Effects of surface tension and intraluminal fluid on mechanics of small airways

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Hill, Mark J., Theodore A. Wilson, and Rodney K. Lambert. Effects of surface tension and intraluminal fluid on the mechanics of small airways. J. Appl. Physiol. 82(1): 233–239, 1997.—Airway constriction is accompanied by folding of the mucosa to form ridges that run axially along the inner surface of the airways. The mucosa has been modeled (R. K. Lambert. J. Appl. Physiol. 71: 666–673, 1991) as a thin elastic layer with a finite bending stiffness, and the contribution of its bending stiffness to airway elastance has been computed. In this study, we extend that work by including surface tension and intraluminal fluid in the model. With surface tension, the pressure on the inner surface of the elastic mucosa is modified by the pressure difference across the air-liquid interface. As folds form in the mucosa, intraluminal fluid collects in pools in the depressions formed by the folds, and the curvature of the air-liquid interface becomes nonuniform. If the amount of intraluminal fluid is small, <2% of luminal volume, the pools of intraluminal fluid are small, the air-liquid interface nearly coincides with the surface of the mucosa, and the area of the air-liquid interface remains constant as airway cross-sectional area decreases. In that case, surface energy is independent of airway area, and surface tension has no effect on airway mechanics. If the amount of intraluminal fluid is >2%, the area of the air-liquid interface decreases as airway cross-sectional area decreases, and surface tension contributes to airway compression. The model predicts that surface tension plus intraluminal fluid can cause an instability in the area-pressure curve of small airways. This instability provides a mechanism for abrupt airway closure and abrupt reopening at a higher opening pressure.

Yager et al. (20) reported observations of airways in which the interstices between the folds were filled with fluid, and this observation added to the interest in mucosal folding. Lambert (12) then suggested that the basement membrane, which contains elastin and collagen, might resist bending and that its bending stiffness might be an important component of airway elastance. Lambert et al. (13) used this model to interpret data that showed correlations between number of folds, airway area, and wall thickness in sheep.

Lambert (12) modeled the airway as a composite structure consisting of an elastic inner layer, which represents the mucosa, an intermediate fluid layer, which represents the submucosa, and an outer layer of smooth muscle, which imposes a compressive stress on the inner layers when it contracts. Surface tension was not included in the model. He computed luminal area as a function of transmucosal pressure for this model. Yager et al. (20) discussed the effect of intraluminal fluid on luminal area and estimated the effect of surface tension on the airway area-transmural pressure curve in the case where the interstices of the folds were completely filled and the air-liquid interface formed a cylindrical surface inside the folds. In this study, we describe a model in which surface tension and intraluminal fluid are added to the Lambert model. The effect of surface tension is analyzed for the case where fluid partially fills the folds. We find that surface tension has no effect on airway area if the amount of intraluminal fluid is small and the fluid lining layer is thin. In that case, the air-liquid interface coincides with the epithelial surface, and the length of the air-liquid interface is constant because the perimeter of the mucosa is constant. Therefore, surface energy is independent of luminal area, and surface tension does not affect airway mechanics. Thus one of the principal consequences of mucosal folding is to remove the compressive effect of surface tension if the airway is relatively dry. However, with fluid volumes on the order of a few percent of luminal volume, fluid pools form in the folds, and the length of the air-liquid interface changes as airway area changes and the shape of the folds changes. In that case, the model predicts that surface tension can cause area-pressure instabilities and fluid-balance instabilities.

METHODS

Model. The model for the airway is the same as that of Lambert (12). The mucosa is modeled as a thin elastic cylinder with Young’s modulus (E), thickness (t), and undeformed radius (R) that is loaded by the pressures that are applied to its inner and outer surfaces. The submucosa is modeled as a fluid in which the pressure (Psub) is assumed to
be uniform. In Lambert’s model, the air pressure in the lumen (\(P_{\text{air}}\)) was applied to the inner surface of the mucosa, and transmucosal pressure, \(P_{\text{air}} - P_{\text{sub}}\), was uniform. For negative values of \(P_{\text{air}} - P_{\text{sub}}\), the mucosa is compressed, and at a critical negative transmucosal pressure, \(P_{\text{cr}} = -(D/R^3)(n^2 - 1)\), where \(D\) is the bending stiffness of the mucosa and \(n\) is the number of folds in the bending mode, the mucosa buckles. He analyzed the buckling of the mucosa for \(P_{\text{air}} - P_{\text{sub}} < P_{\text{cr}}\).

