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REGIONAL DIFFERENCES IN GAS TRAPPING (AIRWAY CLOSURE) BETWEEN APEX AND BASE OF EXCISED RAT LUNGS

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Abstract. Excised rat lungs were ventilated with air under three conditions: (a) while suspended by the trachea and surrounded by air, (b) while inverted and surrounded by saline, and (c) while upright and surrounded by saline. The distribution of transpulmonary pressures over which gas trapping occurred in the lung for each of the three conditions was found by a method previously described by Frazer *et al.* (1979). A distribution having a small standard deviation (SD) indicates more uniform gas trapping in the lung while a larger SD indicates less uniform gas trapping. Results showed that the SD was 0.63 for the inverted lung in saline, 1.10 for the lung in air, and 1.57 for the upright lung in saline.

We conclude that gas trapping in lungs inverted in saline occurs more uniformly than gas trapping in lungs in air or upright in saline. The results obtained in saline in the upright and inverted position also imply that as the lung is deflated surrounded by air, gas trapping initially occurs in the base of the lung before it occurs in the apex. Since gas trapping and airway closure are related, there could also be intrinsic dissimilarities in airway closure between the apex and base of excised rat lungs suspended by the trachea in air.

Airway closure	Posture
Gas distribution	Rat
Lung	Trapped gas

In the past there have been several studies indicating that intrinsic dissimilarities exist between the apical and basal lobes of lungs. For instance it has been shown that pressure–volume ($P_L - V_L$) curves differ between lobes in the apex and lobes in the base of dog (Frank, 1963; Faridy *et al.*, 1967) and human lungs (Silvers *et al.*,

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1979). Other studies have illustrated that there is a preferential distribution of inspired gas to the apical lobes at low lung volumes (Glaister *et al.*, 1973). The object of this study was to determine if such functional inhomogeneities contribute to differences in gas trapping between the apex and base of the lung. Alterations in gas trapping caused by the lungs' orientation in a saline-filled plethysmograph were compared with gas trapping in a lung ventilated in an air-filled plethysmograph. Differences in gas trapping due to the gravity-induced transpulmonary pressure gradient in the saline-filled plethysmograph were used to identify regional variations in the gas trapping mechanism between the apex and base of the lung.

Methods

In this study excised rat lungs were ventilated with air under three different conditions as the lungs were (1) suspended upright in air, (2) inverted in saline, and (3) supported upright in saline. Lungs were removed from male Long Evans hooded rats weighing between 250 and 300 g and anesthetized with sodium pentobarbital (85 mg/kg). A tracheotomy was performed, the diaphragm was opened, and the animals were exsanguinated via the abdominal aorta. For lungs ventilated upright in air and inverted in saline, the heart and lungs were removed from the animal *en bloc*. For lungs ventilated upright in saline, the rib cage in addition to the heart and lungs was excised.

Pressure–volume curves were recorded for lungs under the three different conditions. The system used to ventilate lungs surrounded by air is shown in fig. 1A. Since the lungs were inflated–deflated under near static conditions, transpulmonary pressure, P_L, was defined as $P_L = Pao - Ppl$, where Pao was airway pressure and

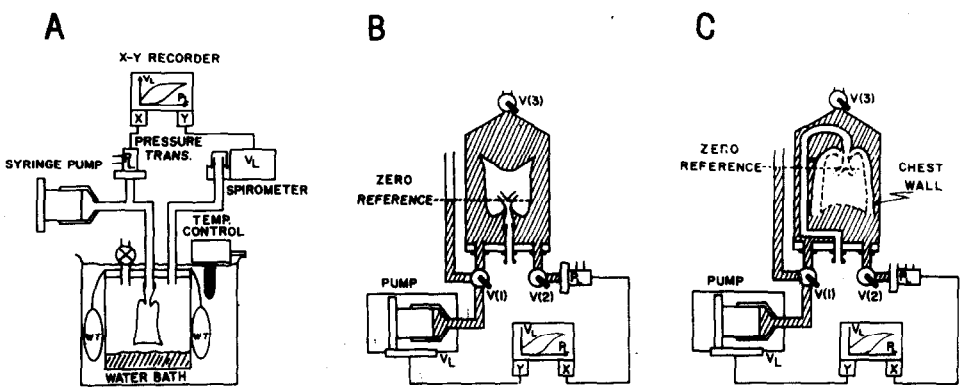

Fig. 1. The schematic diagrams of three different equipment configurations used to record P_L–V_L curves of excised lungs. (A) The system used to record P_L–V_L curves of lungs upright in air. (B) The system used to record P_L–V_L curves of lungs inverted in saline. (C) The system used to record P_L–V_L curves of lungs upright in saline.

