Cardiogenic oscillation phase relationships during single-breath tests performed in microgravity

ANNE-MARIE LAUZON, ANN R. ELLIOTT, MANUEL PAIVA, JOHN B. WEST, AND G. KIM PRISK
Department of Medicine, University of California San Diego, La Jolla, California 92093; and Biomedical Physics Laboratory, Université Libre de Bruxelles, Brussels 1070, Belgium

Lauzon, Anne-Marie, Ann R. Elliott, Manuel Paiva, John B. West, and G. Kim Prisk. Cardiogenic oscillation phase relationships during single-breath tests performed in microgravity. J. Appl. Physiol. 84(2): 661–668, 1998.—We studied the phase relationships of the cardiogenic oscillations in the phase III portion of single-breath washouts (SBW) in normal gravity (1 G) and in sustained microgravity (µG). The SBW consisted of a vital capacity inspiration of 5% He-1.25% sulfurhexafluoride-balance O2, preceded at residual volume by a 150-ml Ar bolus. Pairs of gas signals, all of which still showed cardiogenic oscillations, were cross-correlated, and their phase difference was expressed as an angle. Phase relationships between inspired gases (e.g., He) and resident gas (N2) showed no change from 1 G (211 ± 9°) to µG (163 ± 7°). Ar bolus and He were unaltered between 1 G (173 ± 15°) and µG (211 ± 25°), showing that airway closure in µG remains in regions of high specific ventilation and suggesting that airway closure results from lung regions reaching low regional volume near residual volume. In contrast, CO2 reversed phase with He between 1 G (332 ± 6°) and µG (263 ± 27°), strongly suggesting that, in µG, areas of high ventilation are associated with high ventilation-perfusion ratio (VA/Q). This widening of the range of VA/Q in µG may explain previous measurements (G. K. Prisk, A. R. Elliott, H. J. B. Guy, J. M. Kosonen, and J. B. West. J. Appl. Physiol. 79: 1290–1298, 1995) of an overall unaltered range of VA/Q in µG, despite more homogeneous distributions of both ventilation and perfusion.

ventilation distribution; perfusion distribution; gas exchange; cross-correlation coefficient; helium; sulfurhexafluoride; argon

GRAVITY IS AN IMPORTANT CONTRIBUTOR to the distribution of ventilation (VA) and to ventilatory inhomogeneity (1, 7, 8, 18, 24). The commonly applied gravitational model of VA distribution predicts that, for a vital capacity (VC) maneuver in an upright subject, there will be preferential VA in the dependent zones of the lungs (1, 13, 16, 19). Similarly, perfusion (Q) is also greatest in the dependent zones of the lung (12, 16, 25).

The cardiogenic oscillations in the phase III slope of single-breath washout (SBW) tests are a useful marker of lung inhomogeneity, and the understanding of their amplitude and phase relationships have generated a lot of interest (2–4, 6, 10, 11, 15, 17, 20, 27, 29, 30). Based on the gravitational model, a bolus inhaled at residual volume (RV) will be distributed toward the regions of the lungs that remain open at RV, which are also the nondependent poorly ventilated (high N2 concentration ([N2]) regions of the lungs. Bradley et al. (6) and Yoshioka et al. (29) investigated the phase relationships of the cardiogenic oscillations in VC maneuvers that included a bolus of a test gas. They found that the oscillations in the bolus gas and those in the resident gas (N2) were in phase if the bolus was taken close to RV and out of phase if the bolus was taken close to total lung capacity (TLC). They also showed that the oscillations in the bolus gas and N2 were in phase with cardiac systole when taken close to RV and in phase with diastole when taken close to TLC. Moreover, Bradley et al. (6) showed that gravity influenced their results by performing the test in inverted subjects. They observed a 180° phase shift between the QRS complex and the peaks of the cardiogenic oscillations of the bolus gas from the erect to the inverted position.

If gravity were the sole contributor to ventilatory inhomogeneity, we would expect complete disappearance of the cardiogenic oscillations in weightlessness. However, studies in microgravity (µG), both during parabolic flight (18) and in sustained µG (14, 22), showed that cardiogenic oscillations persisted in both cases. Thus there is evidence for nongravitational inhomogeneity of VA between widely separated lung regions. During the 14-day flight of the space mission Spacelab Life Sciences-2 (SLS-2), SBW tests were performed in sustained µG with a VC inspiration of a test gas mixture containing He and sulfurhexafluoride (SF6), preceded at RV by a 150-ml gas bolus containing Ar. The results of the phase III slopes from these experiments have already been published (23).

