Compliance of peripheral airways deduced from morphometry

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Okazawa, Mitsushi, Peter D. Paré, and Rodney K. Lambert. Compliance of peripheral airways deduced from morphometry. J Appl Physiol 89: 2373–2381, 2000.—Insights into airway mechanics were sought by applying morphometric techniques to rabbit lungs fixed at several lung recoil pressures. Rabbits were treated with either nebulized carbachol followed by iv administration of carbachol or with saline solution (sham). The lungs were held at one of six values of positive end-expiratory pressure (PEEP; 10, 7, 4, 2, 0, and −4 cmH2O) while the animal was killed and formalin was circulated through the lungs. The lungs were removed and left in a bath of formalin for 24 h. Standard airway morphometric measurements were made on membranous bronchiolar slices taken from representative blocks of tissue. Reductions in compliance of peripheral airways deduced from morphometry.


The theoretical understanding of the lung flow-volume curve, developed over the past 30 years, as well as the more recent models of the dose-response relationship of airway resistance in response to airway smooth muscle agonists (2, 3, 5, 8, 11–15, 17, 21, 25), is crucially dependent on knowledge of airway geometry and the airway area-pressure relationship [lumen area (Aℓ) vs. transmural pressure (Ptm)]. The human airway Aℓ–Ptm curves that have been used in the modeling were derived by extrapolating sparse data on large central airways to small peripheral airways that had no data.

Dog data (of which there are more) have also been used (3). This has led to an element of uncertainty concerning the validity of the models, despite the fact that they exhibit many of the features observed in various lung function tests. We sought to reduce the uncertainty about the mechanics of peripheral airways, not by studying single airways but by using morphometric techniques to obtain area data at a number of lung fixation pressures. Average values from many airways of similar size were derived for the parameters of interest at each lung recoil pressure (Pl). This approach has three main advantages over the study of single airways. First, the difficult experimental work lies in performing the morphometry well instead of coping with the technical difficulties associated with the mechanical parameters of tiny airways; second, structural data on the airway wall are obtained at the same time; and, third, the pattern of airway narrowing can be compared in the presence of relaxed and contracted airway smooth muscle. These latter parameters allow a deeper understanding of the airway structure-function relationship. For instance, we can explore how airway narrowing is related to mucosal folding and parenchymal interdependence. Because we obtained data at negative transpulmonary pressures, we had the opportunity to observe airway closure and to elucidate the mechanics of this phenomenon.

Our data show that, as in dogs (18), the smallest airways are relatively more open than larger airways, which is contrary to at least one human model of airway mechanics (14). Airway closure appears to occur through airway flattening (similar to the collapse of latex drainage tubing under suction), independent of whether smooth muscle is activated. Airways in which muscle is activated close at smaller lung volumes than those in which muscle is not activated; thus airway smooth muscle contraction protects the airway against closure. We hypothesize that the reason for this is that the elastic collapse of an airway into a flattened shape is governed by the thickness of the wall, relative to the luminal diameter. The shortening of the airway

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smooth muscle has the effect of both decreasing lumen diameter and increasing the effective wall thickness, thus stiffening the airway.

METHODS

Animal preparation. Sixty mature New Zealand White rabbits were anesthetized using urethane (1,000 mg/kg iv) and α-chloralose (100 mg/kg iv). The rabbits were then tracheostomized and artificially ventilated with 100% oxygen at 40 breaths/min and tidal volume of 7 ml/kg. The vagi were sectioned bilaterally in the neck. A catheter was inserted into the femoral vein for drug and fluid administration. The chest was opened wide by splitting the sternum. Tracheal pressure was measured through the side port of the tracheal tube by using a piezoresistive transducer (Fujikura FPM-02PG, Tokyo, Japan) and was compared with atmospheric pressure to obtain transpulmonary pressure (Pt). Airflow was measured using a pneumotachometer (model 00, Fleisch) and a differential pressure transducer (Validyne MP45) (+5 cmH2O). All pressure and flow tracings were displayed continuously on a monitor that were recorded, as necessary, by a digital data acquisition and recording system (Raytech, Vancouver, BC, Canada). The 60 rabbits were divided into control (Con; n = 30) and carbachol-treated (Carb; n = 30) groups. Each group was further divided into six subgroups according to the peak end-expiratory pressure (PEEP) value: -4, 0, 2, 4, 7, or 10 cmH2O. Thus there were five rabbits in each subgroup.

