Parenchymal Mechanics and Asthma*

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The essence of asthma is impairment of expiratory flow. Expiratory flow requires lung recoil forces to supply the driving pressure and to tether the airways open. Lung recoil forces arise within the parenchymal structures, particularly the air-liquid interface and elastin. Lung recoil is mainly elastic, but shows dissipative properties and contractility, and may be changed by volume history, time dependency, and plasticity. Lung recoil tethers the airway with peribronchial forces approximating pleural pressure but the peribronchial pressure departs systematically from this when the airway constricts, ie, “interdependence.” In asthma, lung recoil may decrease due to changes in surfactant, stretching of connective tissues, and growth. Parenchymal-airway coupling may be changed by local changes in parenchymal properties and particularly by swelling of the adventitia due to edema, inflammation, or matrix remodeling. Such changes in lung recoil and airway coupling may explain some of the reductions of expiratory flow seen in asthma.

The cardinal mechanical abnormality in asthma is impairment of expiratory flow. We have generally focused on abnormalities of the airways, and paid little attention to the tissue that embeds them although its importance to expiratory flow is undeniable; the decrease in the recoil forces of the lung parenchyma during expiration accounts for the dramatic fact that flow rate during a forced expiratory maneuver normally reaches a peak of perhaps 10 L/s but falls to less than 10 mL/s near residual volume. The reasons for this phenomenon are: (1) lung recoil supplies the driving pressure for airflow between the alveolus and the airway at the site of flow limitation, P_A−P_w, and (2) local lung recoil supplies the airway distending force, P_A−P_s, which is a major determinant of the airflow resistance of the upstream segment and of the two main variables that limit flow by the tube wave speed mechanism, namely the area and compliance of the airway at the site of flow limitation. A decrease of lung recoil decreases forced expiratory flow rates for both reasons, accounting for the dramatic dependency of forced expiratory flow on lung volume. How does this mechanism operate in asthma? This article reviews the nature of lung recoil generally, the coupling of that recoil to the airway, and considers the possible roles that changes in general or local lung recoil forces or in the coupling of the airflow to the parenchyma may play in the pathogenesis of asthma.

*Lung Recoil

Lung recoil forces are mostly borne by the alveolar parenchyma. The visceral pleura probably accounts for less than 20% of these forces.1,2 The airway and vascular trees have been thought to be important tension-bearing structures, with axial tensions transmitted from the hilum out to the distal branches where they pass into the perilobular connective tissues and thus to the visceral pleura.3 Against this view are the observations that the hilum is not ordinarily under much tension, that the airways are more readily lengthened when excised than in situ, and that, whereas the disposition of the elements of the bronchovascular trees is radial from the hilum, the lung shows isotropic mechanical properties.4

The alveolar parenchyma, by default, bears the greatest part of the tensions of the lung, transmitting the inflating stresses of the pleura throughout the parenchyma, and supporting the internal structures against the pull of gravity. It can be thought of as a cable and membrane structure which, like a parachute, maintains its configuration and function by tension in its parts (Fig 1). The “membranes” are the pseudoplanar alveolar septa, joining at their borders most typically with two other septa to form an open-cell, foam-like network, each septum bearing tensions in its air-liquid interface and supporting structure of fine connective tissue. Because the structure must be open-celled, some septal borders require special support.5 This is given by a curved stout bundle or “cable” of elastin and collagen as well as a varying amount of smooth muscle. These cables form a chickenwire-like network bounding the alveolar duct. Some cables also circle out to the outer margins of the alveoli that open from the duct but appear not to connect directly to the cables of the neighboring ductal units. The cable system is continuous proximally with the heavier connective tissue of the conducting airways and distally with the fine connective tissue of the septa. The arrangement of these cables and membranes implies a mechanical series relationship, where shortening of one would extend the other and vice versa. Given their substantial differences of composition and form, it is remarkable that the parenchyma retains near geometric similarity over a range of lung volumes; in fixed specimens, interseptal angles remain uniform,6 length densities of the septal borders imply only a slightly greater deflation of the duct than of the surrounding alveoli with deflation,6 and dynamic studies show only modest hysteresis of surface-to-volume ratio.7 These results imply remarkable matching of the passive properties of the cables and membranes.

