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Research Article

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Bronchial Pressure Measurements in Emphysema and Bronchitis *

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Koblet and Wyss were the first to use bronchial pressure measurements to locate the airway obstruction in emphysema and asthma (1). Their results showed that in emphysema expiratory obstruction occurred in large airways whereas in asthma it was in small airways. It had already been established, in particular by Dayman (2), that emphysema was characterized by a marked increase in airway resistance during forced expiration, due to airway compression, and that this increase limited expiratory flow. Subsequently Hyatt, Schilder, and Fry (3) and Fry and Hyatt (4) showed that the inability of the patient with emphysema to breathe was directly attributable to expiratory airway compression and that maximal expiratory flow bore a unique relationship to lung volume. Out of these investigations grew the concept of the "flow-limiting segment," which was regarded as the airway or airways which were the first to narrow enough to limit flow. Thus, Koblet and Wyss's work took on added importance because it suggested that the flow limitation in emphysema was due to narrowing of large bronchi. Our laboratory has confirmed and extended their results by measuring bronchial pressures during cinebronchography (5). It was found that in emphysema the expiratory obstruction as demonstrated by the pressure measurements coincided with collapse of the lobar bronchi visualized cinebronchographically. Furthermore, this collapse appeared to be the result of an increase in bronchial compliance.

These investigations suggested that the collapsing lobar bronchi were flow limiting in emphysema. This was not proven, as the possibility remained that flow was initially limited in smaller airways and that subsequent to this event the lobar bronchi collapsed obstructing flow. The crucial role played by the small airways would thus be masked, and the lobar bronchi would spuriously appear as the flow-limiting segments. The present study was designed to investigate this problem further.

Methods

Subjects. Nine patients were studied. The only criterion for inclusion in the study was chronic airway obstruction with a reduction in forced expiratory volume in the first three-quarters of a second ($FEV_{0.75}$) that was unresponsive to therapy. Thus, all patients with episodic asthma were excluded. Included were six patients who, on the basis of clinical findings and lung function tests, were thought to have emphysema and three patients who were thought to have chronic airway obstruction due to bronchitis without emphysema. The criteria for making this distinction have been previously described (5, 6). The three function tests used in the differentiation are the diffusing capacity, maximal negative static transpulmonary pressure, and over-all lung compliance. For the present purposes it was arbitrarily decided that nor-

TABLE I

Physical characteristics of subjects

Subject	Diagnosis	Age	Sex	Height	Weight
				cm	*kg*
B	Emphysema	48	M	161	57
Br	Emphysema	61	M	169	66
M	Emphysema	63	M	171	55
Mu	Bronchitis	50	M	174	64
S	Bronchitis	53	F	156	49
K	Emphysema	47	M	167	64
Z	Emphysema	64	M	166	69
Te*	Emphysema	66	M	167	64
T	Bronchitis	60	M	170	75

* Panacinar emphysema proven pathologically.

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TABLE II

Results of lung function tests in subjects

Subject	Vital capacity		Functional residual capacity		$FEV_{0.75}$*		D_{LCO}† at rest		$P_{el\ max}$‡ Normal range	C_{TLC}§ Normal range	Pulmonary resistance Normal range
	Measured	Predicted	Measured	Predicted	Before therapy	After therapy	Predicted	Measured	Predicted	<−16	0.10–0.25	1–2
	L	*L*	*L*	*L*	*L/min*			*ml CO/mm Hg/min*		*cm H₂O*	*L/cm H₂O*	*cm H₂O/L/sec*
B	1.63	3.40	6.30	2.98	19	23	96	6.20	15.8	−10	0.621	6.0
Br	1.52	3.74	6.32	3.48	11	18	90	6.45	13.7	−12	0.615	7.3
M	2.10	3.60	4.98	3.48	12	14	85	6.92	12.9	− 7.5	0.845	7.7
Mu	4.19	4.36	5.74	3.74	81	86	110	20.84	16.9	−22	0.364	4.3
S	1.40	2.79	2.61	2.43	14	19	71	6.92	13.9	−17	0.210	7.8
K	1.16	3.72	3.80	3.23	23	20	100	9.69	16.1	−15.5	0.308	3.9
Z	2.88	3.27	3.69	3.23	25	32	77	13.85	12.1	−12	0.494	10.2
Te	2.11	3.27	4.49	3.23	26	23	77	7.43	12.1	−21.5	0.269	11.1
T	4.32	3.74	3.78	3.48	51	71	90	16.45	13.7	−21	0.311	5.5

* Forced expiratory volume in the first three-quarters of a second.
† Steady state diffusing capacity for carbon monoxide with end-tidal sampling.
‡ Static transpulmonary pressure at full lung inflation.
§ Over-all lung compliance ($TLC/P_{el\ max}$).

mality of any two of these tests excluded emphysema. Physical characteristics and lung function tests on all subjects are shown in Tables I and II.

