Undersea Biomedical Research, Vol. 8, No. 3, September 1981

Effectiveness of a breath during exercise in a hyperbaric environment

H. D. VAN LIEW and D. K. SPONHOLTZ

Deparment of Physiology, State University of New York at Buffalo, Buffalo, NY 14214

Van Liew HD, Sponholtz DK. Effectiveness of a breath during exercise in a hyperbaric environment. Undersea Biomed Res 1981; 8(3):147–161.—During vigorous foot-pedal exercise at 6.75 ATA, three subjects had lower total ventilation, larger functional residual capacity (FRC), and higher P_{CO_2} in end-expired and mixed-expired gas than during the same exercise at 1.5 ATA. Compartmental analysis of multiple breath washin suggested that ventilation was more evenly distributed during the high pressure exercise. Mass-balance analysis of inert indicator gases in single breaths showed that at a given pressure, low-diffusivity gases did not mix in the lung as well as high-diffusivity gases. It did not follow, however, that a particular gas was better mixed at low pressure than when its diffusivity was decreased by high pressure; the data showed just the opposite during exercise. The apparent paradox seems to be explained by the change of other conditions for mixing at high pressure, especially the enlargement of the FRC.

functional residual capacity
helium and sulfur hexafluoride
single-breath analysis
multiple-breath washin
diffusion
pulmonary gas mixing
hyperbaric environments
exercise
dynamic compression
flow limitation
end-expired volume

Probably the most important factor that limits a person's ability to perform hard physical work in an environment of dense gas is the greater tendency for dynamic airway compression during expiration (1–6). According to theory, when dynamic compression occurs, the maximal flow attainable at a given lung volume is closely related to the reciprocal of the square root of gas density (4, 6–8).

Several less important factors associated with a dense environment can be expected to modify the physiological impact of the absolute maximum of ventilation imposed by the dynamic compression phenomenon: 1) Inspiratory muscles, which theoretically could change their activity to partially compensate for the expiratory limitation by decreasing the inspiratory time and increasing the inspired volume, may become fatigued (6). 2) If the environment is also hyperoxic, the person can extract more O_2 than normal from his limited alveolar ventilation without becoming hypoxic. Because of the relative hypoventilation, he becomes hypercapnic, which also allows him to expire more CO_2 per breath than normal. Carbon dioxide sensitivity apparently is inversely related to gas density (9), and divers as a group are prone to choose (or

at least to tolerate) greater hypercapnia than nondivers, even when ventilation is submaximal (10–12). 3) Gas mixing in the lung can be expected to be impaired by low gas-phase diffusivity (13, 14), since diffusivity is inversely proportional to environmental density (15). 4) Ventilatory pattern or distribution of ventilation may alter gas exchange effectiveness; some sort of beneficial change in a dense environment has been postulated (16–19).

This communication is concerned with breath effectiveness of men exercising in a hyperbaric, hyperoxic environment at a metabolic rate that caused them to be at or near the limitation caused by dynamic compression.

METHODS

Our experimental strategy was to have our subjects change from breathing air to breathing a mixture that contained low concentrations of four indicator gases, He, Ar, Ne, and sulfur hexafluoride (SF_6). By comparing both the single-breath pattern and the multiple-breath washin pattern of a given indicator gas, we were able to assess changes of overall effectiveness under four conditions: rest and exercise at high or control pressures. By comparing high-molecular-weight indicators with low-molecular-weight ones within a single breath, diffusion effects could be isolated from other influences that changed in the four conditions.

All measurements were made in the hyperbaric chamber at State University of New York at Buffalo (SUNYAB). Subjects were three informed young men, trained in diving techniques, who had been examined six months previously for health and fitness, especially with regard to the cardiopulmonary system. The subjects either breathed chamber air without a mouthpiece or, using a mouthpiece, breathed chamber air or an air-like indicator gas mixture (5.0% SF_6, 4.6% Ar, 4.6% Ne, 4.8% He, 59.8% N_2, and 21.2% O_2) from a bag-in-box system having appropriate valves. Dead space of the mouthpiece was 45 ml. Volume of the bag-box system was continuously measured with a rolling seal spirometer (Collins, Braintree, MA), and concentrations of SF_6, Ar, Ne, He, CO_2, O_2, and N_2 were continuously measured in the mouthpiece, 1 cm from the teeth, with a mass spectrometer (model 1100, Perkin-Elmer, Pomona, CA). The mass spectrometer, located outside the chamber, received its sample through a tube that penetrated the chamber wall; the sample gas was driven by the differential between chamber and room pressure. Outputs of the mass spectrometer and spirometer were recorded with an 8-channel ink-writing polygraph.

To allow low pressure controls and high pressure experimental measurements to be made with the same system, low pressure measurements were made with the chamber pressurized to slightly above atmospheric pressure. Gauge pressure for high pressure exposures was 190 fsw (58 msw) and for low pressure controls was 15 fsw (4.5 msw); these are referred to as 6.75 ATA and 1.5 ATA, respectively.

During a control period while at rest, each subject was connected to the bag-in-box system for monitoring of gas concentrations and collection of mixed expired gas during a 20-breath washin; the subject then stayed on the mouthpiece while breathing air, so that expired concentrations were measured during washout. Then, while breathing air without the mouthpiece, the subject worked on a foot-pedal ergometer at 150 to 175 W. During the fourth or fifth minute of work the subjects again took the mouthpiece for 10–20 washin breaths of the mixture, then 10–20 washout breaths, and then came off the mouthpiece and quit work.

The volume of mixed expired gas collected during the washin procedure was measured with a dry-gas meter, and a sample of the collected gas was sent through the mass spectrometer.

Calculations

Concentrations and volumes were read from the polygraph record; the correction necessary for lag of the mass spectrometer readings behind volume reading was accomplished by aligning the rise of concentration with the beginning of inspiration. We did not attempt correction for time constant (20); timing of the response to a step change of concentration was the same for all gases.

Calculated P_{O_2} and P_{CO_2} values rely on the accurate measurement of total pressure in the chamber, and calculations from mixed expired gas depend on both chamber pressure and the measurement of gas volume. In contrast, the measurements of the inert gases and the spirometer volumes are independent of total pressure, since the same inspired concentration, analysis system, and spirometer were used at high and low pressures. As is seen below, conclusions reached from the inert gases conform generally with conclusions from mixed expired gas, indicating that both kinds of data are valid.

Functional residual capacity (FRC, defined here as end-expired volume) was estimated in three ways: 1) from mixed-concentration of N_2 in a conventional way; 2) from washin data (see next subsection); 3) from end-expired concentration of the best-mixed gas, helium, by the formula:

$$FRC = (V_T - V_D)\left[(C_I/C_{EE}) - 1\right] \qquad (1)$$

where V_T is measured tidal volume, V_D is Fowler dead space estimate for He, and C_I/C_{EE} is the inspired He concentration divided by end-expired He concentration. This assumes that all stratification is between dead space gas and alveolar gas and that there is no parallel heterogeneity. If these assumptions were not valid, the C_{EE} would most likely overestimate the mean mixed concentration; such overestimation would yield an underestimate of FRC by Eq. *1*. Thus large FRC values are not likely due to improper choice of mixed concentration.

