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Stability of intrapulmonary bronchial dimensions during expiratory flow in excised lungs

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HUGHES, J. M. B., HAZEL A. JONES, A. G. WILSON, B. J. B. GRANT, AND N. B. PRIDE. *Stability of intrapulmonary bronchial dimensions during expiratory flow in excised lungs.* J. Appl. Physiol. 37(5): 684–694. 1974.—The length and diameter of intrapulmonary airways (4.8–9.0 mm ID) were measured from tantalum bronchograms in lobes of excised dog lungs. Twenty retrograde catheters were inserted into the lobe around the perimeter and airflow passed from the periphery to the lobar cannula. During expiratory flow the lateral intrabronchial pressure (Pib) in the larger airways was lowered relative to alveolar pressure (PAlv) keeping lung volume constant. Airway dimensions were compared *1*) under no-flow (*static*) conditions when Pib = PAlv and *2*) during expiratory flow (*dynamic*) with Pib < PAlv. When PAlv was held constant at +5 or +10 cmH_2O the change of bronchial diameter per unit change of Pib was significantly less than under static conditions, suggesting that the parenchyma confers a stiffness upon intrapulmonary airways during expiratory flow by virtue of tissue attachments. Interdependence of airway and airspace expansion was less at low lung recoil pressures. At isovolume we estimated that peribronchial pressures decreased relative to pleural pressure by up to 10 cmH_2O. There was no reduction in length as Pib was lowered at constant lung volume.

mechanical interdependence; peribronchial pressure; interstitial pressure; bronchial compliance; airway resistance; flow-volume curves; equal pressure point; forced expiration

IT IS KNOWN that the larger extrapulmonary airways such as the trachea and main bronchi narrow during expiratory flow (11), but the situation for intrapulmonary airways in normal lungs is far from certain. Because of pressure losses upstream from frictional resistance and convective acceleration, intrabronchial pressure relative to pleural pressure will be less at a given lung volume during expiratory flow than in static conditions. Nevertheless, the tendency for intrapulmonary airways to narrow may be offset by tissue forces that operate on the airway wall to minimize changes of bronchial size for a given lung volume. Early studies of Marshall (16) on airways and of Permutt et al. (25) on pulmonary blood vessels suggested that lung volume affected the relationship between vessel diameter and the pressure difference between the lumen and the pleural surface. In other words, there could be substantial changes of perivascular or peribronchial pressure in the absence of changes of pleural pressure. The notion that intrapulmonary airway narrowing at constant lung volume would lead to an increased distending force (from tissue attachments) per unit area of bronchial wall was postulated by Mead et al. (18) in a theoretical study of the interdependence of expansion of structures within the lung.

In this study we have used an experimental model in which intrabronchial pressure could be systematically lowered relative to alveolar pressure at constant lung volume and the relationship between airway diameter (as judged from radiographs) and the intrabronchial-pleural pressure difference explored. The experimental preparation is by no means original. Robert Hooke (5) in 1667 by "pricking all the outer coat of the lungs with the slender point of a very sharp pen-knife" was able to maintain life in a dog at constant lung volume by passing air through the lungs with two pairs of bellows in series. Three hundred years later, for different reasons, Macklem and Mead (13) devised the retrograde catheter technic in which small polythene catheters pass out through the surface of the lung. The use of multiple retrograde catheters was first reported by Culver et al. (3); this preparation, except for minor details, is similar (2).

THEORY

Figure 1 is a schematic diagram of an airway cut in longitudinal section surrounded by lung parenchyma. At equilibrium

$$Pel(br) = Pib - Pexb$$

where Pel(br) is the recoil pressure of the elastic and smooth muscle elements in the bronchial wall, Pib is the lateral pressure in the airway lumen, and Pexb is the extrabronchial pressure, equivalent to the sum of the forces per unit area in the peribronchial space; (Pib − Pexb) is, by definition, the transmural pressure (Ptm) across the bronchial wall.

A similar relationship exists for the lung parenchyma

$$Pel(l) = PAlv - Ppl$$

where Pel(l) is the average recoil pressure of all alveolar walls and surfaces and PAlv and Ppl are the alveolar and pleural pressures, respectively; (PAlv − Ppl) is the transpulmonary pressure (Ptp) under static conditions. The relationship between Pel(br) and bronchial diameter depends upon the elastic properties of the airway wall, just

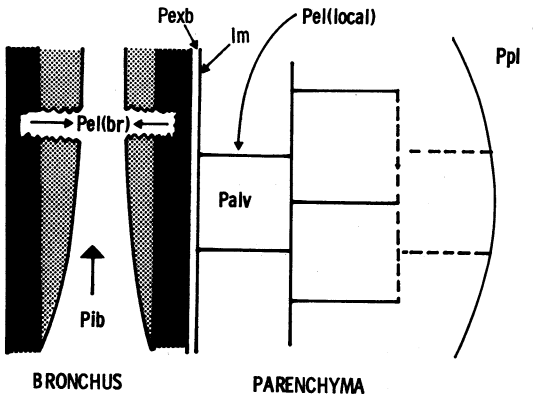

FIG. 1. Schematic representation of bronchial lumen, bronchial wall, peribronchial space, limiting membrane (lm), and surrounding alveolar tissue. Intrabronchial (Pib), extrabronchial (Pexb), alveolar (PAlv), and pleural (Ppl) pressures are indicated as well as elastic recoil pressure of bronchus [Pel(br)] and alveoli locally [Pel(local)]. Bronchial narrowing during expiratory flow (indicated by arrow) is illustrated by lighter shading of bronchial wall. See text for details.

as that between Pel(l) and lung volume depends on the properties of alveolar tissues and surfaces.

Intrapulmonary airways, via bronchioles and alveolar ducts, form a continuous elastic network with the parenchyma. Thus there will be a relationship (in the same sense, but not necessarily one-for-one) between the pressure distending the alveoli (PAlv − Ppl) and that distending the airways (Pib − Pexb). During expiratory flow the pressure losses that occur in the airways from convective acceleration and viscous resistance reduce Pib relative to PAlv. If there is interdependence between airway and airspace expansion, any reduction in bronchial diameter resulting from the fall in Pib will be opposed by surrounding tissue forces acting on the peribronchial space (18). These will tend to decrease Pexb in relation to Ppl thereby increasing (Pib − Pexb) relative to (Pib − Ppl). Therefore the change of bronchial diameter, which will reflect changes in (Pib − Pexb) [and its equivalent Pel(br)], may be less than that predicted solely from the reduction of Pib. During expiratory flow PAlv is greater than Pib, and Pel(l) tends to exceed Pel(br), so that

$$P_{Alv} - Pib = K[Pel(l) - Pel(br)]$$

where K is a factor, related to interdependence, that allows for changes of Pexb in relation to Ppl. Comparing static conditions with expiratory flow

$$\triangle(P_{Alv} - Pib) = K \cdot \triangle[Pel(1) - Pel(br)]$$

For comparisons at the same bronchial diameter Pel(br) will be constant and

$$K = \triangle(P_{Alv} - Pib)/\triangle Pel(l) \qquad (1)$$

If airway size is completely independent of airspace expansion, a change of Pib during expiratory flow will be accompanied by the same change in Pel(br) and K will be unity. In practice, as airways narrow at constant lung volume, the forces in the peribronchial space will operate on a smaller cross-sectional area (18); in addition the length and tension of the local alveolar walls may increase as the surrounding lung distorts to fill the space vacated by the airway wall. As a result Pexb will decrease relative to Ppl. The greater the dependence of airway expansion on lung expansion the larger the value for K. The advantage of *Eq. 1* is that an assessment of interdependence can be made without any assumptions about the absolute value of extrabronchial pressure. A similar expression for interdependence (between adjacent lung lobules) was used by Menkes et al. (21). On the other hand, their experimental design and the structures under study were quite different from ours, and the values for K cannot be compared directly. It is important to emphasize that any change in the elastic properties of the airway wall—produced by a marked change of shape or alteration in smooth muscle tone, for example—may alter the relationship between bronchial diameter and (Pib − Pexb).

