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TRAPPED GAS AT MAXIMUM LUNG VOLUME IN INTACT ISOLATED RAT LUNGS

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Abstract. Excised rat lungs were ventilated with air in a liquid filled plethysmograph that was enclosed in a large pressure chamber, C(B). The lungs were inflated then deflated by removing or adding saline to the plethysmograph while the trachea was attached to a cannula extending through the plethysmograph base. In this system, tracheal pressure, Pao, was equal to gas pressure inside C(B). The gas pressure was held constant at either ambient pressure (Pamb), Pamb + 350 Torr, or Pamb − 350 Torr. When excised lungs were ventilated slowly from their atelectatic state for 10 inflation–deflation cycles with Pao equal to any one of the three pressures, an equivalent amount of gas was trapped in the lungs. If after 10 cycles, however, lungs containing trapped gas were inflated and held at maximum lung volume, the trapped gas spaces could be made to contract or expand in response to rarefaction or compression of the tracheal gas. The amount of expansion and contraction of the trapped gas spaces demonstrates that trapped gas is likely trapped between menisci of a foam that occlude the alveoli or small airways.

Airway closure — Lung pressure–volume curves
Foam formation in lungs — Trapped air

The excised lungs of most animal species including the rat are known to accumulate gas as they are inflated and deflated (Hughes and Rosenzweig, 1970; Faridy and Permutt, 1971; Faridy, 1973). More recently Frazer and Weber (1976) have shown that the accumulation of trapped gas in the ventilated excised rat lung is a function of the inflation–deflation rate. In addition, they have shown that the amount of gas trapped during an inflation–deflation cycle is primarily dependent upon inflation rate and is nearly independent of deflation rate (Frazer and Weber, 1976). It appears that the gas trapping mechanism in excised rat lungs is related to either the formation

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of menisci across the airways (Macklem, 1971; Frazer *et al.*, 1979) or bubbles of a foam (Pattle, 1958; Faridy and Permutt, 1971; Frazer and Weber, 1974, 1975) or airways that close and don't open during subsequent cycles (Glaister *et al.*, 1973). In each case, some gas would be trapped at maximum lung volume, V_{max}, where the airways achieve their largest caliber. The purposes of this study were to determine if trapped gas spaces could be detected in the lung at V_{max}, to determine the mechanics of the trapped gas spaces as they were forced to expand or contract, and to determine, if possible, how the gas was trapped at V_{max}.

Theory

In this investigation trapped gas was detected by selectively expanding or contracting the trapped gas spaces at V_{max}, then keeping those spaces expanded or contracted as the lung was deflated. A change in the minimum volume, V_m (the volume of gas in the lungs at a transpulmonary pressure, PL, of −5 cm H_2O), of the lung following a given cycle reflected the changes in the trapped gas volume. Conversely, if there was no trapped gas at V_{max} there should be no change in the minimum volume upon deflation. Thus, by looking for increases or decreases in the minimum volume following expansion or contraction of the trapped gas, it is possible to detect trapped gas in the lung at maximum lung volume.

Experimentally, the expansion and contraction of the trapped gas spaces were accomplished by placing degassed lungs in a liquid filled plethysmograph, such as chamber C(A) in fig. 1, then increasing or decreasing the pressure in chamber C(B) from ambient pressure, Pamb, by either plus or minus 350 Torr. In this arrangement tracheal pressure, Pao, was the same as the pressure within chamber C(B). Pressure–volume, PL–VL, curves for 10 consecutive inflation-deflation cycles were recorded with Pao maintained at either Pamb + 350 Torr or Pamb − 350 Torr. An inflation–deflation rate was chosen so that the minimum volume of the lung increased during each cycle (Frazer and Weber, 1976). Following the 10 cycles, the lungs were inflated to V_{max}, held at that volume for a stress relaxation period (10 min), then the pressure inside chamber C(B) was changed to Pamb. Additional PL–VL cycles were then recorded with Pao equal to Pamb. First, consider the case where Pao was held at Pamb + 350 Torr (see fig. 2). If any air had been trapped within stable compartments inside the lung at V_{max}, the transmural pressure, P_{TM}, across the wall of the first trapped air space, P_{TM_1}, could be written as:

$$P_{TM_1} = [P_{T_1} - Pao] \quad (1)$$

where P_{T_1} equals the pressure within that space. As Pao was decreased to Pamb, P_{TM_1} would increase. This increasing pressure gradient would tend to expand the region of the lungs containing the trapped gas and would result in an increase in minimum volume upon deflation. Other trapped gas spaces would respond in the same manner.