Procedure. In all subjects bronchial pressures were measured simultaneously with esophageal pressure, lung volume, and flow at the mouth. Two bronchial pressure catheters were employed to record simultaneous pressures in a main-stem bronchus and a segmental bronchus in the same lung. The main-stem catheter was radiopaque and possessed an o.d. of 2.5 mm and an i.d. of 2.0 mm with an end-hole. The catheter in the segmental bronchus was vinyl, o.d. 1.6 mm, i.d. 1.0 mm, with a single side-hole 0.2 mm proximal to a 1-cm radiopaque tip. Both catheters were kept patent by a constant flush of air from a compressed air tank connected to the catheter via a needle valve. This technique has already been described, and sources of error discussed (5). Bronchial pressures were only considered reliable if the instants of zero bronchial pressure coincided with points of zero flow. Esophageal pressure was measured by an esophageal balloon 10 cm long, 3.0 cm in circumference, containing 1.0 to 0.5 ml air, attached to a polyethylene catheter. The 90% response to a square wave of pressure in all three pressure probes was 10 msec or less. All pressures were measured relative to mouth pressure using Sanborn 267B differential pressure transducers.

All catheters were passed transnasally. The esophageal catheter was positioned by inserting it into the stomach, removing it gradually until the pressure it transmitted became negative on deep inspiration, and then withdrawing it an additional 10 to 15 cm. The bronchial catheters were positioned in the desired airway fluoroscopically. The subject sat behind a fluoroscopic screen and breathed from a differentiating spirometer giving both lung volume and flow at the mouth. He performed a series of 10 to 15 vital capacity breaths attempting to increase the flow rate with each breath. Subsequently radiopaque medium was injected into the tracheobronchial tree via the end-hole catheter, and exact catheter positions were noted. Cinebronchographic studies were then carried out during forced expiration and cough. Subsequently the per cent reduction in caliber from the maximum on inspiration to the minimum on forced expiration of selected bronchi on the side catheterized was measured. On the right side the intermediate stem bronchus, the lower lobe bronchus, and a segmental bronchus of the lower lobe were measured. On the left side, the main-stem bronchus, the lower lobe bronchus, and a segmental bronchus of the lower lobe were measured.

From the tracings obtained flow-resistive pressure was estimated from esophageal pressure by subtracting the pressure due to elastic recoil. With tissue resistance assumed to be negligible, flow-resistive pressure can be equated with alveolar pressure.

The bronchial pressures were analyzed by plotting them against pulmonary flow-resistive pressures at a constant lung volume, 75, 50, and 25% vital capacity. Flow at the mouth was also plotted against pulmonary flow-re-

sistive pressure at the same lung volumes giving the isovolume pressure-flow curves as initially described by Hyatt, Schilder, and Fry (3). This method of analysis permitted assessment of the pressure drop at various levels of the bronchial tree from the alveolus to mouth at any point on the isovolume pressure-flow curve. Because the flow in various regions of the lung is nonuniform in obstructive airway disease, one cannot assume that the pressures measured in a bronchus are representative of other bronchi of similar size. Thus the results can only give information on the pressures in the lobe catheterized and cannot be generalized to other lobes. For the same reason it is impossible to give resistance values for different airways except in a general, qualitative way. Nevertheless, it is not unreasonable to assume that maximal flow in different lobes is reached at approximately the same time, and we have therefore used the isovolume pressure-flow curve as an indication of maximal flow in the lobe catheterized.