Washin analysis

On the assumption that the lung could be characterized as a two-compartment system, washin data for one of the indicator gases, SF_6, were analyzed by "curve-peeling" as follows: logarithm of $(1 - C_{EE}/C_I)$ was plotted against cumulative volume expired as $(1 - C_{EE}/C_I)$ descended from 1.0 to 0.02 over the range of useful data; the slow compartment was identified by the straight line drawn through the lowest several points on the curve. The logarithm of the numerical (not the logarithmic) difference between the data points and the slow-compartment straight line was plotted on the same graph; the fast compartment was identified by a straight line through this last plot. The slope, m_1, of the straight lines was assumed to be:

$$m_1 = (1/V_T)\left(\log\left[FRC_1/(FRC_1 + V_{A_1})\right]\right) \qquad (2)$$

and the numerical (not logarithmic) value of the intercept, b_1, assumed to be:

$$b_1 = V_{A_1}/(V_T - V_D) \qquad (3)$$

where V_T is average tidal volume during the washin; FRC_1 is functional residual capacity of the compartment under consideration, either fast or slow; V_{A_1} is the volume of ventilation per breath for the compartment under consideration; and V_D is a Fowler dead space estimate obtained from the pattern of concentration vs. volume of the first washin breath. With the average measured tidal volume and a Fowler dead space estimate, values for FRC and VA for the fast and slow compartments were computed from the slopes and intercepts and an estimate of total FRC obtained as the sum of the FRC of the two compartments.

RESULTS

Means of gas exchange variables for the three subjects are listed in Table 1. Oxygen consumption ($\dot{V}O_2$), CO_2 production ($\dot{V}CO_2$), and respiratory exchange ratio (R) were essentially the same during exercise in the hyperbaric and control environments. Metabolic rate in exercise was almost 10-fold that at rest in the 1.5-ATA control environment. Metabolic rate at rest at 6.75 ATA was elevated, probably because of activity associated with the compression. The subjects were hypercapnic during exercise in the 6.75-ATA environment and had a markedly lower total ventilation ($\dot{V}E$), mainly because of low respiratory frequency (f); average tidal volume (VT) was only slightly below control during exercise in the hyperbaric environment. During exercise, Fowler dead space (VD) for He was somewhat less at the higher pressure, and end-expired fraction of He was less at 6.75 ATA than at 1.5 ATA. The next-to-last column of the table shows estimates of expiratory flow rate during the midportion of the expiration; flow during exercise at 6.75 ATA was about 60% as great as during exercise at the control pressure. Duration of inspiration followed changes of frequency; the ratio of inspiratory duration to breath duration averaged between 0.45 and 0.48 in all cases.

Because respiratory frequency in exercise was less, amounts of O_2 and CO_2 exchanged per breath were markedly greater in the hyperbaric environment than under control conditions, as seen for O_2 in the last column of Table 1. The hypercapnia that resulted from the hypoventilation was reflected in the expired concentration-vs.-volume pattern as elevated P_{CO_2} throughout the breath, with the slope of Phase III unchanged. Fowler dead space for CO_2 was unchanged, or actually smaller, at high pressure (Fig. 1).

Figure 2 shows FRC measured by three methods. The FRC was somewhat enlarged at rest at 6.75 ATA, and values at 6.75 ATA exercise were about 50% larger than at 1.5 ATA.

Figure 3 shows an example of multiple-breath washin results for one subject during exercise. Multiple-breath equilibration rates depend on the ratio of VA/FRC. The marked increase of FRC seen in Fig. 2 may be the main factor behind the slow washin at 6.75 ATA, but poor gas mixing to cause low VA may have also played a role. Since tidal volumes in exercise were approximately the same at the two pressures, the cumulative volume on the horizontal axis is approximately proportional to a breath number scale. Cumulative volumes required for SF_6 to reach 90% of equilibration (a value of 0.10 on the Fig. 3 vertical axis) during exercise for the three subjects were 13 ± 2 vs. 20 ± 2 at 1.5 and 6.75 ATA, respectively, and during rest, 13 ± 4 and 16 ± 4 at 1.5 and 6.75 ATA, respectively. Thus the volume of breathed gas to reach a certain degree of equilibration was the same during rest and exercise at 1.5 ATA but was markedly greater at 6.75 ATA exercise. The ratio of volume to reach 90% equilibration was 1.5 (i.e., volume at 6.75 ATA/volume at 1.5 ATA), approximately the same as the ratio of FRC at 6.75 ATA to FRC at 1.5 ATA.

Compartmental analysis of washin

Results of compartmental analysis of washin of SF_6 are shown in Fig. 4 as bar graphs that represent the averages for the three subjects. In the 8 bars at the *top* of the figure, the height of each bar represents a total quantity and a dashed line in the bar divides the quantity into its fast-compartment component at the top and slow-compartment component at the bottom. The

TABLE 1.
GAS EXCHANGE VARIABLES FOR THREE SUBJECTS*

Conditions of Experiment	$\dot{V}O_2$, liters/min, STPD	$\dot{V}CO_2$, liters/min, STPD	R**	End-Expiratory PCO_2, torr	Mixed-Expiratory PCO_2, torr	$\dot{V}E$, liters/min, BTPS	f, breaths/min	VT, liters/breath, BTPS	VD_{He}, liters/breath, BTPS	$(CEE/CI)_{He}$†	Expiratory Flow, liters/s, BTPS	$\dot{V}O_2$/f, liters/breath, STPD
1.5 ATA Control												
Rest	0.29 ± 0.02	0.28 ± 0.02	0.95 ± 0.02	35 ± 2	25 ± 3	11 ± 1	12 ± 3	0.9 ± 0.3	0.24 ± 0.04	0.23 ± 0.15	0.4 ± 0.1	0.03 ± 0.01
Exercise	2.5 ± 0.2	2.8 ± 0.3	1.12 ± 0.05	45 ± 2	35 ± 3	82 ± 8	24 ± 2	3.4 ± 0.4	0.38 ± 0.19	0.46 ± 0.05	3.7 ± 0.8	0.10 ± 0.01
6.75 ATA												
Rest	0.39 ± 0.02	0.45 ± 0.13	1.15 ± 0.30	35 ± 3	25 ± 1	17 ± 8	11 ± 2	1.5 ± 0.5	0.17 ± 0.03	0.28 ± 0.04	0.6 ± 0.3	0.04 ± 0.01
Exercise	2.6 ± 0.02	2.6 ± 0.2	1.04 ± 0.11	54 ± 4	39 ± 3	57 ± 4	18 ± 2	3.2 ± 0.7	0.32 ± 0.08	0.36 ± 0.05	2.2 ± 0.2	0.14 ± 0.03

*Means ± SD. **R, dimensionless respiratory exchange ratio. †Dimensionless ratio of end-expired to inspired He concentrations.

