Effect of surface tension on alveolar surface area

JAMES P. BUTLER,1,2 RICHARD E. BROWN,1 DIMITRIJE STAMENOVIC,3 JOHN P. MORRIS,4 AND GEORGE P. TOPULOS1,2
(With the Technical Assistance of Lydia S. Stickney5 and Shasta Kielbasa4)
1Harvard Medical School, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham & Women’s Hospital, 2Physiology Program, Harvard School of Public Health, and
3Department of Biomedical Engineering, Boston University, Boston, Massachusetts 02115; and 4Harvard College and 5Harvard Extension School, Cambridge, Massachusetts 02138

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Butler, James P., Richard E. Brown, Dimitrije Stamenovic, John P. Morris, and George P. Topulos. Effect of surface tension on alveolar surface area. J Appl Physiol 93: 1015–1022, 2002. First published February 8, 2002; 10.1152/japplphysiol.00126.2001.—At fixed lung volume (Vl), alterations in surface tension change alveolar surface area (S) and lung recoil (Pl). Wilson (26), using data from fixed lungs (1, 9), quantified the isovolume change in S with Pl. We reexamined this question in fresh excised rabbit lungs, with two important differences. First, we measured fractional changes in S by using diffuse light scattering, avoiding the potential upset of the balance of tissue and surface forces during fixation. Second, we altered surface tension by ventilating the lungs with nebulized polydimethylsiloxane, with much less residual fluid compared with lavage. We found that S decreased at low and mid Vl (treatment surface tension > control) by about half of Wilson’s estimates and was nearly unaffected by treatment at high Vl. This suggests that with increased surface tension there is 1) greater septal retraction in lungs fixed by vascular perfusion compared with unfixed lungs and 2) a greater increase in Pl and less loss of S than would have been predicted.

lungs; mechanics; lung recoil

It is generally agreed that over a wide range of lung volumes (Vl), the architecture of the mammalian lung displays approximate geometric similarity. However, the design of the lung includes an internal degree of geometric freedom in that the division of acinar volume between alveoli and alveolar ducts is determined by a balance of forces: inward-acting tissue forces in the alveolar entrance ring and outward-acting forces arising from septal tissue forces in parallel with surface forces at the air-liquid interface (3, 12, 27). This implies that alveolar surface area (S) can change independently of Vl as a consequence of changes in the surface tension (γ) acting at the air-liquid interface of the alveolar septal surface. There are wide variations in γ, both in normal lungs (especially true for large-volume maneuvers but also true for tidal breathing) and in diseased lungs (such as in acute respiratory distress syndrome), and therefore it is important to assess the magnitude of variations in surface area associated with these changes and their physiological consequences to lung recoil (Pl) and gas exchange.

The interplay between surface forces and tissue forces on the one hand and radially inward- and outward-acting forces on the other hand is shown diagrammatically in Fig. 1. The effect of increased γ is seen to have two effects. First, overall Pl is increased, and second, S of the alveolar septa, especially those with free edges, is decreased. It follows that the tissue forces within those septa (excluding the free edge) are correspondingly reduced and the tissue forces in the free borders of the septa are increased; the net effect is that the increase in Pl is less than that which would have occurred had there been no change in S. Furthermore, γ itself is not an independent variable insofar as it is strongly dependent on both the surface area of the surfactant film as well as the inflation-deflation history. Thus the simplest measure of lung mechanics, i.e., the pressure-volume (P-V) curve, depends on the simultaneous solution to the geometric response to changes in γ, the response of γ to changes in S, and the interaction with tissue forces both within the septa and at their free edges.

In this study, we determined the fractional change in S (ΔS/S), at the same Vl, between control conditions and after changing γ. We then determined the relationship between ΔS/S and the change in Pl (ΔP) caused by changes in γ. This was done over a range of Vl from functional residual capacity (FRC) to total lung capacity (TLC, the volume at 30 cmH2O distending pressure). All measurements were made in fresh excised rabbit lungs, by use of diffuse light scattering technology that, because the lungs are not fixed, permits repeated examination of an individual lung both at different volumes, and before and after altering γ. γ can be altered by lavage with a variety of fluids, followed by reinflation with air [e.g., Smith and Stamenovic (20), Bachofen et al. (1), and Hoppin et al. (13)], but this is known to leave a significant amount of fluid