METHODS

Greyhound dogs were anesthetized with thiopentone sodium (50 mg/kg), given heparin (20,000 IU) intravenously, and exsanguinated. The lungs were excised immediately and the right or left middle lobe dissected free from its neighbors. The bronchial anatomy of these lobes resembles a conifer tree. In the collapsed lobe a plastic introducer (35 cm in length, 3.1 mm OD) was put into the main stem and its tip manipulated in turn into most (about 20) of the main side branches and pushed peripherally; a steel wire with a polyethylene catheter (PE 200) attached was introduced and pushed out through the surface of the lung, as described by Macklem and Mead (13), until its bell-shaped tip (3 mm OD) wedged in a peripheral bronchus. The catheters were gathered together and connected to a source of warmed and humidified air for retrograde inflation of the lobe (Fig. 2). Dry compressed air passed over a water bath heated to 75°C and subsequently cooled in copper tubing surrounded by water at room temperature. The air entering the lung was fully saturated at about 30°C. Preliminary experiments had emphasized the importance of adequate humidification when large volumes of gas are passed through excised lungs.

A tapering polypropylene cannula was passed down the main stem bronchus until its tip (5.0 or 7.0 mm OD) was positioned in a part of the airway surrounded by lung parenchyma on all sides. The central airways beyond the cannula were outlined with tantalum dust under fluoroscopic control. With the lobar cannula closed the lobe could be inflated or deflated (via surface leaks) retro-

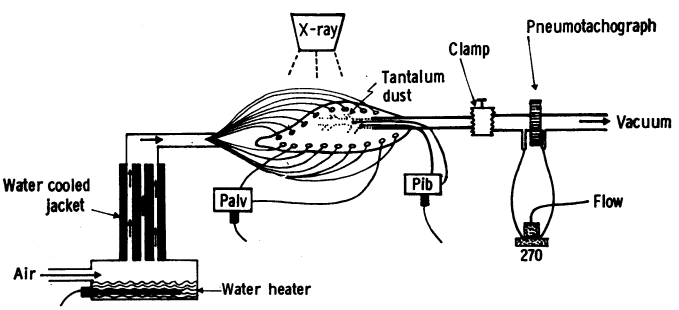

FIG. 2. Diagram of excised lung with multiple retrograde catheters. PAlv and Pib are pressure transducers for measuring alveolar and intrabronchial pressures. [From Butler et al. (2).]

gradely to airway and alveolar pressures between 30 and 0 cmH_2O, while pleural pressure remained atmospheric. Alveolar pressure was measured from two of the retrograde catheters that were separated from the rest and connected to a pressure transducer (Sanborn 268B). Intrabronchial pressure was measured from two catheters (0.86 mm ID, 1.27 mm OD) passed down the lobar cannula and connected to a similar pressure transducer. The ends of these catheters were occluded with a metal plug (1.3 mm diam); lateral pressure was measured from four side holes (0.55 mm diam) opposite to each other and adjacent to the plug. A bias flow kept them patent in between measurements. Alveolar and intrabronchial pressures were measured relative to pleural pressure (atmospheric); they were identical when the lobe was inflated with the cannula closed (static conditions). At any positive alveolar pressure the lobar cannula could be gradually opened so that expiratory flow occurred (dynamic conditions). Flow was monitored with a Fleisch No. 2 pneumotachograph connected differentially to a Sanborn 270 pressure transducer. All pressures and flows were displayed on a Sanborn recorder (model 7700).

Under dynamic conditions we aimed to maintain a constant lung volume by increasing inflow through the retrograde catheters to match expiratory flow. In practice inflow was adjusted to a constant alveolar pressure. Because the airway resistance peripheral to 2–3 mm bronchi is so low in dog lungs at high lung volumes (14), alveolar pressure measured from the retrograde catheters reflects true alveolar pressure very closely even during maximal expiratory flow. Another index of lung volume was the length of the peripheral airways (6). With the lobar cannula fully open, the lobe emptied by virtue of its recoil pressure, and the intraluminal pressure in the main stem bronchi approached atmospheric pressure. By applying negative pressure to the lobar cannula with a vacuum pump, expiratory flow increased further, and intrabronchial pressure could be lowered to subatmospheric values. Once maximal flow was reached, the lateral pressure in airways downstream from the flow-limiting segment was entirely dependent on the setting of the vacuum pump. Radiographs were exposed at known values of PAlv and Pib using nonscreen film (Kodak, Crystallex), a fine focal spot (0.28 × 0.40 mm), and settings kVp 47 and mAs 32. A double-image stereoscopic technic was used [(7), Method A] with a tube separation of 30 cm and anode-film distance of 120 cm. On three occasions true stereoscopic pairs of X-rays were exposed and bronchial cross-section (i.e., shape) analyzed on a stereocomparator in the Department of Photogrammetry at University College, London.

Experimental Procedure and Analysis

With the catheters in position the lobe was inflated to PAlv and Pib +30 cmH_2O with the cannula closed and the pressure readings on the two alveolar and two central bronchial catheters checked for correspondence. The lobar cannula was opened, expiratory flow started, and PAlv and Pib fell (Fig. 3). PAlv was maintained at +10 or +5 cmH_2O by increasing retrograde catheter flow, while Pib was lowered to negative values with the vacuum pump. Under fluoroscopic control the position of the intrabronchial catheters and vacuum setting were adjusted until

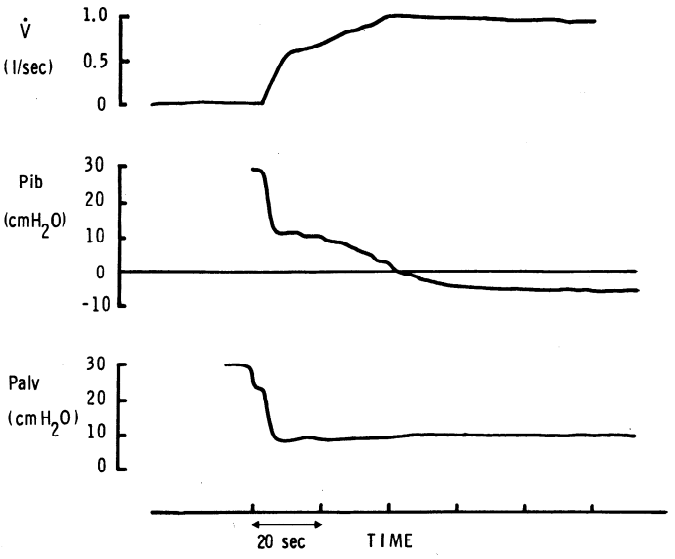

FIG. 3. Tracing from recording of lobar flow (V̇), intrabronchial (Pib) and alveolar (PAlv) pressures during a dynamic maneuver. Lobar cannula is released, flow commences, and PAlv is allowed to fall to +10 cm H_2O and then held constant. Pib is lowered to subatmospheric pressures by vacuum pump. Note the occurrence of flow limitation-reduction of Pib without increase of V̇.

values of Pib for each catheter of down to −15 cmH_2O were found that corresponded with good measuring positions on the bronchogram. Because of the low intrapulmonary resistance in dog lobes at PAlv 10 and 5 cmH_2O, negative intrabronchial pressures were found only within 1–2 cm of the cannula tip. When suitable catheter positions had been found, pairs of static and dynamic measurements were made at PAlv +10 or +5 cmH_2O. All maneuvers started from PAlv +30 cmH_2O; radiographs were exposed 1–4 min after the required PAlv had been reached, but time history was not rigidly controlled. X-rays were also taken under static conditions at PAlv and Pib +30 and 0 cmH_2O and in the collapsed lung with Pib −5 to −15 cmH_2O (suction applied but no flow).

