer analysis (Perkin Elmer MGA 1100) was withdrawn from the mouthpiece, about 1 cm from the subject's teeth. After approximately 20 breaths of wash-in of the mixture, the stopcock was turned so the subject inhaled chamber air, and wash-out of the indicator gases was monitored. Dead space of mouthpiece and valve was 26 ml.

Subjects were instructed to breathe normally. End-expired CO_2 values showed that they did not markedly over- or underventilate. Breaths per min were 8 to 12 at 1.5 ATA, 7 to 11 at 5.5 ATA, and 7 to 11 at 9.5 ATA.

Mass spectrometer outputs were written on an 8-channel polygraph (Grass Model 7). The flow rate of 150 ml/min through the sampling line was controlled by a valve on the mouthpiece. Chamber pressure was used to drive the continuous gas sample to the mass spectrometer outside the chamber. On the assumption that on inspiration all the gases should rise or fall synchronously, we corrected for possible artifacts due to the analysis or recording systems by adjusting the written record so that inspiratory rise of all gases coincided at the midpoint. We then applied the same correction to the exhaled gases. The maximum correction was 0.04 s. The mass spectrometer, calibrated with known gases, was checked by mixing test gas with air and noting the relative changes of the various indicators.

RESULTS

All figures below show results from one subject. Results from the two other subjects were qualitatively the same as those shown.

Figure 1 shows the time courses of the four indicator gases during expiration of the first wash-in breath at 9.5 ATA. The ordinate is concentration, C , relative to inspired concentration, C_i . Helium fell much more rapidly from the inspired level in Phase II of expiration and reached a flatter Phase III or "alveolar plateau" than SF_6 . Neon and Ar were intermediate.

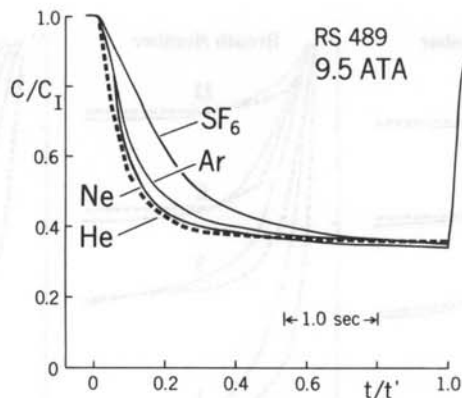


Fig. 1. Concentrations of four indicator gases during expiration of first breath of wash-in at 9.5 ATA for Subject RS. The C/C_1 ordinate makes all indicators exactly comparable even though there were differences in their inspired concentrations (argon has been corrected for Ar in air). Abscissa is relative time, calculated by dividing actual time from first appearance of CO_2 in expiration by duration of CO_2 trace. Sharp rise at right shows that all gases rose synchronously at beginning of inspiration. Note in upper right corner identifies subject and breath.

The angle between Phases II and III is sharper for low molecular weight gases.

Differences between gas concentrations on inhalation or when there was a sudden "square wave" change of concentration presented to the mass spectrometer could be caused by diffusion/convection interactions in the sampling system, unexplained differences in the temporal handling of various gases by the mass spectrometer, or slight misalignments of the pens on the polygraphs. Such differences were negligible in comparison to the differences that appear during the exhalation, as indicated by the way all the gases rise together during inspiration (the upswing at the right of Fig. 1).

Because of the way concentrations are normalized, the entire inhalation preceding the exhalation shown in Fig. 1 contained all four inert gases at C/C_1 values of 1.0. Therefore, since helium concentration is below SF_6 throughout the exhalation, it follows that more He than SF_6 was retained inside the lung. A rough calculation can be made of the magnitude of the difference. If the tidal volume for the breath were one liter and the exhalation rate were constant, the 0.5-s difference near the midpoint of the C/C_1 decline would correspond to a Fowler dead space difference of approximately 125 ml. Alveolar ventilation for He might therefore be 15% greater than for SF_6 , giving $V_T - V_D$ of about 725 for SF_6 if it were 850 for He.

The C/C_1 axis allows easy comparison of the amount of mixing of the gases. For example, if one volume of the inspired gas were mixed with one volume of another gas, the C/C_1 value of each indicator would be 0.5. It is clear from Fig. 1 that early in expiration the gas came from regions of the lung in which He was in lower concentration than SF_6 , as if He had mixed in a larger volume. The four indicators come together and cross over each other at the end of expiration. Because the He trace is nearly flat, end-expired He may be a reasonable estimate of the average C_{He} in the "alveolar plateau" of expiration and also in the lung gas that is not expired, the FRC. However, end-expired SF_6 is clearly lower than C_{SF_6} in most of expiration and probably considerably higher than SF_6 in the FRC.