Protocol. Twenty minutes were allowed for physiological stabilization after instrumentation. The lungs were then degassed by occluding the tracheal tube and allowing complete absorption of oxygen by the pulmonary circulation. Subsequently, a quasistatic pressure-volume curve was obtained at Pt between -15 and +25 cmH2O. This procedure was repeated twice at 10-min intervals. The animals were then ventilated using the same parameters as before, at the chosen value of PEEP for 10 min. Because it was impossible to ventilate the animals using a negative PEEP, the animals in the -4 cmH2O group were ventilated at +4 cmH2O PEEP. End-expiratory pressure was then set to -4 cmH2O before high-frequency oscillation. At each PEEP, the lungs were oscillated with a small tidal volume and high frequency (-0.3 ml and 6 Hz, respectively), while maintaining the chosen PEEP, to measure pulmonary resistance (Raw). At a PEEP of 4 cmH2O, airways were rejected if their short-to-long luminal diameter ratio was < 0.6. At the three highest values of Pt, obliquely cut airways were separated subjectively from airways flattening into an oval shape, based on the relative thickness of the epithelial regions at the ends of the long and short diameters. Flattening airways showed constant epithelial thickness, whereas the epithelium was thicker at the ends of the long diameter in obliquely sectioned airways. Every third eligible, cross-sectioned membranous airway was selected for measurement, until the total number of selected airways reached eight for each slide. Measurements were performed using a Nikon microscope equipped with a camera lucida attachment and a digitizing tablet coupled to an IBM-compatible computer. The measurements are illustrated in Fig. 1. They are as follows: 1) airway basement membrane perimeter (Pbm), the “gold standard” of airway size, and the total area enclosed by the basement membrane (Amo); 2) airway internal perimeter (Pi) and Ai, where Pi is the perimeter of the luminal border and Ai is the area enclosed by Pi; 3) smooth muscle outer perimeter (Pmo) and enclosed area (Amo), as well as the area of the wall occupied by smooth muscle (WAmo); 4) perimeter of adventitial border (Pa) and the total area enclosed by this border (Aa).

Fig. 1. Schematic cross section of airway showing morphometric measurements. r, Radius; P, perimeter; A, area; WA, wall area. Subscripts: a, adventitial border; mo, outer smooth muscle; bm, basement membrane; i, lumen.
and 5) the number of epithelial membrane folds (N). In cases in which the airway was contiguous to an adjacent vessel, a line was drawn, by hand, between the two structures to estimate \( P_{\text{bm}} \). Airways with more than one-third of \( P_{\text{bm}} \) contiguous to an adjacent vessel were omitted from the analysis. From these measurements, we calculated the subdivisions of wall area \((W_{\text{a}} = A_{\text{o}} - A_{\text{w}})\); inner wall area \((W_{\text{a}} = A_{\text{w}} - A_{\text{i}})\). We also calculated area for a fully dilated airway in which the basement membrane is a circle. All such measurements are referred to by adding an asterisk. For example, \( A_{\text{w}}^* \) is the area enclosed by the basement membrane when circular. Measurements conformed to the recommendations of Bai et al. (1).

A selection of the results of these measurements and calculations are reported herein.