In the present study, we used the same SBW tests from the SLS-2 mission to investigate, with the use of cross-correlation techniques, the phase relationship changes from 1 G to µG of the cardiogenic oscillations in CO2, N2, Ar bolus, He, and SF6. We observed distinct phase relationships in 1 G that were consistent with the standard gravitational models of VA and Q in the upright human lung. In µG, these relationships were altered, although distinct correlations still existed. The results shed light on the changes in the distribution of VA, Q, and gas exchange that take place in the absence of gravity and helped to explain previous results (21) that initially appeared somewhat paradoxical.

METHODS

Experimental system. The experimental methods have been published previously (14, 22, 23). Briefly, the SBW tests were performed by using a bag-in-box system. The inspired test gas was contained in a bag of the bag-in-box system and was composed of 5% He-1.25% SF6-balance O2 and was separated from a mouthpiece-valve system by a 150-ml tube, which was filled with 5% He-1.25% SF6-21% O2-balance Ar to
provide an initial bolus. This bolus gas composition was chosen so as to maintain a constant concentration of He and SF\textsubscript{6} throughout the test inspiration. A second bag collected the expired gas. The flow of gas into and out of the bag was measured in a long straight duct in the wall of the box with a Fiehlsch no. 2 pneumotachograph coupled to a differential pressure transducer (MKS Baratron Instruments, Burlington, MA). Determination and corrections for the linearity and asymmetry of the flow-measuring system were done (28). Because the exhalation was made into a bag, the flowmeter measured only dry air. Flow calibration was performed immediately before and after measurements by integrating the flow from a 3-liter calibration syringe (model 5530, Hans Rudolph, Kansas City, MO).

A rapidly responding magnetic-sector mass spectrometer (MGA-1100 or GAMS; Perkin Elmer, Pomona, CA) was used to measure gas concentrations. Gas was sampled through a Teflon capillary tube (−2 m long), the tip of which was placed in the center of the breathing tube at the subject's lips. The mass spectrometer was calibrated in accordance with the manufacturers' instructions to minimize fragment ion cross talk between channels. Sampling of all gases carried on board was performed immediately before and after measurements. The calibration and cross-talk values were determined from these data. The mass spectrometers had a dynamic response (10–90% rise time) of <100 ms. The capillary transit time was measured daily as the time required for a sharp puff of gas containing CO\textsubscript{2} to be detected by the mass spectrometer, and the data were aligned accordingly.

Performance of the SBW. The subject breathed air through the mouthpiece for several breaths and, when comfortable, turned a valve that connected the expired breathing path to the exhaled gas-collection bag in the bag in box to begin the test. The subject was then prompted to exhale to RV at 0.5 l/s with the assistance of a flow-regulating valve. The subject was then encouraged to control flow accurately. The subject was then prompted to exhale to RV at 0.5 l/s with the assistance of a flow-regulating valve.

Subjects and data-collection schedule. Five subjects from the 14-day flight of the SLS-2 mission were studied. Their anthropometric data were as follows (means ± SE): age, 42 ± 3 yr; height, 174.6 ± 4.3 cm; weight, 72.2 ± 5.5 kg; forced vital capacity, 100.6 ± 1.1%pred; and forced expiratory volume in 1 s-to-forced vital capacity ratio, 96.0 ± 3.4%pred. The subjects conserved their assigned numbers from the previous studies (13, 21, 23). All subjects were healthy nonsmokers with normal spirometry and N\textsubscript{2} SBW curves (21, 23), and none reported respiratory symptoms on questioning. The subjects were highly trained, providing for excellent reproducibility of our measurements. The preflight data reported here were collected on days 19, 87, 110, and 123 before launch under normobaric (−760 mmHg) and normoxic (21% O\textsubscript{2}) conditions. Inflight data were collected in the Spacelab under normobaric and normoxic conditions, except for the ambient CO\textsubscript{2} that was between 0.2 and 0.4%. The inflight data were collected on days 3, 7, 9, and 10, and 13. The total number of tests was as follows: in 1 G, subjects 2, 8, 9, 10, and 11 did 5, 4, 4, 4, and 4 tests, respectively; and in µG, they performed 4, 4, 3, 4, and 3 tests, respectively.

Data recording and SBW test analysis. Data were sampled at 160 Hz with a 12-bit analog-to-digital converter in the controlling computer supplied by the National Aeronautics and Space Administration. Data were first corrected for mass spectrometer transit time, and the flow was converted to BTPS conditions. The flow was integrated to give expired volume.

