Interdependence of flow between lobes reduces maximal emptying postresection in dogs

DAVID EWING-BUI AND STEVEN N. MINK

Section of Thoracic Surgery, Department of Surgery, and Section of Respiratory Diseases, Department of Internal Medicine, University of Manitoba, Winnipeg, Manitoba, Canada R3E-0Z3

Received 27 April 2001; accepted in final form 10 September 2001

Ewing-Bui, David, and Steven N. Mink. Interdependence of flow between lobes reduces maximal emptying postresection in dogs. J Appl Physiol 92: 100–108, 2002.—The effect of pulmonary resection on the maximal emptying of the remaining lobes was examined in an open-chest preparation in normal canine lungs and in a unilobar papain emphysema model. The objectives were to determine whether, compared with when both lungs were deflated (BL), maximal emptying of the normal lower lobes or the emphysematous right lower lobe would be altered 1) when acute pneumonectomy of the contralateral lung was performed (OL) and 2) when the lower lobe deflated alone (LA). The alveolar capsule technique was used to measure alveolar pressures (Palv) at 75, 50, and 30% lobar vital capacity (VC). During forced deflation, the maximal rates of deflation (dPalv/dt) and flows (lobar V\(\dot{\text{max}}\)) of the lower lobes were determined under the three different conditions. The Pitot-static tube technique was used to measure intrabronchial pressures and to estimate bronchial area and compliance in which values were obtained at the same central airway during the conditions studied. The results showed that, compared with BL and OL, dPalv/dt and lobar V\(\dot{\text{max}}\) decreased during LA (\(P<0.05\)). These findings were due to a reduction in bronchial area during LA that limited flow at a lower maximal value compared with BL. This decrease in area appeared to be due to a change in bronchial pressure area behavior that resulted in a smaller bronchial area during LA for similar transmural pressures between conditions. There were no differences in findings between normal and emphysematous lobes. This study suggested that removal of lobes may alter the pressure area behavior of central airways. Possible mechanisms considered were differences in axial tension between conditions, negative effort dependence, or parenchymal-bronchial interdependence that may be relevant to understanding the dynamic collapsibility of central as well as intraparenchymal airways.

maximal expiratory flow; regional emptying; choke point; emphysema; lung resection; parenchymal-bronchial interdependence

IN CLINICAL MEDICINE, LOBECTOMIES are frequently performed for both benign and malignant diseases of the lung. However, there is little information available about the dynamic functioning of the remaining lobes postresection, other than reporting the changes in spirometry that occur (6, 18). After resection of pulmonary parenchyma, there are accompanying alterations in the spatial relationships and forces that develop between the remaining lung and chest wall and between the remaining lobes. These alterations may become most apparent during dynamic measurements such as those obtained during forced expiration. If there were interdependence of flow between lobes, such that the removal of parenchyma decreased the flow of the remaining lobes, then after lung resection maximum expiratory flow (V\(\dot{\text{max}}\)) could be reduced to a greater extent than that predicted on the basis of the removal of lung parenchyma alone.

One mechanism by which removal of lobes may decrease maximal emptying of the remaining lobes is by changing the spatial orientation of the bronchi, such that frictional pressure losses (Pfr) to the site of flow limitation were increased after surgery (1, 2, 11). In terms of the wave-speed theory of flow limitation, V\(\dot{\text{max}}\) occurs when, at a site in the airway, gas velocity is equal to the speed at which pressure pulse waves can be propagated along the airway wall (1, 2). This site is termed the choke point (CP), and V\(\dot{\text{max}}\) \(\propto (A^3K^{-1})^{1/2}\), where A* and K are airway area and compliance at CP, respectively. After pulmonary resection, an increase in Pfr would reduce total airway pressure and therefore the lateral airway pressure (Plat) measured at CP (1, 2, 11, 19). In turn, this would lead to a decrease in A* and hence V\(\dot{\text{max}}\) compared with what would be observed without this added increase in Pfr.

