Contributions of Loss of Lung Recoil and of Enhanced Airways Collapsibility to the Airflow Obstruction of Chronic Bronchitis and Emphysema

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ABSTRACT We investigated the contributions of intrinsic disease of the airways, loss of lung recoil and enhanced airway collapsibility to the airflow obstruction of 17 patients with chronic bronchitis and emphysema. Airways conductance at low flow (G_{aw}), maximum expiratory flow ($\dot{V}_{E,MAX}$) and static lung recoil pressure [$P_{st}(L)$] were measured at different lung volumes, and conductance-static recoil pressure and maximum flow-static recoil pressure curves constructed. Low values of $\Delta G_{aw}/\Delta P_{st}(L)$ and $\Delta \dot{V}_E$, max/$\Delta P_{st}(L)$ were attributed to intrinsic airways disease. Airway collapsibility was assessed by comparing G_{aw} with upstream conductance on forced expiration and by the intercept of the maximum flow-static recoil curve on the static recoil pressure axis (P_{tm}').

All patients had reduced G_{aw} at all volumes but in seven $\Delta G_{aw}/\Delta P_{st}(L)$ was normal. On forced expiration, maximum flow in all patients was reduced more than could be accounted for by loss of lung recoil. $\Delta \dot{V}_{E,MAX}/\Delta P_{st}(L)$ was reduced in the patients in whom $\Delta G_{aw}/P_{st}(L)$ was low. In contrast $\Delta \dot{V}_{E,MAX}/\Delta P_{st}(L)$ was normal in three and only slightly reduced in another three of the seven patients with normal $\Delta G_{aw}/\Delta P_{st}(L)$. In these patients G_{aw} greatly exceeded upstream conductance and P_{tm}' was increased.

We conclude that loss of lung recoil could account for the reduction in resting airways dimensions in 7 of the 17 patients. Enhanced airway collapsibility commonly contributed to reduction in maximum flow. In three patients the airflow obstruction could be entirely accounted for by loss of lung recoil and enhanced airway collapsibility.

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INTRODUCTION

Pathological change in the airway wall and lumen leading to narrowing and occlusion is commonly considered to be the most important abnormality in chronic airways obstruction. Nevertheless, it has been recognized for many years that in some patients loss of lung recoil and abnormal dynamic narrowing of airways must contribute to the expiratory difficulty (1, 2). Recent studies have shown that lung recoil pressure is an important determinant of the forces distending the airways during quiet breathing (3, 4), and of the driving pressure for maximum flow on forced expiration (5, 6); in addition, it has been shown that enhanced collapsibility of the airways will reduce maximum flow (6). In this paper we attempt to quantify the contributions of pathological change in the airway or its lumen of loss of lung recoil and of enhanced airway collapsibility to the airflow obstruction of 17 patients with "chronic bronchitis and emphysema." Studies have been made during quiet breathing and during forced expiration, and the results indicate that loss of recoil pressure plays an important role in reducing airway dimensions at low flow and that enhanced airway collapsibility contributes to the reduction in maximum expiratory flow ($\dot{V}_{E,MAX}$).[1] A preliminary report has already been published (7).

[1] *Abbreviations used in this paper:* FEV_1, forced expiratory volume in 1 s; FRC, functional residual capacity; G_{aw}, total airways conductance; G_s, conductance of the airways in the S segment; G_{us}, conductance of the upstream segment; $P_{st}(L)$, static transpulmonary pressure; P_{tm}', critical transmural pressure of flow-limiting airways; SG_{aw}, specific airways conductance; TLC, total lung capacity; $\dot{V}_{E,MAX}$, maximum expiratory flow.