Figure 2 shows how the patterns for SF_6 and He changed during the wash-in at each of the three pressures. Breath number 1 at 9.5 ATA (near the bottom of the right-hand panel) is the breath that was seen in Fig. 1. In the first breath at 1.5 ATA (bottom of left-hand panel), SF_6

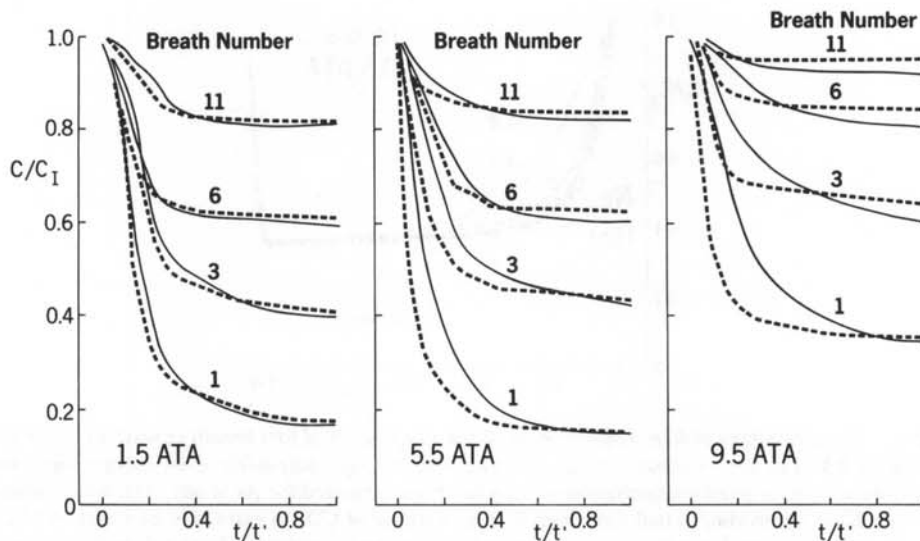


Fig. 2. Comparison of concentration patterns of SF_6 (solid) and He (dashed) for Subject RS as wash-in proceeded; three different environmental pressures. Axes are as in Fig. 1.

and He concentrations are much closer to each other than at 9.5 ATA; the 5.5 ATA breath (middle panel) has an intermediate pattern. The first breath at 9.5 ATA leveled at higher concentrations because in this particular subject tidal volume was larger.

The third breath at each pressure differs from the first in that both SF_6 and He concentrations are higher due to the wash-in process. The pattern of concentrations in the third breath is similar to the pattern of the first in that He has a sharper angulation than SF_6 , but differs in that end-expired He is higher relative to end-expired SF_6 . The high He concentration in the third expiration is explained by a back pressure that develops due to the better mixing of He. The first breath is the only one in which inside-to-outside concentration differences for the two gases are the same before the breath; thereafter He inside the lung is at a higher concentration than SF_6 , and consequently the rapid initial exchange of He decreases until it is about the same as the SF_6 exchange rate. For example, in breaths 6 and 11 at 5.5 and 9.5 ATA (Fig. 2), the amounts of He and SF_6 expired may be nearly the same, judging from the crossover of concentration early in the expiration.

Argon and Ne concentrations, not shown in Fig. 2, were between those of SF_6 and He during Phase II and retained their intermediate angulation throughout wash-in. As the wash-in proceeded, there were crossovers of all four gases that became quite complex. For example, on breath 11 at 9.5 ATA, one of the 4 gases crossed or recrossed another 6 times during the expiration; at end-expiration, concentrations were in order of molecular weight— SF_6 (lowest); Ar; Ne; He.

The patterns of Figs. 1 and 2 are typical for the three subjects, and are consistent with the patterns seen on the wash-out exhalations after the subject begins to breathe air. During the wash-out, the gases rise from a C/C_1 of zero at the left (C_1 corresponds to bag concentration of test gas) to a plateau at the right. The rise was earlier for He than for SF_6 , and on the first breath of wash-out the end-expired values were essentially the same for He and SF_6 . Later in wash-out, end-expired C/C_1 for He was lower than for SF_6 .

Figure 3 shows the wash-in processes plotted semilogarithmically. The ordinates show end-expired concentrations (divided by C_I) subtracted from 1.0, so that the value for any particular breath number indicates the fraction of equilibration yet to be completed. At 1.5 ATA, SF_6 and He washed in simultaneously; at 9.5 ATA, He is closer to equilibrium than SF_6 after 10 breaths, but the two gases are more nearly parallel than would occur if He had not developed the back pressure discussed above in connection with Fig. 2.

DISCUSSION

A satisfactory qualitative explanation of most aspects of our experimental results can be derived from simple physical principles. The crux of the explanation is that the amount of gas diffusing from one location to another in the lungs or in any other configuration is governed by several interdependent variables. A change in one variable can bring about compensations in others that are free to change.