On the radiographs the position of the side holes of the bronchial catheters was visible, and measurements of diameter were made at these points. Airway diameters at pheripheral points in the bronchial tree were also measured, as well as central and peripheral airway lengths. All dimensions were expressed as a percentage of the length or diameter at full inflation of the lung, i.e., PAlv and Pib (static) +30 cmH_2O. Lengths and diameters at Pib +30 cmH_2O were checked two or three times during the course of the experiment; if the measurements differed by more than 2%, the largest value was taken as true maximum diameter. Dimensions at Pib +10, +5, and 0 cmH_2O under static conditions usually represent the mean of two or three measurements. Histologic sections of the lobes, stained with hematoxylin and eosin, were prepared.

RESULTS

Satisfactory results from a technical viewpoint were obtained in eight preparations. Body weight ranged from 20.5 to 27 kg (mean 24) and weight of the middle lobe from 20 to 37 g (mean 27). Two lobes showed some cystic spaces

in the lung parenchyma on macroscopic examination, but their results did not differ from the others. In most cases there was some widening of the perivascular spaces on the histologic sections, but the bronchial and peribronchial tissue looked normal; there was no alveolar edema.

Distribution of Dynamic Pressures

In Fig. 4 the lateral pressure distribution in one preparation at PAlv 10 cmH_2O during expiratory flow (vacuum assisted) is plotted. To demonstrate this, a single bronchial catheter was pulled back toward the bronchial cannula in successive steps under X-ray control; this was not the normal procedure, which was to keep two bronchial catheters in fixed positions throughout the experiment. Most of the convective and frictional pressure loss is concentrated in the 1 cm immediately distal to the bronchial cannula with the pressure gradient becoming progressively steeper near the exit from the lobe. Lobar flows in these experiments ranged from 0.3 to 1.8 $l \cdot sec^{-1}$ (mean 0.58).

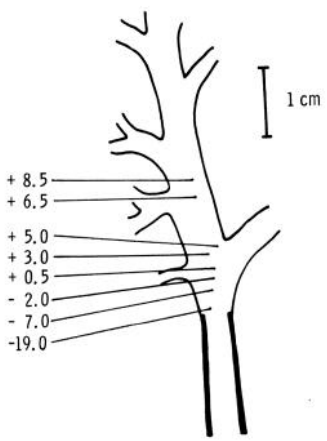

FIG. 4. Tracing from tantalum dust bronchogram with cannula and central airways to show lateral pressure profile under dynamic conditions. All pressures in cm H_2O. Alveolar pressure +10 cmH_2O.

Bronchial Diameter

Figure 5 shows bronchograms obtained under static and dynamic conditions. Had the expansion of airways and airspaces been completely interdependent the caliber of the proximal airway would have followed lung volume, and the diameter in *B* would have been the same as *A* since the alveolar pressure was identical (10 cmH_2O). But if bronchial expansion was independent of airspace expansion, airway diameter in *C* would be similar to that in *B* because the radiographs were exposed at the same intrabronchial pressure. Figure 5 shows that the central intraparenchymal airways narrow to a certain extent in *B* but much less than in the absence of pulmonary parenchymal support in *C*.

In Fig. 6 airway diameter under static conditions at an alveolar pressure of +10 cmH_2O is related to the diameter under dynamic conditions as intrabronchial pressure is lowered during expiratory flow. Results from eight experiments are shown. Static points usually represent the mean value of two measurements, but the dynamic points are single values. The diameters of the central airways (mean diameter at full inflation 6.4 mm) have been compared with measurements in 33 peripheral airways (mean diameter 4.05 mm). The peripheral bronchi show some decrease in diameter in the dynamic maneuver although there was no appreciable change of intrabronchial pressure. This difference can probably be explained on the basis of stress recovery, because there was a longer time history in the dynamic compared with the static measurement between reaching an alveolar pressure of 10 cmH_2O and exposing the radiograph. This time interval was 50 s for static measurements but 240 s for the dynamic, and on the basis

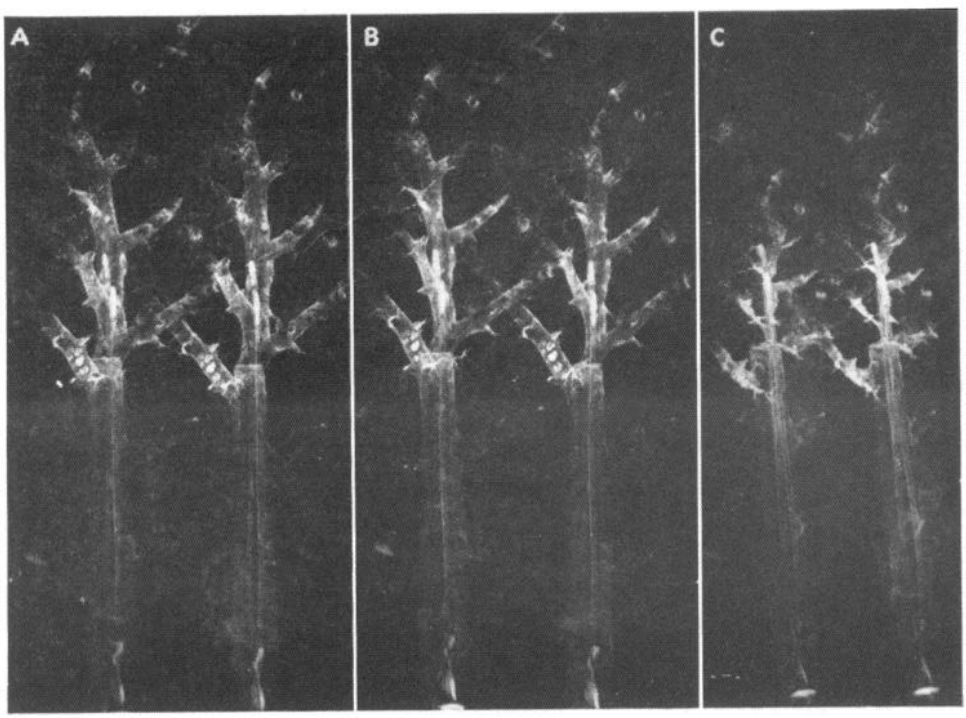

FIG. 5. Tantalum dust bronchogram of excised middle lobe. Note proximal and distal intrabronchial catheters just beyond lobar cannula and, peripherally, the retrograde catheters. *A:* static, PAlv and Pib +10 cmH_2O; *B:* dynamic, PAlv +10 cmH_2O, Pib (distal) −0·5 cmH_2O, Pib (proximal) −10 cmH_2O; *C:* static, PAlv 0 cmH_2O, Pib (distal) −7 cmH_2O, Pib (proximal) −9 cmH_2O. Note some narrowing of bronchus near cannula in *B* compared with *A* at constant PAlv, and also narrowing in *C* compared with *B* at almost constant Pib (proximal).

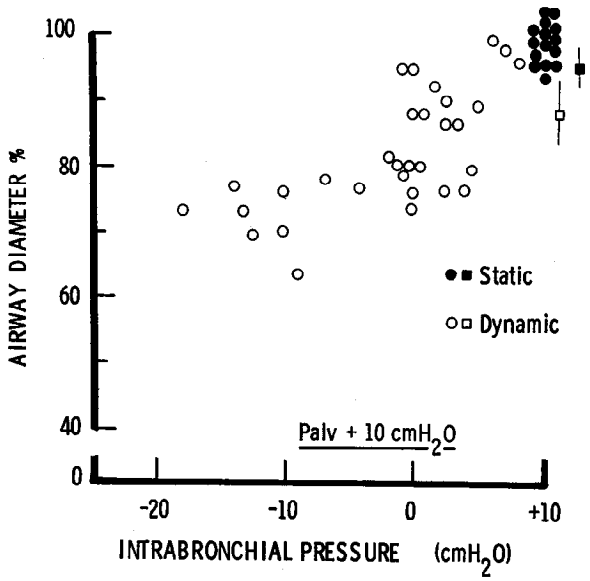

FIG. 6. Plot of airway diameter (% maximum) against intrabronchial pressure (Pib) at alveolar pressure (PAlv) +10 cmH_2O under static (●) and dynamic (○) conditions in eight experiments. Behavior of peripheral airways (■ □) at Pib +10 cmH_2O is also shown for comparison (n = 33). Bars indicate 1 SEM.