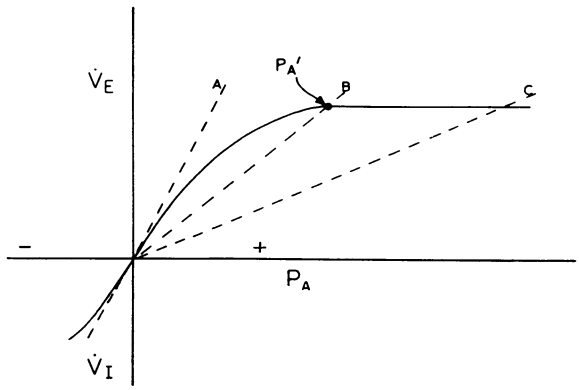

FIGURE 1 Schematic isovolume pressure flow curve in mid-vital capacity. Conductance is represented graphically by the slope of the interrupted lines. Because the pressure-flow relationship is curvilinear, conductance varies with the alveolar pressure applied. A represents the conductance at zero flow [in practice obtained by measuring the pressure-flow slope between zero flow and an inspiratory flow ($\dot{V}_I$) of 0.5 liter/s]. B represents the conductance at the minimum alveolar pressure associated with maximum expiratory flow (P_A'). C represents the conductance at a high alveolar pressure. The reduction in conductance between B and C is accounted for entirely by increased dynamic compression of large airways in the downstream segment, while conductance of the upstream segment is unchanged (see text).

METHODS

Airways are elastic structures whose dimensions vary with changes in lung volume and with the dynamic forces developed during breathing. Both these factors can be controlled by studying the relation between alveolar pressure and flow over a range of pressures at a single lung volume (8). A typical isovolume pressure-flow curve is shown in Fig. 1. On such a curve, total airways conductance (flow/alveolar pressure) is represented graphically by the slope joining any individual pressure-flow point to the origin, so even at a single lung volume, conductance varies continuously with the alveolar pressure applied. In this complex situation there are two conditions under which at least some of the airway dimensions are fixed. The first is during breath-holding, when gas flow is zero and alveolar pressure equals atmospheric pressure. The second is at high values of alveolar pressure, where there is a plateau of expiratory flow at the maximum value and flow becomes independent of the driving pressure. Although on the plateau of an isovolume pressure-flow curve, total airway conductance decreases in parallel with increases in alveolar pressure, the intrabronchial pressure measurements of Macklem and Wilson (9) have shown that over the middle of the vital capacity in normal men this decrease is accounted for entirely by progressive dynamic compression of the largest intrathoracic airways. Measuring $\dot{V}_{E,MAX}$ therefore not only assesses the maximum dynamic performance of the lungs but can also provide information about the dimensions of the smaller airways (upstream segment of Mead, Turner, Macklem, and Little (5), see below) during forced expiration.

In the present patients we have examined these two points on the isovolume pressure-flow curve by measuring conductance close to zero flow and $\dot{V}_{E,MAX}$ at a variety of lung volumes. As shown in Fig. 1, between these two points on the isovolume pressure-flow curve the pressure-flow relation is curved. Although this is usually the relevant part of the curve during tidal breathing, it is much more difficult to analyse and we make no attempt to do so in the present paper.

Static dimensions of the airways: the conductance-static recoil plot. Our aim in this study was to distinguish changes in airway size that are caused by reduction in airway-distending forces from those that reflect a change in the airway wall or lumen itself. We use the term intrinsic disease of the airways to describe the situation where airway narrowing has to be ascribed to changes in the airway wall or lumen.

In intact man the relationship between airway dimensions and airway distending pressure can be approximated by plotting total airways conductance (G_{aw}), measured at low flows, against static transpulmonary pressure [$P_{st}(L)$]. Conductance provides a relatively sensitive measurement of the overall diameters of the tracheobronchial tree, because for laminar flow, conductance is proportional to the fourth power of the radius of the airways. There is empirical evidence that $P_{st}(L)$ is a useful indicator of the forces distending the airways during breath-holding or breathing at low flows. In man, when the relation between $P_{st}(L)$ and volume is altered by strapping the chest wall, airway conductance remains closely related to $P_{st}(L)$ (3, 10). Hyatt and Flath (11) found that in dogs there were only small differences between the diameters of intrapulmonary airways when studied at a given $P_{st}(L)$ in the intact lung and at the same transbronchial pressure after the lung parenchyma had been dissected away. Although these studies indicate that $P_{st}(L)$ is closely related to airway dimensions, this does not necessarily mean that peribronchial pressure is identical with pleural surface pressure. A recent theoretical analysis by Mead, Takishima, and Leith (4) suggests that the forces distending the bronchi would be exactly equivalent to $P_{st}(L)$ only if the specific compliance of alveoli and bronchi were equal and if there were no tension in the limiting membrane of the bronchus. We know of no direct comparisons of specific compliance of bronchi and alveoli in human lungs; it has been suggested that in dog lungs specific compliance of bronchi may be less than that of alveoli (4), although other recent experiments have not shown