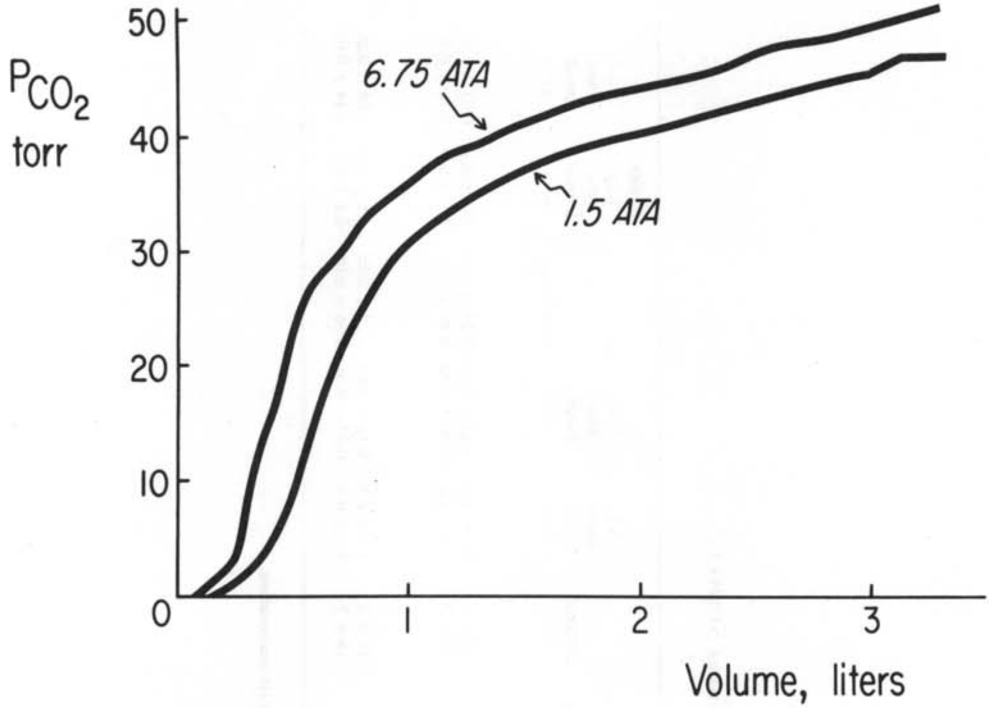

Fig. 1. Patterns of CO_2 in one subject; 3-liter expirations at high and control pressures during exercise.

4 bars at the *top left* show VA (tidal volume minus Fowler dead space), with respiratory frequency noted above the bars. The 4 bars at the *top right* show FRC; number in parentheses in each compartment is VA/FRC, an index of the effectiveness of a single breath on washin of the compartment. The *lower* 8 bars show the VA/FRC values for the four conditions; for each pair of bars, the VA/FRC of the slow compartment is the lesser one to the *left*, and the fast compartment is to the *right*. In all cases, bars representing high pressure data are cross-hatched.

Figure 4 shows that at 1.5 ATA the transition from rest to exercise caused an enlarged $\dot{V}A$ (calculable from VA • f); a slight decrease of total FRC; an increase of the FRC volume of the fast compartment; a change by a factor of about 4 of VA/FRC in both slow and fast compartments; and, most notably, an enlargement of the amount of the VA that went to the fast compartment as seen by its larger VA and high VA/FRC. This last appears to be a wasteful situation in exercise, in that so much of the breath goes to the relatively small FRC volume of the fast compartment.

During exercise at 6.75 ATA, VA and partition of VA were approximately the same as at 1.5 ATA exercise, but the $\dot{V}A$ was considerably less in the higher pressure environment: 54 vs. 75 liters/min. The total FRC at 6.75 ATA was greater than at 1.5 ATA both in rest and exercise, but the change of partition of FRC between rest and exercise was about the same as at 1.5 ATA. A notable difference between the 6.75 and 1.5 ATA cases was in the VA/FRC. At the higher pressure, the VA/FRC changed very little from rest to exercise in the two compartments; the change was only a 30% to 60% increase in contrast to the 4-fold increase between rest and exercise at 1.5 ATA. Differences of resting VA and $\dot{V}A$ between 6.75 ATA and 1.5 ATA are explainable as due to the subjects' greater activity during rest at the higher pressure.

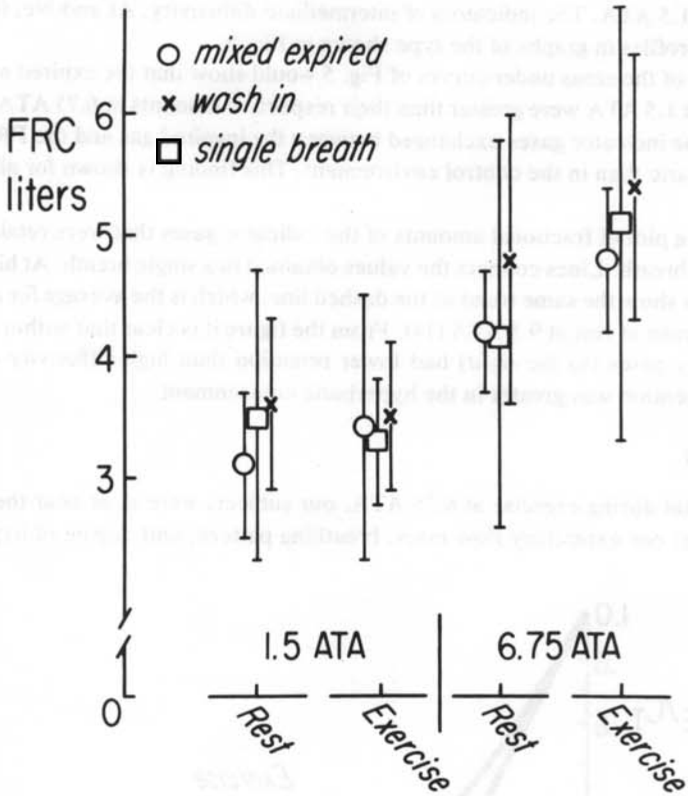

Fig. 2. Mean ± SD of functional residual capacity values measured by three methods.

In all cases, the VA/FRC of the fast compartment was about 3 times the VA/FRC of the slow compartment (*lower panel,* Fig. 4). During exercise the VA/FRC of both compartments at the higher pressure was about one-half the value at the lower pressure; the change was the opposite direction during rest, in which VA/FRC of both compartments at the higher pressure was 1.5 times the value at lower pressure.