Results

Figure 1 is an example of the pressures obtained in a normal subject who was part of another study (7). The lower graph is the isovolume pressure-flow curve. The upper graph shows the relationship between the pressures in a segmental and main-stem bronchus, and pulmonary flow-resistive pressure at 50% vital capacity, on both inspiration and expiration. If the bronchial pressures had equaled flow-resistive pressure, the points would have fallen along the line of identity. If lung tissue resistance is assumed to be negligible, this line describes alveolar pressure. Tissue resistance has been variously estimated between 2 to 40% of pulmonary (airway and tissue) resistance and is linear (8–10). In patients with airway obstruction, tissue resistance is a much lower percentage of the total. In assuming it to be negligible, we are overestimating alveolar pressure slightly but not to a degree that would significantly affect the results described. The lines between the line of identity and the abscissa represent the pressures in bronchi. These pressures are less than alveolar pressure, and the lines fall below the line of identity. The pressure drop from the alveolus to the segmental bronchus is the vertical distance from the line of identity to the segmental bronchial pressure line. The pressure drop from segmental to main-stem bronchus is the vertical distance from the segmental bronchial pressure line to the main-stem bronchial pressure line. The pressure drop from the main-stem bronchus to the mouth is the vertical distance from the main-stem bronchial pressure line to the abscissa.

In this manner, the airways were partitioned into three segments: *1*) alveolus to segmental bronchus, *2*) segmental to main-stem bronchus, and *3*) main-stem bronchus to mouth.

Normally the pressures in the segmental bronchi are approximately equal to pleural pressure during forced expiration, and flow limitation occurs predominantly in the main-stem and lobar bronchi (7).

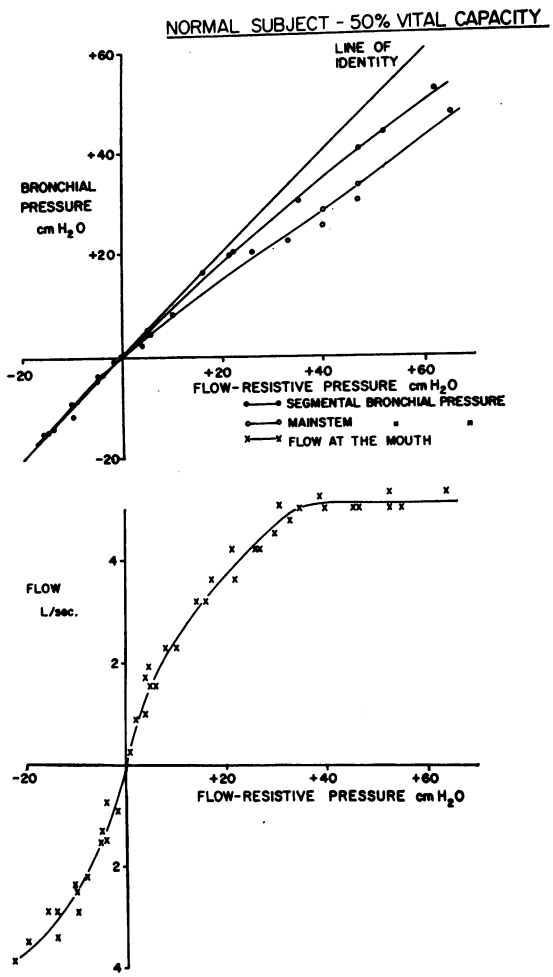

FIG. 1. RESULTS OBTAINED IN A NORMAL SUBJECT, WHO WAS PART OF ANOTHER STUDY (7), AT 50% VITAL CAPACITY. The upper diagram is the plot of segmental bronchial pressure (●——●) and main-stem bronchial pressure (○——○) against flow-resistive pressure. The lower left quadrant is inspiration and the upper right quadrant expiration. The lower diagram is the isovolume pressure-flow curve for the same lung volume.