Removal of lobes may also result in a change in the spatial orientation of the central bronchi, causing a decrease in the longitudinal radius of curvature of these airways, and furthermore would attenuate the lengthening of the central airways during inflation (5). In turn, these effects would result in a reduction in axial tension of the central airways during forced deflation, leading to a decrease in CP area and stiffness compared with preresection (2, 9). Similarly, if CP were to move upstream into lobar and segmental airways postresection, then transmural pressures in the central airways would be more negative compared with preresection, because the pressure drop across the flow-limiting segment would occur in more upstream

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
airs. In the condition in which transmural pressures in central airways were to decrease below those found at the onset of flow limitation, negative effort dependence may develop. In terms of negative effort dependence, once the effort required to produce \( V_{\text{max}} \) is achieved, further increases in effort may cause a paradoxical reduction in \( V_{\text{max}} \) (2). The mechanism may be related to a decrease in the longitudinal radius of curvature of the central airways downstream from the CP when effort is increased above that required to achieve flow limitation that in turn leads to a reduction in axial tension and a decrease in CP area and stiffness (2). Thus negative effort dependence may additionally contribute to a disproportionate decrease in \( V_{\text{max}} \) post-resection (see DISCUSSION).

Moreover, removal of lobes may lead to an alteration in the pressure-area behavior of the central airways by mechanisms that affect peribronchial pressure. In the lung, the visceral pleura is reflected from the parenchyma onto the lobar bronchi, and this reflection extends upward onto the central airways. It has been shown that a negative interstitial or peribronchial pressure develops between the parenchyma and the lobar bronchus, and this negative interstitial pressure is determined by the degree of parenchymal inflation (16, 17, 20, 21, 23). When lobes are removed, it is possible that peribronchial pressure (i.e., pressure between reflected pleura and central airways) may also change upward onto the central airways. It has been shown that a negative interstitial or peribronchial pressure develops between the parenchyma and the lobar bronchus, and this negative interstitial pressure is determined by the degree of parenchymal inflation (16, 17, 20, 21, 23). When lobes are removed, it is possible that peribronchial pressure (i.e., pressure between reflected pleura and central airways) may also become less negative during the forced expiratory maneuver compared with the intact lung. In turn, this effect would result in a reduction in the distending pressure of the central airways, so that \( A^* \) and \( V_{\text{max}} \) would decrease for a given Plat compared with presurgery.

In the present study, we examined the effect of acute lung resection on the maximal flow of the remaining lobes in open-chest dogs. We used an open-chest preparation so that interaction between lobes rather than chest wall-lung interaction would be the primary mechanism studied. We looked at varying degrees of lung resection in which experiments were performed after acute pneumonectomy and when a lobe of interest was deflated alone. In addition, because acute lung resection is performed for tumors in patients diagnosed with emphysema, we also looked at the effect of lung resection on lobar maximal flow in a canine model of unilateral emphysema (11). We investigated whether removal of healthy lung affected maximal emptying of the emphysematous lobe to a greater extent than when all the lobes were healthy. Finally, to examine whether a decrease in lobar emptying after pulmonary resection could be related to an increase in \( P_{\text{fr}} \) or a change in bronchial pressure area behavior, we measured intrabronchial pressures to determine which of the mechanisms could be involved. We were therefore able to estimate the extent to which removal of lobes may affect maximal emptying of the remaining lobes when pulmonary resections are performed in clinical medicine.

**METHODS**

**Animal preparation.** This study was approved by the Central Animal Care Committee at the University of Manitoba. This investigation conforms with the Guide for the Care and Use of Laboratory Animals published by the National Institutes of Health (NIH Publication No. 85-23, revised 1996).

During the experiment, the animals were anesthetized with pentobarbital sodium (30 mg/kg) and placed in the supine position. The chest was widely opened, and the trachea was cannulated with a large-steel tube that just entered the thoracic cavity. The animal was heparinized and phlebotomized, after which the heart was carefully removed. It has been previously shown that lung mechanics in this exsanguinated preparation are very stable over the ~4-h period necessary to conduct this experimental protocol (4, 12, 14). Moreover, the rationale for performing phlebotomy was as follows: In the living animal, lobar compliance is to some extent dependent on the pulmonary blood volume. In the present protocol (see Protocols), different lobes are acutely tied off in the various conditions, and changes in pulmonary blood volume would have to be considered in the interpretation of lobar compliance. In the exsanguinated animal, this would not be necessary. In addition, a living animal would not tolerate the acute resection of large amounts of parenchyma when the lobes were tied off in the different conditions.