We have modified Lambert’s model by including a lining layer of intraluminal fluid with surface tension (\(\gamma\)) at the interface between the fluid and the air in the lumen. If the cylinder is circular and the fluid layer is thin, the curvature of the air-liquid interface is \(\sim 1/R\) and \(P_{\text{n}} = P_{\text{air}} - \gamma/R\), where \(P_{\text{n}}\) is the pressure applied to the inner surface of the mucosa. Therefore, with intraluminal fluid and surface tension, buckling occurs at a less negative value of \(P_{\text{air}} - P_{\text{sub}}\). If the fluid layer is thin, the folds that form when the cylinder buckles quickly penetrate the fluid layer. When that occurs, the curvature of the air-liquid interface is no longer uniform around the circumference of the wall, and the pressure applied to the inner surface is no longer uniform. We have analyzed the buckling of the cylinder under this nonuniform loading.

 Governing equations. A segment of the folded elastic wall is shown in Fig. 1. The elastic wall carries a shear force (\(V\)), a tensile force (\(T\)), and a bending moment (\(M\)) that vary with position (\(s\)) measured along the perimeter of the cylinder. The inclination of the tangent to the wall is denoted as \(\theta\). The equations of equilibrium for the wall are

\[
\frac{dT}{ds} + V(d\theta/ds) = 0 \tag{1}
\]

\[
\frac{dV}{ds} - T(d\theta/ds) = P_{\text{sub}} - P_{\text{n}} \tag{2}
\]

\[
\frac{dM}{ds} - V = 0 \tag{3}
\]

In addition, \(M\) is given by the product of \(D\) and the difference between the curvature of the wall (\(d\theta/ds\)) and the undeformed curvature (\(1/R\))

\[
M = D(d\theta/ds - 1/R) \tag{4}
\]

\(P_{\text{n}}\) that appears in Eq. 2 differs from the uniform \(P_{\text{air}}\) by the pressure difference across the air-liquid interface. The pressure difference across the air-liquid interface is given by the product of surface tension and interface curvature. Surface tension is assumed to be uniform, but the curvature of the air-liquid interface varies around the circumference. The curvature of the interface above the fluid pool must be uniform if \(P_{\text{n}}\) is uniform within the pool. The radius of curvature of this surface is denoted as \(a\). Beyond the boundary of the pool (\(s^*\)), the air-liquid interface coincides with the inner surface of the wall, and the interface curvature is the same as wall curvature (\(d\theta/ds\)). Therefore, \(P_{\text{n}}\) is given by

\[
P_{\text{n}} = P_{\text{air}} - \gamma/a, \quad s < s^* \quad \text{and} \quad P_{\text{n}} = \gamma/(d\theta/ds), \quad s > s^* \tag{5}
\]

Solutions for \(n\) identical symmetric folds around the circumference can be generated from solutions for one interval of length (\(\pi R/n\)), where \(R\) is the radius of the undeformed cylinder. The point \(s = 0\) is taken to be the point of maximum wall curvature at the depth of the fold, and the point \(s = \pi R/n\) is the point of minimum curvature. The boundary conditions for \(V\) and \(\theta\) at these points are

\[
V(0) = V(\pi R/n) = 0 \tag{6}
\]

\[
\theta(0) = \theta(\pi R/n) = \pi/n \tag{7}
\]

The interface above the pool must join the interface on the wall smoothly; that is, the circular arc of radius \(a\) and subtended angle \(\beta\) must meet the wall and be tangent to the wall at \(s = s^*\). This requires that the solution satisfy the following conditions

\[
a = x(s^*)/\sin \theta(s^*) \tag{8}
\]

\[
\beta(s^*) = \theta(s^*) \tag{9}
\]

Finally, the volume of intraluminal fluid (\(V_{\text{fl}}\)) is specified. This is given by

\[
V_{\text{fl}}/2n = \int_0^{s^*} x \sin \theta(s^*) ds - \frac{1}{2} \beta(s^*) a^2 \frac{1}{2} a^2 \cos \theta(s^*) \sin \theta(s^*) \tag{10}
\]

where \(x\) is the perpendicular distance between the midplane and the wall.