Exercise seems to have been associated with heterogeneity of VA/FRC at 1.5 ATA (large ventilation to fast compartment and large value of VA/FRC of the fast compartment), and the heterogeneity was less at 6.75 ATA (equally large fast-compartment ventilation, but enlarged fast-compartment FRC to match it, so VA/FRC of the fast compartment was less). The $\dot{V}A$/FRC for the slow and fast compartments were calculated and compared to the values for the lung taken as a single unit; the result again indicated that distribution of ventilation was somewhat more even during the exercise at the higher pressure, in that the wasteful $\dot{V}A$/FRC of the fast compartment was 1.8 times that of the lung as a whole at 6.75 ATA compared to 2.1 times at 1.5 ATA.

Mass balance analysis of single breaths

The first washin breaths of one subject at exercise are shown in Fig. 5. Tidal volumes happened to be almost the same, so direct comparison between the two breaths is warranted. Both He and SF_6 were at C/CI of about 0.4 at end expiration; the He fell to the plateau more briskly at 6.75 ATA than at 1.5 ATA. Fowler dead space for He would clearly be less at 6.75

ATA than at 1.5 ATA. The indicators of intermediate diffusivity, Ar and Ne, fell between the SF_6 and He profiles in graphs of the type shown in Fig. 5.

Integration of the areas under curves of Fig. 5 would show that the expired amounts of both He and SF_6 at 1.5 ATA were greater than their respective amounts at 6.75 ATA; it follows that amounts of the indicator gases exchanged between the inspired gas and the FRC were greater in the hyperbaric than in the control environment. This finding is shown for all three subjects in Figure 6.

Figure 6 is a plot of fractional amounts of the indicator gases that were retained in the FRC after the first breath. Lines connect the values obtained in a single breath. At high pressure the three subjects show the same trend as the dashed line, which is the average for a larger number of breaths in men at rest at 9.5 ATA (14). From the figure it is clear that within a single breath, low-diffusivity gases (to the *right*) had lower retention than high-diffusivity ones, but for a given gas, retention was greater in the hyperbaric environment.

DISCUSSION

We infer that during exercise at 6.75 ATA, our subjects were at or near their maximal gas exchange rate; our expiratory flow rates, breathing pattern, and degree of hypercapnia were

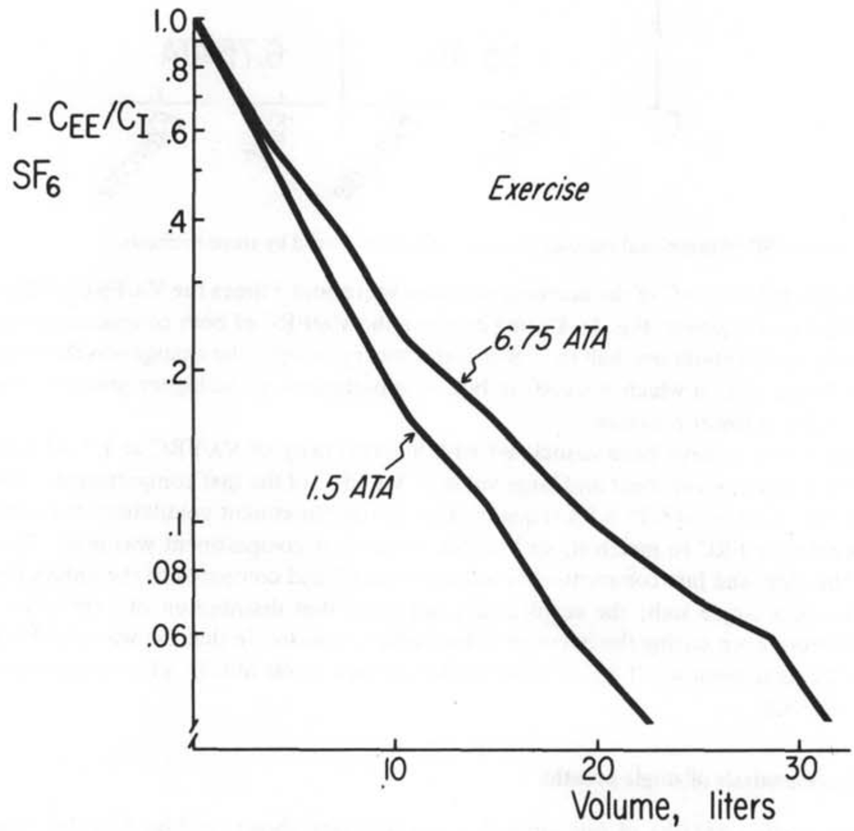

Fig. 3. Multiple-breath washin results for sulfur hexafluoride for one subject during exercise. Vertical axis shows fraction of disequilibrium between the inspirate (C_I, concentration) and the end-expired gas (C_{EE}, concentration). Horizontal axis shows cumulative volume of gas expired.

near those reported by others during the flow-limited condition at similar gas densities (1, 2, 4–6, 21–24), but our subjects did not complain of the severe dyspnea found in some studies (3, 6, 21, 24).

Although FRC changes but little in exercise at normal pressures (25), increased FRC has been reported previously in exercise at high pressure (3, 4, 6). In our experiment the mixing benefit of the enlarged FRC (see APPENDIX) and perhaps the longer breath duration over-