During the experimental protocol, measurements were obtained with the animal placed into a pressure-corrected volume-displacement plethysmograph (15). Lung volumes (VT) were measured by a Krogh spirometer, and total expiratory flow was measured by a pneumotachograph (Fleisch no. 4) mounted between the plethysmograph box and spirometer. Pressure at the airway opening (Pao) was referenced relative to plethysmograph box pressure (Ppl). Transpulmonary pressure was calculated from Pao – Ppl, in which pressures were measured with a differential pressure transducer (MP-45; Validyne, Northridge, CA). The lungs could be inflated from a positive-pressure source with air or forcibly deflated (−100 to −200 mmHg) by a negative-pressure reservoir attached to the airway opening. The frequency response of this system has been found to be adequate in phase and amplitude, and its characteristics have previously been described (15).

The technique of Fredberg et al. (3) was used to measure alveolar pressure (Palv). A pressure capsule (13-mm surface diameter) with a 5-mm hole, continuous with a 5-mm threaded sleeve, was glued to the parenchymal surface of one or both of the lower lobes (see individual protocols, further below). The lung parenchyma visible through the hole in the capsule was punctured with a small needle. A miniature differential pressure transducer (8510B; Endevco, San Juan Capistrano, CA) was screwed into the threaded sleeve of the capsule. Palv was recorded on an oscillograph and displayed on an oscilloscope (Tektronix, Beaverton, OR) (4, 12).

In a subset of experiments (see below), a pressure sensor device termed a Pitot-static tube was used to measure lateral (Plat) and end-on (Pend) intrabronchial pressures (4, 10, 19). The Pitot-static tube measured 2.5 mm outer diameter and 2.5 cm in length and was built as described by Macklem and Mead (7). The lateral port was located ~1 cm from the tip of the Pitot-static tube. Plat and Pend were in turn referenced relative to Ppl. Two polyethylene tubes [Intramedic PE-205 (Parsippany, NJ); 1.5 mm ID, 65 cm long], with numbered markings to identify airway locations of interest, were attached to the respective ports of the Pitot-static tube, and the other ends were connected to individual pressure transducers (Validyne MP-45). The Pitot-static tube was advanced
both lungs were forcibly deflated (both-lung deflation); in RLL on four occasions emphysema was produced in the RLL. The details of this effect was examined in a subset of experiments in which removal of healthy lung on a remaining emphysema lobe, (DISCUSSION).

 Determinations, and lobar flows subtended by the Pitot-static tube was positioned at an airway site where Plat did not vary with negative pressure applied to the airway opening, but slightly downstream Plat decreased abruptly and varied with negative pressure applied to the airway opening. Bronchial cross section was estimated at 75, 50, and 30% lobar VC and was inferred from the intrabronchial pressure determinations, and lobar flows subtended by the Pitot-static tube at the respective Vl. (see Data analyses). Furthermore, after bronchial area was assessed at the CP site, the Pitot-static tube was pulled slightly upstream and bronchial area was calculated at this new upstream site. From the change in bronchial areas at the two sites and the corresponding change in lateral pressures, an estimation of K could be determined at the three Vl (10, 11) (see Data analyses; see DISCUSSION).

 Unilobar emphysema model. To determine the effect of removal of healthy lung on a remaining emphysema lobe, this effect was examined in a subset of experiments in which emphysema was produced in the RLL. The details of this canine lobar emphysema model have previously been described (11, 13). The enzyme papain was instilled into the RLL on four occasions -2 wk apart. For this procedure, the animals were anesthetized with pentobarbital sodium (30 mg/kg), after which the animal was placed in the supine position. A flexible bronchoscope was then passed into the trachea and advanced down the right lung until the bronchopulmonary segments of the RLL were visualized. Through a port in the bronchoscope, a solution containing -2.5 ml of the enzyme papain (type IV, Sigma Chemical, St. Louis, MO) mixed in 25 ml of normal saline was placed into a localized area of the RLL, such that after the fourth instillation the entire lobe would be injured. After each of the four instillations, the animal was ventilated for 6-7 h with its right side maintained in the dependent position and with its head slightly elevated. This maneuver prevented the papain mixture from spilling to the other lobes of the lung. When papain is given in this manner, it has been found that a rather diffuse unilobar emphysematous lesion is produced (12). The animals were returned to their cages when stable.