Data analysis. The data from each group of animals were pooled at each \( P_L \) for each treatment to obtain mean values for Con and Carb airways. The airways were also subdivided into bins based on \( P_{bm} \) at each \( P_L \). After some preliminary analysis of airway number and the distribution of airway sizes, we decided to use the bins shown in Table 1. Means and standard errors of relevant measures of airway size and deformation were calculated for the pooled data and by bin. Measured and derived quantities were normalized on the basement membrane length, except \( A_i \), which was normalized on the maximal lumen area \((A_i^* = P_i^2/4\pi, \text{where } P_i \text{ is the internal perimeter of the lumen})\). Lung volumes (V) were normalized on the volume at \( P_L = 25 \text{ cmH}_2\text{O} \), the greatest inflation pressure that we used. The number of airways examined at each \( P_L \) is shown in Table 2.

### RESULTS

There were no significant differences in the pressure-volume relationships between Con and Carb groups, except at \( P_L = 0 \) and 7 cmH\(_2\)O (t-test, \( P < 0.05 \)). \( R_{sw} \) data are summarized in Fig. 2. Because there were no significant changes in \( R_{sw} \) in the Con group caused by the sham treatment, these data are not shown. There were no significant differences in baseline \( R_{sw} \) between Con and Carb groups at each \( P_L \). In the Carb group, elevation of \( R_{sw} \) occurred in all animals after the administration of nebulized carbachol. A further elevation occurred after iv administration of carbachol. There were significant differences between the means for both treatments at \( P_L = 0, 2, \) and 4 cmH\(_2\)O (paired \( t \)-test, \( P < 0.05 \)). At 7 cmH\(_2\)O, only the elevation caused by iv carbachol was statistically significant, whereas, at 10 cmH\(_2\)O, only the nebulized treatment produced a statistically significant increase in \( R_{sw} \). Thus the delivery of nebulized carbachol at a concentration of 256 mg/ml did not achieve maximal muscle activation. Examination of the morphometric data showed that the progressive increase in \( R_{sw} \) with decreasing \( P_L \) is caused, in part, by a progression of muscle shortening from central to peripheral airways as \( P_L \) is reduced.

Both Con and Carb airways (365 and 549 airways, respectively) were selected for analysis. The frequency distribution of \( P_{bm} \) was not different (Kolmogorov-Smirnoff test, \( P < 0.001 \)) between Con and Carb groups.

Figure 3 shows the mean, normalized \( A_i/P_L \) curves (i.e., \( A_i/A_i^* \) vs. \( P_L \)) for the pooled data for both the Con and the Carb cases. At \( P_L \) ranging from 0 to 7 cmH\(_2\)O, the lumens of the Carb airways were smaller than the lumens of the Con airways. Also, the steepest decrease in lumen area occurred at lower values of \( P_L \) in the Con airways than in the Carb airways. These results are not surprising. The surprising result is that, at \( P_L = -4 \text{ cmH}_2\text{O} \), the two curves crossed, and the Carb airways were significantly more open than the Con airways (Welch test, \( P < 0.01 \)). This result was true for all airway sizes, although not all differences achieved statistical significance (Fig. 4). Another surprising result that was true across all airway sizes was that the Con airways were more open at \( P_L = 7 \text{ cmH}_2\text{O} \) than at 10 cmH\(_2\)O (Figs. 3 and 4), except for the small airways for which there were insufficient data at \( P_L = 7 \) and 10 cmH\(_2\)O. It is also worth noting that, for all sizes of Carb airways, there were no changes in lumen area between \( P_L = 0 \) and 2 cmH\(_2\)O. Thus there should have been no change in \( R_{sw} \) in this pressure range. It can be seen in Fig. 2 that this was the case.

<table>
<thead>
<tr>
<th>( P_L ), cmH(_2)O</th>
<th>No. of Control Airways</th>
<th>No. of Carbachol Airways</th>
</tr>
</thead>
<tbody>
<tr>
<td>-4</td>
<td>68</td>
<td>92</td>
</tr>
<tr>
<td>0</td>
<td>89</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>105</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>49</td>
<td>95</td>
</tr>
<tr>
<td>7</td>
<td>32</td>
<td>105</td>
</tr>
<tr>
<td>10</td>
<td>22</td>
<td>81</td>
</tr>
<tr>
<td>Total</td>
<td>365</td>
<td>549</td>
</tr>
</tbody>
</table>

\( P_L \), lung recoil or transpulmonary pressure.