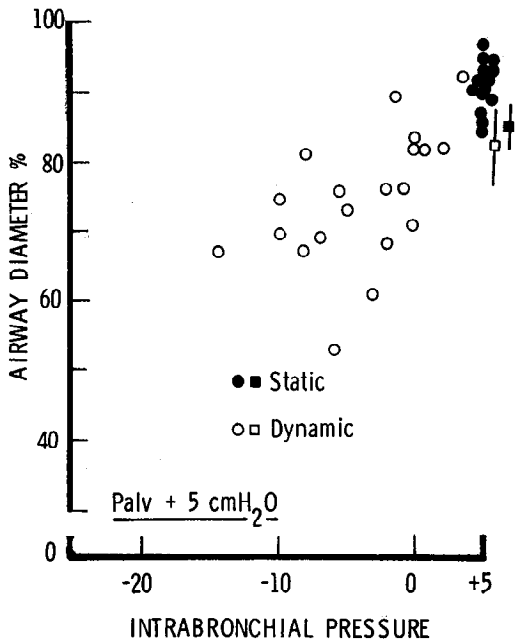

FIG. 7. Plot of airway diameter (as % maximum) against intrabronchial pressure (Pib) at constant alveolar pressure +5 cmH_2O under static (●) and dynamic (○) conditions in eight experiments. Behavior of more peripheral airways (■ □) at Pib +5 cmH_2O is also shown for comparison (n = 33). Bars indicate 1 SEM.

of previous data (6) this could result in a reduction of diameter of 5–10%. The changes of intrabronchial pressure occurring in the more central airways were accompanied by relatively modest reductions in diameter. A reduction of intraluminal pressure of 10–25 cmH_2O relative to alveolar pressure caused a diameter change of only 20% (or 15% if some degree of stress recovery is allowed). In Fig. 7 the behavior of the same airways at an alveolar pressure of 5 cmH_2O is plotted. The results are similar, although the slope of the curve of the points for the central airways at negative intrabronchial pressures is steeper than at PAlv +10 cmH_2O. This suggests that less parenchymal support is given at lower lung recoil pressures.

In Fig. 8 the diameters of the central airways in Figs. 6 and 7 under static and dynamic conditions are compared at the same intrabronchial pressures. The continuous line shows bronchial diameter under no-flow conditions (Pib = PAlv) as the lung is deflated from maximum (Pib +30 cmH_2O) to minimum (Pib 0 cmH_2O) volumes. The interrupted lines show bronchial diameters at PAlv +10 cmH_2O and PAlv +5 cmH_2O as intrabronchial pressure is systematically lowered. The vertical distance between the static and dynamic lines shows the extent to which bronchial diameter differs from that predicted on the assumption of independent expansion of airways and airspaces. The horizontal distance between the curves measures, in terms of pressure, the support given to the airway wall by the expansion of the lung. For example, at an intrabronchial pressure of −10 cmH_2O the bronchial diameter under static conditions (i.e., collapsed lung) was 53% of maximum, but at the same pressure in the lung inflated to PAlv +10 cmH_2O the diameter was 72%. Under static conditions a diameter of 72% corresponds to an intrabronchial pressure of +0.5 cmH_2O. Therefore we reason that under dynamic conditions the extrabronchial pressure must have decreased by 10.5 cmH_2O to maintain a diameter of

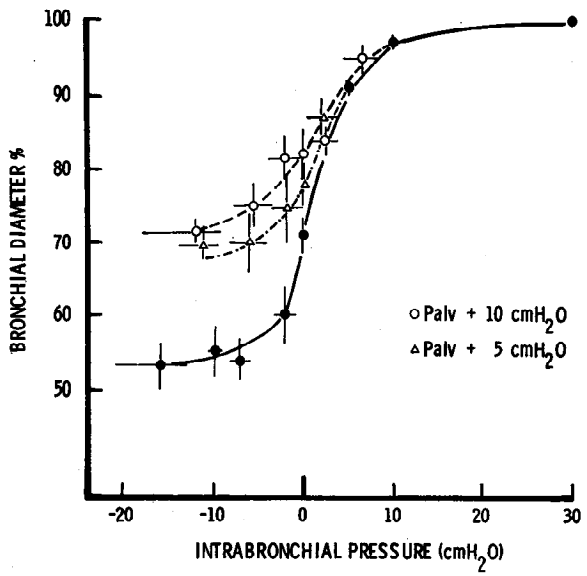

FIG. 8. Airway diameter (as % maximum) plotted against intrabronchial pressure under static (continuous line) and dynamic (interrupted lines) conditions at alveolar pressures of +10 cmH_2O and +5 cmH_2O. Mean results from eight experiments; vertical bars 1 SEM; horizontal bars give range of pressures over which airway diameters were measured.

72%. This implies that the peribronchial pressure must have been at least 10 cmH_2O more negative than pleural pressure.

Measurements of Bronchial Area

From stereoscopic X-ray pairs the cross-sectional area of a bronchus can be reconstructed by photogrammetric technics using a stereocomparator as shown in Figs. 9 and

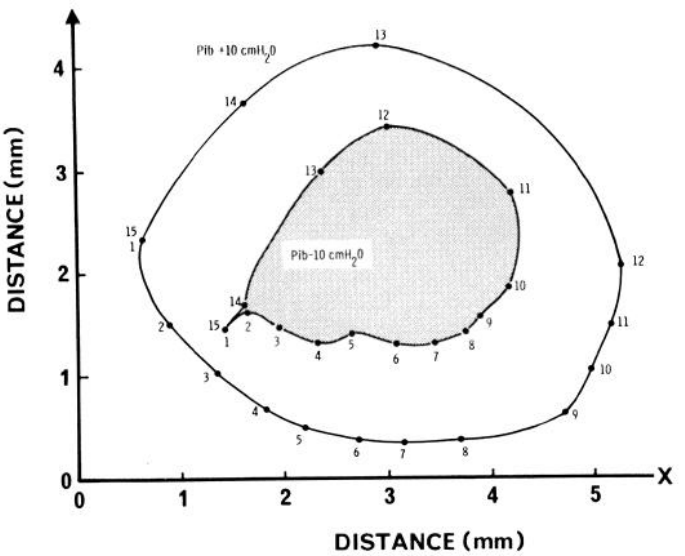

FIG. 9. Bronchial area in cross-section (from stereoscopic measurements) at constant lung volume under static [Pib +10 cmH_2O (outer ring)] and dynamic [Pib −10 cmH_2O (inner ring)] conditions. Note concentric narrowing. Alveolar pressure +10 cmH_2O in both instances. Numbers indicate measurement sites.