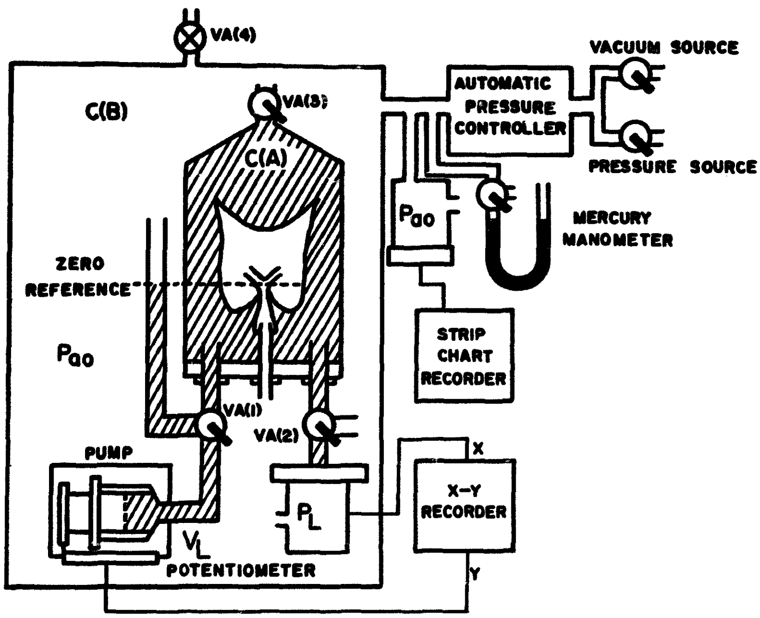

Fig. 1. Schematic diagram of the experimental apparatus for recording rat lung pressure volume curves. Valve VA(1) with all three ports open permits setting the zero reference prior to recording a PL–VL curve. The reference port is closed as the lung is inflated-deflated. Normally, VA(2) is open between the pressure transducer and the plethysmograph; the third port is open only when filling the pressure transducer and tubing with fluid. Air escapes through VA(3) as C(A) is filled with fluid; the valve is closed when recording a PL–VL curve. The mercury manometer is used to calibrate the pressure transducer, Pao.

A similar argument can be made when trapped gas spaces are exposed to an increasing tracheal pressure from Pamb – 350 Torr to Pamb. In this case the trapped gas spaces would tend to decrease in size and show a decrease in the minimum volume of the lung upon deflation. It should be noted that if there were no trapped gas in the lung at V_{max} (or if gas could escape easily from the trapped gas spaces), it would be expected that a change in Pao would not result in a change in the total amount of trapped gas when the lung was deflated. Gas could theoretically be trapped in the lung at V_{max} by having menisci in the airways, or foam (bubbles) within the alveoli and airways or airway closure.

Methods

The experimental procedures employed in this study required a ventilation system in which lung volume could be measured as the absolute value of Pao was varied over a range of Pamb ± 350 Torr. The system shown in fig. 1 was used to satisfy these demands by employing a plethysmograph containing an incompressible liquid (saline). With lungs in the plethysmograph, tracheal pressure was the same as that within chamber C(B). The carina was chosen as the zero pressure reference. As liquid was removed from chamber C(A) with a syringe type pump (Harvard

Apparatus Model #901), the pressure surrounding the lungs decreased and the lungs inflated. Deflation was achieved by pumping the saline back into the chamber. Volume was measured with a linear motion potentiometer attached to the plunger of the syringe; transpulmonary pressure was measured with a capacitance type transducer (Setra Model #233). Both pressure and volume were recorded on an X–Y recorder. The pressure inside chamber C(B), lung tracheal pressure, could be held constant at Pamb, or Pamb plus or minus 350 Torr, with a Cartesian Manostat pressure controller (Model #8). The pressure inside chamber C(B) was measured with a strain gauge transducer (Statham Model #P6-15D-350) and recorded on a strip chart recorder.