### Table 2. No. of airways studied at each \( P_L \)

<table>
<thead>
<tr>
<th>( P_L ), cmH(_2)O</th>
<th>No. of Control Airways</th>
<th>No. of Carbachol Airways</th>
</tr>
</thead>
<tbody>
<tr>
<td>-4</td>
<td>68</td>
<td>92</td>
</tr>
<tr>
<td>0</td>
<td>89</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
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<td>4</td>
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<td>95</td>
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<td>7</td>
<td>32</td>
<td>105</td>
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<tr>
<td>10</td>
<td>22</td>
<td>81</td>
</tr>
<tr>
<td>Total</td>
<td>365</td>
<td>549</td>
</tr>
</tbody>
</table>

### Table 1. \( P_{bm} \) ranges used in determining bins

<table>
<thead>
<tr>
<th>Label</th>
<th>( P_{bm} ) Range, mm</th>
<th>No. of Control Airways</th>
<th>No. of Carbachol Airways</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>&lt;0.8</td>
<td>113</td>
<td>225</td>
</tr>
<tr>
<td>1-mm</td>
<td>0.9–1.1</td>
<td>129</td>
<td>153</td>
</tr>
<tr>
<td>1.5-mm</td>
<td>1.4–1.6</td>
<td>62</td>
<td>70</td>
</tr>
<tr>
<td>Large</td>
<td>&gt;2</td>
<td>61</td>
<td>101</td>
</tr>
</tbody>
</table>

\( P_{bm} \), basement membrane perimeter.
A finding that does depend on airway size is apparent in Fig. 4. The value of $A_i/A_i^*$ at $P_L = 0$ cm H$_2$O is greater for small airways than for larger airways. This is true for both Con and Carb airways.

Our observation that the smallest airways are relatively more open than larger airways [which has also been reported for dogs (18)] can be elucidated from further examination of the histological sections. Fig. 5 shows representative photomicrographs of cross-sectioned airways. In the Con group (Fig. 5, D–F), airways were predominantly round at $P_L = 4$ cm H$_2$O and were narrowed and flattened at smaller $P_L$ values. In the Carb group (Fig. 5, A–C), airways were round and unfolded at $P_L = 10$ cm H$_2$O (not shown) and circularly narrowed with many folds at 4 cm H$_2$O. At $P_L = 0$ cm H$_2$O, Carb airways tended to remain rounded, with many folds. At $P_L = -4$ cm H$_2$O, these airways tended to be no longer circular but were somewhat flattened, although the flattening was to a lesser extent than in Con airways. Thus it appears that there were two different modes of reduction of lumen area as $P_L$ was reduced. The Con airways flattened and then developed many epithelial folds, whereas the Carb airways developed many folds then flattened.

**DISCUSSION**

We believe that this is the first reported observation of airway collapse and closure by flattening. It is a puzzling observation as the conceptual model of our experiment was that of a uniformly deflating lung, with snapshots of its morphology taken at six different recoil pressures. An initially circular airway should have stayed circular. We propose that our observations can be understood by using the theory of elastic buckling that was used to explain the mechanics of the folding of the epithelial membrane. When the pressure on the outside of a circular elastic tube is greater than...
the pressure inside the tube by a critical amount, the tube undergoes elastic buckling into an oval shape that becomes progressively flatter as the $P_{tm}$ difference is increased. In the case of the epithelial membrane, this flattening is not observed because the membrane is subject to the geometrical constraint of not being able to penetrate the airway smooth muscle layer. It must, therefore, develop folds instead of flattening. We propose that the total airway wall is not so constrained and is thus able to collapse into an oval shape.