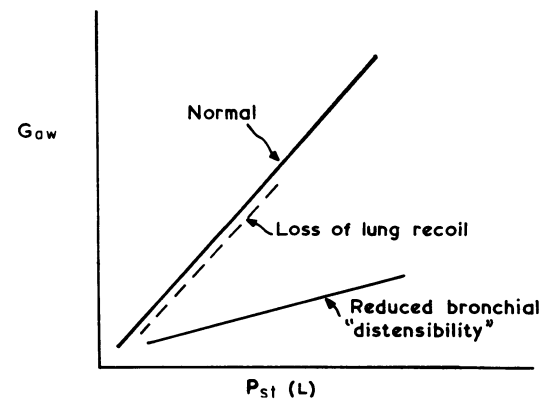

FIGURE 2 Schematic conductance-static recoil plot. Loss of lung recoil does not affect the conductance-static recoil slope. A reduced slope indicates a reduction in the overall distensibility of the tracheobronchial tree.

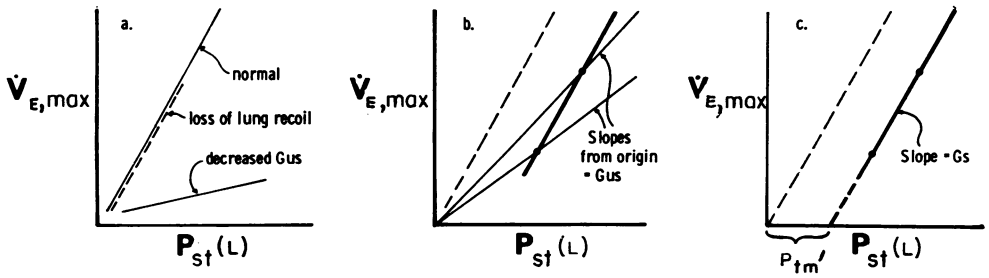

FIGURE 3 Schematic maximum flow-static recoil plots. *a*. Loss of lung recoil does not affect the maximum flow-static recoil slope. A decrease in the maximum flow-static recoil slope indicates a decrease in upstream conductance. *b*. Parallel displacement of maximum flow points (heavy continuous line) to higher values of static recoil pressure. In the analysis of Mead et al. (5) this change is also interpreted as a decrease in upstream conductance. Interrupted line indicates a normal maximum flow-static recoil curve. *c*. Graphical interpretation of the maximum flow-static recoil curve (heavy continuous line) shown in *b* using the analysis of Pride et al. (6). See text.

consistent differences (12). If specific compliance of the bronchi were less than that of the alveoli, then the forces distending the bronchi would be systematically greater than transpulmonary pressure (4). In plotting conductance against $P_{st}(L)$, we are using recoil pressure as an indicator of the forces distending the airways and not necessarily implying that $P_{st}(L)$ is precisely equivalent to the tissue forces distending the airways.

The change in conductance with change in static recoil pressure ($\Delta G_{aw}/\Delta P_{st}(L)$) is a function of the radial distensibility of the bronchial tree and is analogous to the measure of bronchial distensibility in an isolated bronchus obtained by plotting bronchial diameter versus transbronchial pressure. $\Delta G_{aw}/\Delta P_{st}(L)$, however, represents the lumped distensibility of all the bronchial tree and will be affected by changes in any of the bronchial generations. A reduction in $\Delta G_{aw}/\Delta Pst(L)$ may indicate either stiffness of individual airways or loss or complete occlusion of parallel airways (Fig. 2); this is exactly comparable to the way in which a reduced lung compliance may reflect stiffening of individual alveoli or loss of alveoli. With loss of lung recoil without any intrinsic abnormality of the airway wall or lumen, $\Delta G_{aw}/\Delta P_{st}(L)$ will be within the normal range.

Dynamic performance of the lungs: the maximum flow-static recoil plot. Mead et al. (5) have shown that $V_{E,MAX}$ at any lung volume where there is a plateau of flow on the isovolume pressure-flow curve can be analysed in terms of the relationship between $P_{st}(L)$ and the conductance of the airways upstream to equal pressure points (conductance of the upstream segment, G_{us}):

$$V_{E,MAX} = P_{st}(L) \cdot (G_{us}). \quad (1)$$

In normal subjects from about 70% down to about 30% of the vital capacity equal pressure points become fixed on forced expiration at lobar or segmental bronchi (9), and so in these circumstances the upstream segment corresponds approximately to the intrapulmonary airways. At lower lung volumes in normal subjects and throughout the vital capacity in some patients with chronic airflow obstruction (13) the equal pressure points are situated in more peripheral airways.