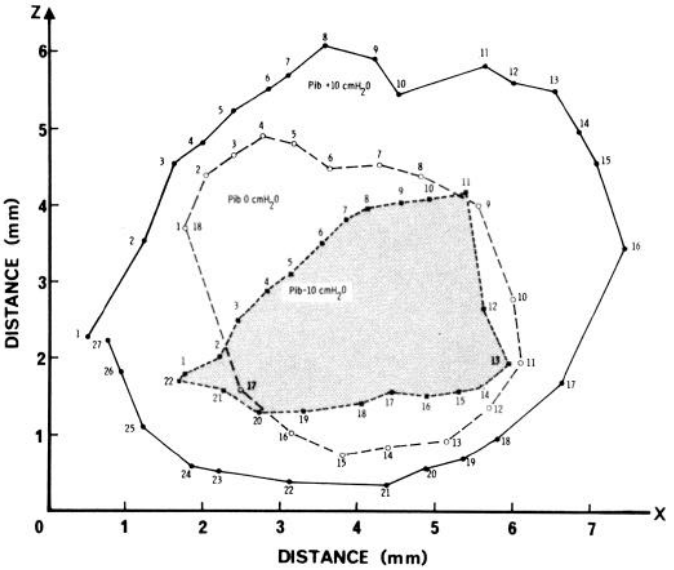

FIG. 10. Bronchial cross-section (from stereoscopic measurements) at different lung volumes under static conditions. Note approximately circular shape at Pib +10 and 0 cmH_2O with some flattening in the compressed and collapsed lung (Pib −10 cmH_2O).

10. Bronchial area is plotted in Fig. 9 under static and dynamic conditions at an alveolar pressure of 10 cmH_2O. Under dynamic conditions the intrabronchial pressure has been lowered by 20 cmH_2O to −10 cmH_2O. The decrease of diameter under compression is concentric, which is not surprising if the airway is supported by lung tissue on all sides. These measurements were repeated in another lung with similar findings. Nevertheless, in the absence of parenchymal support some distortion of bronchial shape occurs, as seen in Fig. 10. Under static conditions there is comparatively little change of shape until negative pressures (Pib −10 cmH_2O) are reached. Differences between bronchial diameter and area were assessed in the following way. Bronchial areas were measured by planimetry and diameters calculated from them on the basis of a circular shape; these were compared with the largest diameter actually observed on the X axis. Expressed as percentage of the diameter at Pib +10 cmH_2O (100%), the differences between observed and calculated diameters were 1.5% at Pib −10 cmH_2O (dynamic), 4.75% at Pib 0 cmH_2O (static), and 11.25% at Pib −10 cmH_2O (static). Four measurements were made at Pib +10 cmH_2O and two at the other pressures. These estimates show that intrapulmonary bronchi maintain a fairly regular shape except when compressed in a collapsed lung. Calculations of area from the largest diameter overestimated the planimetered area by 20–25% except at Pib −10 cmH_2O (static) when the average difference was 88%. Expressed as a percentage of the planimetered area at Pib +10 cmH_2O the calculated area overestimated the true one at Pib −10 cmH_2O (static) by 12.5%. Depending on the orientation of the bronchus and X-ray tube, measurements of diameter may as easily underestimate true bronchial area.

Airway Length

Measurements of airway length have been plotted against alveolar pressure in Fig. 11. The mean and standard error

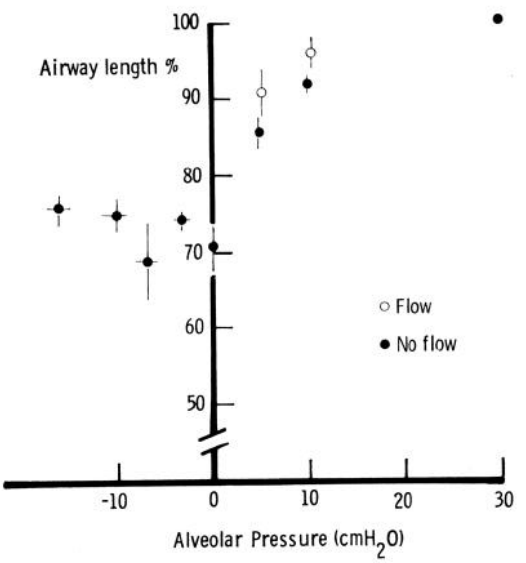

FIG. 11. Airway length (as % maximum) plotted against alveolar pressure under static (●) and dynamic (○) conditions. Mean results of all segments (n = 29) measured in eight experiments. Bars indicate 1 SEM.

of the average airway length in each experiment (based on measurements from 3–6 segments) are shown under static and dynamic conditions. Changes of airway length are related to changes in the cube root of lung volume (6), and therefore airways shorten as transpulmonary (alveolar) pressure is lowered. The mean values for all experiments show an increase in length of 2–4% at the same P_{Alv} on transferring from static to dynamic conditions. For individual airway segments (28 in number) the mean percentage change (related to maximum length) in any pair of measurements was 4.6 at P_{Alv} 10 cmH_2O and 4.5 at P_{Alv} 5 cmH_2O. For the segment adjacent to the cannula where negative intrabronchial pressures existed during the dynamic measurements, there was surprisingly no shorten-

ing. These segments increased in length in the dynamic situation by 8% at PAlv 10 cmH_2O and 5.4% at PAlv 5 cmH_2O.

DISCUSSION

In this study measurements of airway dimensions have demonstrated that at a constant lung volume the parenchyma confers considerable stiffness on 5–9 mm airways when their internal pressure is reduced relative to alveolar pressure by expiratory flow. Nevertheless before this data can be accepted on a quantitative basis, the limitations of our preparation and methods need to be reviewed.

Accuracy of bronchial diameter measurements. Stereoscopic X-ray theory (7) has shown that when airway diameter exceeds the width of the focal spot of the anode by five times or more (as in these experiments), airway diameter can be estimated acccurately assuming a circular shape to within 2%. The repeatability of the measurement of bronchial diameter was assessed by measuring 10 airways (5.0–7.3 mm ID) on three separate occasions. Measurements were made blind. The largest difference between the measurements for any airway was 0.15 mm (2.3%); the mean maximum difference was 0.08 mm (1.3%).

Distortions produced by cannula. In preliminary experiments nearly all the pressure drop in the bronchial tree downstream from 2 mm bronchi was found to be confined to the 1–2 cm adjacent to the lobar cannula even when flow was maximal. The achieve a pressure in intraparenchymal airways less than pleural pressure, the lobar cannula had to be pushed well into the lung as shown in Figs. 2 and 5 and negative pressure applied to it from a vacuum pump. Unfortunately the most proximal side branches were occluded, and it was common to find the proximal part of the lobe overinflated in the dynamic measurements; proximal alveolar pressures were generally 20–30 cmH_2O compared with 10–5 cmH_2O in the more distal part of the lobe. Although the airways studied were not in the obstructed part, some degree of local hyperinflation probably contributed to the increases in airway length at constant PAlv in the dynamic compared with the static measurements, although there seemed to be little effect on airway diameters (cf. peripheral airways in Figs. 6 and 7).

Measurement of alveolar pressure. Alveolar pressure was recorded indirectly from retrograde catheters in 2–3 mm bronchi. The peripheral resistance of dog lungs is known to be low, and this was confirmed by our measurements of pressure profiles (Fig. 4). Therefore pressure differences between the retrograde catheter and nearby alveoli must have been small. Homogeneity within the lobe under dynamic conditions is rather more difficult to substantiate. As already mentioned, obstruction and hyperinflation of the proximal part of the lobe may have extended distally to affect the segments under scrutiny. As a check we sampled alveolar pressures in various sites through the lobe under dynamic conditions with a fine (28 gauge) needle, concentrating on the region near the cannula where intrabronchial pressures and diameters were being measured. Although a wide spectrum of pressures was recorded (in four experiments), the majority of the readings were $\pm$ 2 cmH_2O of the retrograde catheter pressure measured simultaneously.

Measurement of lateral intrabronchial pressure (Pib). From the Bernoulli equation[1] we calculated the loss of kinetic energy from the alveolus to most proximal site where intrabronchial pressure was measured. Convective acceleration accounted for over 50% (mean 68%) of this pressure loss. Consequently the measurement of Pib could be influenced significantly by technical factors such as the presence of the catheter in the airway lumen and its degree of angulation (yaw) with the airstream (15). In model experiments we compared the pressures recorded by the intrabronchial catheters with directly measured side pressures in straight tubes of 6–6.5 mm ID. Flows were adjusted to give velocities similar to those measured under dynamic conditions (1.0–3.5 $cm \cdot s^{-1}$). Only small differences in pressure (<2.0 cmH_2O) were recorded, and no effect of yaw was found. Although the velocity profile in a lobar bronchus with side branches is considerably more complex than in a single tube, these measurements suggest that the presence of the catheter per se did not introduce a large error into the measurement of lateral pressure.