An intraparenchymal airway becomes subjected to a collapsing stress through the interdependence mechanism. The basis for this has been developed in several modeling studies in which the airway is thought of as a tube embedded in the foamlike parenchyma (7, 11–13, 15, 16). It may be helpful to think of the airway as a circular tube that must be inserted into a circular hole in the parenchyma. When the diameter of the unfilled parenchymal hole, in which the tube is embedded, is the same size as the outer diameter of the tube, the stress on the outside of the tube is the same as the stress on the pleural surface (16). If the tube is bigger than the (unfilled) hole, the local peribronchial stress will tend to compress the airway, whereas, if the hole is larger than the airway (as we expected would happen when the airway smooth muscle shortened), the local stress will tend to keep the airway open. This is usually referred to as the “interdependence effect.” Experiments that examined the relationship between airway and parenchymal hole sizes in excised dog lungs showed that, for the values of $P_L$ that occur around functional residual capacity and for larger airways, the peribronchial stress is no more than $\sim 1$ cmH$_2$O different from pleural pressure (7, 19). We believe that our data show that collapsing pressure must occur in the case of our small rabbit airways. To demonstrate this, we must determine whether the airway changes size with $P_L$ in the same way as the parenchyma. For a uniformly deflating lung, such as we assume to have in the present study, linear dimensions scale on the cube root of lung volume and areas scale on the two-thirds power of lung volume. Hence, to aid comparison between airway cross-sectional area and the area of a hole in the parenchyma, in which the airway would be a snug fit at total lung capacity, we have plotted normalized airway total cross-sectional area ($A_o/A_o^*$) and volume ($V/V^*$)$^{2/3}$ against $P_L$ (Fig. 6). It is apparent that $A_o/A_o^*$ for the smaller Con airways (small and 1-mm bins) does not change in the same way with $P_L$ as would an unfilled hole in the parenchyma of a uniformly deflating lung. The hole is much smaller than the airway at $P_L < 7$ cmH$_2$O (the larger airways deviate from uniform deflation at $P_L < 2$ cmH$_2$O). Thus, for the small and 1-mm Con airways at these $P_L$s, the

Fig. 5. Representative micrographs of airways from 2 groups at $P_L = −4, 0,$ and $4$. A–C: Carb airways at $P_L = 4, 0,$ and $−4$ cmH$_2$O, respectively. D–F: Con airways at $P_L = 4, 0,$ and $−4$ cmH$_2$O, respectively.
parenchyma adjacent to an airway must be compressed relative to the parenchyma distant from the airway (Fig. 5D). From this observation, it follows that instead of the peribronchial stress being equal to pleural pressure, it must be closer to or even exceed lumen pressure. That is, parenchymal interdependence is causing the airway to compress rather than remain open. When this compression is sufficiently great, the airway wall buckles elastically, and the airway starts to flatten (Fig. 7). The mechanics of this are similar to those for the initial buckling of the epithelial membrane (9), but, instead of the epithelial membrane, it is the entire thickness of the airway wall that is involved in the buckling. This buckling has been described by Hill and colleagues (6), who showed that it is governed by the mechanical and geometrical properties of not only the wall but also the parenchyma. They predicted that it could occur at a P_l as low as 1 cmH_2O. Our results, which indicate a buckling pressure between 2 and 4 cmH_2O, are in accord with this prediction. The greater value that we observed could indicate that the stiffness of the folding membrane is greater than assumed by Hill and colleagues. Once buckling has commenced, the peribronchial stress probably becomes nonuniform around the perimeter of the airway, with greater stress on the ends of the long diameter than on the ends of the short diameter. In the appendix, we show that the peribronchial stress around a small Con airway at P_l = 2 cmH_2O is ~2.4 cmH_2O, which results in a collapsing Ptm difference of 0.4 cmH_2O. The same calculation for P_l = 0 cmH_2O yields a collapsing Ptm difference of 6 cmH_2O. Further support for our flattening argument is given in Table 3, in which we present the mean values for the ratio of the short-to-long diameters of the airways at each P_l < 4 cmH_2O (at P_l ≥ 4 cmH_2O, we excluded airways for which this value was <0.6, as explained above.) It is apparent from the data in Table 3 that the airways flatten (i.e., the ratio decreases) with decreasing P_l and that this flattening is greater for the Con airways than for the Carb airways. For small and 1-mm Con airways at P_l < 2 cmH_2O, it appears that the epithelial membrane becomes more folded (Figs. 5 and 8) as the long diameter of the flattened cross section becomes shorter under the influence of the compressive stress on the ends of the long diameter of the airway.