 Protocols. In experiment 1, measurements were obtained in six dogs in which emphysema was produced in the RLL (experiment 1A). In five other control dogs, the RLL was instilled with saline solution over a similar interval (experiment 1B). Alveolar capsules were placed on both lower lobes (3, 4, 8, 12). Measurements were obtained under three conditions. In condition 1, measurements were obtained while both lungs were forcibly deflated (both-lung deflation); in condition 2, either the entire right or left lung was deflated and tied off with cotton tape, and parameters of forced expiration were obtained from the untied lung alone (one-lung deflation); and in condition 3, measurements were obtained when either the RLL or left lower lobe (LLL) deflated alone; in the latter case, the airways to all lobes except the lobe of interest were transiently occluded with cotton tape (lower lobe deflation alone). The conditions were studied in random order in the two groups, so that the effect of time or of tying the lobes would not be a factor in the interpretation of the results.

 In experiment 2, because the major effect of acute lung resection was determined to occur between both-lung deflation and lobar deflation alone, this experiment was repeated in another group of animals with emphysema RLL (n = 5; experiment 2A) and with healthy lungs (n = 11; experiment 2B). In experiment 2, an alveolar capsule was placed only on the RLL, because two-lobes in experiment 1 showed findings similar to one another. In experiment 2, the order of the conditions was again randomized. Intrabronchial pressures were examined in all dogs in the emphysema group and 6 of the 11 dogs in the control group. In the intrabronchial experiments, a Pitot-static tube was advanced down the airway and was positioned just upstream from the CP site identified at the specific Vl when the RLL deflated alone (4, 10, 11). This location was usually located in central airways just downstream from the entrance to the RLL in both the healthy and emphysematous lobes. When the RLL was deflated alone, the CP location did not move between 75 to 30% lobar VC and remained at this same site.

 In experiments 1 and 2, the protocol for each condition was as follows. In the different conditions, the portions of the lung to be studied were twice inflated to total lung capacity (transpulmonary pressure -30 cmH2O) to standardize for volume history. After the third inflation, the airway was opened to a negative pressure reservoir to produce forced deflation. Total Vmax, Vl, and Palv were recorded at 200 mm/s on the oscillograph, and flow and Palv could also be plotted as a function of volume on the oscilloscope. Palv was differentiated with respect to time to obtain dPalv/dt (4, 8, 12).

 For each of the groups, the emptying rates (i.e., dPalv/dt) of the right, left, or both lower lobes (where appropriate) were examined at the same inflations during the conditions (i.e., 30, 50, and 75% of the respective lower lobe VC). From the emptying rates and the volume pressure (dV/dPalv) assessed at the respective Palv, lobar flows could be ascertained (4, 12) (see Data analyses).

 Data analyses. In both experiments 1 and 2, as previously indicated, Palv were differentiated with respect to time (dPalv/dt) at the specific alveolar volumes analyzed in the individual experiments (4, 8, 12). In experiment 2, multiplying dPalv/dt by the slope of the static volume-pressure curve (dV/dPalv) measured at the same absolute volume or Palv also allowed computation of lobar maximal flow = (dPalv/ dt x dV/dPalv) - dV/dt (4, 8, 12). The agreement between measured and calculated values has been good in previous studies (4, 12).

 In those experiments in which intrabronchial pressures were obtained, pressure losses due to convective acceleration (Pca) were calculated as the difference between Pend and Plat measured from the Pitot-static tube ports (4, 10, 11, 19). Pca was calculated from the Bernoulli equation (Pca = ½ ρV2A-2) where ρ is gas density (1.10 g/l) and V is the flow subtended by the Pitot-static tube. These parameters were used to estimate area at the Pitot-static site. Compliance at this airway site was calculated from ΔA/ΔPlat where ΔA was the difference in area between CP site and an airway site ~1 cm upstream and ΔPlat was the difference in Plat at these sites (10, 11). This upstream site was still located in the same generation airway as where the CP was identified (see DISCUSSION). Pfr from alveoli to the site of the Pitot-static tube were calculated from Pfr = (Palv - Pend). Frictional resistance was calculated from Pfr/Vl, where Vl was the flow subtended by the Pitot-static tube (4, 10, 12).
Statistical analyses. In the individual groups, one-way analysis of variance for repeated measures (within ANOVA) or two-way ANOVA for two repeated measures (within ANOVA) was used to assess differences between parameters when repeated measurements were obtained. Between different groups, a two-way ANOVA (between-within ANOVA) was used to assess differences in lower lobe emptying patterns. When multiple comparisons were obtained, the Student-Newman-Keuls multiple-range test was used to determine where significant differences occurred in the analysis. Results are reported as means ± SE.