Equations 1–4, for the loading described by Eq. 5 and given values of \(P_{\text{air}} - P_{\text{sub}}, V_{\text{fl}}, n\), and \(\theta\), were integrated numerically from \(s = 0\) to \(s = \pi R/n\). Because the values of \(T\) and \(d\theta/ds\) at \(s = 0\) are not imposed by the boundary conditions and the values of \(a\) and \(s^*\) are not known a priori, the solution method required a search through values of \(T(0), d\theta/ds(0), a, \beta, s^*\) to find solutions that satisfied the boundary conditions at \(s = \pi R/n\), given by Eqs. 6 and 7, and the conditions at \(s^*\) given by Eqs. 8–10. Solutions were obtained for a series of values of \(P_{\text{air}} - P_{\text{sub}}\) up to the value of \(P_{\text{air}} - P_{\text{sub}}\) at which the sides of the folds touched at the midplane of the fold.

Particular values of the parameters were used in the calculations. On the basis of the data of Codd et al. (2), Young’s modulus \(E\) was taken to be 200 cm H\(_2\)O, the thickness-to-radius ratio (\(t/R\)) was taken as 0.04, and the bending stiffness \(D/R^3\) was taken to be 0.0015 cm H\(_2\)O. The value of \(R\)
was chosen to be 0.5 mm. Solutions were obtained for two values of \( \gamma \), 10 and 20 dyn/cm, respectively; for a series of values of \( V_n \), ranging from 1 to 4% of the area of the undeformed cylinder, \( \pi R^2 \); but for only one value of \( n \), \( n = 16 \). This value of \( n \) was chosen because it lies in the middle of the range of \( n \) observed by Lambert et al. (13).

RESULTS

The area-pressure curves that were computed from the model are shown in Fig. 2. In these curves, airway area (\( A \)), normalized by the undeformed area (\( A_o \)), is plotted against the pressure difference across the liquid lining and mucosa, \( P_{air} - P_{sub} \). For pressures greater than the buckling pressure, the cylinder remains circular. The specific elastance, \( A_o [d(P_{air} - P_{sub})/dA_o] \) of the circular cylinder is \( Et/2R \). Therefore, for \( P_{air} - P_{sub} \) greater than the critical buckling pressure, the curves shown in Fig. 2 have slope \( 2R/Et \). At the buckling pressure, area decreases sharply with decreasing pressure. The curves for fluid volumes <1% nearly coincide with Lambert’s curve for \( n = 16 \) (12). With intraluminal fluid, the buckling pressure is increased by \( \gamma/R \). However, if the amount of fluid is small, the fluid pools are small, the air-liquid interface nearly coincides with the wall surface, and the area-pressure curve is nearly the same as the area-pressure curve for the dry airway. If the amount of intraluminal fluid is greater, the area-pressure curves depart from those for dry airways. The shapes of a half-fold at various points along the pressure curves are also shown. The pressure in the fluid pool (\( P_{fl} \)) relative to gas pressure (\( P_{air} \)) is plotted vs. \( V_{fl} \) at fixed values of \( P_{air} - P_{sub} \) in Fig. 3.

DISCUSSION

Modeling assumptions. The model for the mucosa that is analyzed here is an idealized and simplified model. First, the geometry is idealized. It is assumed that the folding is uniform along the axis of the airway so that the deformation is two-dimensional. It is also assumed that the 16 folds around the circumference are identical, whereas the folding seen in airways is irregular. The material properties of the the airway are also modeled simply. The mucosa is modeled as a linear elastic material. Although geometric nonlinearities are included in the analysis of the folding, material nonlinearities are not considered. Finally, the submucosa has been modeled as a fluid in which the pressure is uniform. The material properties of the submucosa are unknown. It appears that the submucosa must be highly deformable because the deformations that occur during mucosal folding are large, but it is not known that the submucosa is completely inelastic. Also, the submucosa is thin compared with the depth of the folds. Contact forces between the mucosa and the surrounding smooth muscle layer or blood vessels in the submucosa may impose a nonuniform stress on the submucosal side of the mucosa.