Ppl was pleural pressure. Lungs suspended in air were ventilated with positive airway pressure (Pao), and Ppl was equal to atmospheric pressure. The description of the equipement and its accuracy for measuring PL – VL curves of lungs suspended in air have been published previously (Frazer *et al.*, 1979). In this study, saline-filled plethsmographs were used to introduce gravity-induced transpulmonary pressure gradients. Two different systems were used to ventilate lungs with air as they were surrounded by saline (fig. 1B, 1C). In both cases the lungs were inflated–deflated with negative pleural pressures (Ppl) and Pao was equal to atmospheric pressure. With the lungs in saline, Ppl varied between the apex and base of the lung. Both liquid-filled plethysmograph systems were calibrated so that transpulmonary pressure was measured at the level of the lung carina. Lungs inverted and surrounded by saline were ventilated with air using the system shown in fig. 1B. This system and its accuracy have also been described previously in detail (Frazer and Weber, 1976). In order to reverse the gravity-induced gradient, lungs were ventilated upright in saline using the system shown in fig. 1C. In this case the rib cage was left intact and was supported by hooks in the plethysmograph to keep the lungs from inverting and floating towards the top of the chamber.

A series of five sets of PL – VL curves was recorded for lungs ventilated with air while suspended by the trachea in air. Another series of six sets of PL – VL curves was recorded for lungs ventilated with air as they were inverted in saline, and a third series of seven sets of PL – VL curves was recorded for lungs ventilated with air as they were supported upright in saline. Each set of PL – VL curves consisted of six inflation–deflation cycles at a rate of 7.64 ml/min. Before recording each set of curves, the lungs were vacuum degassed using the method described by Stengel *et al.* (1980). During the first cycle lungs were inflated from a transpulmonary pressure of 0.0 cm H_2O to a maximum transpulmonary pressure of 30 cm H_2O (PLmax), and then deflated to an end-expiratory pressure PLmin. The value of PLmin was the same for each inflation–deflation cycle in a given set of curves. During cycles two through five, the lungs were inflated to PLmax and deflated to PLmin. During the sixth cycle the lungs were inflated from PLmin to PLmax and deflated to -5 cm H_2O. For the lungs suspended by the trachea in air PLmin was $+7$ cm H_2O for the first set of curves and decreased in order to $+1$, -2, -5 and -8 cm H_2O for the second through fifth sets of curves. The values of PLmin for upright and inverted lungs surrounded by saline was $+6$ cm H_2O for the first set of curves and $+3$, $+2$, $+1$, 0.0, -3 cm H_2O (for lungs supported upright in saline only) and -5 cm H_2O for the sets of curves that followed. A representative series of PL – VL curve sets for lungs ventilated upright in saline is shown in fig. 2.

The fraction of gas trapped in the lungs following a set of PL – VL curves was calculated by dividing the amount of gas trapped in the lungs at -5 cm H_2O (Vm) following the sixth inflation–deflation cycle by the maximum lung volume during the same cycle (Vmax). The variable (Vm/Vmax) was equal to the normalized minimum volume of the lung. By recording several sets of PL – VL curves for each lung in which PLmin was held at different values, it was possible to determine the

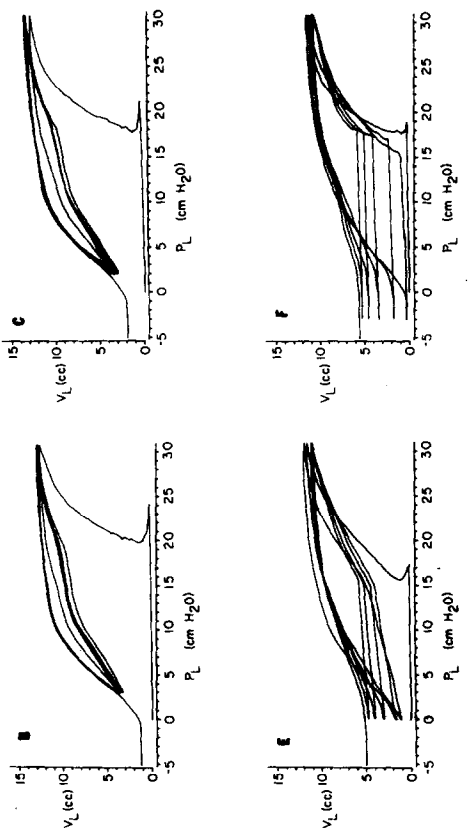

Fig. 2. Seven sets of pressure–volume curves for a typical rat lung ventilated at 7.64 ml/min showing how the amount of trapped air increased following 6 inflation–deflation cycles as the end expiratory pressure, $P_{L}min$, was progressively reduced from (A) +6 cm H_2O, to (B) +3 cm H_2O, (C) +2 cm H_2O, (D) + 1 cm H_2O, (E) 0.0 cm H_2O, (F) −3 cm H_2O, and (G) −5 cm H_2O.

relationship between PLmin and Vm/Vmax for lungs under the three different conditions examined in this study.