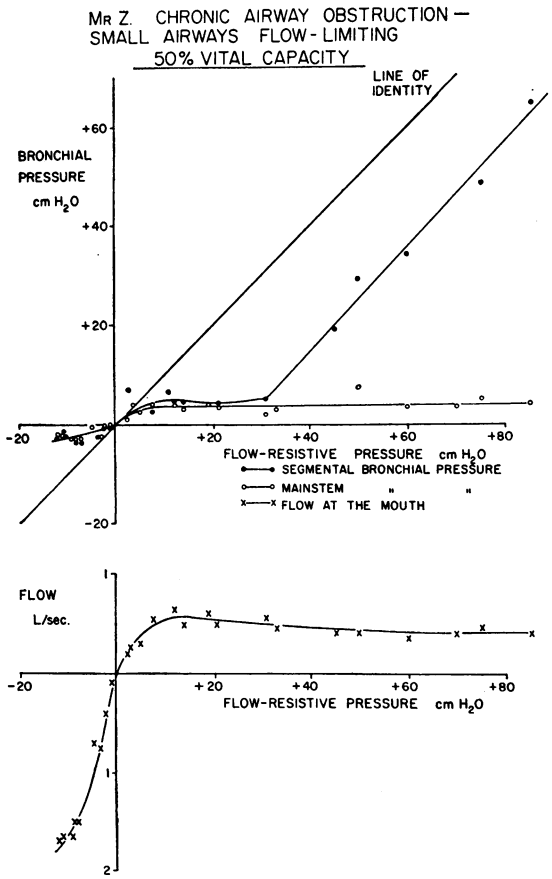

FIG. 2. RESULTS OBTAINED IN A PATIENT WHOSE SMALL AIRWAYS WERE FLOW-LIMITING AT 50% VITAL CAPACITY. The symbols and method of plotting are the same as in Figure 1.

All patients had abnormal pressures and fell into one of three groups: *1*) those in whom the small airways were flow limiting, *2*) those in whom the large airways were flow limiting, and *3*) those in whom both small and large airways appeared to limit flow.

Figure 2 is an example of the pressures obtained in a patient in whom the small airways were flow limiting. Two of the nine patients fell into this category. With the isovolume pressure-flow curve as an index of peak flow in the lobe catheterized, the flow-limiting segment is the one where the pressure drop down its length increases once maximal flow is reached. This diagram illustrates that it is the pressure drop from the alveolus to segmental bronchus that increases after peak flow is reached. Later on, a large pressure drop develops between the segmental and main-stem bronchus, but the lobar bronchus, which lies between, cannot in any way be considered as flow limiting. The initial flow limitation clearly occurs in the smaller airways as these airways increase their resistance sufficiently to limit flow before the lobar bronchi do. If this case had been studied during a single forced expiration with an alveolar pressure of greater than 80 cm H_2O, the lobar bronchi would spuriously appear to be flow limiting. It is only by studying the pressure relationships over a wide range of alveolar pressures and at the same lung volume that the role of the

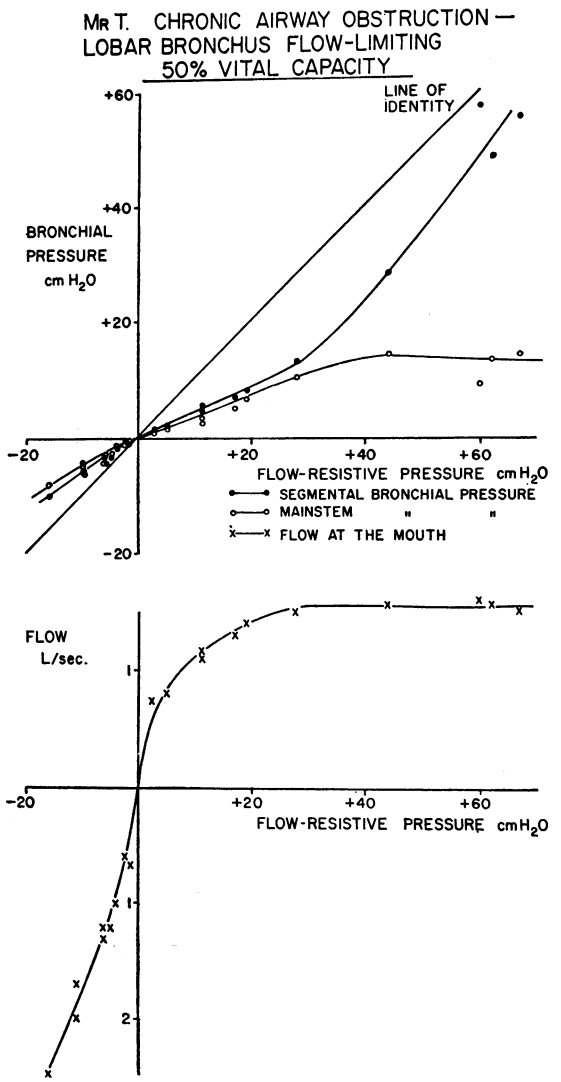

FIG. 3. RESULTS IN A PATIENT WHOSE LOBAR BRONCHUS WAS FLOW-LIMITING AT 50% VITAL CAPACITY. The symbols and method of plotting are the same as in Figure 1.