Which materials bear tension? It was recognized early on that the surface component is very important; obliterating the air-liquid interface by inflation with saline reduces transpulmonary pressure by at least half.8 The tissue component generally is attributed to type I collagen and elastin. In the dog, about half of parenchymal type I collagen is found in the cables referred to above, and the other half in the fine network in the alveolar septal interstitium.9 Early on it was thought that type I collagen served primarily to protect lung tissue from overdistention and came under tension only at high lung volumes. It ap-

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pears, however, to be present in a complex network configuration and to be closely associated with elastin, so that it may, in fact, share in forcebearing over a wide range of lung volumes. Elastin is the obvious candidate for maintaining tissue tensions over a range of lung volumes, with its cardinal characteristic being a large range of extensibility (twofold), which in fact approximates that needed for expanding the lung (volumetrically eightfold) from 0 to 30 cm of water distending pressure.

Wilson and Bachofen have modeled the interplay of these components by treating the cable system as a helix of elastic elements, tensed by the surface tension of radially disposed septa. Using energy arguments and known properties of interfacial tension, they were able to predict observed lung behavior reasonably well, supporting the concept that lung recoil depends on a mechanical series interaction of the connective tissue cables with the alveolar membrane. We have taken a complementary approach. We defined $\sigma_{1ss}$ and $\sigma_\gamma$ as the recoil stresses attributable to interfacial and connective tissues acting on a transection of air-filled lung. We then estimated these stresses using stereologic estimates of the length of the interface and cross-sectional area of elastin seen on lung sections and data from the literature for surface tension and elastin stress. Although we have limited confidence in the assumptions, the resulting calculations fit reasonably well with typical volume-pressure data for the canine lung. We found (Fig 2A, left) that on a cross-section of lung, the calculated total contribution of elastin, $\sigma_{el}$, exceeds that of interfacial tension, $\sigma_\gamma$, over the full range of lung volume. When we restricted the question to the septum (Fig 2B, right), we found the elastin contribution greater than that of interfacial tension at lower lung volumes, whereas interfacial tension contributed more than elastin at higher lung volumes. The possibility that septal connective tissues bear tensions at low volumes contrasts sharply with one current view that septal connective tissues are slack. The basis for that view, namely redundancy or pleating of the alveolar septa in the three-way junctions where septa typically meet, we think may be an artifact of the experimental preparation. We have shown that such an appearance depends on the volume history of the preparation and is found only when the lungs have been first allowed to collapse and then have not been fully distended to over approximately 20 cm $H_2O$; under physiologic circumstances, we think that the septa are fully deployed. We further argue that some tissue tension is essential for maintaining the configuration of the internal surfaces of the alveolar parenchyma. Elastin has long-term force-length stability; the alveolar air-liquid interface does not. Elastin, then, can provide long-term stability to the configuration of the alveolar surfaces, anchoring them in space, whereas interfacial tension could not. We conclude that the fine elastin framework in the septum is under some tension even at low lung volumes.

**Contractile Elements**

The lung is a modestly contractile organ. Lung recoil, as measured by volume-pressure curves or the length-tension behavior of subpleural parenchymal strips, can be rapidly and reversibly altered by a variety of agents known to affect smooth muscle. It has been held that a regulated local decrease in parenchymal compliance may serve the physiologic function of changing ventilation locally, narrowing the distribution of $V/Q$ within the lung.

There are three types of contractile elements that might contribute. The first is the smooth muscle in the small airways and blood vessels. Narrowing and shortening of those structures could pull in on the surrounding paren-
parenchyma, tensing its passive elements. The second is the smooth muscle in the alveolar duct. Alveolar ductal smooth muscle is seen in many species, but to our knowledge, it has not as yet been quantified in any species. Its location in the alveolar ductal unit suggests that its contraction would tense the radially disposed septa, increasing alveolar surface area to some extent and narrowing the alveolar duct. A third possible source is the abundant contractile interstitial cell described by Kapanci et al.\textsuperscript{12} Although these cells are not typical smooth muscle cells histologically, they have much more actin than do noncontractile cells.

Which of these three systems is responsible for the observed alterations of lung recoil is not known. In a theoretical study based on Weibel’s anatomic data and modeling the parenchyma as an elastic continuum, we predicted small effects on lung recoil (<20%) from constriction of small airways and vessels.\textsuperscript{13} Constriction of ductal smooth muscle, however, should be more powerful. The role of the Kapanci cells is unclear, particularly because of their orientation transverse to the septum, which seems would not give the cell much mechanical purchase in the plane of the septum.