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in the lung (4). The septa of partially filled alveoli are thus not equivalent to two-dimensional membranes with (altered) γ at the air-liquid interface. Thus, in the lavage preparation, the alveolar architecture is changed owing both to the direct effects of changes in γ and to partial alveolar flooding. We therefore chose to alter γ by ventilating the lung with nebulized polydimethylsiloxane (hereafter abbreviated as siloxane), the volumetric dose of which was several orders of magnitude less than techniques employing lavage. We found that the shifts in the pressure-volume characteristics with exposure to nebulized siloxane were remarkably similar to those found in air-filled lungs following lavage with the same fluid (20), a technique generally thought to effect an approximately constant γ preparation (13, 28).

Using these techniques, we found that ∆S/∆P systematically decreased with increasing Vt. Near FRC it was about half that concluded by Wilson (26), using data of Bachofen et al. (1) and Gil et al. (9) obtained from fixed lungs. At high Vt, ∆S/∆P was very close to zero.

**MATERIALS AND METHODS**

Two groups of New Zealand White rabbits were used for these experiments: one group (n = 9) for characterizing the effects of nebulized siloxane on pulmonary mechanics (pressure/volume curves, residual siloxane, and regional variability); the other group (n = 7, surface-to-volume ratio (S/V) study) for measuring the effect of alterations in γ, as quantified by changes in Plt, on pulmonary surface area.

**Effects of nebulized siloxane.** The deflation P-V characteristics were studied after three different types of exposure to constant γ siloxane. In exposure type 1 (repeat nebulized siloxane, n = 3), lungs were excised and control P-V data were collected. The lungs were then ventilated with nebulized siloxane, and posttreatment P-V data were collected. Ventilation with nebulized siloxane and P-V data collection were then repeated two more times. In exposure type 2 (nebulized siloxane vs. lavage, n = 3), excised lungs were studied under control conditions, after a single nebulized siloxane treatment, and after siloxane lavage and reflation with air. In exposure type 3 (nebulized siloxane in vivo, n = 3), anesthetized animals were ventilated with nebulized siloxane, the lungs were excised, and postnebulization P-V data were collected.

**Animal preparation.** Each of the 16 animals (mean body wt 3.7 kg) was anesthetized with ketamine (30–50 mg/kg im) and xylazine (1–3 mg/kg im). Additional pentobarbital sodium (10–20 mg/dose iv) was given via an ear vein as needed to maintain adequate anesthesia. Thirteen rabbits (treatment types 1 and 2 and animals used for the S/V study) received heparin (1,000 units/kg) and were exsanguinated via the carotid arteries. They were then intubated, the trachea was clamped at positive airway opening pressure (Pao), and the lungs were excised. Three rabbits (treatment type 3) were intubated below the larynx through a midline incision and ventilated with nebulized siloxane. The animal then received heparin (1,000 units/kg) and was exsanguinated via its carotid arteries. The lungs were then excised.

**Experimental setup and ventilatory histories.** Each pair of rabbit lungs was suspended by the trachea, and the endotracheal tube was connected to an adjustable constant-pressure source for control of airway opening pressure (Pao). The lungs were kept moist with 0.9% saline. Between measurements, the lungs were ventilated at 20 breaths/min (Harvard respiration pump, Harvard Apparatus, Millis, MA), and during measurements they were held at a constant airway pressure. The ventilator was operated as a “pressure ventilator” with the addition of pop-off valves to its inspiratory and expiratory limbs. The pop-off valve on the ventilator’s inspiratory limb was set to open at Pao ∼ 25 cm H2O, whereas its passive expiratory limb’s valve was set to open at positive end-expiratory pressure of 2–3 cm H2O (pretreatment) or 7–10 cm H2O (posttreatment). This increase in positive end-expiratory pressure posttreatment was done to prevent atelectasis and maintain FRC near control levels, because the siloxane treatment raises the lung’s γ and recoil pressure, especially at low Vt. Before each measurement, the lung was cycled three times between Pao of 3 and 30 cm H2O and then set to the target Pao on the lung’s deflation limb. During measurements, Pao was held constant by connecting the lung to an air source with a “T” side branch submerged to a measured depth in a water column. Because there is no gas flow during measurements, Pao is a direct measure of Plt. At each target Pao ranging from 2.5 (pretreatment) and 5 (posttreatment) to 30 cm H2O, both Vt and S were measured, as described below.