RESULTS

In experiments 1A and 1B, the emptying rates of the lower lobes were examined at identical Palv in the three conditions. At 30, 50, and 75% lobar VC, the Palv measured for each lobe are shown in Table 1. At the respective Vt, the Palv for the emphysematous RLL in experiment 1A were lower than those of the other lobes. In experiment 1A, the lobar VC for the emphysematous RLL was slightly higher than that found for the contralateral LLL, but the results did not reach statistical significance between groups (0.83 ± 0.13 liter for the RLL and 0.76 ± 0.18 liter for the LLL). In experiment 1B, lobar volumes were very similar to one another and measured 0.60 ± 0.25 and 0.63 ± 0.24 liter, respectively.

The results obtained in dPalv/dt in experiments 1A and 1B are shown in Figs. 1 and 2, respectively. When either the RLL or LLL deflated alone, dPalv/dt measured at 75% VC was lower than when both lungs were deflated, whereas this effect was less apparent at 50 and 30% VC. When one lung was deflated, dPalv/dt measured at 75% VC was again generally higher compared with when the lower lobe was deflated alone.

During whole right lung deflation, dPalv/dt measured at 75% VC for the RLL was higher than that found during both-lung deflation, and this difference reached statistical significance in experiment 1B. On the other hand, during left lung deflation, dPalv/dt measured at 75% VC for the LLL was lower than that found during both-lung deflation, and this reached statistical significance in experiment 1A (see DISCUSSION). In the condition in which the lower lobe was deflated alone, the emphysematous RLL in experiment 1A deflated more slowly than its contralateral LLL or the normal RLL in experiment 1B.

In experiments 2A and 2B, the Palv examined are shown in Table 2. The findings in dPalv/dt were similar to those in experiment 1 and showed that emptying rates for the RLL were much higher during both-lung deflation compared with lobar deflation alone (see Fig. 3). In experiment 2, maximal lobar flows were also calculated (see Fig. 4). During both-lung deflation, maximal flows for the RLL during both-lung inflation increased approximately four times in experiment 2A and two to three times in experiment 2B group compared with lobar deflation alone. These results were not significantly different between groups 2A and 2B.

The intrabronchial measurements obtained with the Pitot-static tube located at the identical airway site during both-lung deflation and lobar deflation alone are shown in Table 3. In experiment 2B, although Plat...
were similar between conditions, bronchial cross section measured at 75 and 50% VC was higher during both-lung deflation (see Fig. 5). In experiment 2A, similar results were observed, although statistical significance was not achieved in this group.

In both experiments 2A and 2B, bronchial compliance was examined at the same airway site during lobar deflation alone and both-lung deflation. In the present analysis, K was calculated to give an estimation of airway compliance. The results showed that during one-lobe deflation, airway compliance decreased compared with both-lung deflation, and this finding reached statistical significance in the emphysema group (experiment 2A) (see Table 3). In experiment 2A, K calculated at all VL during both-lung deflation were significantly higher than those obtained in experiment 2B.

In Table 3, there were no changes in Pfr or Res between both-lung deflation and lobar deflation alone in experiments 2A and 2B. In both experiments, Pfr and Res were generally higher at low VL compared with the respective high VL.

**DISCUSSION**

The present study shows that there is interdependence of flow between lobes, such that the presence of
adjacent lobes improved the emptying of the lower lobe during forced deflation. When the lower lobe was deflated alone, its rate of deflation was lower than when deflated in the presence of adjacent lobes. This effect was most apparent at high VL. A number of possible mechanisms were considered for this finding. One mechanism invoked was that there was a relative increase in Pfr during one-lobe deflation and that this resulted from torsion of the bronchus along its long axis that occurred to a greater extent when the lobe deflated alone.