**Dissipative Properties**

The lung, like all solid biologic structures, is imperfectly elastic and shows hysteresis when passively cycled. Over a range of conditions, about one tenth of the energy put into the lung during inflation is lost (dissipated as heat) and consequently lung recoil is less at any given volume during deflation than it was during inflation. The hysteresis is far from a Newtonian flow resistance; the loops from pressure-volume studies or from force-length studies of parenchymal strips are profoundly insensitive to flow rate. In fact, the energy lost is nearly proportional to the elastic energy stored. Alternatively, the frictional stress is a fraction (the structural damping coefficient, $\eta$) of the elastic stress. In the more familiar terms of resistance, $R$; frequency, $\omega$; and elastance, $E$; $\omega R = \eta E$. This is not only a simplifying formulation, but may turn out to reflect the basic biochemical mechanism of energy dissipation in smooth muscle (J. Fredberg, personal communication). The effect is not small; at low frequencies, lung tissue resistance can be the major component of total pulmonary resistance.\textsuperscript{14} Although surface tension and connective tissues may contribute, it is of particular importance that $\eta$ may be changed by agents that affect smooth muscle.

**Volume History, Time Dependency, and Plasticity**

There are additional phenomena that may significantly reduce lung recoil. The lung has substantial compliance during inflation to very high volumes, and after higher inflations, a substantial portion of the deflation curve is shifted to lower pressures (Fig 3). This immediate volume history effect may reflect a rapid (seconds) time dependency of lung recoil by relaxation of surface tension due to recruitment of pulmonary surfactant from the subphase or by stress relaxation of the connective tissue components as well. There are also time dependencies on a longer scale. Although there is remarkable (and fortunate!) stability of the recoil properties of the healthy lung over decades (mechanism unknown), both reversible and irreversible changes may occur. With sustained distention and increase of the mean alveolar surface area, pulmonary surfactant is generated to reestablish the appropriate concentration of surfactant and surface tension. Distention can affect growth. It is not known to what extent it can lead to yield or remodeling of lung connective tissues.

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**Figure 2.** Left. Lung volume vs calculated contribution of several tension-bearing components to net parenchymal stress. Volume is given as fraction of lobar volume at 30 cm H$_2$O distending pressure ($FV_{L,30}$). Contributions of tension in air-liquid interface, $\sigma_g$ (volume $V$, curve 1), and of transected elastin, $\sigma_{el}$ ($\Delta$, curve 2), were based on known properties and stereologic data. Their sum is also displayed (closed circle, curve 3), as is mean distending pressure at which lobes were held on deflation limb during fixation ($P_1$, O, curve 4). Right, Lung volumes vs contributions to net parenchymal recoil of septal elastin, $\sigma_{el,u}$ (triangles), and septal interfacial tension, $\Delta_s$ (X) (after Oldmixon and Hoppin$^9$).
To summarize, lung recoil resides primarily in the alveolar parenchyma, which is a cable and membrane tensed structure with major forces borne in the air-liquid interface, but with an essential contribution by septal elastin. Recoil may be changed generally and locally by its dissipative properties, its contractility, and the effects of volume history, time dependency, and plasticity.

AIRWAY-PARENCHYMAL LINKAGE

Lung recoil accounts wholly or in large part for the lung volume dependency of airway length, diameter, conductance, maximal expiratory flow, and the dramatic effects of pulmonary fibrosis or emphysema on airways function. As a starting point, the airways can be considered to be exposed on their outer surfaces to a pressure (peribronchial pressure, \( P_a \)) equal to pleural pressure (\( P_{pl} \)). Pleural pressure, in turn, is less than alveolar pressure, \( P_a \), by virtue of recoil forces of the surrounding parenchyma. The anatomic linkage by which this is accomplished differs along the tree from large airways to small. The trachea lies in the loose tissues of the mediastinum and so, like the esophagus, is in effect exposed to \( P_{pl} \). An invagination of the visceral and parietal pleura surrounds the largest intrapulmonary airways, whereas more distally there is only an adventitia separating the airway from the surrounding parenchyma. In the smallest conducting airways, the distal bronchioles, the connective tissues of the alveolar parenchyma appear to connect directly to those of the airway wall. Yet it remains the case throughout the tree that the traction generated by the recoil of the surrounding lung is applied to the outside of the airway.

Although we start with the notion that \( P_a = P_{pl} \), significant departures must occur with the sort of distortion that occurs when the airway changes diameter disproportionately to the surrounding lung, eg, with bronchoconstriction. In this circumstance, parenchymal tensions become nonhomogeneous and forces develop that oppose the change in diameter, eg, by lowering the \( P_a \) with bronchoconstriction. This phenomenon was first proposed as the result of a deformation of elements of an elastic network and was dubbed “interdependence.”\(^\text{15}\) Subsequently, on the basis of theoretical and experimental evidence, the lung was modeled as an elastic continuum and the restorative forces of interdependence (ie, \( \Delta P_r \)) were determined as a function of the shear modulus, \( \mu \), which, in turn, is a direct function of lung recoil, \( \mu \sim 0.7P_a \), \( \Delta P_r \sim 0.7P_L \) \((1 - D/D_0)\), where \( D \) is the diameter of the tunnel formed by the peribronchial parenchyma and \( L \) designates the homogeneous, undistorted diameter. The absolute restorative forces of interdependence, then, are substantial and are greatest at high lung volumes.