**Vt measurement.** At Pt ∼ 10 cm H2O, three pleural markers (short pieces of black suture) were cemented to the middle
portion of the costal pleural surface of one diaphragmatic lobe (S/V experiments) or both left and right lobes (siloxane-treatment experiments) by use of a small drop of cyanoacrylate glue, ~1.5 cm apart in a triangular pattern. The edge lengths were measured either with calipers (for the S/V experiments) or from photographs of the pleural markers together with a ruler held parallel to the lung surface (siloxane-treatment experiments). The area of the triangle was calculated as the 3/2 power of the area inscribed by the suture markers (14), normalized to its value at TLC pretreatment. (TLC is defined as Vl at Pao = 30 cmH2O). Note that Vl as thus defined is an estimate of the sum of gas and tissue volume. Pressure and volume data were fitted by least squares to the exponential expression of Salazar and Knowles (18)

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V = V_0 + VC[1 - \exp(-Pao/P_0)]
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where V0 is Vl at zero transpulmonary pressure, VC is the change in volume from V0 to its asymptotic value at high transpulmonary pressures (essentially equivalent to 30 cmH2O), and P0 is the pressure at which Vl reaches 69% of its asymptotic value from the PL = 0 state.

S measurement. Fractional changes in S, or, equivalently, surface-to-volume ratio, were determined by using diffuse scattering of laser light (693 nm). These changes were measured, during control conditions, with TLC used as the reference state. After nebulized siloxane treatment, measurements were repeated, using pretreatment isovolume points as the reference states. For a description of the theories, techniques, and interpretations involved when using diffuse light scattering in measuring lung architecture, see Butler et al. (6, 7), Suzuki et al. (21), Miki et al. (16), and Topulos et al. (22). Briefly, one optical fiber was used to place a point source of light normal to the pleural surface of the lung lobe, and three receiving fibers detected the backscattered light by using a intensity at fixed and known distances from the optical source. In the diffuse far field of scattering, the intensity falls off with distance r from the source proportionate to \(k_{diff}l_{opt}/r^3\exp(-k_{diff}r)\), where \(k_{diff}\) is the diffuse extinction coefficient and \(l_{opt}\) is the optical mean free path for scattering. Fitting a linear function to the logarithm of the \(r^2\)-weighted intensity suffices to determine \(k_{diff}\), the logarithm of \(k_{diff}l_{opt}\), and hence the fractional changes in \(l_{opt}\) from any reference state. These can be converted to fractional changes in surface area by observing that \(l_{opt}\) is proportional to \(l_m^2\) (21), where \(l_m\) is the mean linear intercept of air-liquid interfaces in the lung and that \(l_m\) is proportional to \((SV)^{-1}\), i.e., the inverse of S/V.

Treatment of the lungs with nebulized siloxane. After control measurements, the lung was ventilated for 5 min at 20 breath/min. Treatment was then begun with nebulized siloxane (5 ml polymethylsiloxane; viscosity 20 cS, molecular weight ~2,000, γ 20.6 dyn/cm; Nye Lubricants, New Bedford, MA) in the inspiratory limb of the ventilator by using a continuous flow of ~13 l/min compressed air into the nebulizer (Misty-Neb, Allegiance, McGraw Park, IL). The time necessary for nebulizing the entire 5 ml of siloxane was between 5 and 10 min. Gas leaving the circuit during nebulization passed through HEPA filters (OF612HE Omega filter, Atrix International, Burnsville, MN) to avoid contaminating the room with siloxane aerosol. The size distribution of the siloxane aerosol leaving the nebulizer was characterized (Aerosizer, model MACCII, API, Amherst, MA). The count median aerodynamic diameter of the mist leaving the nebulizer was 1.8 ± 1.3 μm (mean ± geometric SD). After treatment, the lung was ventilated for either 5 min (siloxane-characterization measurements) or 30 min (S/V measurements).