Cardiogenic oscillation phase analysis. The gas concentration vs. time signals were resampled at 40 Hz and smoothed with a moving average square window of 0.225-s duration. A segment of 3–5 s, proportionally adjusted to each subject's VC, was then isolated from the middle of the phase III portion of the test (see Ref. 23 for the determination of the phase III slope) and from the corresponding volume signals. The slope of each segment was estimated by linear regression and was subtracted so that the resulting gas-concentration signals oscillated around zero. The gas-concentration signals were then transformed to the volume domain by performing a cubic spline interpolation, thus providing gas-concentration data at equally spaced volume intervals. Further calculations were performed in the volume domain to account for any variation in flow rate. The cross-correlation coefficient functions were then calculated for several combinations of gas-concentration vs. volume signals. Cross-correlation (•) is a technique for estimating the similarity between two signals (5). It consists in overlaying the two signals, moving one of them point by point with respect to the other one, and calculating the product of their amplitude at each point. The integral of these products is then calculated. The phase shift of one signal relative to the other, at which the integral is maximal, is where the signals are most correlated (or in phase). This was done as follows

\[ t_{xy}(\tau) = C_{xy}(\tau)/\sqrt{C_{xx}(0)C_{yy}(0)} \]  

where \( t_{xy} \) is cross-correlation coefficient function; \( x \) and \( y \) are two different gas concentration vs. volume signals; \( C_{xy} \) is cross-correlation function of \( x \) and \( y \); \( C_{xx} \) and \( C_{yy} \) are autocorrelation functions of \( x \) and \( y \), respectively; and \( \tau \) is the phase shift (in ml) of the cross-correlation function.

The cross-correlation function \( C_{xy}(\tau) \) is defined as

\[ C_{xy}(\tau) = \int_{-\infty}^{\infty} x(t) y(t + \tau) dt \]

where \( x \) is the signal vs. time in (ml).

To express the phase relationship of the cardiogenic oscillations of the various gases studied in terms of degrees, a complete cycle (360°) was defined as the volume expired between each electrocardiogram QRS complex. The volume between R waves was estimated for each SBW test over the whole phase III slope segment used for cross-correlation, and all angular references were made with respect to this mean value. Figure 1 shows an example of an out-of-phase cross-correlation between Ar and He in 1 G. It can be seen that the two signals have to be shifted by 180° with respect to each other to get a maximal positive correlation.

Unpaired t-tests were performed to evaluate the statistical significance level. Significance was accepted at the \( P < 0.05 \) level, and the results are expressed as means ± SE.

RESULTS

The cross-correlation coefficients of the following gas combinations were calculated: He-N\textsubscript{2}, He-SF\textsubscript{6}, Ar bolus-He, Ar bolus-N\textsubscript{2}, CO\textsubscript{2}-Ar bolus, CO\textsubscript{2}-He, and CO\textsubscript{2}-N\textsubscript{2}. Because of the noise in the SF\textsubscript{6} signal and because He and SF\textsubscript{6} are inspired simultaneously and must, therefore, behave similarly in terms of convective gas transport, other cross-correlations in which SF\textsubscript{6} was used were uninformative and have been omitted. The resulting phase value of each cross-correlation coefficient was determined as the first maximum observed to the right...
of 0° (see Fig. 1 for the determination of the maximum). A phase value around 0 or 360° shows a positive correlation, whereas a phase value around 180° shows a negative correlation. Figure 1 shows that a shift of the two signals by 180° with respect to one another is needed to obtain a maximal positive correlation. That is, when the signals are shifted by −180°, a maximal correlation is seen, indicating that when the signals are in their nonshifted state they are out of phase. Figures 2–4 show the phase values of all tests in a double-plot format; i.e., the results are plotted twice, with the x-axis repeating the portion 0–360°. The double-plot format allows the visualization of the out-of-phase (−90–270°) and the in-phase (−270–450°), i.e., second 90°) data points as two distinct clusters. The means of the 1 G and μG values for all subjects were also computed over the period 90–450° and are shown on the top of each graph of Figs. 2–4 (see mean over 360°). Note that some of the data points are superimposed. The total number of tests performed by each subject is listed in methods. Six of 273 correlations were discarded because their first maximum to the right of 0° was not obvious, i.e., an inflection point or a quasipla-

teau was seen instead of a maximum. If a biphasic maximum was observed, the middle point was chosen.