The question still remains as to why the very smallest airways collapse the least. Elastic buckling theory shows that a tube's intrinsic resistance to buckling increases with the cube of the thickness-to-radius ratio. We have no direct measure of this. However, be-

### Table 3. Ratio of short-to-long lumen diameters for all airways at given lung recoil pressures

<table>
<thead>
<tr>
<th>P_l, cmH_2O</th>
<th>Con</th>
<th>Carb</th>
</tr>
</thead>
<tbody>
<tr>
<td>−4</td>
<td>0.449 ± 0.022</td>
<td>0.697 ± 0.014</td>
</tr>
<tr>
<td>0</td>
<td>0.641 ± 0.014</td>
<td>0.742 ± 0.009</td>
</tr>
<tr>
<td>2</td>
<td>0.761 ± 0.008</td>
<td>0.758 ± 0.009</td>
</tr>
</tbody>
</table>

Values are means ± SE. Con, control airways; Carb, carbachol-treated airways.
cause $WA_\text{g}/A_{\text{bm}}^*$ is approximately twice the thickness-to-radius ratio of the fully distended airway, it can be seen in Fig. 9 that the smaller airways had relatively thicker walls, and this could explain their resistance to elastic buckling.

The data in Fig. 8 show that, for all airway sizes, the Carb airways had more epithelial folds than Con airways at positive $P_L$. Close to $P_L = 0 \text{ cmH}_2\text{O}$, the number of folds is approximately the same for both treatments. The data also show that the number of folds increases with airway size. According to the study by Lambert and colleagues (10), the number of folds is determined not by airway size but by the normalized thickness of the region between the subepithelial reticular layer and the muscle layer (called the “submucosa” by those authors, referred to as “gap” in the present study and the area of the wall cross-section that it occupies as $WA_\text{g}$). Their analysis shows an inverse relationship between gap thickness and fold number. Thus the data in Fig. 8 indicate that the normalized gap thickness should be greater as the size of the airway decreases. We calculated this thickness ($WA_\text{g}/A_{\text{bm}}^*$) and present the results in Fig. 10. These data are in qualitative agreement with the predictions (10). When we plotted our data in the same three-dimensional manner as Lambert et al. did with their sheep data, we obtained a graph that looked very similar to their Fig. 3B (10). That study also predicted the dependence of fold number on lumen area. Our results for the pooled data (pooled data are used to reduce the noise) are shown in Fig. 11. Two things are apparent from this figure. First, the number of folds increases as the lumen area decreases. This is in accord with the analysis of Lambert and colleagues (10) and is contrary to that of Wiggs et al. (24) and Seow et al. (20). Comparison of our Fig. 11 with Fig. 2 in Ref. 10 suggests a value of $\sim 0.07$ for $WA_\text{g}/A_{\text{bm}}^*$, which is in agreement with our rabbit data (Fig. 10). Second, the relationship between fold number and lumen area appears to be the same for Con and Carb airways, despite the different sequences of collapse and manner of loading of the membrane.

There are two other studies in which theories of epithelial membrane folding have been developed (20, 24). Because the values for $WA_\text{g}/A_{\text{bm}}^*$ used in those studies are greatly in excess of those observed experimentally, both in this study and others (10, 18), the biological relevance of those theories is called into question.