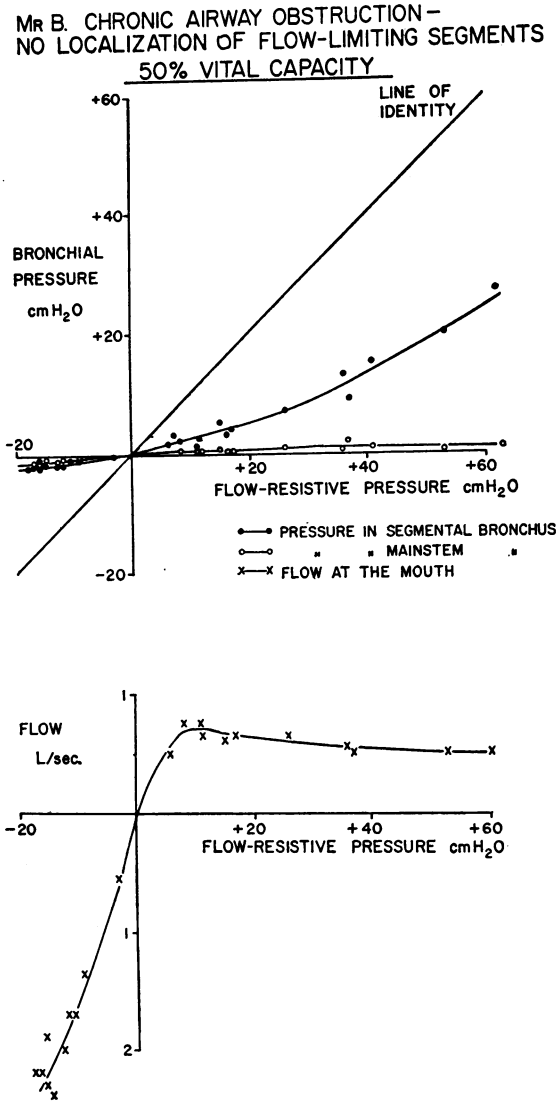

FIG. 4. RESULTS OBTAINED IN A PATIENT IN WHOM BOTH LARGE AND SMALL AIRWAYS APPEARED TO LIMIT FLOW SIMULTANEOUSLY. The symbols and method of plotting are the same as in Figure 1.

small airways becomes aparent. On inspiration there was a large pressure drop from the segmental bronchus to the alveolus, whereas the pressure drop down the length of the lobar bronchus was negligible. Thus inspiratory obstruction is predominantly in small airways.

An example of the pressures obtained in the group in which the lobar bronchus was flow limiting is seen in Figure 3. Once maximal flow is reached, the pressure drop from the segmental to main-stem bronchus is the only one to increase, and therefore, narrowing of the lobar bronchus must have limited flow. This was so even though there was a large pressure drop from the alveolus to the segmental bronchus. On inspiration the lobar obstruction disappears, and the obstruction is entirely in the small airways as in the previous example. Of the nine patients, five fell into this category and three of these were thought to have bronchitis without emphysema.

Figure 4 is an example of the third group in which there were two patients. Once peak flow was reached the pressure drop down both the small airways and the lobar bronchus increased. Flow limitation cannot be localized to either small

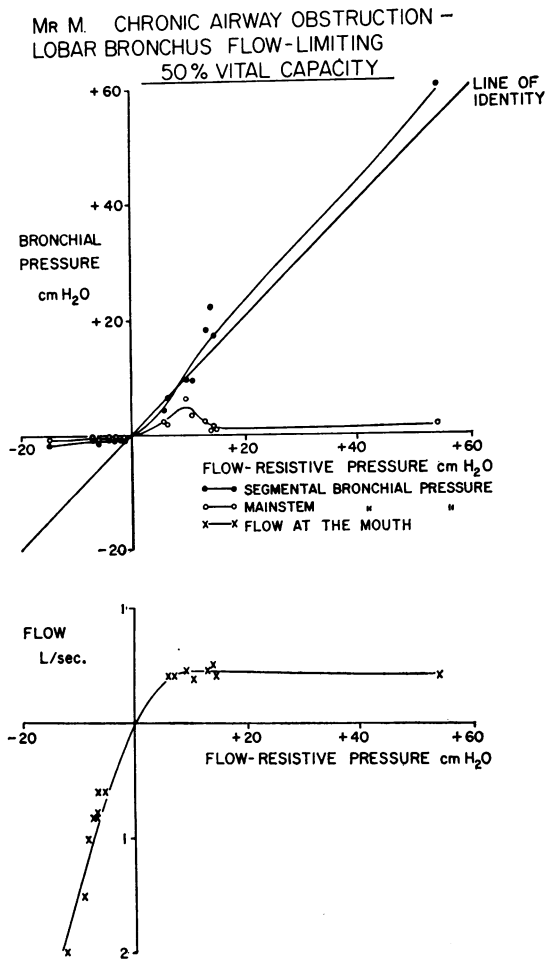

FIG. 5. EXAMPLE OF A PECULIAR FINDING SEEN IN TWO PATIENTS WHOSE LOBAR BRONCHI WERE FLOW-LIMITING. The symbols and method of plotting are the same as in Figure 1. The pressures in the segmental bronchus appear to be greater than the alveolar pressure as detected by the esophageal balloon during expiration.