Eq. 1 can be expressed graphically by plotting maximum flow against static recoil pressure (Fig. 3*a*). With loss of lung recoil pressure $\Delta V_{E,MAX}/\Delta P_{st}(L)$ will remain in the normal range. A reduction in $\Delta V_{E,MAX}/\Delta P_{st}(L)$ indicates a decrease in upstream conductance. In addition a parallel displacement of maximum flow points to higher static recoil pressures without any change in $\Delta V_{E,MAX}/\Delta P_{st}(L)$ will be interpreted in the analysis of Mead et al. as a decrease in upstream conductance, which is particularly marked at low recoil pressure (Fig. 3*b*).

Pride, Permutt, Riley, and Bromberger-Barnea (6) developed a slightly different equation to predict $V_{E,MAX}$ at any lung volume with a plateau of flow on the isovolume pressure-flow curve:

$$V_{E,MAX} = (P_{st}(L) - P_{tm'}) \cdot (G_s). \quad (2)$$

where $P_{tm'}$ is the critical transmural pressure (difference between lateral airway and extra-airway pressure) at which the flow-limiting airways narrow sufficiently to restrict flow, and G_s is the conductance of the airways in the S segment during forced expiration. In this analysis the S segment comprises all the airways between the alveoli and those which form the flow-limiting segment. Hence the S segment will be shorter than the upstream segment of Mead et al. (5) if $P_{tm'} > 0$ and longer than the upstream segment if $P_{tm'} < 0$. This equation distinguishes two different abnormalities of the airways, a decrease in conductance of the smaller airways (G_s) and an enhanced collapsibility of flow-limiting airways (shown by an increase in $P_{tm'}$), which in the analysis of Mead et al. would both be interpreted as a decrease in upstream conductance. If G_s and $P_{tm'}$ are unaffected by changes in lung volume, their values can be derived from a maximum flow-static recoil plot, G_s being represented by the slope of the maximum flow-static recoil points themselves ($\Delta V_{E,MAX}/\Delta P_{st}(L)$) and $P_{tm'}$ by their intercept on the static recoil axis (Fig. 3*c*). In this analysis parallel displacement of maximum flow points to higher recoil pressures would be interpreted as being due to an increase in $P_{tm'}$, implying enhanced collapsibility of flow-limiting airways (Fig. 3*c*).

Experimental procedure. In each subject we measured total airways conductance, $V_{E,MAX}$, and $P_{st}(L)$ over as wide a range of lung volumes as was possible. Total airways conductance (G_{aw}) was measured in a variable pressure, constant volume body plethysmograph by the panting technique (14). As discussed above, the aim was to measure conductance close to zero flow so that there would be no dynamic effects on airway dimensions. Patients with severe