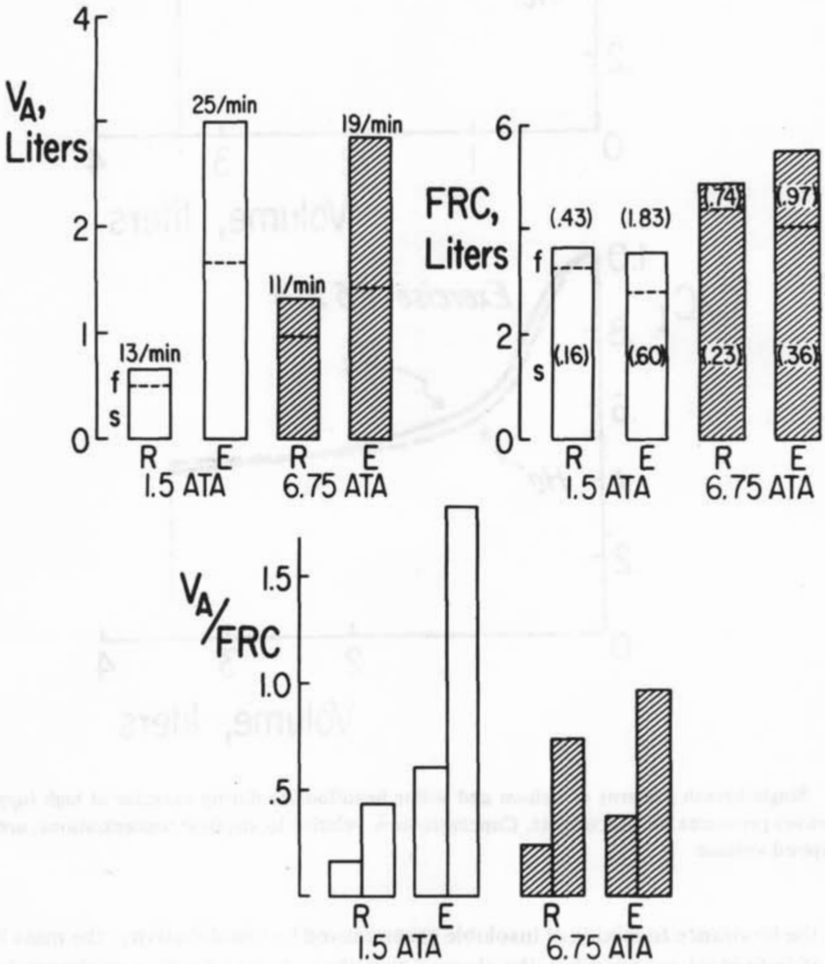

Fig. 4. Results of 2-compartment analysis of sulfur hexafluoride washin data. R, rest; E, exercise; *open bars,* 1.5 ATA; *cross-hatched bars,* 6.75 ATA. *Upper left:* total height of each of the 4 bars shows V_A, calculated from average V_T during the multiple-breath procedure minus the V_D that was estimated by the Fowler procedure from the first breath. The V_A value is partitioned into a fast *(above)* and slow *(below)* compartment estimated by curve peeling. Respiratory frequency is given above each V_A bar. *Upper right:* total height of each of 4 bars is total FRC calculated from sum of the two compartments derived by curve peeling. Total FRC is partitioned into fast *(above)* and slow *(below)* compartments. Ventilation per volume on a single-breath basis (V_A/FRC) is shown in parenthesis within each compartment in the bars and is represented by the bars in the *lower part* of the figure, the slow compartment being to the *left* of each pair.

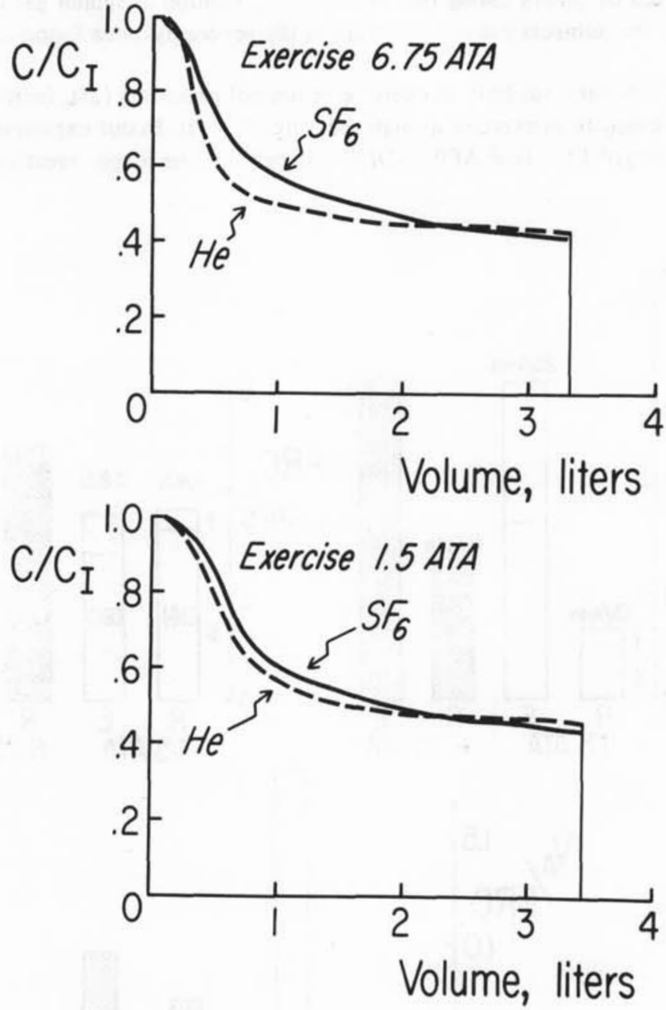

Fig. 5. Single-breath patterns of helium and sulfur hexafluoride during exercise at high *(upper)* and control *(lower)* pressures for one subject. Concentrations, relative to inspired concentrations, are plotted against expired volume.

balanced the hindrance to mixing of insoluble gases caused by low diffusivity; the mass balance analysis of individual exercise breaths showed that the amount of gas to exchange between inspirate and the residual gas in the FRC was greater in the hyperbaric than in the control environment. Other aspects of the changes at high pressure might be considered beneficial also. Distension of airways caused by large lung volume can be expected to make resistance to airflow less than it otherwise would have been and to decrease the resistance to gas mixing by diffusion and convection. The decreased respiratory frequency at high pressure allows gas flows to be less for a given tidal volume and allows more time for diffusive mixing. The washin analysis suggested that ventilation distribution was more even at high pressure.

Unfortunately, a simplistic view that these changes are adaptive mechanisms for compensating for high pressure effects may not be warranted, since cause-and-effect relationships are