Hooded male rats of the Long Evans strain weighing between 250 and 300 g were anesthetized with sodium pentobarbital (65 mg/kg) given intraperitoneally. A tracheotomy was performed, and the animals were ventilated with 100% O_2 for 10 to 15 min using a positive pressure respirator (Harvard Apparatus Model #665). An open bilateral pneumothorax was achieved by opening the abdominal cavity and sectioning the diaphragm. Following the O_2 washout, the lungs were allowed to collapse passively and the trachea was clamped so that the oxygen remaining in the lungs was absorbed by the blood (Dale and Rahn, 1952). When the lungs had become atelectatic, they were quickly excised by cutting the rib cage on both

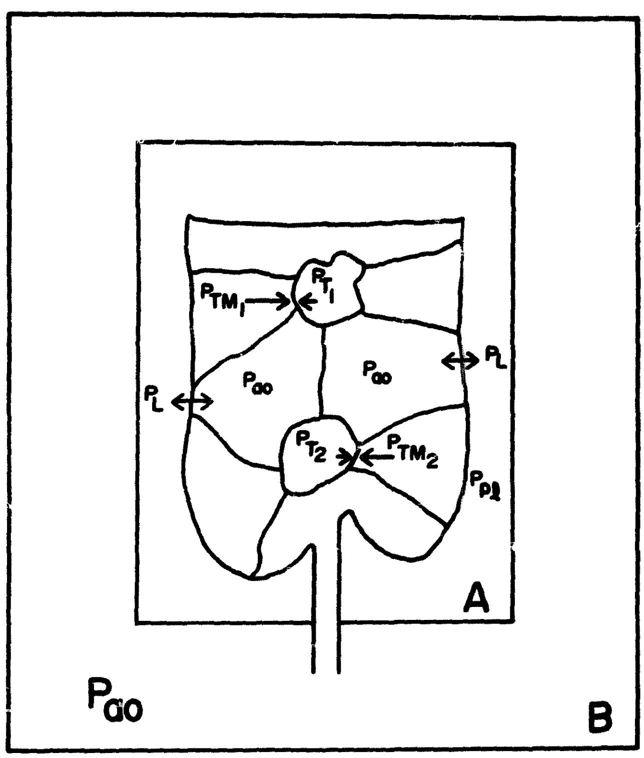

Fig. 2. Schematic representation of a lung held at constant volume within a fluid-filled plethysmograph (A) inside an air-filled chamber (B). PL is the transpulmonary pressure, Ppl is the lung surface pressure, P_{T_1} and P_{T_2} are the pressures within two trapped gas spaces and P_{TM_1} and P_{TM_2} are the transmural pressures across the trapped gas space walls.

sides of the mid line and removing the lungs and heart *en bloc*. After their removal the lungs were inverted and connected to a cannula that extended from the trachea to the outside of the water-filled plethysmograph. Approximately 20 min elapsed between the dissection and the beginning of an experiment.

Three pressure-volume curves (10 inflation–deflation cycles each) were recorded for each lung. Initially, a control curve was obtained to ensure that the lung opened normally and had no leaks. A control curve consisted of 10 continuous inflation–deflation cycles between a maximum pressure, P_{max}, of 30 cm H_2O and a minimum pressure, P_{min}, of -5 cm H_2O. The rate of change of lung volume was constant at 3.82 ml/min.

Following the control curve, the lungs were degassed in a vacuum jar to ensure that they had the same volume history (Mead and Collier, 1959; Edmunds *et al.*, 1967). Then two additional experiments were performed on each lung. The order of the experiments was alternated to ensure that it had no effect on the results. The lungs were again degassed between the experiments. In both experiments the lungs, plethysmograph, pump, and transducers were placed inside the large pressure–vacuum chamber, C(B), shown in fig. 1. The pressure in chamber C(B), which equaled tracheal pressure, was then increased or decreased from Pamb to either Pamb plus or minus 350 Torr. Chamber pressure was maintained while pressure–volume curves were recorded for 10 continuous inflation–deflation cycles between the same minimum and maximum transpulmonary pressures (-5 cm H_2O and 30 cm H_2O) and the same inflation–deflation rate (3.82 ml/min) as the controls. After the tenth cycle, the lungs were inflated an eleventh time to P_{max}. Lung volume was held constant by turning off the syringe pump for a ten minute stress relaxation period; tracheal pressure was then allowed to return to ambient pressure. A second 10-min stress relaxation period was observed at V_{max} before the lungs were deflated at the control rate. Next, 4 additional inflation–deflation cycles, 12 through 15, were recorded with Pao equal to ambient pressure. The variable V_m/V_{max}, where V_m represents the volume of trapped gas in the lung following a specified cycle measured at -5 cm H_2O (minimum volume), equaled the normalized minimum volume of the lungs and was used to represent the fraction of air trapped in the lungs after any cycle (Frazer and Weber, 1976). The change in normalized minimum volume of the lungs following deflation in the eleventh cycle in turn reflected the change in size of the trapped air spaces.