Particular values for the parameters of the model have been chosen. The values of some of these parameters are uncertain, and the values of some are known to vary over a wide range. The model equations can be nondimensionalized (12), and the nondimensionalization yields scaling laws for the dependence of the variables on the parameter values. These laws allow the results reported here to be scaled for other parameter values. For example, the bending stiffness \( D \) of the mucosa is not well established, and the size of airways, which is described by the parameter \( R \), varies over a wide range. Scaling laws show that the pressure differences shown in Fig. 2 are proportional to \( D/R^3 \).
Because D is proportional to $t^3$, $D/R^3$ would be independent of airway size if the material properties of the mucosa were the same for all airways and mucosal thickness were scaled with $R$. Observed values of $n$ also vary considerably. Roughly speaking, $P_{air} - P_{sub}$ for a given deformation scales with $n^2$. The value of $\gamma$ in the airways is also uncertain. Alveolar surface tension has been measured and is known to change as lung volume changes, but the distribution of $\gamma$ along the airways is unknown. The effect of $\gamma$ scales with $\gamma/R$. Thus, for a given surface tension, the effects of intraluminal fluid and surface tension are greater in smaller airways than in larger airways. If the value of $R$ had been chosen to be 1 mm instead of 0.5 mm, the curves for $\gamma = 20$ dyn/cm for that airway would be the same as the curves for $\gamma = 10$ dyn/cm that are shown. We chose to analyze the deformation of a small airway to emphasize the effect of surface tension. Finally, we show results for intraluminal fluid volumes of 1–4% of undeformed luminal area. Yager et al. (21) found intraluminal fluid volumes of ~2% of luminal area at both high and lower lung volumes. For fluid volumes greater than ~6%, the fluid simply floods the space between the folds, and the air-liquid interface is circular. In that case, transmucosal pressure is uniform, and the effect of surface tension on mucosal folding can be obtained from Lambert’s results (12).

We assumed that the mucosa folded in a 16-lobe mode. The buckling pressure for this mode is larger than the buckling pressure for lower values of $n$, and one would expect that buckling with lower values of $n$ would be favored. Nonuniformities in mucosal properties around the circumference of the airway could affect the buckling mode. Lambert (12) suggested that the higher value of $n$ is imposed by the geometric condition that the folded mucosa fit within the surrounding ring of smooth muscle, and Mitzner and Wagner (15) suggested that folds form over blood vessels that impose an initial deformation on the mucosa. Thus, although the mechanism is unknown, multifold buckling occurs, and we have chosen a value of $n$ that lies in the middle of the observed range. However, the computed curves do not take account of the mechanisms that produce multifold buckling, and the sharp change in the slope of the curves shown in Fig. 2 seems unrealistic. It seems likely that the transitions between the segment of the curve for $A/A_o > 1$ to the segments for $A/A_o < 1$ are smoother than those shown in Fig. 2.

Smooth muscle contraction simultaneously imposes both a compressive pressure difference across the mucosa and maintains a circular outer boundary that confines the mucosa. If there were no smooth muscle tone and transmural pressure were negative, the entire airway wall, mucosa, submucosa, and smooth muscle could buckle in the lower energy two-lobe mode. Excised airways with no muscle tone collapse in this two-lobe mode. However, in intact airways, the surrounding parenchyma also tends to maintain a circular outer boundary for the airway. Certainly, reports of ridges in the surface of airways are not restricted to preparations in which smooth muscle has been activated by bronchoconstrictive agents. In the appendix, we analyze the effect of the surrounding parenchyma on the critical buckling pressure and conclude that, in the absence of smooth muscle tension, the critical buckling pressure for 16-lobe buckling of the mucosa within a circular outer boundary is smaller than the critical pressure for two-lobe buckling of the entire airway wall if transpulmonary pressure is >1 cmH$_2$O. Because passive or active smooth muscle tension and parenchymal stiffness both contribute to maintaining a circular outer boundary, the outer boundary of intact airways may remain circular, and the model described here may be an appropriate model for elasctance of the mucosa of normal airways.