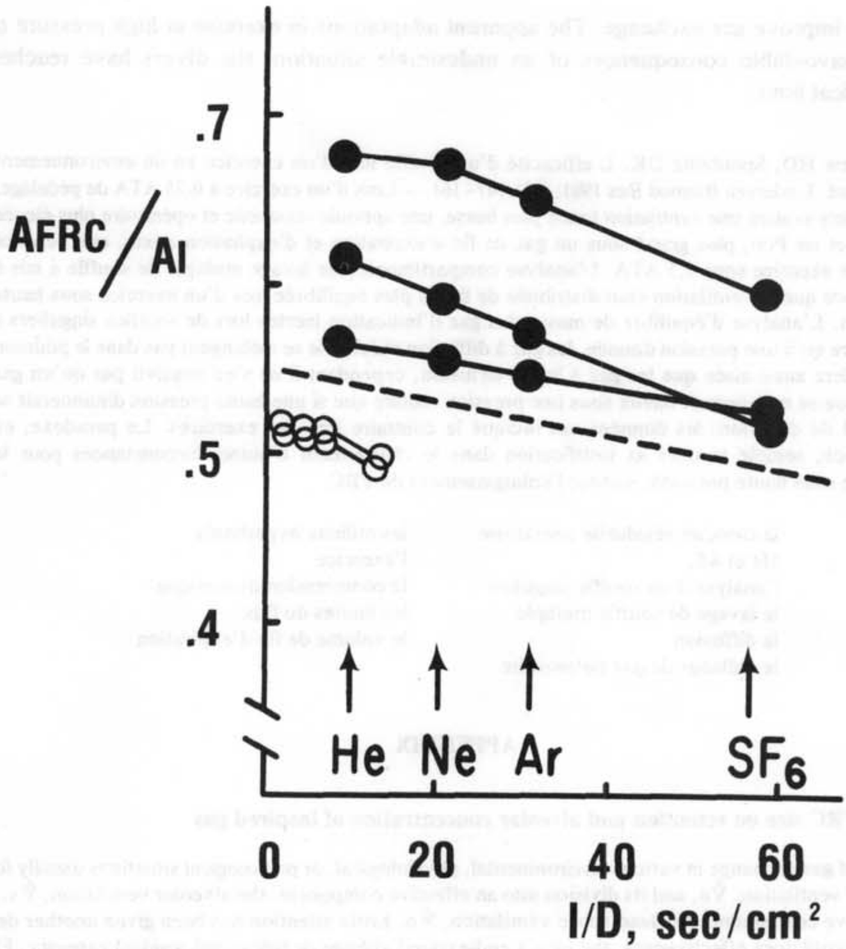

Fig. 6. Amount in functional residual capacity, A_{FRC}, relative to inspired amount, AI, of indicator gases retained in the FRC after a single breath of the indicator mixture is plotted against the reciprocal of the molecular diffusivity: *Closed circles,* 6.75 ATA exercise; *open circles,* 1.5 ATA exercise. Lines connect points for a single breath. *Dashed line,* average slope of a larger number of breaths in subjects at rest, from a previous study. *Arrows,* individual indicators at 6.75 ATA; at 1.5 ATA each indicator has a low value of I/D, so the points for all 4 gases are near the I/D for He at 6.75 ATA.

not clear. It seems quite likely that the subjects had no choice but to change in the directions that were observed. When an exercising diver is limited in the expiratory flow he can achieve, breath duration will perforce be greater if tidal volumes are to be adequate, and the diver may allow his FRC to enlarge so as to conserve the time or the muscular energy that would be required to bring the lung down to the usual end-expired volume. Exercise tidal volumes may be limited by an end-inspiratory volume that is near TLC when FRC is large. Force generated by inspiratory muscles may be less effective than normal because of high recoil pressures at high lung volumes and because of an inefficient, short configuration of the diaphragm. Improved distribution of ventilation may occur because parts of the lung that are relatively overventilated during exercise at normal pressure are distended and unable to ventilate as well at high pressure; if the more even ventilation does not result in more even $\dot{V}_A/\dot{Q}$ throughout the lung, it will not improve gas exchange. The apparent adaptations in exercise at high pressure may be the unavoidable consequences of an undesirable situation; the divers have reached a physiological limit.

Van Liew HD, Sponholtz DK. L'efficacité d'un souffle lors d'un exercice en un environnement hyperbaré. Undersea Biomed Res 1981; 8(3):147–161.—Lors d'un exercice à 6,75 ATA de pédalage, trois sujets avaient une ventilation totale plus basse, une aptitude résiduelle et opératoire plus élevée (FRC), et un P_{CO_2} plus grand sous un gaz de fin d'expiration et d'expiration mixte, que pendant le même exercice sous 1,5 ATA. L'analyse compartimentée de lavage multiple de souffle a mis à l'évidence que la ventilation était distribuée de façon plus équilibrée lors d'un exercice sous haute pression. L'analyse d'équilibre de masse des gaz d'indication inertes lors de souffles singuliers a démontré qu'à une pression donnée, les gaz à diffusion réduite ne se mélangent pas dans le poumon de manière aussi aisée que les gaz à haute diffusion, cependant il ne s'en ensuivit pas qu'un gaz spécifique se mélangerait mieux sous une pression réduite que si une haute pression diminuerait sa capacité de diffusion; les données ont indiqué le contraire lors des exercices. Le paradoxe, en apparence, semble trouver sa justification dans le changement d'autres circonstances pour le mélange sous haute pression, surtout l'énlargissement du FRC.

la capacité résiduelle opératoire
He et SF_6
l'analyse d'un souffle singulier
le lavage de souffle multiple
la diffusion
le mélange de gaz pulmonaire
les milieux hyperbarés
l'exercice
la compression dynamique
les limites du flux
le volume de fin d'expiration

APPENDIX

Effect of FRC size on retention and alveolar concentration of inspired gas

Studies of gas exchange in various environmental, physiological, or pathological situations usually focus on the total ventilation, $\dot{V}_E$, and its division into an effective component, the alveolar ventilation, $\dot{V}_A$, and an ineffective component, the dead space ventilation, $\dot{V}_D$. Little attention has been given another determinant of ventilatory effectiveness, the lung's end-expired volume or functional residual capacity, FRC. Its importance to amount of insoluble gas exchanged per breath can be seen from simple mass-balance derivations: Amount, A_I, of an indicator gas taken into the alveolar portion of the lungs in a single breath is the same before and after mixing with FRC gas:

$$A_I = C_I V_A = C_M (V_A + FRC) \qquad (1A)$$

In Eq. *1A*, C_M is concentration after mixing, C_I is inspired concentration, V_A is "alveolar" or effective part of a breath, and FRC is FRC volume. The V_A in Eq. *1A* can be defined as tidal volume minus dead space volume, $(V_T - V_D)$, so Eq. *1A* requires the assumption of an "equivalent" dead space that accounts both for differences of upper to lower airway concentrations (stratification) and variability between exchange unit concentrations (parallel heterogeneity). The amount of the indicator gas retained in the lung, A, and fraction retained, A/A_I, can be used to characterize the breath effectiveness.

$$A = C_M\, FRC = (C_I V_A \cdot FRC)/(V_A + FRC) \qquad (2A)$$

$$A/A_I = C_M\, FRC/C_I V_A = FRC/(V_A + FRC) \qquad (3A)$$

Equations *2A* and *3A* show clearly that FRC is a strong determinant of the amount of inspired gas that remains in the lung after each breath. Hyperbaric environments can be expected to have conflicting effects on amount exchanged as defined by the equations. For any particular tidal volume, decreased diffusive mixing decreases V_A by increasing the effective dead space, but high airway resistance can be expected to increase the FRC (3, 4, 6, 26, 27).