A study was performed to determine the validity of assuming that the lung does not respond to changes in Pao when it does not contain any trapped gas. A finger cot placed in Chamber C(A) in place of the lung was examined as Pao was varied between Pamb plus or minus 350 Torr. The finger cot contained no trapped gas and it had nearly the same maximum volume as the lung. Theory would predict that the balloon should not respond to pressure changes in chamber C(B).

The results of this study were dependent upon the accuracy of the ventilation system. It was found that the saline-filled plethysmograph did not behave as a perfect system and minor corrections were necessary to account for the finite compliance and/or temperature changes in the system when there were large changes in Pao. The magnitude of the corrections was determined by varying Pao between Pamb ± 500 Torr with no lungs in the plethysmograph, with the tracheal cannula sealed, and with zero transmural pressure maintained across chamber C(A).

Results

A typical 10 cycle pressure–volume control curve for a lung ventilated at 3.82 ml/min in a saline filled plethysmograph is shown in fig. 3A. Figures 3B and 3C are examples of PL–VL curves for the same lung ventilated at the same rate but with Pao equal to Pamb + 350 Torr and Pamb − 350 Torr respectively. The pressure–volume curves in figs. 3B and 3C were similar to control curves.

The normal PL–VL relationship for the eleventh through sixteenth cycles are given in figs. 4A and 4B. In fig. 4A Pao had originally equaled Pamb + 350 Torr for the first 10 cycles. Then during the eleventh cycle with Pao still equal to Pamb + 350 Torr the lung was inflated from point 1 (shown in fig. 4A) to P_{max}. Upon reaching

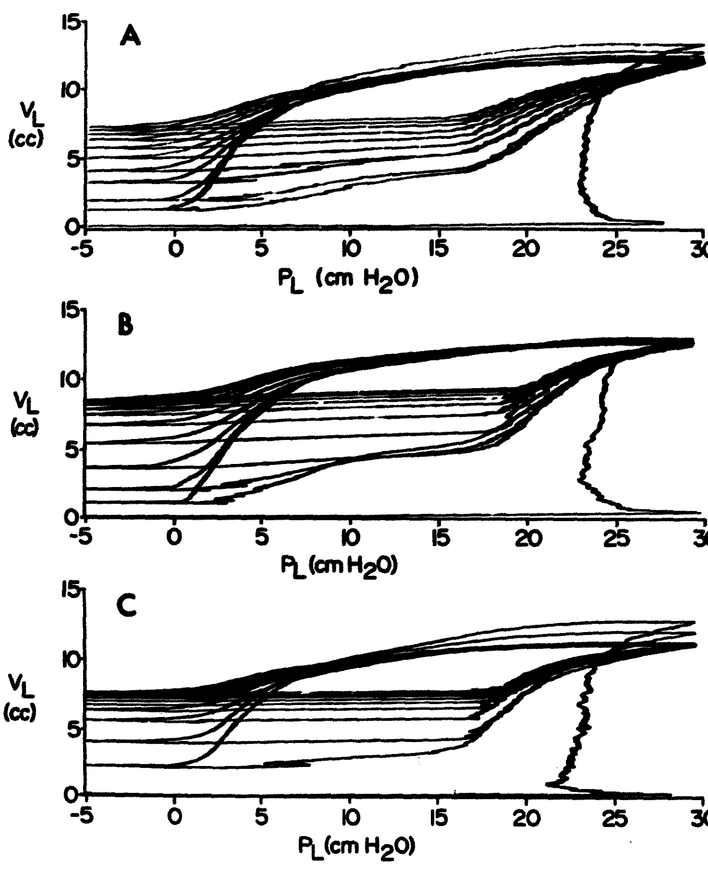

Fig. 3. Effects of tracheal pressure on recorded PL–VL curves. Panel A shows a control curve recorded with Pao = Pamb. In B, the lungs were inflated-deflated with Pao held at Pamb + 350 Torr. In C, the same lungs were inflated-deflated with Pao held at Pamb − 350 Torr.