Finally, our analysis describes the configuration of the mucosa and intraluminal fluid in static equilibrium. The equilibrium configuration depends on $P_{air} - P_{sub}$, and if $P_{air} - P_{sub}$ changes, the system must relax from the old to the new configuration. The relaxation time for redistribution of intraluminal fluid can be estimated by using the equations that describe two-dimensional viscous fluid flow. The volume flow rate ($Q$) in the fluid layer is given by $Q = (h^3/12\mu)(\Delta p/d)$ where $h$ is the thickness of the layer, $\mu$ is fluid viscosity, and $\Delta p$ is the difference between the pressures at two points separated by a distance (d). To change the shape of the fluid layer, a volume of the order of $dh$ must be collected, and the time required to transport this volume of fluid is $dh/Q$. For a value of $\mu$ equal to the viscosity of water, $\Delta p$ equal to the difference between pressure in the pool and pressure in the thin layer, and $h$ and $d$ equal to pool dimensions, the relaxation time is 0.1 s. Thus, for changes of configuration that occur over time scales that are >0.1 s, our assumption that pressure is uniform in the pool seems justified. However, $Q$ is proportional to $h^3$. An initially uniform layer of fluid would redistribute on a time scale of 0.1 s, but as the fluid layer on the ridge thins, flow becomes smaller and the rate of thinning decreases. In addition, our solution contains a discontinuity in the curvature of the air-liquid interface and hence, a discontinuity in fluid pressure, at the boundary between the pool and the thin layer. Our model does not address the complex mechanics of the fluid layer that covers the ridge; we have simply assumed that this layer is relatively thin.

Airway mechanics. The primary purpose of this work is to investigate the effects of surface tension and intraluminal fluid on the folding of the mucosa that occurs when airways are compressed. A primary, and perhaps surprising, result is that surface tension has no effect on airway compression if the amount of intraluminal fluid is small. This result can be understood immediately by considering the effect of the folds on surface energy. By folding, the perimeter of the airway remains nearly constant as airway area decreases. If the amount of fluid is small so that the pools of intraluminal fluid are small, the air-liquid interface lies near the inner surface of the airway, and the area of the air-liquid interface and hence the surface energy also remain constant. If surface energy is independent of airway area, surface tension cannot affect the pres-
ure-area curve. This result can also be obtained from Eq. 2. If the air-liquid interface coincides with the airway wall, the value of \( P_{air} \) is \( P_{air} = \gamma (d/ds) \). Another term in Eq. 2, \( T(d/ds) \), has the same form as the term \( \gamma (d/ds) \). Therefore, a change in \( \gamma \) can be balanced by an equal and opposite change in \( T \), leaving all other equations unchanged. Thus surface tension can be balanced by wall compression with no change in the area-pressure curve, and Lambert’s original model (12), in which surface tension was neglected, is valid for any value of surface tension if the airway is relatively dry. Conversely, changes in luminal area would have little effect on surface tension in that case. In the parenchyma, surface tension changes because alveolar surface area changes with lung volume. In the airways, if the amount of intraluminal fluid is small, airway perimeter is nearly independent of airway luminal area, and airway wall area changes only by the change in airway length as lung volume changes. Therefore, the direct effect of lung volume on surface tension in the airways is weak.

The combination of intraluminal fluid and surface tension affect the area-transmucosal pressure curves as shown in Fig. 2. Before buckling of the mucosa, the fluid forms a thin layer around the circumference of the lumen, and the pressure in the fluid layer is lower than luminal pressure because of the pressure drop across the air-liquid interface. Therefore, the compressive pressure applied to the mucosa is \( >P_{air} - P_{sub} \) by \( \gamma/R \) or 0.2 and 0.4 cmH_2O for \( R \) of 0.5 mm and \( \gamma \) of 10 and 20 dyn/cm, respectively. Thus, with intraluminal fluid, buckling occurs at values of \( P_{air} - P_{sub} \) that are greater than the value for the dry tube. For 1% fluid volume, the fronts of the folds quickly push through the thin fluid lining, and fluid collects in the depths of the folds. However, the curvature of the surface of the pools nearly equals the curvature of the mucosa, and the region covered by the pools is small so that the area-pressure curves are displaced only slightly to the right along the pressure axis. For 2% fluid, the area-pressure curve lies a bit farther to the right down to \( A/A_0 \) of \( \approx 0.2 \).