In terms of wave-speed theory, the effect of an increase in Pfr would be to reduce the total pressure head along the airway (i.e., Pend) (1, 2). This, in turn, would cause a relative reduction in Plat, such that bronchial cross section would be lower during one-lobe deflation compared with both-lung deflation. However, with the Pitot-static tube located at the identical airway site, the results showed (see Table 3) that Plat, Pend, and Pfr were not different between conditions to substantiate that such a mechanism was involved.

Another mechanism could be related to the effect of negative effort dependence. Elliott and Dawson (2) state that, according to the LaPlace relation, the transmural pressure across an elastic membrane is dependent on longitudinal as well as radial tension. For an elastic tube, this means that the product of longitudinal curvature will contribute an additional term to the tube stiffness that depends on the area-distance characteristics of the tube. When the longitudinal curvature of an airway is large (i.e., large radius of curvature), the resultant area and stiffness will be increased compared with when the radius of curvature is small. These concepts would pertain whether or not a particular airway is the site of the CP.

During one-lobe deflation alone, a more negative pressure would be found in the central and lobar airways compared with both-lung deflation, because the CP would move upstream from the trachea (see further below) to the lobar bronchus during one-lobe deflation. In terms of Elliott and Dawson (2), such an effect may lead to a decrease in the longitudinal radius of curvature of the airways downstream from the RLL bronchus that would in turn decrease the axial tension of the RLL bronchus compared with both-lung deflation. Although reservoir pressure was adjusted during each condition to obtain the value just required to achieve $V_{\text{max}}$, central airways during one-lobe deflation were most likely exposed to a more negative pressure than that required at the onset of flow limitation. This could result in negative effort dependence, in which $V_{\text{max}}$ becomes reduced when effort is increased over that required to just achieve maximal flow. However, if negative effort dependence played a role in the present study, RLL airway stiffness would have decreased rather than increased compared with both-lung deflation (see Table 3). Thus, from these results, negative effort dependence does not appear to be the mechanism involved.

Changes in axial tension related to parenchymal inflation also need to be considered as an explanation for the different findings observed between conditions. Hughes et al. (5) reported that, in intact bronchi of dog lungs, lobar length decreased ~30% as transpulmonary pressure decreased from 30 to 0 cmH$_2$O. The removal of lobes may have reduced the axial tension of the central airways, because inflation of lobes whose bronchi are ordinarily attached to the central airways would not be found. Again, however, such a change during lobar deflation alone would be expected to decrease airway compliance rather than to increase it as was observed in the present study (2).

Another explanation for the present results is that there was a change in bronchial pressure-area behavior between one-lobe and both-lung deflation and that this change reflected a difference in peribronchial interstitial pressure between conditions. From the results obtained in Fig. 5 and Table 3, when the lower lobe deflated alone, bronchial cross section was lower...
Table 3. Intrabronchial pressure measurements in experiment 2

<table>
<thead>
<tr>
<th></th>
<th>75% VC</th>
<th>50% VC</th>
<th>30% VC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LA</td>
<td>BL</td>
<td>LA</td>
</tr>
<tr>
<td>Plat, cmH2O</td>
<td>3.9 ± 0.8†§‡</td>
<td>3.2 ± 0.2†‡</td>
<td>1.3 ± 0.2†</td>
</tr>
<tr>
<td>Pend, cmH2O</td>
<td>4.9 ± 0.8†‡</td>
<td>4.5 ± 0.2†‡</td>
<td>1.9 ± 0.5†</td>
</tr>
<tr>
<td>Pfr, cmH2O</td>
<td>0.2 ± 0.3</td>
<td>0.8 ± 0.5</td>
<td>0.7 ± 0.6</td>
</tr>
<tr>
<td>Res, cmH2O·L⁻¹·s</td>
<td>0.17 ± 0.2†</td>
<td>0.45 ± 0.6</td>
<td>1.24 ± 0.9</td>
</tr>
<tr>
<td>K, cm²/cmH2O</td>
<td>0.12 ± 0.16</td>
<td>1.2 ± 0.5§§</td>
<td>0.12 ± 0.08</td>
</tr>
</tbody>
</table>