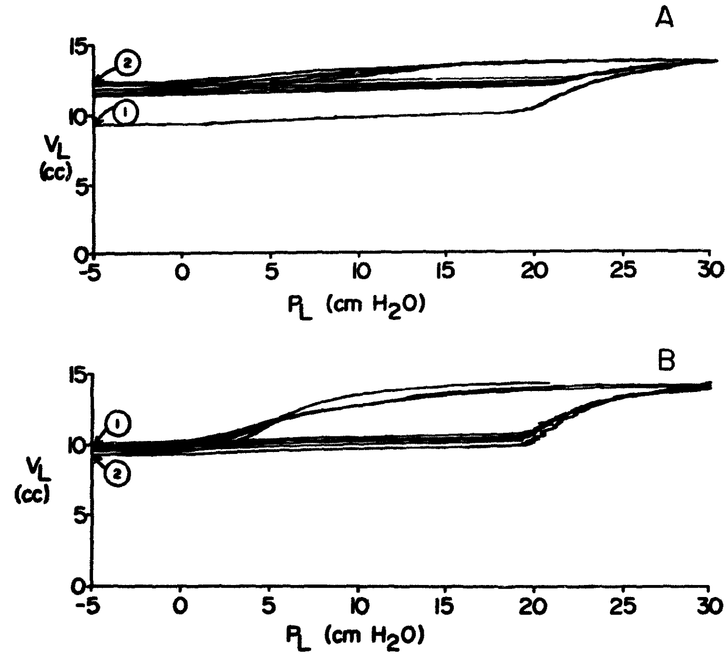

Fig. 4. The eleventh through sixteenth PL–VL cycles are shown for a lung ventilated with the tracheal pressure at either Pamb plus (panel A) or minus (panel B) 350 Torr. In both panels, the eleventh cycle started at Point 1 and approached maximum lung volume where Pao was allowed to assume ambient pressure. The lungs were then deflated and ended at Point 2.

P_{max} lung volume was held constant for 10 min and then Pao was allowed to decrease to Pamb. After a second 10-min period, the lung was deflated to point 2. There was a significant increase in V_m/V_{max} during cycle 11. As the lungs were inflated–deflated during cycles 12 through 15 with Pao equal to Pamb, V_m/V_{max} slowly decreased. The PL–VL relationship in fig. 4B shows the second case where the lung had been ventilated for 10 cycles with Pao equal to Pamb – 350 Torr. Here, the eleventh cycle again started at point 1. Then the lungs were inflated to P_{max} and held at constant lung volume for 10 min after which Pao was increased from Pamb – 350 Torr to Pamb. Following another 10-min period the lungs were deflated back to point 2. At point 2 the amount of trapped gas was less than it had been prior to the eleventh cycle, but additional gas was trapped during the next 4 cycles.

The normalized minimum volume for cycles 1 through 15 is given for both experiments in figs. 5A and 5B. The mean value and standard error are indicated (n = 3). At point Pao = Pamb in fig. 5A, tracheal pressure was allowed to decrease to ambient pressure; and the relative amount of trapped gas in the lungs increased by an additional 40% and then decreased. Conversely, when Pao was allowed to increase to Pamb at the point Pao = Pamb in fig. 5B, the amount of trapped gas decreased by 10% and increased on subsequent cycles.

In both figs. 5A and 5B the three control curves recorded with Pao equal to ambient pressure are shown for comparison. Even though the amount of trapped gas tended to be greater after 10 cycles when tracheal pressure was either greater