TABLE I

Results in Normal Subjects and Patients with Airflow Obstructions

Normal subjects	Sex	Age	Height	FEV_1	VC	$\dot{V}_{max}$ at 50% VC	TLC	TLC	FRC	C_{st}(L) at FRC	G_{aw} at FRC	SG_{aw} at FRC	$\Delta G_{aw}/\Delta Vol$	$\Delta G_{aw}/\Delta P_{st}$(L)	P_{tm}'	G_s
number		*yr*	*m*	*liter*	*liter*	*liter/s*	*liter*	*% predicted*	*liter*	*liter/cm H_2O*	*liter/s/cm H_2O*	*G_{aw}/liter lung vol*			*cm H_2O*	*liter/s/cm H_2O*
1	M	27	1.71	3.5	4.6	4.9	6.2	98	3.1	0.23	1.01	0.32	0.54	0.092	−3.8	0.47
2	M	48	1.74	3.5	5.0	8.2	8.0	117	4.3	0.36	0.66	0.15	0.45	0.183	+0.8	0.97
3	M	36	1.78	4.0	5.9	5.5	7.6	110	4.3	0.28	0.79	0.18	0.32	0.108	0	0.50
4	M	34	1.86	3.9	5.2	3.9	8.2	111	4.9	0.36	0.60	0.12	0.46	0.180	+1.7	0.80
5	M	33	1.67	4.0	5.0	5.0	6.3	105	3.4	0.24	0.76	0.22	0.27	0.055	−2.2	0.53
6	M	40	1.64	3.4	4.2	6.2	6.1	107	3.3	0.25	0.56	0.17	0.34	0.075	−0.5	0.74
7	M	32	1.86	5.6	7.0	5.9	8.8	116	4.3	0.37	1.57	0.36	0.38	0.116	−3.0	0.66
8	M	39	1.87	5.2	6.2	7.0	8.1	106	4.0	0.28	1.25	0.31	0.45	0.120	0	0.66
9	M	27	1.73	3.4	4.8	2.8	5.8	89	3.2	0.31	0.42	0.13	0.37	0.108	0	0.48
10	F	29	1.83	5.0	6.1	4.8	8.2	118	4.2	0.28	0.66	0.16	0.30	0.078	−0.9	0.48
Mean		34.5	1.77	4.15	5.40	5.42	7.33	107.7	3.90	0.30	0.83	0.212	0.39	0.111	−0.8	0.63
SD		6.6	0.08	0.82	0.87	1.52	1.10	9.0	0.61	0.05	0.35	0.087	0.08	0.043	1.7	0.17
SEM		2.1	0.03	0.26	0.27	0.48	0.35	2.9	0.19	0.02	0.11	0.027	0.03	0.013	0.5	0.05
Patients																
11	M	60	1.70	1.1	3.3	0.9	7.6	122	5.7	0.28	0.28	0.05	0.11	0.037	+0.6	0.23
12	F	65	1.54	1.0	2.1	0.5	5.2	131	3.5	0.42	0.25	0.07	0.35	0.110	+3.4	0.40
13	M	69	1.52	0.8	2.4	0.5	6.0	130	4.7	0.28	0.17	0.04	0.06	0.019	+2.5	0.22
14	M	57	1.67	0.9	2.8	1.3	7.1	118	5.0	0.36	0.24	0.05	0.14	0.035	+4.5	0.38
15	M	61	1.73	1.4	3.3	0.6	7.6	125	5.1	0.67	0.18	0.03	0.21	0.075	+2.9	0.42
16	M	66	1.81	1.7	3.5	1.6	8.9	124	6.9	0.83	0.37	0.05	0.26	0.110	+5.6	0.75
17	M	67	1.62	0.7	2.2	0.7	7.6	136	6.6	0.32	0.39	0.06	0.16	0.045	+3.4	0.55
18	M	57	1.67	1.6	3.4	1.2	8.4	141	5.9	0.45	0.47	0.08	0.27	0.096	+1.6	0.37
19	M	54	1.60	0.4	2.6	0.7	8.0	148	6.5	0.45	0.17	0.03	0.10	0.038	+3.7	0.27
20	M	64	1.67	0.6	2.3	0.4	7.4	123	6.2	0.21	0.26	0.04	0.11	0.022	+1.0	0.11
21	M	66	1.71	1.4	3.2	0.7	9.0	143	6.9	0.31	0.16	0.02	0.10	0.030	+3.9	0.25
22	M	64	1.71	1.1	2.8	0.6	6.8	107	4.9	0.35	0.27	0.05	0.10	0.026	+5.8	0.26
23	M	42	1.69	0.7	2.2	0.4	5.7	92	4.6	0.19	0.10	0.03	0.11	0.030	+2.1	0.17
24	M	59	1.74	0.7	2.4	1.1	8.3	125	6.3	0.71	0.14	0.02	0.08	0.026	+5.0	0.41
25	M	68	1.73	1.5	4.0	0.4	7.8	120	5.9	0.83	0.40	0.07	0.18	0.184	+2.2	0.44
26	M	68	1.63	1.2	3.1	0.7	7.4	131	5.6	0.26	0.41	0.07	0.70	0.156	+3.3	0.36
27	M	56	1.68	0.5	3.0	0.5	8.8	147	7.0	0.47	0.36	0.05	0.17	0.090	+0.6	0.19
Mean		61.4	1.67	1.02	2.86	0.74	7.51	127.2	5.72	0.44	0.27	0.048	0.19	0.066	+3.1	0.34
SD		6.9	0.07	0.40	0.55	0.35	1.09	14.2	0.98	0.21	0.11	0.018	0.15	0.050	1.6	0.16
SEM		1.7	0.02	0.10	0.13	0.08	0.27	3.4	0.24	0.05	0.03	0.004	0.04	0.012	0.4	0.04