At that value of \( A/A_0 \), fluid fills most of the space within the fold and the air-liquid interface is near the neck between adjacent folds. The neck is narrow and the radius of curvature of the air-liquid interface is small as it passes through the neck. As a result, pressure in the fluid pool is much more negative than luminal pressure, and the region covered by the pool is subjected to a large compressive stress. This buckled configuration is maintained by the negative pressure in the pool, and \( P_{air} - P_{sub} \) is more positive. In fact, this configuration occurs at positive values of \( P_{air} - P_{sub} \) for both \( \gamma = 10 \) and \( \gamma = 20 \) dyn/cm. After the air-liquid interface passes through the neck, its radius of curvature increases, pressure in the fluid pool is less negative, and more negative values of \( P_{air} - P_{sub} \) are required to decrease area further. The same sequence occurs as \( A/A_0 \) decreases with 3% fluid. However, the air-liquid interface passes through the neck at a slightly higher value of \( A/A_0 \) the minimum radius of curvature as the interface passes through the neck is larger, and the maximum value of \( P_{air} - P_{sub} \) is smaller than for 2% fluid. The sequence is illustrated by diagrams that show three configurations, all of which occur at \( P_{air} - P_{sub} = -0.5 \).

The combination of surface tension and intraluminal fluid can produce convoluted area-pressure curves. The segments of the curves with positive slope are locally stable branches. That is, if \( P_{air} - P_{sub} \) is held constant, more work is required to deform the tube along the equilibrium curve than would be provided by the given \( P_{air} - P_{sub} \). The segments of the curve with negative slope are locally unstable. Thus configuration b shown in Fig. 2 is unstable. If \( P_{air} - P_{sub} \) were held constant, the tube would jump to either configuration a or c. The combination of stable and unstable segments leads to hysteresis in airway closing and opening. For example, in the instance where \( \gamma = 10 \) and there is 3% fluid volume, area would decrease smoothly along the upper segment of the area-pressure curve down to \( A/A_0 = 0.25 \) as \( P_{air} - P_{sub} \) decreased to \( -0.6 \). For a further decrease in \( P_{air} - P_{sub} \), \( A/A_0 \) would drop to the value \( A/A_0 = 0.1 \) on the lower segment of the curve. If \( P_{air} - P_{sub} \) were then increased, area would increase along the lower segment until \( P_{air} - P_{sub} \) reached \( -0.3 \). For any further increase, \( A/A_0 \) would jump from 0.15 to 0.8. For some values of \( \gamma \) and fluid volume, namely, \( \gamma = 10 \) dyn/cm and 2% fluid or \( \gamma = 20 \) dyn/cm and 2-4% fluid, positive values of \( P_{air} - P_{sub} \) are required to reopen the airway.

Recent studies (3, 16, 18) have shown that a positive transmural pressure is required to open airways that have closed. The airways appear to open abruptly at a critical positive transmural pressure. In some modeling studies, the positive opening pressure has been assessed to the pressure required to drive a miniscus axially into the closed segment of the airway (3). Our model describes a different mechanism that could maintain the airway nearly closed at small positive transmural pressures and produce a sudden opening at a critical pressure. The mechanism does not require an axial nonuniformity between open and closed segments of the airway; it is an instability in the opening of an axially uniform tube with fluid-filled folds.