Siloxane lavage. After control data and data after a single nebulized siloxane treatment were obtained (as above), the lungs of rabbits in the type 2 exposure group (nebulized siloxane vs. lavage) were lavaged with the same fluid. The lungs were filled by connecting the trachea (starting from a Pt of 0) to a siloxane-filled reservoir held 30 cm above the lung. Filling required 80–88 ml of siloxane and took ~15 min. To drain the siloxane from the lungs of two animals, the reservoir was then lowered to ~100 cm below the level of the lungs. The siloxane was withdrawn from the lungs of the third animal by aspiration with a syringe and passive drainage. After 15–20 min, 22–25 ml of siloxane remained in the lungs. The lungs were then ventilated with air for ~5 min, and then postlavage P-V data were collected as described above.

Siloxane dose deposited. In separate experiments, the volume of siloxane deposited per gram of lung tissue was determined in three excised rabbit lungs and one excised dog lobe ventilated with nebulized siloxane and in one rabbit lobe ventilated in vivo with nebulized siloxane. The mass of elemental Si in each of 23 samples (1.3 ± 0.5 g) was determined by atomic absorption spectroscopy (Gaithersburg Laboratories, Knoxville, TN). Also analyzed were untreated control lungs prepared in an identical manner, to which known volumes of siloxane were added after homogenization (used to calculate Si recovery efficiency). The volume of siloxane deposited per gram of lung tissue was computed from recovery efficiency (~0.63), the density and composition of the siloxane, and the mass of each sample.

RESULTS

Effects of siloxane exposure on the P-V curves. The P-V characteristic of the lung changed consistently after all of the exposures to siloxane, with no important differences between a single nebulization, multiple nebulizations, or lavage. Figure 2 shows a comparison of P-V curves under control conditions; one, two, or
LUNG SURFACE AREA AND ALTERED \( P_L \)

The volume of siloxane deposited was determined to be \( 0.0045 \pm 0.0006 \) \( \text{ml/g lung} \) (mean \( \pm \) SD). This dose of siloxane, if spread uniformly at TLC [at which rabbit lung density \( \approx 0.858 \) and \( S/V \) is \( \approx 350 \text{ cm}^{-1} \) (9)], would result in a siloxane film layer \( \approx 0.01 \) \( \mu \text{m} \) thick at TLC and about twice that at FRC. Equivalent results were found in the dog lobe. This thickness is a negligible fraction of alveolar diameter and on the order of magnitude of the 0.1-\( \mu \text{m} \) thickness of the normal surfactant layer (12). There is, however, considerable uncertainty regarding the nature and degree of spreading (see DISCUSSION).

Pooled pressure-volume data (mean \( \pm \) SD) for the \( S/V \) experiments, both pre- and posttreatment, together with their exponential fits, are shown in Fig. 4.

The difference in \( P_L \) (posttreatment minus control) at any given \( V_L \) is a measure of the difference in surface forces after treatment and is denoted \( \Delta P \). At any \( V_L \) below \( \approx 95\% \) TLC, \( P_L \) increased posttreatment (\( \Delta P > 0 \)), and conversely above this volume. This volume defines a crossover point at which the posttreatment \( P_L \) is the same as control, i.e., the point at which \( \gamma \) after siloxane is the same as that in the normal lung (see DISCUSSION for comments on film spreading). This is consistent with the idea (20) that, at this crossover volume, the in vivo \( \gamma \) is similar in magnitude to that of the siloxane and should therefore induce little geometric distortion from the control state. Our results are also consistent with other observations of the volume at which normal \( \gamma \) is \( \approx 20 \text{ dyn/cm} \), which range from mid 80\% TLC (19, 20) to mid 90\% TLC (26, 13).

After treatment with siloxane, it was not possible to determine \( V_L \) by pleural markers below \( P_a \approx 5 \text{ cmH}_2\text{O} \) because at such low distending pressures areas of the lung began to collapse, thus distorting its pleural surface. The gross appearance of such collapsed areas posttreatment was strikingly similar to that of a degassed lung.

Alveolar \( S \), \( V_L \), and \( \Delta P \). Pretreatment \( S \) varied strongly as a function of \( V_L \). Figure 5 shows a log-log plot of \( S \) vs. \( V_L \) (mean \( \pm \) SE). Control data points are shown, together with the regression line (constrained to go through the origin because both \( S \) and \( V_L \) are normalized to their values at TLC). The slope is 0.65, which is not significantly different from \( 3/4 \).