VC = vital capacity; $\dot{V}_{max}$ at 50% VC = maximum expiratory flow at 50% of expiratory VC; C_{st}(L) at FRC = static lung compliance expressed as the slope of the expiratory PV curve between FRC and 0.5 liter above FRC; G_{aw} = total airways conductance, measured at an inspiratory flow of 0.5 liter/s; SG_{aw} = specific airways conductance, value of airways conductance divided by the thoracic gas volume (in liters) at which it was measured; $\Delta G_{aw}/\Delta Vol$ = slope of relationship between airways conductance and thoracic gas volume; $\Delta G_{aw}/\Delta P_{st}$(L) = slope of relationship between airways conductance and static recoil pressure of the lung.

airflow obstruction show considerable looping of the expiratory pressure-flow curve during panting, so we measured the slope between zero flow and an inspiratory flow of 0.5 liter/s, during panting at about 2 breaths/s. Dynamic changes on inspiration at these flow rates are small. An average of 15 measurements over a range of lung volumes was made and a line of best fit drawn by eye through the points. Total lung capacity (TLC) was determined by obtaining thoracic gas volume by panting against a closed shutter (15) and then adding the volume inspired as the patient made a full inflation on opening the shutter. The mean of at least four measurements was taken. Functional residual capacity (FRC) and residual volume were derived from separate records of tidal breathing and vital capacity maneuvers. $V_{E,MAX}$-volume curves were obtained with the patient seated within a variable-volume body plethysmograph (16) and breathing out to the room via a Fleisch No. 3 or 4 pneumotachograph. The box-spirometer system was pressure-compensated and the amplitude and phase of volume signals showed no change with increasing frequency up to 6.5 cycle/s. The pressure drops across the pneumotachograph screens were linear up to flows of 400 liter/min (No. 3) and 600 liter/min (No. 4). Expiratory flow was plotted against change in thoracic gas volume on a Tektronix 564 storage oscilloscope (Tektronix, Inc., Beaverton, Ore.). A series of full vital capacity maneuvers was performed with efforts varying up to maximum and the largest expiratory flows at a given volume were recorded (17). $P_{st}(L)$ was measured with an esophageal balloon containing 0.5 ml air (18) at frequent intervals in the vital capacity, volume being measured with the patients seated within the variable-volume body plethysmograph. A mean pressure-volume curve was constructed for each patient from at least three closely reproducible curves; occasional curves with more positive esophageal pressures were ignored. Static expiratory compliance was taken as the slope of the expiratory pressure-volume curve between FRC and 500 ml above FRC. The forced expiratory volume in 1 s (FEV_1), and vital capacity were measured with a timed spirometer.

From these measurements, conductance-static recoil and maximum flow-static recoil plots were constructed as follows: (*a*) Conductance-static recoil plot, conductance at each lung volume was read off the conductance-volume curve and plotted against static recoil pressure for this volume. In all subjects an attempt was made to measure both inspiratory and expiratory pressure-volume curves, but in most subjects the expiratory pressure-volume curves were more repeatable. There was relatively little hysteresis between inspiratory and expiratory pressure-volume curves in the patients and so expiratory pressure-volume curves were used in all except one patient in whom esophageal spasm at full inflation prevented reliable expiratory curves being obtained. (*b*) Maximum flow-static recoil plot, $P_{st}(L)$ obtained on the expiratory pressure-volume curve was plotted against the value of $\dot{V}_{E,MAX}$ found at the same volume on the $V_{E,MAX}$-volume curve. Flows close to peak expiratory flow were ignored, since these are effort-dependent. The slope of the maximum flow-static recoil points, $\Delta\dot{V}_{E,MAX}/\Delta P_{st}(L)$, was estimated between 70% and 30% of the vital capacity to obtain G_s; the intercept of this slope on the pressure axis was used to estimate P_{tm}'.

All volumes were expressed at body temperature and pressure.

Subjects studied. 10 normal subjects (9 men and 1 woman, average age 34.5 yr) and 17 patients with chronic airflow obstruction (16 men and 1 woman, average age 61.4 yr) were studied. Only two of the normal subjects were cigarette smokers and none had any history of serious respiratory disease. The patients all had chronic cough and expectoration and were present or ex-smokers. They had been under observation for at least 2 yr during which time there had been little variation in airways obstruction, either spontaneously or after adrenergic bronchodilator drugs or (in most cases) after controlled trial of prednisolone. Attempts were made to select patients who showed the clinical and physiological features of either the "emphysematous" or the "bronchial" types of chronic airways obstruction (19).