Figures 3 and 11 show pooled data. These graphs more clearly show the behavior of the airways than the binned data. However, they must be treated with caution, as we did not sample equally in all bin sizes. Our data tended to be clustered in the two bins of smaller airway size because there were many more of these airways to sample. Thus the pooled data are biased.
toward small airways. Our conclusions are not crucially dependent on the pooled data.

Because only small volume oscillations were applied immediately before the fixation process, it is unlikely that the Carb airway geometry reported in this study conforms to what would exist in vivo when tidal pressure swings are superimposed on the bronchoconstricting stimulus. There is increasing evidence that tidal stretching of airway smooth muscle is an important modulator of airway tone and may be the most important safety factor preventing excessive airway narrowing (4, 22). Although tidal breathing would probably attenuate the degree of muscle shortening and airway narrowing we observed, it is unlikely that it would alter the basic conclusions of this study. The qualitative differences in the behavior of the relaxed and constricted airway at low distending pressures would still be operating.

In summary, our data show that, in a deflating lung, unchallenged (Con) airways flatten with very little mucosal folding and then develop mucosal folds with further lung deflation. On the other hand, challenged (Carb) airways develop many folds as the lung deflates and flatten only at collapsing P_tms values. The observed pattern of folding is in accord with the predictions of the model analysis of Lambert and colleagues (10). Whereas Carb airways have less lumen area than Con airways at distending P_tms, they are more open at collapsing pressures. Our results show that “parenchymal interdependence” imposes a collapsing stress on Con airways at positive P_t, which raises the question of whether parenchymal interdependence provides significant support for bronchoconstricted airways at low positive P_t. If it is not significant, then folding of the epithelial basement membrane may provide the only...
mechanical resistance to smooth muscle shortening under these circumstances.

APPENDIX

It is possible to estimate the peribronchial deformation of the parenchyma and thus to estimate the peribronchial stress \( (P_x) \). The normalized radius of an airway is approximately equal to the smooth muscle outer perimeter divided by the basement membrane perimeter \((P_{mo}/P_{bm})\). The normalized radius of a hole in the parenchyma is approximately equal to the cube root of the normalized volume \([(V/V^*)^{1/3}]\). Thus the strain, \( \varepsilon \), is given by the following equation

\[
\varepsilon = \frac{P_{mo}/P_{bm} - (V/V^*)^{1/3}}{(V/V^*)^{1/3}} = \frac{P_{mo}/P_{bm} - 1}{(V/V^*)^{1/3}}
\]

For a small Con airway at \( P_t = 2 \, \text{cmH}_2\text{O} \), \( \varepsilon \) has a value of 0.6. Using the expression for the shear modulus of rabbit parenchyma deduced by Stamenovic and Yager (23), \( \mu = (0.5 \times P_t) + 3 \, \text{cmH}_2\text{O} \), to calculate the peribronchial stress change from the uniformly inflated state \( (\Delta P_x) \), yields \( \Delta P_x = 2.4 \, \text{cmH}_2\text{O} \). The same calculation for \( P_t = 0 \) results in \( \Delta P_x = 6 \, \text{cmH}_2\text{O} \). Because we are using pleural pressure \( (P_{pl}) \) as reference, the peribronchial stress for an airway that deflates uniformly with the parenchyma is \( P_x = 0 \) and airway lumen pressure is \( P_t \). Thus, for a small Con airway at \( P_t = 2 \, \text{cmH}_2\text{O} \), the pressure on the outside is 2.4 \( \text{cmH}_2\text{O} \) and inside is 2 \( \text{cmH}_2\text{O} \), resulting in a collapsing \( P_{tm} \) of 0.4 \( \text{cmH}_2\text{O} \). This calculation is less than rigorous because it uses linear elasticity theory, which is probably not accurate for such large deformations. However, the calculation was not made with quantitative accuracy in mind but, rather, to show the plausibility of our hypothesis that the parenchyma near a Con airway can be compressed enough to provide a collapsing \( P_{tm} \).

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