Also shown in Fig. 5 are posttreatment values of \( S \), which were systematically less than control at \( V_L \) at

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**Fig. 3.** Comparison of P-V data (means \( \pm \) SD) in lungs used for siloxane exposure characterization with the data of Smith and Stamenovic (20). \( \bullet \), control (\( n = 6 \)); \( \circ \), after a single treatment with nebulized siloxane (\( n = 6 \)). These are the same data as in Fig. 2, with SD bars added. The deflation P-V data of Smith and Stamenovic (20) are shown as \( \bigcirc \), presiloxane control; \( \bullet \), air filled after siloxane lavage.

**Fig. 4.** Pooled P-V data (means \( \pm \) SD) in lungs used for lung \( S/V \) measurements (\( n = 7 \)). Exponential fits following Salazar and Knowles (18) are also shown. \( \bigcirc \), Control; \( \bullet \), postsiloxane exposure. Note that the two P-V curves cross at a \( V_L \) somewhat above 90\% TLC. Below this point, recoil is increased with treatment, consistent with increased \( \gamma \), and vice versa above the crossover volume.
which recoil was significantly increased. At high Vl, the differences were not significant.

A cross plot of control S and posttreatment S at each of Vl = 0.4, 0.6, 0.8, and 1.0 TLC is shown in Fig. 6 as a function of ΔP (control S points are shown on the ΔP = 0 axis).

A reduction of these data to the change in S (posttreatment minus control) at these same four volumes is shown in Fig. 7 vs. ΔP. Also shown in both Figs. 6 and 7 are estimates of S and ΔS vs. ΔP from the work of Wilson (26). These lines were derived from Fig. 1 of that work. The intercepts at ΔP = 0 were shifted slightly to coincide with our measurements; the slopes were taken from the chord slopes of the air-filled and detergent-rinsed preparations below TLC and from the tangent slope of the line at TLC.

At volumes below ~80% TLC, Pl was increased, consistent with an increase in γ; this in turn is necessarily associated with a decrease in surface area. Above 80% TLC, differences were not significant.

**DISCUSSION**

Our measurements of the change in parenchymal surface area, at fixed volumes when γ is artificially changed, are similar to but quantitatively smaller than that seen by others [Bachofen et al. (1) and Gil et al. (9) as synthesized by Wilson (26)]. There are two differences in the experimental preparations that may account for this. First, our measurements were performed in fresh, unfixed lungs by use of diffuse light scattering, whereas the classical measurements of surface area have been done in fixed and sectioned lungs by using stereological principles and morphometric measurements made under light microscopy. Second, our intervention to change the lung’s γ involved ventilation with nebulized siloxane, which resulted in a deposited volume significantly smaller than is seen with previous lavage techniques. We remark on each of these. After these methodological issues, we give some interpretations of our findings in terms of their physiological and pathophysiological implications.

*How are forces “fixed” when chemically preserving a lung?* The inwardly acting forces in the tissue comprising the alveolar entrance rings are essentially at all times balanced by the combination of outwardly acting tissue forces in the alveolar septa together with the γ present at the air-liquid interface. For the resulting geometry (fractionation of volume between ducts and alveoli, or, equivalently, the determination of the alveolar septal area at that given Vl) to remain unchanged during fixation requires that the forces that are mechanically in series change quantitatively in an identical fashion over time. If this is not the case, then there will be a distortion of the geometry during fixation before the final state is reached when sections can be cut. The change in the force/length characteristics of connective tissue (primarily elastin and collagen) as well as smooth muscle during aldehyde fixation is not well known. Similarly, there are no studies to our knowledge of the time course of changes in γ in the lung (be they associated with native surfactant or with any of the perturbing fluids or detergents used to artificially change γ) during vascular perfusion with osmium tetroxide or glutaraldehyde. Moreover, leak-
age of any fluid into the alveolar space may transiently increase γ before fixation and result in a larger decrease in surface area. The question of whether there is geometric distortion during fixation, particularly as manifested in changes of surface area relative to that present in vivo, thus remains open. It is important to note that we are not questioning the value of classical fixation techniques in preserving the ultrastructure at the cellular and subcellular level, nor do we question the appropriateness of using stereological techniques to infer three-dimensional properties such as S/V from morphometric measurements made on sections. Rather, it would seem important in the future to characterize the temporal evolution of stiffening of proteins and surface films in the presence of aldehyde perfusates. This would resolve the possibility that differences in our data, obtained on fresh, unfixed lungs, from classical studies are due to architectural alterations in the lung parenchyma associated with perfusion fixation of prestressed tissues.