Fluid instabilities. In addition to the mechanical instability that can occur for certain values of \( \gamma \) and fluid volume, a fluid instability can also occur. The mechanism is described by Fig. 3, in which pressure in the fluid pool, relative to luminal pressure, is plotted against fluid volume at a fixed value of \( P_{air} - P_{sub} \). This figure shows that at \( P_{air} - P_{sub} = -0.3 \), fluid pressure decreases as fluid volume increases because the radius of curvature of the air-liquid interface decreases as the volume of the pool increases. In that situation, a uniform distribution of fluid along the axis of the airway is unstable. If fluid volume were slightly greater at one point along the axis, pressure would be lower at that point and fluid would flow toward it. Pressure would fall further at the point where volume was high and would rise at other points, driving further flow. For \( \gamma = 20 \) dyn/cm, fluid accumulation would be terminated by a mechanical instability that occurs at a fluid volume of 3%.
Both the mechanical and the fluid instability mechanisms are driven by the decrease in radius of curvature as the air-liquid interface approaches the neck between adjacent folds. Folds that are one-half or more filled with fluid are susceptible to these instabilities. Therefore, it would be unlikely to find airways in which folds are one-half filled with fluid; it would be more likely to observe airways that are nearly dry or airways in which the folds are filled past the neck.

Comparison with airway elastance. Our modeling of the effects of surface tension and intraluminal fluid describes potential mechanisms for instabilities that may play a role in airway closure and reopening, and we have argued that this model of mucosal bending is pertinent both to airway compression driven by smooth muscle contraction and compression by transmural pressure differences due to flow. However, there is a fundamental question about the significance of these results; it is not clear that the magnitudes of mucosal bending stiffness and surface tension are large enough for these mechanisms to be significant. Because surface tension affects the area curves shown in Fig. 2, surface tension is significant, relative to mucosal bending stiffness, in 1-mm airways. However, it is not clear that the magnitudes of both bending stiffness and surface tension in small airways are significant. Figure 2 shows the relationship between area and transmucosal pressures. Transmucosal pressure is important if it is significant compared with the pressure generated by smooth muscle tension or if it is a significant fraction of transmural pressure. The range of pressures shown in Fig. 2 is small, on the order of 1 cmH₂O. Maximum smooth muscle contraction generates compressive pressures of 30–40 cmH₂O (4). Therefore, mucosal bending stiffness offers little resistance to maximum smooth muscle contraction. However, the bending stiffness of the mucosa may have been underestimated. Also, airway wall thickening occurs in asthma, and bending stiffness is proportional to the cube of thickness. A doubling of mucosal thickness would produce an increase of nearly a factor of ten in bending stiffness.

Although it appears that the mechanisms described here would not be significant during maximum muscle contraction, they may be significant at lower levels of smooth muscle tension. To determine whether they contribute significantly to normal airway elastance, the theoretical curves shown in Fig. 2 should be compared with experimental curves of airway area vs. transmural pressure. A precise comparison is not possible at present for a number of reasons. First, the pressures shown in Fig. 2 are the difference between gas pressure in the lumen and pressure in the submucosa. The pressure difference across the muscle and other elastic components of the airway wall must be added to the pressure differences shown in Fig. 2 to obtain transmural pressure. Therefore, plots of airway area vs. transmural pressure would be expected to be shifted to the right along the pressure axis, and the slopes of the curves would be reduced because of the elastance of the smooth muscle and other components of the airway wall, but the magnitudes of these shifts are unknown.

Also, the relationship between area, the area of the undeformed mucosa, and maximum airway area for large transmural pressures would be needed to align the ordinate in Fig. 2 with the ordinate of experimental area-pressure curves. At present, the transmural pressure at which mucosal folding begins is not known.

Although a precise comparison between the theoretical curves shown in Fig. 2 and experimental data is not possible, an approximate comparison can be made between the magnitude of the elastance of the model mucosa and the magnitude of airway elastance. The value of specific elastance, A₀ (dP_air – P_sub)/dA₀, for the model curves is ~1 cmH₂O. Gunst and Stropp (4) report area-transmural pressure curves of fluid-filled 4-mm canine airways. To obtain a value of specific elastance that is comparable to the model elastance, an approximate A₀ value for the canine airways is needed. The report of Yager et al. (21) shows that the epithelium of airways of guinea pig lungs fixed at a transpulmonary pressure of 5 cmH₂O is fairly smooth. The mucosa of sheep airways fixed at zero transpulmonary pressure (13) have deep folds. We will assume that folding begins at a transmural pressure of ~2 cmH₂O and take this value as the value of A₀. Then, the data of Gunst and Stropp (4) yield a value of specific elastance of 2–3 cmH₂O. The model mucosa would provide a significant fraction of the elastance of these 4-mm airways, and because airway elastance decreases with decreasing airway size (7, 14), mucosal elastance would provide a larger component of the elastance of smaller airways.