Values are means ± SE. Plat and Pend, are lateral and end-on pressure losses, respectively; Pfr, frictional pressure losses; Res, frictional resistance; K, airway compliance; LA and BL, lobar deflation alone and both lungs, respectively; VC, a fraction of right lower lobe capacity. ANOVA and SNK *P < 0.05 vs. 50% VC; †P < 0.05 vs. 30% VC. By 2-way ANOVA and SNK, ‡P < 0.05 both lung vs. lobar deflation alone; §P < 0.05 experiment 2A vs. 2B.

Fig. 5. Bronchial area is plotted on the ordinate against percent lobar VC on the abscissa for the emphysema (experiment 2A; n = 5; A) and control experiments (experiment 2B; n = 6; B). Results were obtained during both-lung deflation and LA. Statistical analyses included 1- and 2-way ANOVA and SNK.

than that found during both-lung deflation (see Fig. 5), even though Plat were similar between conditions (see Table 3). It is important to recognize that the bronchial pressure-area relationship is curvilinear, such that it is relatively noncompliant at the extremes of high and low lateral pressures, whereas it is fairly compliant between these pressures (5, 10). As shown in Table 3, for similar Plat were measured at different portions of the bronchial pressure-area curve during one-lobe and both-lung deflation. In turn, this could occur despite unchanged Plat between conditions, if peribronchial and therefore transmural pressures differed between conditions.

Peribronchial pressure is determined by the interaction between the bronchus and the parenchyma and termed parenchymal-bronchial interdependence. Sasaki et al. (20) reported previously that lobar bronchi were much less collapsible in situ than when dissected free because of radial traction of peribronchial tissues. In a subsequent experiment, they examined the influence of lung parenchyma on dynamic bronchial collapsibility of excised dog lungs (21). They concluded that the presence of lung parenchymal attachments significantly reduced dynamic bronchial collapsibility compared with static collapsibility. The magnitude of peribronchial pressure has been investigated in various studies and has been found to approximate lung recoil pressure. Nakamura et al. (16, 17) deduced that in intact lobes, peak peribronchial parenchymal stress averaged ~29 cmH2O at total lung capacity. Because bronchial transmural pressure of intraparenchymal airways is determined by peribronchial interstitial pressure, the loss of parenchymal attachments would have a significant effect on bronchial cross section during forced deflation.

In the literature, bronchial-parenchymal interdependence is usually considered a factor contributing to
dynamic collapse in lobes and lobar segments (21, 23). Yet the present study would argue that it may also play a role in influencing collapse of the central airways as well, at least those airways situated close to the lobar airways. In the lung, the visceral pleura is reflected from the parenchyma onto the lobar bronchi, and this reflection extends upward onto the central airways. The peribronchial interstitium of the central airways (i.e., potential space between reflected pleura and bronchus) is contiguous among the lobes, and therefore removal of lobes may affect the peribronchial interstitial pressure of the central airways that are in close proximity to the lobar airways. In the intact lung, inflation may cause a radial traction at the bronchial junctions and therefore help keep the remaining airway open. When some lobes are removed, peribronchial pressure may exert less negative radial traction during the forced expiratory maneuver compared with the intact lung. In the present study, the major effect of pulmonary resection was observed at 75% lobar VC, whereas changes were less marked at 50 and 30% lobar VC. This finding is consistent with the results of others who observed that the effect of lobar parenchymal-bronchial interdependence on preventing bronchial collapsibility were greater at high vs. low transpulmonary pressures (21, 23). Accordingly, the present study shows that removal of lobes may affect the emptying of the remaining lobes and that parenchymal-bronchial interdependence may be relevant to the understanding of collapsibility in the central as well as lobar airways.