Results

The mean value of Vm/Vmax (±SEM) was calculated for the specified sets of PL–VL curves recorded for lungs suspended in air (N = 6) and plotted *vs* PLmin as shown in fig. 3. The continuous curve drawn through the points represents the best fit of a curve proportional to the normal probability distribution function. Also shown in fig. 3 is the result of similar calculations made for lungs upright in saline (N = 6) and lungs inverted in saline. In each case as PLmin was lowered, the fraction of gas trapped in the lungs increased until a plateau was reached. It is difficult to compare curves in fig. 3, however, since zero transpulmonary pressure was arbitrarily defined as the pressure difference at the level of the carina in the saline-filled plethysmograph.

The slopes of the curves in fig. 3 are proportional to normal probability density functions in fig. 4. Since only the range of transpulmonary pressures over which gas trapping occurs was important in this study, all three normal curves were plotted assuming that they had the same mean transpulmonary pressure. As a result, in fig. 4, PLM is equal to the difference between the mean pressure and transpulmonary pressure for each density function. These densities represent the

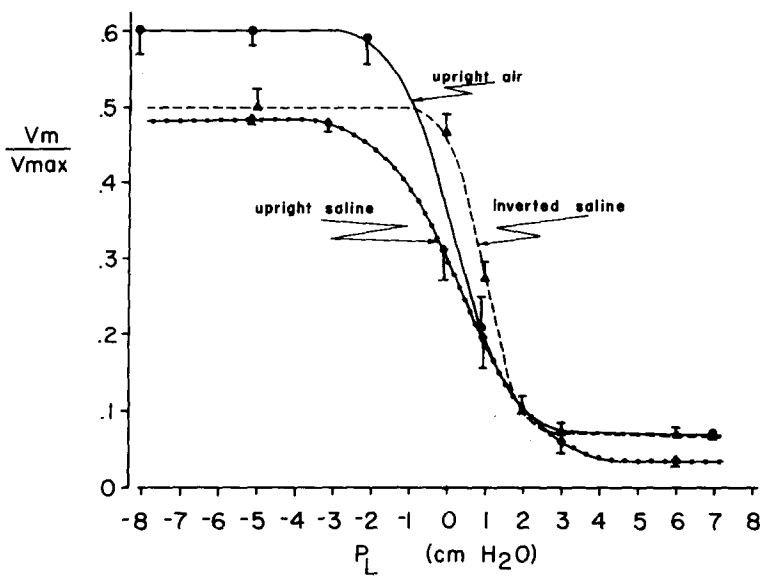

Fig. 3. Mean values (±SEM) of the normalized minimum volume of the lung, Vm/Vmax, *vs* end-expiratory pressure PLmin following inflation–deflation cycles of lungs ventilated upright in air, inverted in saline and upright in saline (N = 6).

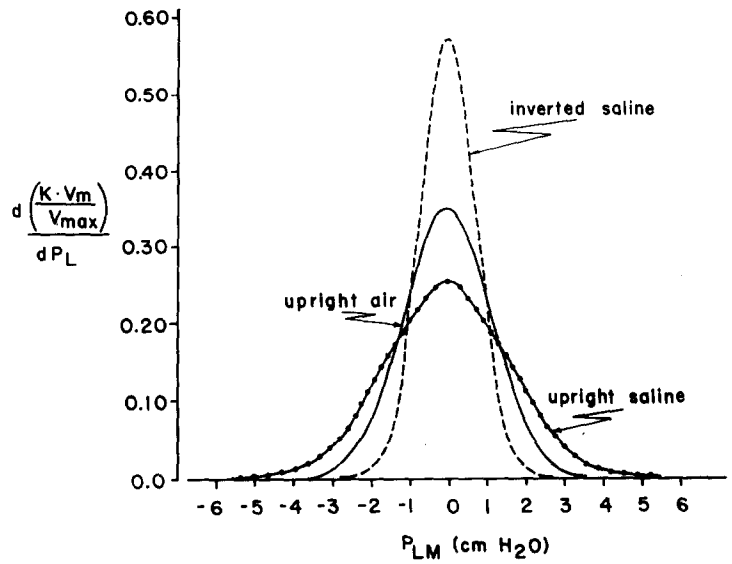

Fig. 4. The absolute value of the slopes of the curves in fig. 3 plotted as a function of normalized transpulmonary pressure, PLM, where PLM equals (PLmean – PL) for each distribution.

relative change in gas trapping at each transpulmonary pressure. The narrowest density function is associated with lungs inverted in saline (SD = 0.63), and the widest represents the lung upright in saline (SD = 1.57). In air, the width of the density function is midway between the two saline curves (SD = 1.1). In other words, gas trapping occurs over the smallest transpulmonary pressure range for lungs inverted in saline and over the largest range for lungs upright in saline.