From the gravitational model of ventilation distribution, we expect the cross-correlation coefficient of He and N₂ to be out of phase in 1 G, because He is an inspired gas and N₂ is a resident gas. The inspiration of a gas must necessarily imply dilution of the resident gas and a resulting out-of-phase relationship between such gases, irrespective of the effects of gravity. Thus He and N₂ should remain out of phase in 1 G and μG. This is what is seen in Fig. 2A, where the mean cross-correlation coefficient for He and N₂ is 211 ± 9° in 1 G and 163 ± 7° in μG, both values being close to 180°. Similarly, simultaneously inspired gases should be in phase both in 1 G and in μG, which is the case with He and SF₆ with values of 336 ± 7° and 306 ± 25°, respectively (Fig. 2B).

Comparison of both continuously inspired and resident gases with Ar bolus gas showed no overall change between 1 G and μG. Ar bolus and He were out of phase in 1 G (173 ± 15°), and this was unaltered in μG (211 ± 25°) (Fig. 3A). Ar bolus and N₂ (the resident gas) were in phase in 1 G (15 ± 12°) and remained so in μG (293 ± 27°), although there was a significant (P < 0.01) shift toward the out-of-phase condition (Fig. 3B). It is worth noting at this point that the cardiogenic oscillations in N₂ are much less well defined than those for Ar bolus, He, and CO₂. This renders comparisons between the cardiogenic oscillations in N₂ and those in the other gases more difficult and likely explains the greater scatter in the phase shifts seen in the comparisons between N₂ and other gases.

There were, however, significant and consistent changes in the phase relationships among the gases affected only by V″ (inspired, resident and bolus) and CO₂, which reaches the lung through gas exchange and is, therefore, a marker of pulmonary Q. In 1 G, CO₂ and Ar bolus were clearly out of phase (187 ± 6°), a consistent observation in every test performed. Although somewhat scattered in some subjects, this relationship was reversed in μG (315 ± 31°, P < 0.01) (Fig. 4A). Similarly, CO₂, which was in phase with inspired He in 1 G (186 ± 6°), reversed phase and was out of phase in μG (263 ± 27°, P < 0.01) (Fig. 4B). N₂ was clearly out of phase in 1 G with CO₂ (180 ± 21°) and significantly moved toward (but did not completely reach) an in-phase condition (261 ± 26°, P < 0.05) in μG (Fig. 4C).

DISCUSSION

The cardiogenic oscillations superimposed on the phase III slope of SBW tests result from the complex summation of transient alterations in the proportion of the total flow coming from different lung units and containing gases of different concentrations (9). Fuku-

chi et al. (11) have shown that the cardiogenic oscillations are induced by the direct beating action of the heart on areas of the lungs containing different gas concentrations. By infusing saline in the pericardium of a dog, these authors insulated the lungs from the pressure waves generated by the heartbeat and elimi-

Fig. 1. Example of cross-correlation coefficient (⁎) calculation for subject 8 in 1 G. Top: Ar concentration ([Ar]) as a function of volume. Middle: He concentration ([He]) as a function of volume. Bottom: cross-correlation coefficient of [Ar] and [He] as a function of volume or degree. The first maximum to right of volume = 0 liter (or 0°) is chosen as shown by arrow.
nated the cardiogenic oscillations in N₂ sampled in peripheral airways.

The cardiogenic oscillations have long ago been recognized as a useful tool in the understanding of the distribution of V̇A in health and disease. In 1961, Fowler and Read (10) studied the amplitude and phase relationships of the cardiogenic oscillations in subjects inhaling a tidal breath of a test gas containing 21% O₂-20% Ar-balance N₂. In their erect subjects, they found that Ar was in phase with CO₂ and out of phase with O₂. Their results were interpreted in terms of the gravitational model, that is, an upper zone of the lungs having a high ventilation-perfusion ratio (V̇A/Q̇) and a lower zone having a low V̇A/Q̇. Therefore, Ar inspired throughout the breath was distributed preferentially to the dependent zones where there is also high Q (high CO₂ concentration), whereas O₂, which was also distributed preferentially to the dependent zones, was removed by gas exchange, lowering its concentration in the dependent zones. To study the effect of gravity on their results, Fowler and Read repeated these tests in supine subjects. They reported a decrease in the amplitude of the O₂ and CO₂ oscillations and a phase shift between the different gases. CO₂ was now out of phase with Ar and O₂. Because the time relationship between Ar and the electrocardiogram had remained the same, Fowler and Read concluded that when the subject is lying down the blood flow must increase dramatically in the poorly ventilated regions of the lungs.