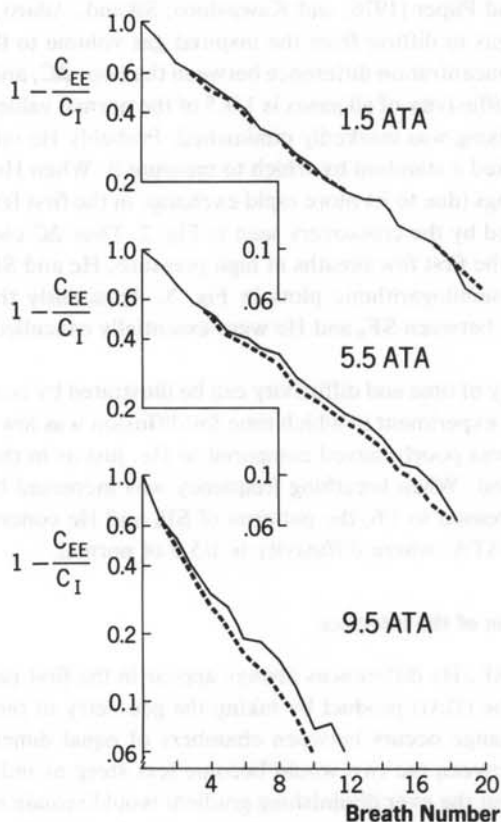


Fig. 3. Semilogarithmic plots of wash-in process at 3 pressures; Subject RS. Helium (dashed) is closer to equilibrium than SF_6 (solid) after first few breaths at 5.5 and 9.5 ATA. The 9.5 ATA wash-in proceeded more rapidly than the others because subject chose a breathing pattern of larger tidal volumes.

The diffusion-area-time product

The equation for diffusion within a simple geometry illustrates how some of the factors that influence diffusion in the lung may interact. Consider diffusion of an indicator gas from one well-mixed chamber to another through a barrier. All the indicator is originally in chamber 1. Indicator amount (V_2) in chamber 2 at any time (t) is governed by the equation:

$$V_2 = V_1^0 (m) (1 - e^{-n(DAt)}) \quad (1)$$

where V_1^0 is amount in chamber 1 at zero time, m and n are constants defined by the geometry of the two chambers and permeability of the membrane, D is the molecular diffusivity of the indicator and A is the area of the exchange surface.

The importance of Eq. 1 for the present discussion is that, under the influence of a given concentration difference, the amount of indicator to diffuse depends on the product (DAt). According to this, D , A , and t should each be equally effective in governing the amount exchanged. For example, a decrease of diffusivity to 1/10 of normal, as at 10 ATA, should be completely compensated for by a 10-fold increase of A or t , or by a combination of changed A and t that leads to a product that is 10 times the normal product (5×2 or 3.16×3.16).

If we envision the lung as two chambers in diffusion contact, one originally containing inspired gas and the other originally filled with residual gas, as done previously by Sikand, Magnussen, Scheid, and Piiper (1976) and Kawashiro, Sikand, Adaro, Takahashi, and Piiper (1976), the amount of gas to diffuse from the inspired gas volume to the residual gas volume would depend on the concentration difference between the two, ΔC , and on the (DAt) product.

At 9.5 ATA, where diffusivity of all gases is 1/9.5 of the normal value, separation of SF_6 and He showed that SF_6 mixing was markedly diminished. Probably He mixing was less also, but in our protocol, we lacked a standard by which to measure it. When He came to have a higher concentration in the lungs (due to its more rapid exchange in the first few breaths), He wash-in was slowed, as indicated by the crossovers seen in Fig. 2. Thus ΔC changes exerted a buffering effect so that after the first few breaths at high pressure, He and SF_6 concentrations were nearly parallel on the semilogarithmic plots in Fig. 3. Apparently the effects of the 6-fold difference of diffusivity between SF_6 and He were essentially cancelled by the ΔC differences between the two.

The interchangeability of time and diffusivity can be illustrated by comparison of the present data with results of our experiment in which time for diffusion was low during rapid breathing (Van Liew 1978); SF_6 was poorly mixed compared to He, just as in this experiment in which diffusivity was decreased. When breathing frequency was increased by a factor of 6 so that diffusion time was decreased to 1/6, the patterns of SF_6 and He concentrations resemble the results in Fig. 2 at 5.5 ATA, where diffusivity is 1/5.5 of normal.

Mouthward translocation of the interface

The finding that the SF_6 -He differences always appear in the first part of expiration can be discussed in terms of the (DAt) product by taking the geometry of the lung into account.