**APPENDIX**

The effect of the surrounding parenchyma on the buckling of an airway can be modeled by representing the surrounding parenchyma as an elastic continuum and adding this feature to the model for a thin-walled elastic tube. This model can be analyzed by combining two results from classic elasticity theory. The first is the analysis of buckling of a thin-walled tube supported by a Winkler foundation (1). A Winkler foundation provides a restoring stress that is proportional to the local displacement. The critical buckling pressure (P_crW) for a thin-walled tube supported by a Winkler foundation is given by the equation

\[ P_{crW} = -\frac{(n^2 - 1)(Dw/R^3) - kR/(n^2 - 1)}{(2\pi)^2} \]  

where \( n \) is the number of folds in the buckling mode, \( Dw \) is the bending stiffness of the tube wall, \( R \) is the tube radius, and \( k \) is the spring constant of the Winkler foundation. The first term on the right side of Eq. A1 describes the buckling pressure of an isolated thin-walled elastic tube. The second term describes the additional compressive pressure required to overcome the restoring forces provided by the foundation. In the buckled state, the normal stress applied by the foundation and the radial displacement of the tube are both proportional to \( \cos(n\psi) \) where \( \psi \) is the azimuthal angle around the axis of the tube. The ratio of the two is \( k \). The effective \( k \) of an elastic continuum can be obtained from a second result from classic elasticity theory (19). The stress and displacements in an elastic body loaded by normal stresses acting at a circular inner boundary can be expressed as series that reduce to Fourier series in the azimuthal angle at the boundary. The ratio of normal stress to radial displacement for each term in the series provides \( k \) for that order. The
ratio depends on the order, or buckling mode (n), and is given by

\[ k = E_{\text{par}} (n^2 - 1)/R (2n + 1 - v) \]  

(A2)

In Eq. A2, \( E_{\text{par}} \) and \( v \) are the Young's modulus and Poisson's ratio of the parenchyma. Substituting this value for \( k \) into Eq. A1 yields the following expression for \( P_{c\text{W}} \)

\[ P_{c\text{W}} = - (n^2 - 1)/(Dw/R^3) - E_{\text{par}}/(2n + 1 - v) \]  

(A3)

The objective here is to compare the buckling pressures for two different buckling geometries, buckling of the entire wall in the \( n = 2 \)-lobe mode and buckling of the mucosa in the \( n = 16 \)-lobe mode, with the outer boundary of the airway remaining circular. If \( P_{c\text{W}} \), the buckling pressure given by Eq. A3 for \( n = 2 \), is more negative than \(-0.4\), the critical pressure for mucosal buckling shown in Fig. 2, mucosal buckling will occur. Thus we seek the value of \( E_{\text{par}} \) for which \( P_{c\text{W}} < -0.4 \) cmH₂O

\[ 3(Dw/R^3) + E_{\text{par}}/(5 - v) > 0.4 \]  

(A4)

The value of the bending stiffness of the airway wall (Dw) is unknown. It is clear that Dw must be greater than the bending stiffness of the mucosa (D) because the airway wall includes the mucosa and the smooth muscle layer and is much thicker than the mucosa. However, a conservative estimate of the value of \( E_{\text{par}} \) for which Eq. A4 is satisfied is obtained by assuming that \( Dw < 10^2 \) D and that the first term in Eq. A4 is negligible. The value of \( v \) for the parenchyma is \(-0.4\). Thus a conservative estimate of the value of \( E_{\text{par}} \) that will prevent buckling of the entire airway in the \( n = 2 \)-lobe mode is \( E_{\text{par}} > 2 \) cmH₂O. Young's modulus has not been measured at very low transpulmonary pressures, but an extrapolation of the data of Lai-Fook et al. (11) to lower pressures yields the estimate \( E_{\text{par}} > 2 \) cmH₂O for transpulmonary pressure >1 cmH₂O.

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