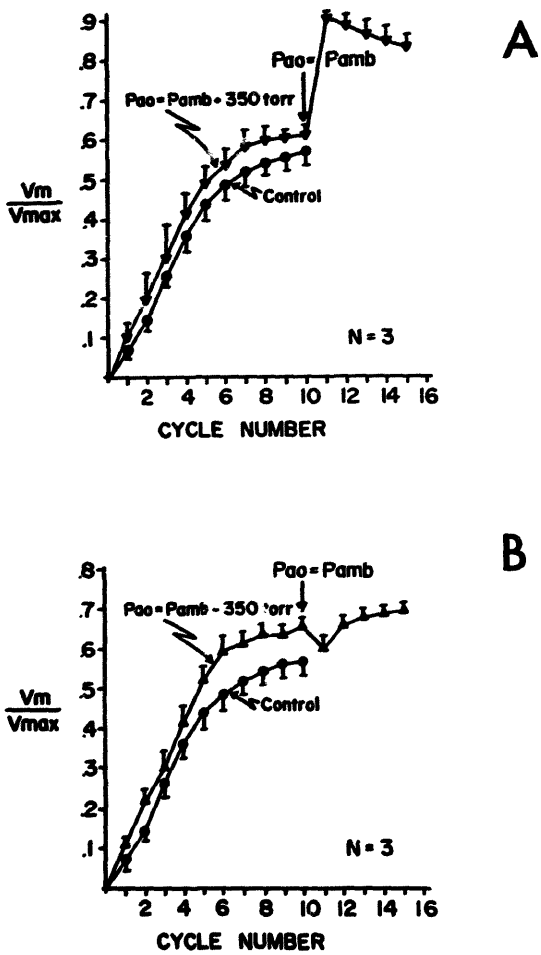

Fig. 5. Normalized minimum volume per cycle of three lungs ventilated from the atelectatic state with Pao initially either greater (Panel A) or less (Panel B) than ambient pressure. In both panels A and B, Pao assumed ambient pressure during the eleventh cycle with the lung held at V_{max}. The normalized minimum volume of the 3 control lungs using the same plethysmograph is shown for comparison for the first ten cycles.

or less than ambient pressure, the increase could not be shown to be significant using an analysis of variance. Since the control curves were always recorded first, we feel that the slight increase in V_m/V_{max} was not related to tracheal pressure but to the order in which the curves were recorded. It has been previously observed that repeated ventilation and degassing of lungs can cause a slight increase in the amount of gas trapped in the lungs per cycle (Frazer *et al.*, 1979).

The experiments designed to determine how lungs containing no trapped gas would respond to changes in Pao were consistent with theoretical predictions. When the balloon was ventilated for ten cycles with Pao equal to either Pamb plus 350 Torr or Pamb minus 350 Torr, there was no change in the minimum volume as Pao assumed ambient pressure.

Results of the study to determine the necessary corrections that must be made to lung volume measurements as Pao was changed showed that a correction of less than 0.25 ml was needed when Pao was varied between Pamb and Pamb + 350 Torr, and a correction of less than 0.75 ml was needed when Pao was varied between Pamb and Pamb – 350 Torr. These corrections accounted for all errors involved in changing Pao including those due to system compliance and/or temperature changes. Lung volume measurements were always corrected by the appropriate amount when Pao was changed during the course of an experiment.

Discussion

Several physical properties of the trapped gas spaces were examined in this study. For instance, when gas is trapped while excised lungs are being ventilated with Pao equal to either Pamb plus or minus 350 Torr, air accumulates within the lung in a similar manner as it does when Pao equals Pamb. This suggests that the trapped gas space itself, instead of responding to changes in the absolute value of Pao, responds only to pressure differences between the inside and outside of the trapped gas space.

An additional property of the gas trapping mechanism in the lung is that when the lung is inflated–deflated between the same maximum and minimum pressures at a constant rate, the total amount of gas trapped appears to reach an equilibrium value. When lungs were ventilated at a rate of 3.82 ml/min for 10 consecutive cycles, the maximum amount of trapped gas reached approximately 65% of V_{max} (Frazer and Weber, 1976). If the percentage of trapped gas was artificially increased to greater than 65% of V_{max} by decreasing Pao from Pamb + 350 Torr, the total volume of the trapped gas spaces decreased during subsequent cycles (fig. 5A). If, on the other hand, the size of the trapped gas space was artificially reduced by increasing Pao, the volume of the trapped gas spaces increased during additional PL–VL cycles (fig. 5B).

Our results indicate that at least a portion of the gas trapped in the excised lung as it is ventilated remains trapped at maximum lung volume. Neither the exact volume of gas trapped nor the mechanism of how the gas is trapped at V_{max}, however, could be determined in this study. Although it has been suggested that some airways open at high transpulmonary pressures (Glaister *et al.*, 1973), we feel that there is good evidence that at a transpulmonary pressure of 30 cm H_2O all airways capable of opening are pulled open by their parenchymal attachments. It is possible, however, that foam or menisci stabilized by alveolar surfactant may still be present within the small airways of the lung at P_{max} causing a functional type of airway closure at high transpulmonary pressures.