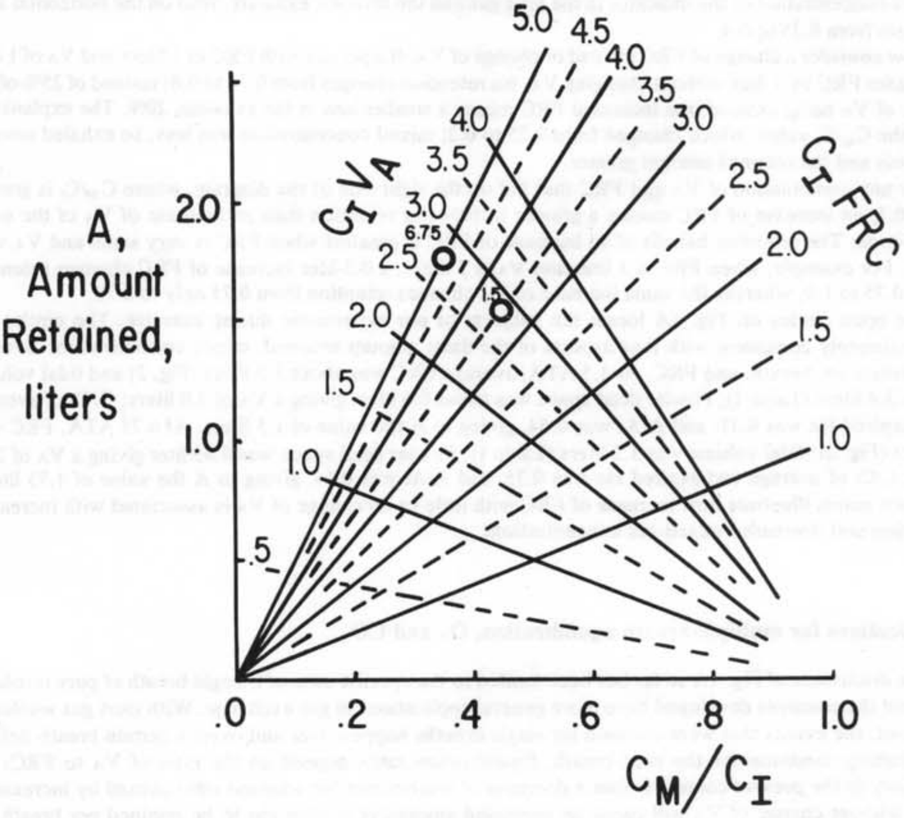

Fig. 1A. Display of interrelationships between A, amount of an inert indicator gas that is retained in the FRC after a single breath; V_A, volume inspired minus dead space volume; C_M, mixed concentration in the FRC and alveolar part of the expirate after inspiration; C_I, unmixed inspired concentration; and FRC. To follow examples in the text, let $C_I = 1.0$, the case for an inspiration of pure indicator. The treatment here has no provision for heterogeneity in the lung, except that a heterogeneous lung would have a large V_D and therefore a small V_A for any given tidal volume. *Open circles*, subject at 6.75 ATA and 1.5 ATA.

Figure 1A is a graphical representation of interrelationships between the variables of Eq. *2A*. It is used to develop the following concepts: *1)* that when V_A is large, amount retained may be increased more by an increase of FRC than by an increase of tidal volume; and *2)* that concentration of the mixture of inspired gas with FRC gas increases when V_A is increased, but it decreases when FRC is increased.

The isopleths on Fig. 1A are for constant values of the products, $C_I V_A$ and C_IFRC; the diagram is easiest to comprehend if breaths of pure indicator are considered, in which $C_I = 1$; the isopleths are then simply for constant V_A and constant FRC. Any point on the diagram shows the result of a single breath: before the breath there is no indicator in the lung, and afterward there is an amount A; before the breath, concentration of indicator in the lung is zero, and afterward C_M/C_I has reached some positive value. The FRC isopleths have positive slopes, consonant with the commonplace idea that when FRC is unchanged, a large breath yields a larger amount and concentration of inspirate in the lung than does a small breath. In contrast, the V_A isopleths have negative slopes: for a given breath size (i.e., a given V_A), a large FRC yields a large amount of indicator retained after one breath, but the mixed indicator concentration is less than when the FRC is small.

Consider a specific example of increasing V_A with constant FRC. When a person with FRC of 3 liters doubles V_A from 1 to 2 liters, the amount retained, read on the upright axis, changes from 0.75 to 1.2 liters. Obviously 25% of the indicator gas in the 1-liter V_A and 40% in the 2-liter V_A were exhaled (not retained).

Mixed concentration of the indicator in the lung gas and the alveolar exhalate, read on the horizontal axis, changes from 0.25 to 0.4.

Now consider a change of FRC instead of change of V_A. If a person with FRC of 3 liters and V_A of 1 liter increases FRC by 1 liter without changing V_A, his retention changes from 0.75 to 0.8; instead of 25% of the 1 liter of V_A being exhaled, the increased FRC means a smaller loss in the exhalate, 20%. The explanation is in the C_M/C_I value, which changed from 0.25 to 0.2; mixed concentration was less, so exhaled amount was less and the retained amount greater.

For any combination of V_A and FRC that fall on the right side of the diagram, where C_M/C_I is greater than 0.5, an increase of FRC causes a greater increase of retention than an increase of V_A of the same magnitude. The retention benefit of an increase of FRC is greatest when FRC is very small and V_A very large. For example, when FRC is 1 liter and V_A is 3 liters, a 0.5-liter increase of FRC changes retention from 0.75 to 1.0, whereas the same increase of V_A changes retention from 0.75 only to 0.78.

The open circles on Fig. 1A locate the subjects of our experiment during exercise. The circles are approximately consistent with four aspects of the data: amount retained, mixed concentration, alveolar ventilation per breath, and FRC. At 1.5 ATA, average FRC was about 3.5 liters (Fig. 2) and tidal volume about 3.4 liters (Table 1); Fowler dead space was about 0.6 liter, giving a V_A of 2.8 liters; C/C_I of average end-expired He was 0.43; and A/A_I was 0.54, giving to A the value of 1.5 liters. At 6.75 ATA, FRC was 5 liters (Fig. 2); tidal volume was 3.2 liters (Table 1); Fowler dead space was 0.45 liter giving a V_A of 2.75 liters; C/C_I of average end-expired He was 0.35; and A/A_I was 0.64, giving to A the value of 1.75 liters. The two points illustrate how increase of FRC with little or no change of V_A is associated with increased retention and decreased mixed-gas concentration.

Implications for multiple-breath equilibration, O_2 and CO_2

The discussion of Fig. 1A so far has been limited to the specific case of a single breath of pure insoluble gas, but the concepts developed have more general applications in gas exchange. With inert gas washin or washout, the events that were outlined for single breaths happen over and over; a certain breath defines the starting condition for the next breath. Equilibration rates depend on the ratio of V_A to FRC; the corollary in the present context is that a decrease of washin rate (or washout rate) caused by increase of FRC without change of V_A will cause an increased amount of washin gas to be retained per breath (or washout gas to be eliminated per breath). Although washin rate is slower with a big FRC, amount of gas retained per breath is greater.

Although "alveolar" oxygen and carbon dioxide are often considered to be constant over time, they actually fluctuate (16, 28). Each inspiration brings new O_2 into the lung, raising the O_2 concentration above the base line of the time average of O_2 concentration, and removal via the blood lowers the O_2 to a nadir before the next inspiration. A single breath of air mixes with FRC gas and thereby changes the lung O_2 concentration by an amount that is analogous to the C_M of Fig. 1A. Of the O_2 brought into the lung by the breath, some is lost in exhalation and some can be considered retained in the same manner as an inert gas, with the difference that concentration of O_2 is also continuously changing due to O_2 uptake by blood. If most of the exhalation volume is expelled from the lung soon after inspiration, or if exhalation is followed by a pause so that O_2 continues to fall in lung gas, the expired gas will contain O_2 at a relatively high concentration. By minimizing the fluctuations of O_2 concentration, a large FRC may decrease the amount of O_2 exhaled.