Effect of time history. Changes in airway diameter due to differences in time history between the static and dynamic measurements were apparent from the measurements of peripheral airways (see Figs. 6 and 7, and RESULTS section). To correct for this the dynamic curves in Fig. 8 should be shifted to the left. On the other hand, the increase in airway length dynamically (see Fig. 11) would have the opposite effect, and for this reason we have not attempted to correct for these factors.

Measurement of airway diameter at low lung volumes. Measurements of airway caliber from two-dimensional radiographs usually ignore shape or changes of shape. Using stereoscopic technics bronchial cross-sections were reconstructed in three preparations. The measurements in Figs. 9 and 10 show that the larger intrapulmonary airways assume a regular, almost circular shape except when subjected to compressive forces in a collapsed lung. To this extent the static curve at negative intrabronchial pressures in Fig. 8 does not truly reflect changes in bronchial area. Nevertheless, this part of the static curve is not required for the assessment of interdependence (see subsection *Calculation of K*) or in the calculation of the additional pressures operating on the airway wall in the dynamic situation.

Analysis of Interdependence

Figure 12 presents the data of Fig. 8 with the dynamic results at PAlv 5 cmH_2O and standard errors omitted for clarity. At point *E* in the dynamic curve intrabronchial pressure (Pib) is -5.6 cmH_2O, whereas in the static or quasi-homogeneous condition a similar bronchial diameter occurs at Pib $+0.8$ cmH_2O (point *C*). At *E* and *C* the airway has by definition the same Pel(br) and transmural pressure (i.e., Pib $-$ Pexb)—assuming no change in shape or elastic properties—so the extrabronchial pressure (Pexb) must have decreased by 6.4 cmH_2O (distance *CE*). There are several explanations for this decrease of Pexb. Mead et al. (18) put forward a model of pulmonary elasticity in which the pressure distending airways and airspaces in the inflated lung was influenced by changes in their area relative to the area of the tissue surrounding them. For intra-

[1] $Pca = \rho v^2/2g$, where Pca is pressure due to convective acceleration, ρ is density of air, v is velocity, and g is acceleration due to gravity.

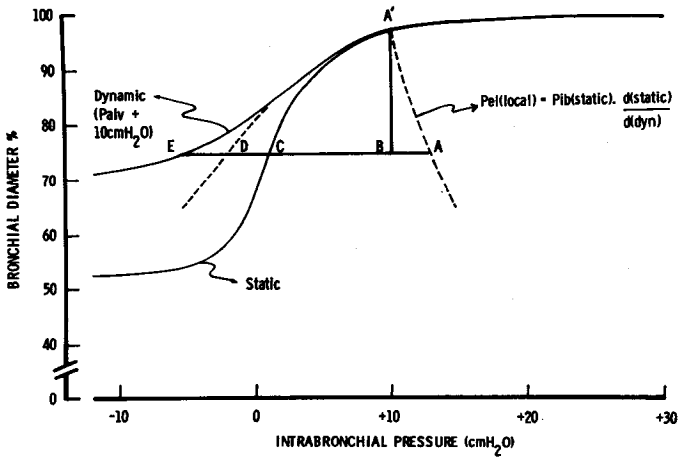

FIG. 12. Simplified display of data of Fig. 8 plotting airway diameter against intrabronchial pressure under static and dynamic conditions. Interrupted lines represent the additional stress on the airway wall under dynamic conditions by virtue of its change in surface area. Pel(local) = local alveolar tissue recoil pressure (see Fig. 1); Pib and d(static) = intrabronchial pressure and bronchial diameter under static conditions at point A'; d(dyn) = bronchial diameter on dynamic curve. See text and APPENDIX for details.

pulmonary airways Pexb depends upon alveolar pressure, the number of alveolar tissue attachments, their tension, and the area upon which they operate (the external diameter of the airway wall). If lung volume, transpulmonary pressure (Ptp), and local alveolar wall tension remain constant, bronchial narrowing will be accompanied by an increase in bronchial transmural pressure by means of a decrease in Pexb, because the same number of tissue attachments with the same tension operate on a smaller surface area. In addition local alveolar tissue tension may increase even though overall lung volume and Ptp remains constant. The relative contribution of changes of surface area, on the one hand, and tissue tension, on the other, to the change of Pexb can be assessed by calculating the change of Pexb expected solely on the basis of the decrease in bronchial diameter (see APPENDIX for details). At a diameter of 75% the decrease in surface area accounts for an additional local tissue recoil pressure of 2.8 cmH_2O (AB); when this pressure is subtracted from the static Pib at this diameter (point C), the contribution of the decrease in circumference (CD) to the decrease in Pexb (CE) under these dynamic conditions can be seen. At this airway diameter it contributes 44% of the decrease in Pexb; at 80% and 72.5% diameter the change of surface area accounts for 72% and 33%, respectively. The remaining portion of the decrease in Pexb (i.e., DE) is probably related to increases in radial tension from the surrounding lung tissue, which distorts as the airway within it narrows. The increase in tissue tension is closely related to the degree of bronchial narrowing, contributing 1.0 cmH_2O to the lowering of Pexb at a bronchial diameter of 80% and 6.4 cmH_2O at 72.5% diameter. If this tissue distortion had been shared by all alveolar walls to a great distance, the resulting change in stress on the airway wall would have been negligible. Our results at bronchial diameters < 80% max suggest that the strain is taken up locally with corresponding changes in tissue tension and peribronchial stress. Other tests of Mead et al.'s model of pulmonary elasticity in lung tissue (23), lobules (28), arterial vessels (1), or segments (20, 21) have also concluded that interdependence is greater than can be accounted for on the basis of change of surface area alone. On the other hand, the decrease in airway diameter at PAlv +10 cmH_2O from 97 to 82% max can be explained wholly by surface area changes, so it would appear that a certain amount of slack can be taken up by the surrounding tissue without appreciable changes of tension. It is of interest that localized pleural distortion leads to parenchymal compression closely limited to the pleural surface and sharply demarcated from normally expanded lung (27). This suggests that negative interdependence of airways and airspaces would occur during fast inspiration, the increase in (Pib − Ppl) relative to (PAlv − Ppl) leading to airway widening, compression of the surrounding tissue, and a decrease in peribronchial stress.

The possibility remains that part of the distance CE could be explained by a true change in the elastic properties of the airway wall. There was a longer time available for stress recovery of smooth muscle tone in the measurement at E compared with C; this would have lessened the distance CE, not increased it. Airway length was different, being 92% max at point E and 75% max at C. Nevertheless, Hyatt and Flath (8) have shown that pressure-diameter curves for excised dissected-out airways are independent of moderate changes of length. Airway shape, from Figs. 9 and 10, did not change significantly. For these reasons it seems likely that the majority of the difference between the static and dynamic airway curves is due to increases in extrabronchial pressure.

Calculation of K. This measure of interdependence based on *Eq. 1* (see section THEORY) is shown in Fig. 13 for the dynamic curves at PAlv 10 and 5 cmH_2O. The interdependence factor (K) is plotted against airway diameter and static intrabronchial pressure. K is calculated for points of equal airway diameter (e.g., E and C, Fig. 12). At E (PAlv − Pib) equals the distance BE; on the static curve at C there is no difference. Pel(l) at E is +10 cmH_2O and at C +0.8 cmH_2O. Therefore $K = BE/BC$. The magnitude of interdependence assessed in this way is greater at higher lung volumes (PAlv +10 cmH_2O) as predicted from a theoretical study by Lambert and Wilson (9). Also shown in Fig. 13 are predictions from the model of Mead et al. (18), i.e., $K = AC/BC$, which emphasizes again that some but not all of the bronchial narrowing during expiration can be explained on the basis of surface area changes.