If it is assumed that all the gas trapped in the lungs at V_{max} is confined in compartments free to expand or contract in response to changes in transmural pressure, the limits of the volume change can be calculated using Boyle's Law. In our experiments the limits of expansion and contraction of an infinitely compliant trapped gas space would cause an approximate 50% increase or 50% decrease in the volume of trapped gas. Actual measurements indicated that V_m increased by 40% but decreased by only 10%.

Since V_m very nearly increased as predicted when Pao was decreased, it is likely that the compliant trapped gas spaces respond to an increase in transmural pressure by simply increasing in size. When the transmural pressure was decreased, however, the trapped gas spaces were reduced in size but not nearly as much as predicted by Boyle's Law. In the latter case it is unlikely that the smaller than predicted reduction in volume could be due solely to the compliant behavior of the trapped gas spaces since those spaces would have to withstand transmural pressures of between 250 and 300 Torr following the small 10% change in volume. Our explanation of the smaller than predicted volume change is that additional gas must have entered the trapped gas spaces as Pao increased.

We feel that the overall behavior of the trapped gas spaces is due to the physical properties of menisci that occlude the very small airways and/or alveoli in the lung. Consider a meniscus pushed down one of these airways toward the alveoli. As the meniscus reaches successive airway bifurcations, it divides and its total cross-sectional area increases. Since energy is required to stretch the film, a pressure difference is generated across the film as it is pushed toward the lung periphery (Frazer and Khoshnood, 1979). Conversely when the meniscus approaches the trachea, its area decreases and energy is recovered from the film. If each meniscus contains alveolar surfactant, which is likely the case, a greater pressure difference would be generated across the meniscus as it travels toward the alveoli than when it moves toward the trachea. It is unlikely, however, that a pressure difference greater than a few cm H_2O could ever be developed across a meniscus. The larger pressure difference generated as the trapped gas spaces shrink in size could serve as a driving force for gaseous diffusion across the meniscus wall causing additional gas to enter the trapped gas space. The addition of this gas to the trapped gas space would prevent it from shrinking to its theoretical minimum size predicted by Boyle's Law. When the trapped gas spaces expand, however, menisci move toward the trachea and their total area decreases. The pressure difference generated across each meniscus would be small in this case and very little diffusion from the trapped gas spaces would occur. If menisci were responsible for the trapped gas, during expansion of the trapped gas spaces the volume of the trapped gas would closely follow Boyle's Law.

Next, consider how the trapped gas space would respond if the trapped gas was contained exclusively in bubbles that did not occlude the airways. In this case, if alveolar surfactant lined the bubble, a larger pressure difference would be generated across the bubble wall as it expanded than when it contracted (Enhorning, 1977). Thus, more gas would diffuse from bubble trapped air spaces during expansion. It would be expected that if the trapped gas was exclusively trapped in bubbles, it would more closely follow Boyle's Law during compression than during expansion. This was not found to be the case in this study. It still remains to be determined, however, whether the gas is trapped at V_{max} by a small amount of foam that occludes the airways upon expansion or by gas initially trapped behind menisci.

Since the lungs were immersed in a liquid in this study, there was a range of transpulmonary pressures along the lung pleura from the base to apex. It has been shown by Frazer and Weber (1976), who compared the amount of gas trapped in lungs ventilated in both an air and liquid filled plethysmograph, that the effects of the gradient is to slightly reduce the amount of gas trapped in the lungs. In other words, the pressure gradient in the liquid filled plethysmograph does not appear to affect appreciably the gas trapping mechanism in the lungs.

At the present time the rate of menisci or foam production and breakage in a normal lung is not known. In some pathological conditions such as severe edema, however, large amounts of froth or foam having normal lung surface properties (Pattle, 1965) can be generated in the lung and then accumulate in the airways (Faridy, 1973). When this occurs, the foam or menisci can obstruct the airways (Frazer *et al.*, 1979) and alter the normal distribution of air in the lungs. As a result, the ventilation–perfusion pattern is altered in the lung (Williams, 1953). Smaller increases in foam or meniscus formation which may be associated with abnormal lung function are difficult to detect at the present time in the lungs of living animals. It has already been shown, however, that foam in the airways of the lung can alter closing volume measurements (Sergysels *et al.*, 1977). In the future, menisci or foam may prove to potentiate closing volume abnormalities and alterations in RV, FRC, and TLC which are now associated with many pathological conditions in the lungs.

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