The effect of weightlessness on the distribution of V̇A and pulmonary Q has also been studied by performing SBW tests during short periods (~27 s) of µG generated by parabolic flight profiles (18). Michels and West (18) had their subjects inspire a VC of a test gas containing an initial bolus of Ar followed by 100% O₂. They found a very large reduction in the cardiogenic oscillation amplitude if the whole test maneuver was performed in µG or if only the preliminary exhalation to RV was performed in µG while the remainder of the test was done in 1 G. A special test was also devised to investigate the distribution of Q. The subjects hyperventilated while breathing air for a period of 5 s, after which they held their breath for 15 s. This was then followed by a controlled expiration to RV. This test was designed to emphasize the distribution of CO₂ due to Q and eliminate the inhomogeneity of CO₂ due to V̇A. These
maneuvers were performed in 1 G, µG, and ~1.8 G, with the breath held and the exhalation being performed at the same G loading. These tests revealed marked cardiogenic oscillations in O₂ and CO₂ in 1 G that were reduced in µG and increased in ~1.8 G. However, the periods of hypergravity preceding the µG phase of the flights raise questions about residual effects persisting through the period of µG. Nonetheless, SBW results from tests performed in sustained µG during spaceflight show clearly that there is persisting inhomogeneity of V˙A and Q in µG (14, 22). Although their amplitude was reduced in µG, the cardiogenic oscillations were still present (14, 22).

In the present study, we examined the phase relationships between gases in SBW tests performed in 1 G and in sustained µG. We expected that He and N₂ would be ~180° out of phase in 1 G because areas of high ventilation must have high He concentration ([He]) and low [N₂] (N₂ is a resident gas and is thus diluted by He-containing inspirate; therefore, high He must imply low N₂). We expected to see the same phase relationship in µG because, even though we may not see a top-to-bottom distribution in V˙A, the regions of the lungs receiving preferential V˙A will remain the areas with low [N₂]. Similarly, He and SF₆ maintained a constant phase relationship regardless of gravity. Because both He and SF₆ were inspired simultaneously, this was expected. It is, however, interesting to note that subjects 2 and 8 in the present study did not demonstrate a clear in-phase relationship between He and SF₆ in µG. Furthermore, subjects 2 and 8 also behaved differently from the other subjects in a previous study (23). Their phase III slope difference decreased more than for the other two subjects in going from 1 G to µG (Fig. 4, Ref. 23). Also, their decrease in phase III slope induced by the breath holding was less than for the other subjects, both in 1 G and µG.

Comparison of Ar bolus with N₂ and He provides information regarding the site of airway closure with respect to the distribution of V˙A. In 1 G, areas of high V˙A (the bases of the lungs) are associated with low Ar bolus concentration, as reflected in the out-of-phase condition with He in Fig. 3A. This is generally interpreted as being a consequence of dependent airway closure, where the base of the lung is closed at RV and so a bolus inspired at RV is preferentially distributed to the apices. The fact that in µG these gases remain out of phase shows that the regions of the lungs that close
at RV are those regions with high specific $\dot{V}_{A}$. This is consistent with the idea that these regions are predisposed to airway closure because of the low regional lung volume they reach at RV. Because the regions with high ventilation (high [He]) also have low $N_2$, we expected an opposite relationship between Ar bolus and $N_2$ than the one observed between Ar bolus and He. Indeed, Ar bolus and $N_2$ were in phase in 1 G and remained so in $\mu$G (Fig. 3B), although there was a significant shift toward the out-of-phase condition, presumably due to a noisier $N_2$ signal.

The most striking phase shift seen in the cardiogenic oscillations in subjects going from 1 G to $\mu$G was observed in the CO$_2$ data (Fig. 4). In 1 G, CO$_2$ and Ar

Fig. 4. Cross-correlation coefficients for CO$_2$-Ar bolus (A), CO$_2$-He (B), and CO$_2$-N$_2$ (C). Format is same as in Fig. 2.
bolus were almost exactly out of phase with a value of 187 ± 6°. The 1-G results are predictable when the gravitational model of VA and Q distribution is used. High pulmonary Q, which results in high alveolar CO₂ concentration, is present in the dependent zones of the lung because of the weight of the blood itself, whereas the Ar bolus inspired at the beginning of the VC is distributed to the nondependent zones of the lung, which are the regions that remain open at RV. In µG, a marked phase shift between CO₂ and Ar bolus was seen with a new in-phase value of 315 ± 31° (Fig. 4A). The phase shift observed indicates that, in µG, the more highly perfused regions of the lung are now the same regions that remain open at RV.