In summary, we would draw the following conclusions from Figs. 12 and 13.

1) Interdependence is relative. Diameter changes of 15–20% can occur without appreciable changes of tension in the surrounding tissue. This leaves room for bronchomotor tone to operate at a given lung volume.

2) The part played by the parenchyma assumes increasing importance as further narrowing of the airway lumen takes place. Airway closure is thus prevented from occurring too easily.

3) The effect of interdependence is greatest at high lung volumes and transpulmonary pressure, leaving airways more vulnerable to closure when lung recoil is low.

4) At a given lung volume dynamic narrowing of the

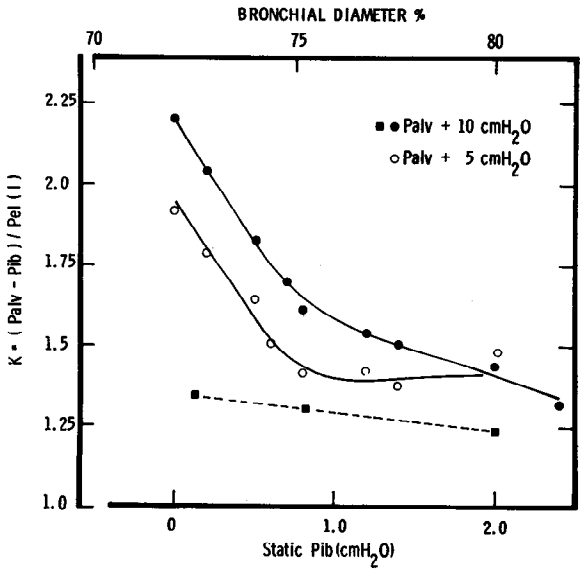

FIG. 13. Plot of K [constant of proportionality between ΔPib and ΔPel(br)] against static Pib (point C in Fig. 12) and bronchial diameter (as % maximum) under dynamic conditions at fixed alveolar pressures +5 and +10 cmH_2O. Interrupted line represents calculations on the basis of the model of Mead et al. (18) at PAlv +10 cmH_2O. See text for details.

segment upstream from the equal pressure point (EPP) (to the right of Pib 0 cmH_2O) will occur, although airway diameter will be up to 12% greater than predicted on the basis of the change in Pib.

Relationship of Airway and Airspace Interdependence to Flow Limitation

Although there are substantial differences between an excised dog lung preparation and normal man, we believe these results have established the principle that intrapulmonary airways narrow less during expiratory flow than would be predicted on the basis of intrabronchial pressure measurements. Marshall and Holden (17) showed in man from bronchographic measurements that there was some protection of intrapulmonary airways from high intrathoracic pressures and flows generated by coughing. The relative stability of the caliber of intrapulmonary airways during expiratory flow contrasts sharply with the lack of support available to the lobar and main bronchi. At the entrance to a lobe the behavior of the extrapulmonary airways will be similar to that shown by the static curve in Fig. 12. Several experimental findings may be explained on this basis. For example, over a large portion of the vital capacity (VC) during maximum expiratory flow the locus of the EPP (19) remains fixed in lobar or segmental bronchi. Since the site of the EPP appears to be quite uniform among different species and under different conditions (14, 15) one imagines that the elasticity of pulmonary parenchyma prevents the intrapulmonary airway narrowing, which would otherwise allow the EPP and the flow-limiting segment downstream from it to enter the lung. Interdependence declines in magnitude at lower lung recoil pressures (cf. values for K in Fig. 13), and this lack of support presumably allows the EPP to progress rapidly upstream at lung volumes below 30% VC (14). By using a physical model to simulate maximal expiration, Pardaens et al. (24) found that the flow-volume relationships of lungs were mostly dependent on the elastic properties of the lungs and bronchi. Using the anatomy of Weibel (29) they found a more peripheral location (5th airway generation) of the EPP below 70% VC than previously reported, but had they taken intrapulmonary airway stability into account, a lobar location of EPP would probably have been found.

What advantages or disadvantages accrue from intrapulmonary airway stability? During maximal expiration as in coughing the central location of flow-limiting segments will promote more uniform emptying of the lung periphery (22). On the other hand, the lack of dynamic compression in these airways except at low lung volumes means that clearance of bronchial secretions is heavily dependent on ciliary action.

Flow-Limiting Segment

Although interdependence was not sufficient to prevent flow limitation occurring in this preparation (Fig. 3), this should not be taken as evidence that narrowing of this degree would occur in the intact lung at this lung volume during maximal flow. I_t depended on the intrapulmonary position of the bronchial cannula, which, in turn, was merely a device to overcome the low flow resistance of excised dog lobes and produce intrapulmonary intrabronchial pressures less than pleural. As already mentioned the location of the EPP at volumes above 30% VC is in extrapulmonary airways, and an increase in driving pressure once the EPP has developed will not in theory move the position of the EPP or the flow-limiting segment (26). In this respect Fig. 3 is somewhat misleading. At the onset of maximum flow Pib (measured at the site of the distal catheter) was +1.5 cmH_2O, becoming more negative with an increase in driving pressure. Therefore the EPP (by definition the site where Pib = 0 cmH_2O) must have moved peripherally during maximum flow at isovolume. Nevertheless in this preparation the tip of the lobar cannula, flow-limiting segment, and pressure site were in close proximity so that further narrowing of the flow-limiting point during maximum flow (consequent on the increase in driving pressure) could easily have distorted and changed the diameter and pressure of the segment next to it.

Emphysema

A decrease in maximum flow ($\dot{V}_{max}$) resulting from lack of airway support from the parenchyma was foreseen many years ago by Dayman (4). Airway conductance (Gaw) is reduced, reflecting a reduction in static airway dimensions, probably on the basis of a loss of lung recoil (10). The loss of lung recoil [Pst(l)] reduces maximal flow at a given lung volume for several reasons: *a*) the driving pressure for the segment upstream from the EPP is reduced; *b*) the resting dimensions of the airways may be less at the lower Pst(l); *c*) interdependence between airways and airspaces is less effective at lower Pst(l) (see Fig. 13). Nevertheless after taking these factors into account, Leaver et al. (10) found that $\dot{V}_{max}$ was reduced out of proportion to the loss of lung recoil. If the loss of elasticity and parenchymal distortion, which reduced lung recoil, also affected the normal inter-

dependence between airway and airspace expansion, then loss of $\dot{V}_{max}$ would be greater then loss of Pst(l), and upstream conductance (Gus) would be lowered disproportionately in relation to Gaw, as found by these authors (10). The migration of the EPP into the lung beyond the lobar bronchi seen in some subjects with emphysema (11) may reflect a relative lack of interdependence, although the increase in peripheral airways resistance may also play a part. The high residual volumes, air trapping, and low ventilation-perfusion ratios in emphysema may also reflect a loss of interdependence in its other role, that of preventing peripheral airway closure.