Discussion

We have shown that gas trapping occurs in rat lungs as a function of end-expiratory pressure (Frazer *et al.*, 1979). The index of gas trapping, Vm/Vmax, plotted as a function of end-expiratory pressure forms a reverse sigmoid shaped curve (fig. 3). The slope absolute value of the sigmoid curve is well approximated by a scaled normal probability density curve and illustrates the change or distribution of gas trapping, with respect to transpulmonary pressure (fig. 4).

When lungs were ventilated with air, in this study, it was possible to determine the gas trapping distribution as a function of transpulmonary pressure without a transpulmonary pressure gradient from apex to base. It was not possible, however, to determine if gas trapping in all regions of the lung follows the same distribution or if the distribution represents a summation of regional differences in gas trapping between the apex and base of the lung.

One way to determine if a regional difference in gas trapping exists between the apex and base is to ventilate the lung while it is suspended in a transpulmonary pressure gradient created by gravity in a saline-filled plethysmograph. If gas trapping, in all regions of the lung, were to occur over the same average transpulmonary pressure range, one would expect a transpulmonary pressure gradient of any orientation to increase the range of gas trapping pressures. If there were a regional difference in gas trapping between the apex and base of the lung, however, one would expect a transpulmonary pressure gradient to make gas trapping either more uniform or less uniform depending upon the orientation of the lung within the transpulmonary pressure gradient.

Now, consider the results of this study in which excised lungs were ventilated in a saline-filled plethysmograph in either an upright or inverted orientation. It was found that ventilating the lungs in saline caused gas trapping to occur over either a broader (upright orientation) or narrower (inverted orientation) transpulmonary pressure range than lungs ventilating in air. The experimental evidence indicates, therefore, that there is a regional difference in gas trapping between the apex and base of a lung ventilated in air in the absence of a transpulmonary pressure gradient.

These results also mean that gas trapping in the base of the lung occurs before gas trapping in the apex as the lung is deflated in air, when there is no transpulmonary pressure gradient. This is illustrated by the fact that gas trapping occurred over a smaller transpulmonary pressure range, or more homogeneously throughout the lung, when the lungs were inverted in saline than when they were upright in air (fig. 4). For lungs inverted in saline the transpulmonary pressure at the base of the lungs exceeded the transpulmonary pressure at the apex because of the transpulmonary pressure gradient produced by the saline. This should favor gas trapping in the apex to occur before gas trapping in the base. Since gas trapping occurred more uniformly when the lungs were ventilated while inverted in saline, we conclude that gas trapping in lungs suspended in air, when there is no transpulmonary pressure gradient, occurs at higher transpulmonary pressures in the base than in the apex. Conversely, with gas trapping in the base of the lung occurring at higher transpulmonary pressures than in the apex when the lung is suspended in air, ventilating the lungs upright in saline should enhance the regional differences in gas trapping. Figure 4 shows that this is the case since gas trapping occurred over the largest transpulmonary pressure range when the lungs were ventilated upright in saline.

Our results indicate, therefore, that structural differences must also be present in rat lungs and that they contribute to differences in gas trapping pressures between apical and basal lobes.

Our laboratory has recently presented evidence that gas trapping is caused by the formation of menisci across the airways as lungs are deflated (Frazer *et al.*, 1979; Frazer and Weber, 1980; Frazer and Khoshnood, 1979). These menisci do not allow alveolar gas to communicate freely with tracheal gas and represent a

functional form of airway closure. Hence, we consider gas trapping to be a direct consequence of airway closure. This study implies, therefore, that structural dissimilarities between the apex and base of the lungs cause the airways in the base to close before the airways in the apex as the lung is ventilated in air.

It is interesting to note that Likens and Mauderly (1983) have recently shown that closing volumes can be measured for rats *in vivo*. Since the transpulmonary pressure difference for a rat lung in the supine position would not exceed 2 or 3 cm H_2O, and the maximum transpulmonary pressure gradient would not be greater than 1 cm H_2O/cm, it is likely that their closing volume measurements reflect our predicted nonhomogeneities in airway closure between the apex and base of the lungs rather than a transpulmonary pressure gradient.

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