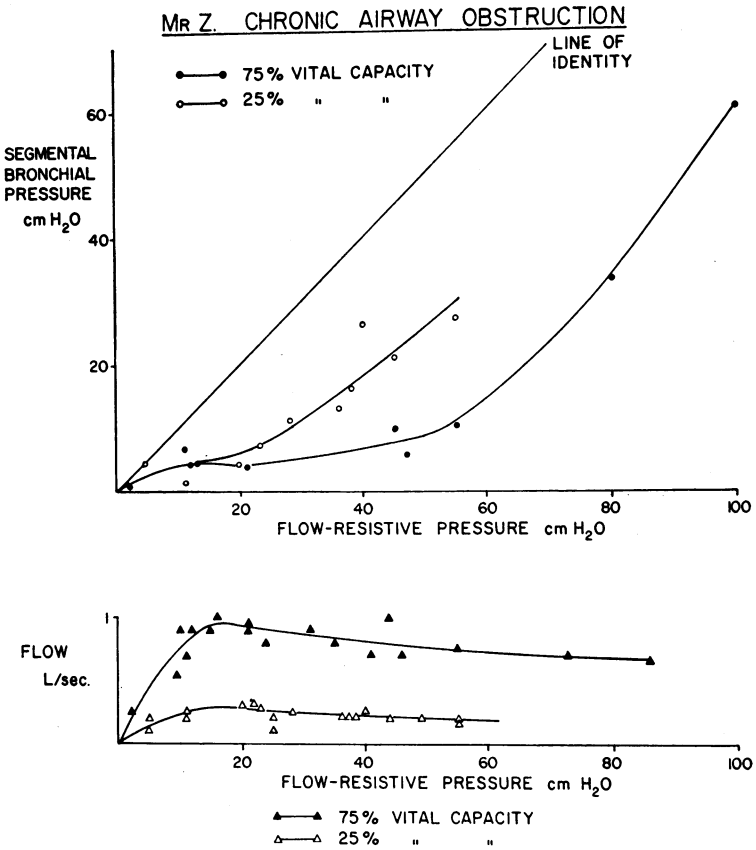

FIG. 6. EFFECT OF LUNG VOLUME ON SEGMENTAL BRONCHIAL PRESSURE. Pressures at 75% (●——●) and 25% (○——○) vital capacity are shown. The lower diagram shows the isovolume pressure-flow curves at 75% (▲——▲) and 25% (△——△) vital capacity.

TABLE III

Per cent reduction in caliber of various bronchi from maximum on inspiration to minimum on forced expiration

Subject	Intermediate stem or mainstem bronchus	Lower lobe bronchus	Segmental bronchus of lower lobe
Small airways or both small and large airways flow-limiting			
B	37.5	60.0	62.5
Z	44.5	80.0	67.0
Te	37.5	70.5	58.0
Mean	39.6	70.2	62.5
Lobar bronchi flow limiting			
K	50.0	60.0	38.0
M	25.0	86.0	22.0
Mu	23.0	82.0	44.5
S	52.5	50.0	50.0
T	41.0	66.5	50.0
Mean	38.3	68.9	40.9

or large airways as both levels of the bronchial tree appear to contribute.

Figure 5 is an example of a peculiar finding seen in two patients with emphysema. In this case the lobar bronchus was clearly flow limiting. The pressure recorded within the segmental bronchus, however, was considerably larger than the pressure in the alveoli as estimated by the esophageal balloon.

Figure 6 demonstrates the effect of lung volume on the pressure measured. The data of Hyatt, Schilder, and Fry (3) and Briscoe and DuBois (11) show that the resistance during expiration is much greater at a low lung volume as compared to a high one and peak flow is likewise considerably less. This is illustrated in the isovolume pressure-flow curves at 75 and 25% vital capacity shown at the bottom of Figure 6. The top of Figure 6 shows that the pressure drop from the

alveolus to the segmental bronchus decreased from 75 to 25% of vital capacity, approximately 50%, whereas the flow diminished by about 67%. The resistance increase in these airways is in the order of 50%. However, the pressure drop from segmental to main-stem bronchus increased 100%, and the resistance down the lobar bronchi increased about 600%. This effect of lung volume on lobar bronchial resistance during expiration was seen in all patients studied.