APPENDIX

Analysis of Contribution of Surface Area Changes to Changes in Bronchial Transmural Pressure (Ptm)

Figure 1 shows schematically the peribronchial space surrounding the bronchial wall. On its alveolar side this space is bounded by a limiting membrane (*lm*), which forms part of and is continuous with the lung parenchyma. The peri- or extrabronchial pressure (Pexb) equals the alveolar pressure (PAlv) minus the local lung recoil pressure [Pel(local) in Fig. 1]; we assume the latter is equivalent to the sum of the outward-acting alveolar tissue forces per unit bronchial area (Σ Fo/Abr). (The contribution of the limiting membrane to the sum of these pressures is probably small and can be neglected.) Thus

$$\text{Pexb} = \text{PAlv} - \text{Pel(local)}$$

According to the analysis of Mead et al. (18) Pel(local) in the alveolar tissue next to a bronchus will only equal the average tissue recoil pressure for the whole region if the space for the bronchus within the parenchyma at a given transpulmonary pressure exactly matches the size of the bronchus distended outside the lung to the same pressure. In this situation Pexb will equal Ppl. Nevertheless at the same lung volume and for a constant outward-acting tissue force (Σ Fo), any reduction in bronchial surface area will lead to an increase in Pel(local). Thus the difference between Pib and Pexb, or bronchial transmural pressure (Ptm), is

$$\text{Ptm} = \text{Pib} - [\text{PAlv} - \text{Pel(local)}] \qquad (2)$$

To calculate changes of Pel(local) resulting from changes in bronchial diameter (at constant lung volume), an absolute value for local tissue recoil pressure must be chosen corresponding to the static situation. In Fig. 12 we have assumed [as did Mead et al. (18) in a similar analysis] that in the static situation at Pib +10 cmH_2O (i.e., *A'*) local alveolar wall recoil equals overall lung recoil, i.e., Pel(local) = Pel(l) so that Pexb = Ppl. There is some experimental justification for this; under static conditions following a maximal or submaximal inflation, airways and airspaces in excised lungs have the same relative changes of dimensions (6), and bronchial diameters in lungs at a given Ptp have a similar size when subsequently dissected out and exposed to the same pressure (8). Therefore at point *A'*, Pel(local) = Pel(l) = Pib(static). In the dynamic situation bronchial diameter decreases from *A'* to *A*, and surface area decreases in direct proportion to the diameter change since airway length remains constant (Fig. 11), and Pel(local) increases according to the formula shown in Fig. 12.

At *A'* in Fig. 12 Pib, PAlv, and Pel(local) each have a value of +10 cmH_2O, and from *Eq. 2* Ptm = +10 cmH_2O. At *E* Pib −5.6 cmH_2O, PAlv +10 cmH_2O, while Pel(local) has increased to +12.8 cm H_2O (see point *A*), giving a Ptm for the bronchus of −2.8 cmH_2O. But in the static situation at the same bronchial diameter Ptm = +0.8 cmH_2O [assuming Pel(local) = Pel(l) under static conditions]. For Ptm to be +0.8 cmH_2O at point *E*, Pel(local) must have increased by +6.4 cmH_2O, but only 2.8 cmH_2O (44%) of this increase can be accounted for by changes in surface area alone.

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REFERENCES

1. Benjamin, J. J., P. Murtagh, and S. Permutt. A study of pulmonary interdependence with tantalum arteriograms. *Federation Proc.* 30: 555, 1971.
2. Butler, J., J. A. R. Friend, J. M. B. Hughes, H. A. Jones, N. B. Pride, and A. Wilson. An isovolume lung preparation for studies of flow-dependent changes in bronchial calibre. *J. Physiol., London*, 231: 79–80, 1973.
3. Culver, B., J. Friend, V. Loverde, and J. Butler. The flow limiting segment in the airway. *Physiologist* 16: 293, 1973.
4. Dayman, H. Mechanics of airflow in health and emphysema. *J. Clin. Invest.* 30: 1175–1190, 1951.
5. Hooke, R. Account of an experiment made by M. Hook of preserving animals alive by blowing through their lungs with bellows. *Phil. Trans. Roy. Soc.* 2: 539–540, 1667.
6. Hughes, J. M. B., F. G. Hoppin, Jr., and J. Mead. Effect of lung inflation on bronchial length and diameter in excised lungs. *J. Appl. Physiol.* 32: 25–35, 1972.
7. Hughes, J. M. B., F. G. Hoppin, Jr., and A. G. Wilson. Use of stereoscopic x-ray pairs for measurements of airway length and diameter in situ. *Brit. J. Radiol.* 45: 477–485, 1972.
8. Hyatt, R. E., and R. Flath. Influence of lung parenchyma on pressure-diameter behavior of dog bronchi. *J. Appl. Physiol.* 21: 1448–1452, 1966.
9. Lambert, R. K., and T. A. Wilson. A model for the elastic properties of the lung and their effect on expiratory flow. *J. Appl. Physiol.* 34: 34–38, 1973.
10. Leaver, D. G., A. E. Tattersfield, and N. B. Pride. Contributions of loss of lung recoil and of enhanced airways collapsibility to the airflow obstruction of chronic bronchitis and emphysema. *J. Clin. Invest.* 52: 2117–2128, 1973.
11. Macklem, P. T., R. G. Fraser, and D. V. Bates. Bronchial pressures and dimensions in health and obstructive airway disease. *J. Appl. Physiol.* 18: 699–706, 1963.
12. Macklem, P. T., R. G. Fraser, and W. G. Brown. Bronchial pressure measurements in emphysema and bronchitis. *J. Clin. Invest.* 44: 897–905, 1965.
13. Macklem, P. T., and J. Mead. Resistance of central and peripheral airways measured by retrograde catheter. *J. Appl. Physiol.* 22: 395–401, 1967.
14. Macklem, P. T., and J. Mead. Factors determining maximum expiratory flow in dogs. *J. Appl. Physiol.* 25: 159–169, 1968.
15. Macklem, P. T., and N. J. Wilson. Measurement of intrabronchial pressure in man. *J. Appl. Physiol.* 20: 653–663, 1965.
16. Marshall, R. Effect of lung inflation on bronchial dimensions in dog. *J. Appl. Physiol.* 17: 596–600, 1962.
17. Marshall, R., and W. S. Holden. Changes in calibre of the smaller airways in man. *Thorax* 18: 54–58, 1963.
18. Mead, J., T. Takishima, and D. Leith. Stress distribution in lungs: a model of pulmonary elasticity. *J. Appl. Physiol.* 28: 596–608, 1970.
19. Mead, J., J. M. Turner, P. T. Macklem, and J. B. Little. Significance of the relationship between lung recoil and maximum expiratory flow. *J. Appl. Physiol.* 22: 95–108, 1967.
20. Menkes, H., G. Gamsu, R. Schroter, and P. T. Macklem. Interdependence of lung units in isolated dog lungs. *J. Appl. Physiol.* 32: 675–680, 1972.
21. Menkes, H., D. Lindsay, L. Wood, A. Muir, and P. T. Macklem. Interdependence of lung units in intact dog lungs. *J. Appl. Physiol.* 32: 681–686, 1972.
22. Millette, B., P. C. Robertson, W. R. D. Ross, and N. R.

ANTHONISEN. Effect of expiratory flow-rate on emptying of lung regions. *J. Appl. Physiol.* 27: 587–591, 1969.
23. MORGAN, M. S., S. V. DAWSON, F. G. HOPPIN, JR., AND G. C. LEE. Quantification of interdependence. *Physiologist* 16: 399, 1973.
24. PARDAENS, J., K. P. VAN DE WOESTIJNE, AND J. CLEMENT. A Physical model of expiration. *J. Appl. Physiol.* 33: 479–490, 1972.
25. PERMUTT, S., J. B. L. HOWELL, D. F. PROCTOR, AND R. L. RILEY. Effect of lung inflation on static pressure-volume characteristics of pulmonary vessels. *J. Appl. Physiol.* 16: 64–70, 1961.
26. PRIDE, N. B., S. PERMUTT, R. L. RILEY, AND B. BROMBERGER-BARNEA. Determinants of maximal expiratory flow from the lungs. *J. Appl Physiol.* 23: 646–662, 1967.
27. ROBERTSON, C. H., D. L. HALL, AND J. C. HOGG. A description of lung distortion due to localized pleural stress. *J. Appl. Physiol.* 34: 344–350, 1973.
28. TAKISHIMA, T., AND J. MEAD. Tests of a model of pulmonary elasticity. *J. Appl. Physiol.* 33: 576–581, 1972.
29. WEIBEL, E. R. *Morphometry of the Human Lung*. Berlin: Springer-Verlag, 1963, p. 9–122.