**IMPLICATIONS TO EXPIRATORY FLOW LIMITATION IN ASTHMA**

The effect of the parenchyma on expiratory flow limitation depends on three critical factors, each of which may be changed in asthma: (1) general lung recoil, because it determines the driving pressure, \( P_a - P_{br} \), and (2) local (peribronchial) recoil, and (3) airway-parenchymal coupling, because they apply the distending forces to the outer surface of the airway, \( P_a \).

General lung recoil at a given lung volume is reduced in asthma.\(^\text{17}\) Some of this may be reversible. There is now clear evidence from careful radiologic studies of patients with asthma that there are significant increases of total lung capacity and reductions of elastic recoil that are reversible over the time scale of weeks, mechanism not specified.\(^\text{18}\) Some of the decrease in recoil in asthmatics appears to be irreversible, reflecting a growth response to the hyperinflation of asthma during the growing years,\(^\text{19}\) or a plastic response to sustained inspiratory efforts, eg, competitive swimmers have large lungs.\(^\text{20}\) It is tempting to speculate that the asthmatic in remission has relatively normal lung recoil (and forced expiratory performance) because of the important contribution of surface tension, but that sustained hyperinflation during exacerbations induces surfactant production. Furthermore, any developed slackness of the asthmatic’s connective tissue would then be more apparent, allowing a lower lung recoil to develop than would be the case in the normal subject.

Local (peribronchial) lung recoil should be particularly susceptible to each of these phenomena where there are higher tensions in the force-bearing elements surrounding narrowed airways.

In addition, the tethering effect of parenchymal recoil should be reduced by changes in the adventitial compartment that couples airway and parenchyma. Processes that would favor adventitial swelling would include increased capillary pressures and increased interstitial oncotic pressures in the presence of inflammation. Bronchoconstriction may favor fluid accumulation because of the effects of in-

![Figure 3](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21711/)
terdependence and hyperinflation on peribronchial pressure. Changes in the cellular and matrix components of the adventitia are seen in biopsy specimens of asthmatic lungs. Peribronchial edema is seen in lungs administered meth-

acholine\textsuperscript{21} and blood vessel engorgement with a variety of interventions.\textsuperscript{22} The effect of such swelling of the adventitial compartment would be to change the effects of interdependence between the airway and parenchyma. Swelling, by allowing the parenchyma to relax back toward the position it held prior to bronchoconstriction, would increase $P_\infty$, narrowing the airway at a given lung volume, making it more readily closed and less readily opened.\textsuperscript{21}

The effects of activation of parenchymal contractile elements are harder to predict. Contraction of airways smooth muscle may increase lung recoil to a degree, but presumably would decrease expiratory flow by narrowing the airways primarily. Contraction of alveolar ductal smooth muscle, however, should increase expiratory flow because of the increases of both the driving pressure and airway tethering forces. Activation of contractile elements may also affect hysteretic properties. Such effects have been extensively examined in the context of the relative hysteresis of parenchyma and the airway;\textsuperscript{23} if the hysteresis of airway and parenchyma is matched, the diameter of the airway will track with lung volume; if the hysteresis of the parenchyma exceeds that of the airway, the diameter of the airway wall will lead lung volume (narrower during deflation); if airway hysteresis exceeds that of the parenchyma, airway diameter will lag lung volume (widener during deflation). Thus, when a deep inhalation causes an increase in forced expiratory flow rate at a given lung volume ($M/P>1$), the explanation could be high airway hysteresis, low parenchymal hysteresis, or both. High airway hysteresis would be expected for length-forcing of activated airway smooth muscle.\textsuperscript{24} In the parenchyma, however, the effect of contractile element activation is less clear. Because the contractile element, eg, alveolar ductal smooth muscle, is mechanically in series with the septa, it could latch up, stiffening the parenchyma and conceivably reducing its hysteresis.

**Conclusion**

To clarify the potential role of changes in the parenchyma and its coupling to the airway in asthma, there is particular need for systematic studies of pathologic changes of the peribronchial parenchyma and adventitia. We need to know more about the causes and dynamics of fluid transport and extension of inflammatory processes both radially between compartments of the airway wall and along the axis of the bronchovascular interstitium. We need to know more about the effects of sustained bronchial constriction, of sustained hyperinflation, and of inflammatory conditions on lung recoil and on airway-parenchymal linkage.

**References**