**Diffuse light scattering.** In addition to the uncertainties associated with chemical fixation, there are also a number of unanswered questions regarding the use of diffuse light scattering to obtain stereological information. Chief among these is the relationship between fractional changes in the optical mean free path (which we feel confident we can measure) and the corresponding fractional changes in the geometric mean free path (which is the desired quantity, inversely proportional to S/V). The relationship between the optical and geometric mean free path was established by Suzuki et al. (21), by comparison with microscopic morphometry on preparations fixed by vascular glutaraldehyde and osmium tetroxide perfusion, assuming that the fixed preparation is reasonably faithful to the in vivo architecture (17). It is important to note that the measurements we report here are expressed as fractional changes in S/V, not absolute values. We therefore cannot make any direct comparison with that portion of Wilson’s work that quantifies the specific relationship between γ and S/V. Furthermore, we have explicitly extrapolated the calibration of Suzuki et al. (21) to the posttreatment preparation; the magnitude of the error involved here is unknown, but we suspect that it is small, because films significantly less than a wavelength of light in thickness have little effect on the optical properties of surfaces. On the other hand, an upper bound on this effect can be calculated in a manner similar to that in Butler et al. (6), treating the coated septa as an optical composite (siloxane-tissue-siloxane; index of refraction 1.4:1.33:1.4). The scattering cross sections with and without the siloxane film present amount to ~5%, which we take as negligible. In summary, even in light of the above uncertainties, diffuse light scattering has the singular advantage of being applicable to fresh, unfixed lungs, and, in consequence, individual preparations can be used as their own controls, either for comparison at different VL (see Figs. 6 and 7) or for comparison at a variety of isovolume points before and after treatment (see Figs. 6 and 7).

**Altering the lung’s γ.** There is little doubt that treatment with nebulized siloxane significantly alters the γ in the lung. This could result from the siloxane spreading into a thin and continuous film at high VL, where the surfactant γ is greater than 21 dyn/cm, and, through unknown mechanisms, remaining spread at low VL, even though that is not the energetically favored state. In this case, the lung would have an approximately constant γ, independent of VL. By contrast, it is also possible that the siloxane contaminates the entire surfactant film sufficient to raise γ well above normal values at low VL, although not necessarily to the siloxane-air interfacial value. This possibility is supported by the observation that contamination from protein leakage in diseases characterized by increased capillary permeability can lead to significant surfactant dysfunction, with elevated γ. In this case there is no reason to believe that γ posttreatment is constant. We have no experimental evidence to resolve this question, which must therefore remain open. Nevertheless, it is important to recognize that, whether or not γ is constant, exposure to nebulized siloxane results in consistent changes in PL, and the values we report here for the change in surface area per change in recoil pressure would still be valid, insofar as this ratio is an estimate just of the tangent δS/δPL|VL. In particular, the specific value of γ does not enter into our calculations; in this sense one can consider the “dose” in our treatment to be the change in PL, albeit through the agency of the nebulized siloxane.

Despite these uncertainties in γ after treatment with nebulized siloxane, we are confident that the resulting change in acinar architecture is close to that after a pure γ alteration. In contrast to the lavage preparation, the nebulized technique leaves a much smaller volume of siloxane in the lung. Compared with the 0.0045 ml/g lung mass we found with the nebulization method, Smith and Stamenovic (20) report their lungs retained 0.4 ml/g after siloxane lavage, and Bachofen et al. (1) reported a similar amount (5 ml retained in the lungs of 3-kg rabbits) after detergent lavage. These amounts are ~10% of alveolar volume at FRC and ~100 times greater than the volume of liquid retained by using the nebulization method described here. With any substantial amount of remaining fluid, there can be a significant alteration of the local alveolar architecture. Figure 7 in Bachofen et al. (4) is a striking example of this. See also Bachofen et al. (5) for a discussion of the alterations of alveolar architecture in fluid-filled and fluid-rinsed preparations.