Table III shows the maximal percentile reduction in caliber of the segmental, lobar, and main-stem bronchi during cough or forced expiration in the eight cases in whom these measurements proved possible. Those whose small airways limited flow have been combined with those whose flow was limited by both small and large airways, as in both these groups the pressure in the segmental bronchi was considerably less than normal. There is no significant difference in the behavior of the intermediate or main-stem bronchi or the lower lobe bronchi among the three groups. However, there was a marked difference in the reaction of the segmental bronchi. In those whose small airways participated in limiting flow the mean reduction in caliber was 58% or greater, averaging 62.5%, whereas in those whose lobar bronchi were flow-limiting it was 50% or less, averaging only 40.9%.

The separation by pressure measurements into those patients in whom flow limitation occurred due to collapse of the lobar bronchi and those in whom flow limitation was due to narrowing of smaller airways cannot be made by measurement of lobar bronchial caliber. In both groups collapse occurred to the same degree. Differentiation can be made by the reaction of the segmental airways, which narrow pathologically in those patients whose small airways limit flow.

Discussion

These results indicate that the inspiratory obstruction in emphysema and bronchitis lies somewhere in the small airways between the segmental bronchi and the alveoli. During expiration, however, there are two levels of obstruction, one in the small airways and one in the large airways, usually in the lobar bronchi. The small airway obstruction is relatively fixed, is present throughout both inspiration and expiration, and is little

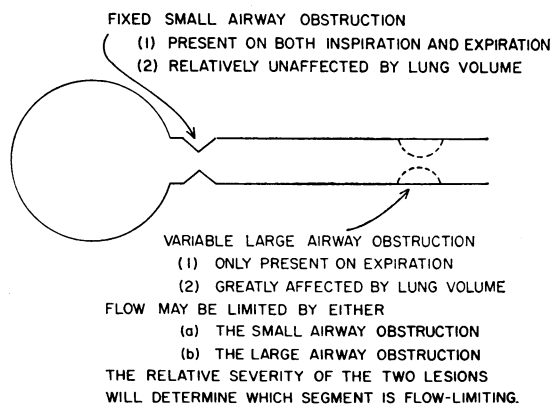

FIG. 7. DIAGRAMMATIC CONCEPT OF THE NATURE OF AIRWAY OBSTRUCTION AND FLOW LIMITATION IN BRONCHITIS AND EMPHYSEMA.

affected by changes in lung volume. The large airway obstruction is highly variable, is only present on expiration, and is greatly affected by changes in lung volume. These concepts are illustrated in Figure 7. The relative severity of the two lesions presumably determines which segment is flow limiting.

Because of the nonuniformity of pressure and flow in different regions of the lung in emphysema and bronchitis, the flow-limiting segments may also vary regionally. As established earlier, the results apply only to the lobe catheterized. In any one subject, therefore, there may be regions where the large airways are flow limiting and regions where the small airways limit flow. In this respect, the fact that the three patients thought to have bronchitis but not emphysema were flow limited by lobar bronchi is not necessarily of much significance. Nevertheless, it does demonstrate that major airway collapse and obstruction occur to a distinctly pathological degree in patients without physiological evidence of alveolar destruction. It also occurs in patients with bronchiectasis (12), and unpublished cinefluorographic evidence shows that it occurs in extrapulmonary airways (intrathoracic trachea and main-stem bronchi) as well. Collapse of large airways, therefore, is not necessarily a result of loss of parenchymal support. In those whose small airways participated in flow limitation the pressure within the lobar bronchi at the upstream end was less than normal. In those whose lobar bronchus limited flow it was generally equal to or greater than normal. The compressing force on the lo-

bar bronchus must have been greater than normal in the patients in the former group but equal to or less than normal in the latter. Reference to Table III shows that in spite of this difference in compression, the per cent of caliber reduction of the lobar bronchi was very nearly equal, and pathologically large compared to the mean normal value of 49% established by Fraser (13).

If lobar bronchial collapse is due neither to loss of alveolar support nor to an increased compression, then it must be due to a lesion within the bronchial wall itself, leading to an increase in bronchial compliance. Such lesions have been described pathologically by Wright (14), and by Kiener, Koblet, and Wyss (15).