A similar phase shift from 1 G to µG was seen between CO₂ and He. Again, as predicted from the gravitational model, both CO₂ and He are distributed preferentially to the dependent zones of the lung at 1 G. Because these areas have both high VA and Q, an in-phase condition was seen in 1 G for CO₂ * He with a value of 332 ± 6°. In µG, however, this became an out-of-phase condition with a value of 263 ± 27° (Fig. 4B). Thus, in µG, the areas of low VA (low [He]) are now associated with areas of much higher perfusion than was the case in 1 G. Whether this change in the pattern of VA/Q distribution results from areas of low ventilation being associated with areas of high perfusion or simply from uneven ventilation in the face of uniform pulmonary perfusion cannot be determined from these data. However, in a previous study (22), specifically designed to investigate pulmonary perfusion inhomogeneity in µG, cardiogenic oscillations were shown to be reduced to ~60% of their preflight standing size, implying a persistent inhomogeneity of perfusion (22). This study, therefore, supports the former interpretation. The CO₂ and N₂ data (Fig. 4C) also reflect similar results, where in 1 G these gases are out of phase, as would be expected from the standard gravitational model. In µG, a shift occurs toward an in-phase condition. This does not quite reach our arbitrary condition to be classified as in phase, but this may simply be a reflection of the difficulty in detecting the small cardiogenic oscillations of N₂ in µG.

Prisk et al. (21) studied gas exchange in sustained µG during the SLS-1 and SLS-2 experiments. Briefly, they obtained plots of instantaneous respiratory exchange ratio (R) against expired volume from slow VC expirations. R was calculated from CO₂, O₂, and N₂ concentrations. As suggested by West et al. (26), the slope of R vs. expired volume (corrected for continuing gas exchange) reflects VA/Q inhomogeneity, although incomplete gas mixing probably also contributes. The range of VA/Q seen over phase IV was reduced in µG, consistently with a more homogeneous distribution of VA/Q between regions of lung that close at RV and regions of lung that remain open at RV. However, somewhat surprisingly, the range of VA/Q seen over phase III in µG was identical to that seen in 1 G. Given the previously observed reductions in the inhomogeneity of VA (14) and pulmonary Q (21), this result seemed somewhat paradoxical. The observations in the present study regarding the cardiogenic oscillations in CO₂ provide a potential answer to this paradox. In 1 G, areas of high VA are associated with areas of high Q (the gravitationally dependent portions of the lung). This is clearly observable in the CO₂ vs. He data (Fig. 4B). The effect of this correlation of VA and Q is to reduce the overall range of VA/Q seen in the normal upright human lung. In µG, however, the areas of low VA are now associated with areas of relatively higher Q, and vice versa. This has the effect of widening the range of VA/Q present for a given degree of inhomogeneity of VA and Q. Thus, despite an overall reduction in the inhomogeneity of VA/Q in µG, the inhomogeneity of VA/Q is unchanged.

In conclusion, using cross-correlation techniques on cardiogenic oscillation data, we investigated the effect of µG on the distribution of gas in the lung. The results show that, as was the case in 1 G, the regions of the lung that close at RV are also in µG those regions with high specific VA. This is consistent with the idea that these areas reach a lower regional lung volume at RV, thus predisposing them to regional airway closure. In sharp contrast to the situation in 1 G, areas of low VA have a relatively higher Q than that in 1 G, leading to a widening of the range of VA/Q in µG. This may explain previous observations of an overall unaltered range of VA/Q in µG despite a more homogeneous distribution of both VA and Q.

The authors acknowledge the dedicated collaboration of the crew of Spacelab Life Sciences-2. We also thank Raoul Ludwig, Janelle Fine, Mary Murrell, Marsha Dodds, and Brian Dubow for their technical and administrative assistance.

This work was supported by National Aeronautics and Space Administration Grant NAGW 897. A.-M. Lauzon was supported by the Canadian Lung Association and by the Fonds pour la Formation à la Recherche en Santé du Quebec, Canada. M. Paiva was supported by contract Prodex with the Belgian Federal Office for Scientific Affairs.

Address for reprint requests: G. K. Prisk, Dept. of Medicine, 9500 Gilman Dr., Univ. of California, San Diego, La Jolla, CA 92093-0931. Received 7 April 1997; accepted in final form 25 September 1997.

REFERENCES