When diffusion exchange occurs between chambers of equal dimension, the steep initial gradient or interface between the two would become less steep as indicator moves from one chamber to the other, but the ever diminishing gradient would remain in place at the interface between the two. In the lung, there is a vast divergence of summed cross section of airways and of lung volume as the airways divide on the paths to the alveoli. This dictates that a steep gradient that is set up at some location will move toward the mouth as indicator diffuses from larger airways into exchange units (LaForce and Lewis 1970; Paiva 1973). The steep fall of SF_6

and He in the first part of expiration (Phase II of expiration) shows the extent of the mouthward movement of the steep gradient between inspired gas and resident gas in the lung.

At both low and high pressures, the high diffusivity of He allows the He gradient to move farther mouthward than the SF₆ gradient. At high pressure, both gases probably do not move as far mouthward, but since the He gradient is in upper airways having low volume even at 9.5 ATA, high pressure has little effect on the He profile. According to this reasoning, at high pressure the SF₆ gradient's mouthward movement is so delayed that it remains in lower airways and a relatively large volume of gas with a concentration equal to the inspired concentration is still mouthward of the gradient.

Low diffusivity causes the steep gradient to remain in a region of large cross-sectional area in a way that buffers the effect of low diffusivity. In a normal environment and for He at pressure, diffusion practically ceases when the gradient moves into the relatively narrow cross section of upper airways. In a hyperbaric environment, the steep gradient for SF₆ stays in a large cross section so that diffusion exchange, although hampered by low diffusivity, is aided by large area.

Oxygenation in dense environments

The high concentrations of SF₆ during the course of the first-breath expirations at 5.5 and 9.5 ATA show that low diffusivity is associated with poor gas mixing. Mixing of SF₆ is unequivocally poor compared to He in the sense that better mixing would have left more SF₆ in the FRC after the breath.

There have been several reports that delivery of O₂ or CO into arterial blood is facilitated by breathing dense gas (Martin, Zutter, and Anthonisen 1972; Johnson and Van Liew 1974; Kvale, Davis, and Schroter 1975; Wood, Bryan, Bau, Weng, and Levison 1976; Worth, Takahashi, Willmer, and Piiper 1976; Gledhill, Froese, Buick, and Bryan 1978), leading to speculation that gas mixing may be improved by the changes in mechanical processes that occur with dense gases. Our demonstration that mixing is poor in dense environments indicates that the improved oxygenation or CO uptake must rather be due to more favorable distribution of inspired gas.

One explanation for the improved oxygenation of capillary blood at high pressure could be that the distribution is more even, perhaps brought about by more efficient cardiac mixing in a dense environment (Wood et al. 1976). There is another possibility that is essentially the opposite: oxygenation may be improved by more unevenness. If there are appreciable numbers of low-ventilation, low-perfusion units distributed throughout the lung (Martin, Das, and Young 1976; Ewan, Jones, Nosil, Obdrzalek, and Hughes 1978), oxygen may normally diffuse into such units, thus decreasing the O₂ delivery to nearby well-ventilated, well-perfused units. Low diffusivity may improve the performance of the lung by decreasing the waste of O₂ incurred by its delivery into poorly perfused units.

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Van Liew, H. D., E. D. Thalmann, and D. K. Sponholtz. 1979. Le dépendance diffusive du gaz pulmonaire mélangeant à 5.5 et 9.5 ATA. *Undersea Biomed. Res.* 6(3):251-258. — La diffusivité de la phase gazeuse est proportionnelle inversement à la pression, et pour ça le mélange des gaz inspirés dans les poumons peut être compté d'être pauvre dans les environnements hyperbares. Les sujets ont fait des souffles multiples "wash-in" d'un mélange (4% chacun de SF₆, Ar, Ne, et He; 21% O₂, 63%

N₂) à 1,5, 5,5, et 9,5 ATA. Aux pressions plus hautes, il y avait des différences prononcées des concentrations entre les gaz indicatifs, mesuré par le spectromètre masse à la bouche durant une seule expiration. Comparé aux gaz plus lourds, les gaz légers sont tombés plus tôt d'une concentration de l'espace morte au niveau "alvéolaire," et ont eu une concentration moyenne expirée plus basse, indiquant que plus des gaz légers ont été retenus chez la Capacité Fonctionnelle Résiduelle (CFR) après le souffle. Pourtant, les taux de "wash-in" pour les indicateurs ont été à peu près de même; un taux initial rapide pour He a diminué ainsi qu'il était à peu près de même que le taux de SF₆, parce que dans les souffles postérieurs une contre pression a développé pour He. Les résultats illustrent la principe fondamentale que la quantité du gaz qui diffuse d'une location à une autre dans un réservoir dépend non seulement de la diffusivité, mais aussi d'une façon indépendante de l'inclinaison du concentration, le temps pour diffuser, et la configuration du réservoir.

diffusivité
diffusion de la phase gazeuse
échange des gaz respiratoires

air hyperbare
mélangeant des gaz pulmonaires

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