The same reasoning can be applied to CO_2 exchange. In inspiration, CO_2-free gas mixes with FRC gas, causing a lowered CO_2 concentration. The smaller the FRC relative to V_A, the more the end-inspiratory CO_2 level will go below the time-average of CO_2 in the lung. The lowered CO_2 in the early part of the breath cycle is of course balanced later by elevated CO_2 caused by delivery via blood, but if most of the volume is exhaled early, gas low in CO_2 will be exhaled. With a large FRC, the same volume of inspiration causes only a small dilution of the CO_2 in the lung, so that exhalation carries out CO_2 at high concentration, and therefore the quantity carried is larger than otherwise.

Supported in part by NHLBI Grant PO1-HL-14414 and ONR contract N00014-76-000472.—*Manuscript received for publication January 1981; revision received May 1981.*

REFERENCES

1. Lanphier EH. Pulmonary function. In: Bennett PB, Elliott DH, eds. The physiology and medicine of diving and compressed air work, 2nd edition. Baltimore: Williams and Wilkins Company, 1975:102–154.
2. Vorosmarti J Jr, Bradley ME, Anthonisen NR. The effects of increased gas density on pulmonary mechanics. Undersea Biomed Res 1975; 2:1–10.
3. Spaur WH, Raymond LW, Knott MM, et al. Dyspnea in divers at 49.5 ATA: mechanical, not chemical in origin. Undersea Biomed Res 1977; 4:183–198.
4. Wood LDH, Bryan AC. Exercise ventilatory mechanics at increased ambient pressure. J Appl Physiol: Respir Environ Exercise Physiol 1978; 44:231–237.
5. Vorosmarti J Jr. Influence of increased gas density and external resistance on maximum expiratory flow. Undersea Biomed Res 1979; 6:339–346.
6. Hesser CM, Linnarsson D, Fagraeus L. Pulmonary mechanics and work of breathing at maximal ventilation and raised air pressure. J Appl Physiol: Respir Environ Exercise Physiol 1981; 50:747–753.
7. Macklem PT, Mead J. Factors determining maximum expiratory flow in dogs. J Appl Physiol 1968; 25:159–169.
8. Haynes JH, Kylstra JA. Estimate of maximum expiratory flow based on the equal pressure point concept and Weibel's lung model. Undersea Biomed Res 1974; 1:45–58.
9. Gelfand R, Lambertsen CJ, Peterson RE. Human respiratory control at high ambient pressures and inspired gas densities. J Appl Physiol: Respir Environ Exercise Physiol 1980; 48:528–539.
10. Florio JT, Morrison JB, Butt WS. Breathing pattern and ventilatory response to carbon dioxide in divers. J Appl Physiol: Respir Environ Exercise Physiol 1979; 46:1076–1080.
11. Kerem D, Melamed Y, Moran A. Alveolar P_{CO_2} during rest and exercise in divers and non-divers breathing O_2 at 1 ATA. Undersea Biomed Res 1980; 7:17–26.
12. Sherman D, Eilender E, Shefer A, Kerem D. Ventilatory and occlusion-pressure responses to hypercapnia in divers and non-divers. Undersea Biomed Res 1980; 7:61–74.
13. Van Liew HD, Thalmann ED, Sponholtz DK. Diffusion-dependence of pulmonary gas mixing at 5.5 and 9.5 ATA. Undersea Biomed Res 1979; 6:251–258.
14. Van Liew HD, Thalmann ED, Sponholtz DK. Hindrance to diffusive gas mixing in the lung in hyperbaric environments. J Appl Physiol: Respir Environ Exercise Physiol 1981; 51:243–247.
15. Paganelli CV, Kurata FK. Diffusion of water vapor in binary and ternary gas mixtures at increased pressures. Respir Physiol 1977; 30:15–26.
16. Johnson LR, Van Liew HD. Use of arterial P_{O_2} to study convective and diffusive gas mixing in the lungs. J Appl Physiol: Respir Environ Exercise Physiol 1974; 36:91–97.
17. Kvale PA, Davis J, Schroter RC. Effect of gas density and ventilatory pattern on steady-state CO uptake by the lung. Respir Physiol 1975; 24:385–398.
18. Wood LDH, Bryan AC, Bau SK, Weng TR, Levison H. Effect of increased gas density on pulmonary gas exchange in man. J Appl Physiol: Respir Environ Exercise Physiol 1976; 41:206–210.
19. Gledhill N, Froese AB, Buick FJ, Bryan AC. $\dot{V}_A/\dot{Q}$ inhomogeneity and AaD_{O_2} in man during exercise: effect of SF_6 breathing. J Appl Physiol: Respir Environ Exercise Physiol 1978; 45:512–515.
20. Mitchell RR. Incorporating the gas analyzer response time in gas exchange computations. J Appl Physiol: Respir Environ Exercise Physiol 1979; 47:1118–1122.
21. Anthonisen NR, Utz G, Kryger MH, Urbanetti JS. Exercise tolerance at 4 and 6 ATA. Undersea Biomed Res 1976; 3:95–102.
22. Dwyer J, Saltzman HA, O'Bryan R. Maximal physical-work capacity of man at 43.4 ATA. Undersea Biomed Res 1977; 4:359–372.
23. Morrison JB, Butt WS, Florio JT, Mayo IC. Effects of increased O_2-N_2 pressure and breathing apparatus on respiratory function. Undersea Biomed Res 1976; 3:217–234.
24. Thalmann ED, Sponholtz DK, Lundgren CEG. Effects of immersion and static lung loading on submerged exercise at depth. Undersea Biomed Res 1979; 6:259–290.
25. Stubbing DG, Pengelly LD, Morse JLC, Jones NL. Pulmonary mechanics during exercise in normal males. J Appl Physiol: Respir Environ Exercise Physiol 1980; 49:506–510.
26. Garrard CS, Lane DJ. The pattern of stimulated breathing in man during non-elastic expiratory loading. J Physiol 1978; 279:17–29.
27. Stubbing DG, Pengelly LD, Morse JLC, Jones NL. Pulmonary mechanics during exercise in subjects with chronic airflow obstruction. J Appl Physiol: Respir Environ Exercise Physiol 1980; 49:511–515.
28. Bondi KR, Van Liew HD. Fluxes of CO_2 in the lung gas studied by continuously recorded arterial pH. J Appl Physiol: Respir Environ Exercise Physiol 1973; 35:42–46.