**Physiological significance.** In his investigations into the relationships among PL, surface area, and γ, Wilson (25, 26) concluded that at any given VL, increased γ leads to an increase in PL through both its direct effects (quantitatively given by P = (%)γS/V) and its indirect effects via a net increase in ductal tissue forces due to their serial arrangement with alveolar septa. (This is true independent of parenchymal geometric distortion, but note that decreases in S will reduce tissue forces within the septa, because they are in parallel with the septal surface.) An equivalent expres-
sion of this phenomenon is to observe that, in the absence of geometric distortion, an increase in $\gamma$ would lead to increased $P_L$ in excess of that which is observed; the presence of distortion allows the lung to relax to a new equilibrium state at a lower $P_L$. The extent to which this occurs can be quantified by the change in surface area with changes in $P_L$ under isovolume conditions. The fact that we found less area change with changes in recoil then implies that alterations in $\gamma$ such as found in disease would be expected to have a more serious impact on $P_L$ than would have been predicted. Indeed, the smaller the change in area with $P_L$, the closer $P_L$ is to the observed $\Delta P$.

Wilson’s arguments are based on the conservation of energy when external (pressure/volume) work is done by the lung; the internal energy is present as elastic stored energy in the tissue and as surface energy associated with $\gamma$. Missing from his formulation is the term associated with the energy of adsorption or desorption of molecules from the liquid lining layer when $\gamma$ is changed. The effect of this term on Wilson’s results is unknown to us but invites future investigation.

Our control measurements of the dependence of surface area on $V_L$ show that $S$ varies roughly as $V_L^{0.6}$. This is consistent with our laboratory’s previous observations (21) made in dog lungs and corresponds to approximately geometric similarity in parenchymal architecture over most of the vital capacity. Gil et al. (9), using morphometric measurements in rabbit lungs, found an exponent closer to one-third, but there was significant scatter in the data. On the other hand, both our results and Gil et al.’s are inconsistent with the recent observations of Carney et al. (8), who on the basis of subpleural observations of alveolar geometry concluded that volume changes were effected primarily by recruitment; this would correspond to a power law exponent of 1.0. In addition, their data seem inconsistent with this conclusion, because for fixed alveolar volume recruitment requires the total alveolar number to increase approximately proportional to $V_L$. This in turn implies a nearly constant alveolar number density, contrary to their Fig. 4. Moreover, at a $V_L$ of ~50% TLC, a quantitative estimate from that figure of the volume fraction occupied by alveoli exceeds 1.0.

Several forms of pulmonary pathology as well as developmental deficiencies are known to produce damage to or deficiencies of surfactant function (see, e.g., 10, 11, 15, 24). At the level of lung mechanics, our data suggest that the primary consequence of increased $\gamma$ is simply increased local recoil. The loss of area with abnormally high $\gamma$ may compromise gas exchange as well, because of both the simple loss of available area as well as increased tissue thickness and decreased conductance for diffusive gas transport. However, our observation that area loss is less than previously thought suggests that the lung is less at risk for this to occur, although the cost for this protection is a commensurately increased recoil pressure, as remarked above. Changes in $\gamma$ are also present in normal lungs, especially during large volume excursions but even during tidal breathing. Our finding that there is a relatively smaller amount of area distortion with changes in $\gamma$ is consistent with the observations of Butler et al. (7), who found the expected pressure relaxation and recovery but essentially no geometric adaptation after step changes in volume, and the observations of Miki et al. (16), who found essentially no hysteresis in surface area during normal tidal breathing in live rabbits. At high $V_L$, our observation of a negligible change in surface area is consistent with the observations of Bachofen et al. (2), who found little hysteresis in $S$ at high $V_L$ and concluded that tissue forces play a dominant role.

In summary, our experiments demonstrate that a very small amount of aerosolized siloxane results in significant, systematic, and reproducible changes in the lung’s pressure-volume relationship. The increased $P_L$ at all but the highest $V_L$ are consistent with the $\gamma$ of the siloxane-exposed lung being greater than the $\gamma$ in the normal lung. With increased $\gamma$, we found a reduction in surface area under isovolume conditions, but of a magnitude significantly less than that found by Wilson (26). We speculate that the major source of this discrepancy lies in the difference between the balance of forces that determine surface area in chemically fixed lungs and in freshly excised lungs. Physiologically, we conclude that increased $\gamma$ associated with respiratory diseases or with industrial exposure to siloxane aerosols in the workplace has a larger effect on $P_L$ and a smaller effect on $S$ than would have been predicted from the work of Wilson (26).

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