The effect of lung volume on the large airway resistance is curious. In the normal subjects the same segments also show a marked increase in resistance during expiration as volume diminishes (7). In emphysema and bronchitis, this phenomenon will aggravate any large airway obstruction that is present. In fact, both patients whose small and large airways were flow limiting at 50% vital capacity or less showed no evidence of large airway limitation at 75% vital capacity.

It is interesting to speculate on the nature of the small airway resistance. It is possible that it is predominately bronchospastic and as such amenable to bronchodilator therapy. Its relief would be accompanied by a significant decrease in inspiratory resistance and work of breathing. During expiration, however, the large airway obstruction would predominate and expiratory flow would be only slightly improved. It is a puzzling clinical occurrence to observe decrease in wheezing and considerable subjective amelioration after bronchodilators in patients with chronic airway obstruction in whom objective measurements using the FEV, maximal midexpiratory flow rates, or peak flow rates fail to demonstrate improvement. It is possible that this is not detected because the wrong measurements have been made. The measurement of inspiratory resistance would be necessary. Gandevia (16) has suggested that when the large airways are flow limiting the timed vital capacity curve is linear, whereas when the small airways are flow limiting it is exponential. A change in shape of the curve (becoming linear after bronchodilators) might indicate a decrease in small airway obstruction.

The finding in two subjects whose lobar bronchi were flow limiting that the pressure in the segmental bronchus was greater than alveolar pressure requires explanation. For expiratory flow to occur the pressure in the alveoli distal to the segmental bronchus must have been greater than the pressure within the bronchus. It has been established that the esophageal balloon reflects the most negative pressure along its length (17). Our results may be explained if there are large variations in alveolar pressure throughout the lung and in pleural pressure across the surface of the lung in bronchitis and emphysema. The esophageal balloon might then measure an alveolar pressure that is considerably less than the pressure in the alveoli distal to the bronchial pressure catheter.

These results have an important bearing on the cough mechanism in chronic airway obstruction. For cough to be effective in riding the airways of secretion there must be a rapid velocity of air as well as an efficient ratio of particle size to tube diameter. In normal lungs there is both a high flow rate and a significant decrease in the caliber of the airways. Both of these mechanisms serve to increase velocity, which has been estimated to approach the speed of sound (18), although this is probably an overestimate (7). In airway obstruction, however, the flow rates are grossly restricted. To achieve a high velocity narrowing must be considerably greater than normal. Table III shows that this occurs in the segmental bronchi in patients whose small airways participate in flow limitation. In patients whose lobar bronchi limit flow, the airways upstream are held open by the high intraluminal pressure. Thus the velocity is low and the ratio of particle size to tube diameter relatively ineffective. In all patients cough is ineffective, but in those whose large airways limit flow, retention of secretions will be more severe. This in turn must contribute to the morbidity and might contribute to the pathogenesis of chronic bronchitis and emphysema.

Finally these results indicate that tracheal reconstructive surgery as has been suggested by others (19) would be of no benefit whatsoever in any of these patients. In none of our subjects was the trachea flow-limiting. It is conceivable that in the occasional case tracheal collapse might limit flow

and operative repair might produce some benefit. Nonetheless these cases must be extremely rare.

Summary

Bronchial pressures were measured in a segmental and main-stem bronchus in nine patients with chronic airway obstruction, simultaneously with lung volume, flow at the mouth, and esophageal pressure during a series of vital capacity breaths in which the subject attempted to increase flow rate with each breath. Subsequently, radiopaque material was instilled into the tracheobronchial tree, and cinefluorographic films were taken during forced expiration and cough. The technique permitted identification of the flow-limiting airways, location of the obstruction, and measurement of the caliber changes in the airways.

The results showed that there are two levels of obstruction in emphysema and bronchitis. One is in the small airways, is relatively fixed, present on both inspiration and expiration, and little affected by changes in lung volume, and the other obstruction is in the large airways, is highly variable, present only on expiration, and markedly affected by changes in lung volume. In five patients, expiratory flow limitation was due to the large airway obstruction; in two patients it was due to obstruction in the small airways; and in two others both large and small airways appeared to limit flow simultaneously. The relative severity of the two lesions apparently determines which obstruction is flow limiting.

In those patients in whom collapse of the large airways limited flow, there was significantly less narrowing of the segmental bronchi during forced expiration compared to the other patients. The cough mechanism is therefore more seriously impaired in the former group.

Acknowledgments

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