In terms of the protocol, it should be recognized that the Pitot-static tube was placed at the CP site during one-lobe deflation and remained at this site during both-lung deflation although it was not the CP site during both-lung deflation. On the basis of previous experiments, the CP site found during both-lung deflation would be identified at the carina, where CP area would average 2.5 cm$^2$ and K would average 0.15 cm$^2$/cmH$_2$O (4, 10, 11, 15). Furthermore, it should be noted that the measurement of $K$ is only an estimate. $K$ was determined from $\Delta A/\Delta P_{\text{Plat}}$ in which measurements were obtained at the RLL bronchus and ~1 cm upstream (see Data analyses). This approach assumes that the tube law (i.e., bronchial area vs. transmural pressure curve) of the airway is constant at the two sites. However, in the experiment, both sites were located in the same airway generation (this fact was checked at the end of the experiment), so this assumption remains a reasonable possibility. Nevertheless, it is necessary to note that this is a limitation of this measurement technique.

Furthermore, the present results are somewhat different than those previously described by Solway et al. (22) and Mink et al. (14), who reported results of flow limitation in a transistor model and in canine models of regional lung disease, respectively. Both groups of investigators supported the concept of interdependence of flow between regions as outlined by Wilson et al. (24). The principles of this theory are that in nonhomogeneous lung disease, in which regions of the lung share a common downstream CP, when flow is reduced from one region, the other region will compensate for this reduction in flow (22, 24). In this case, the other region will increase its contribution to total flow to maintain a central CP. In terms of the present study, the predictions would be that, when lobes were removed during lobar deflation alone, the lower lobe would increase its rate of emptying until a new CP was formed at the carina or a more upstream site. However, in contrast to what was predicted, a reduction in lower lobe emptying was found in the present study.

On closer inspection, however, the findings predicted by Solway et al. (22) can be observed in the present study. In experiment 1A (Fig. 2), when the left lung was removed, right lower $dP_{\text{Palv}}/dt$ measured at 75% VC were higher compared with both-lung deflation, and in experiment 1A similar results were observed, although statistical significance was not found. Accordingly, when the left lung was removed, the RLL increased its rate of deflation compared with both-lung deflation, until a CP was reached at the carina or more upstream site. On the other hand, when the right lung was removed, an increase in LLL $dP_{\text{Palv}}/dt$ was not apparent, and, in fact, a decrease in LLL $dP_{\text{Palv}}/dt$ was observed in experiment 1A.

The above inconsistencies suggest that multiple factors are involved when interdependence of flow between regions is considered. In this regard, Mink et al. (14) found that when an obstructed LLL and normal left upper lobe (LUL) emptied into a common downstream central CP in a canine model, the removal of the LUL resulted in an increase in LLL $dP_{\text{Palv}}/dt$ compared with two-lobe deflation, and these results followed the predictions of Wilson et al. (24). However, in a model in which an obstructed LLL and LUL did not share a common downstream CP, the removal of the LUL was associated with a reduction in LLL $dP_{\text{Palv}}/dt$ compared with two-lobe deflation, and these results are similar to those reported in the present study. Thus it appears that at least two factors may be involved when lobar interdependence of flow is considered, and these factors work in opposite directions. When bronchial pressure-area behavior is unchanged between conditions, removal of lobes in which a common CP is shared results in an increase in $dP_{\text{Palv}}/dt$ of the remaining lobes; however, if bronchial pressure area behavior is changed between conditions, then $dP_{\text{Palv}}/dt$ may decrease when lobes are removed. The latter finding was the predominant one observed in the present study. The extent to which each one would predominate in a given situation is not yet clear.

In summary, this study shows that when the lower deflated alone, a significant decrease in $dP_{\text{Palv}}/dt$ occurred compared with two-lung and one-lung deflation. This effect was due to interdependence of flow between lobes, such that the presence of adjacent lobes maintained bronchial cross section to a greater extent than when the lobe deflated alone. Possible mechanisms considered were differences in axial tension between conditions, negative effort interdependence, or the possibility that parenchymal-bronchial interdependence may be relevant to understanding the dynamic collaps-
ibility of central as well as intraparenchymal airways. It must be recognized, moreover, that the present study was performed in the open-chest preparation. Whether interdependence of flow between lobes would be applicable to a similar extent in the closed chest preparation is not clear, although the results and mechanisms discussed should be operative in both situations. Whereas the applicability of animal models to the human condition must be viewed cautiously, the present findings have implications with respect to the mechanics discussed should be operative in both situations.

This research was supported by the Dr. Paul H. T. Thorlakson Foundation Fund and The CHEST Foundation

REFERENCES