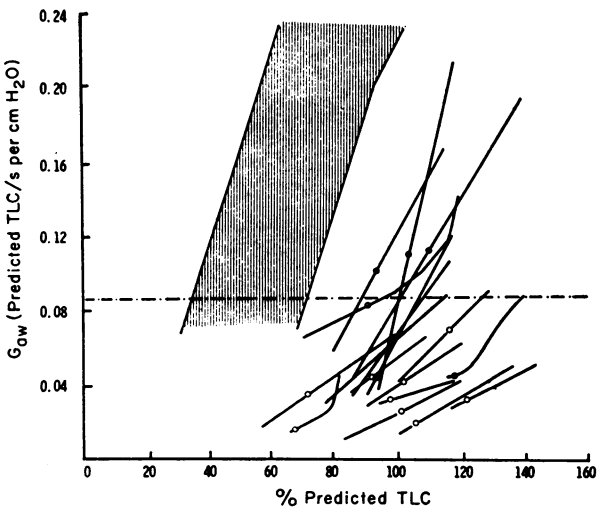

FIGURE 4 G_{aw} (measured at low flow rates) plotted against lung volume. To correct for differences in size of the subjects lung volume is expressed as percent of predicted TLC and for conductance flow rate is expressed as predicted TLC per second. The shaded area indicates the normal range which extends upwards to higher levels of conductance. The horizontal interrupted line indicates a normal value of conductance at FRC, corresponding to 0.5 liter/s/cm H_2O for a man with a TLC of 6 liter. The open circles indicate the values of conductance when the patients were asked to pant after a period of quiet breathing (see text).

RESULTS

Anthropometric data and measurements of static and dynamic lung volumes, static lung compliance, and airways conductance in the normal subjects and the patients with airways obstruction are summarized in Table I. The patients were smaller than the normal subjects and the predicted total lung capacity (TLC) (20) of the largest normal subject was 192% of the TLC predicted for the smallest patient. In the Table, flow rates have been expressed in liters per second, but in Figs. 4–8, an attempt has been made to correct for these great differences in size by expressing all flow rates as predicted TLC per second. In normal children and adolescents maximum flow rates and conductance values have been shown to be closely related to TLC (21).

FEV_1, lung volumes, and static lung compliance. FEV_1 was reduced, and functional residual capacity and residual volume were increased in all the patients with

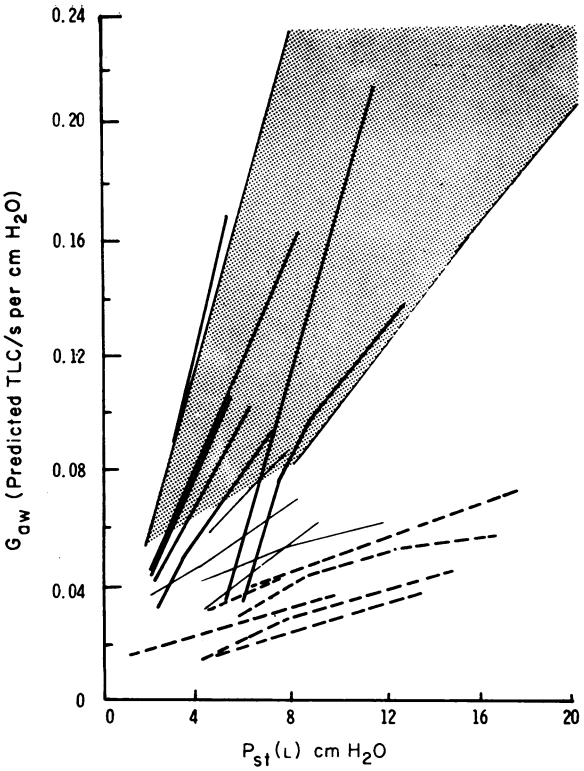

FIGURE 5 G_{aw} (measured at low flow rates and expressed as predicted TLC per second per centimeter H_2O) plotted against lung recoil pressure. The shaded area indicates the lower part of the normal range. The results from all 17 patients are shown. In the three following figures (6, 7, and 8) only the patients who had a normal conductance-static recoil slope (indicated by the thick, continuous lines) and those with a very abnormal conductance-static recoil slope (indicated by the interrupted lines) are shown. The patients with intermediate values of conductance-static recoil slope are indicated by thin, continuous lines.

airflow obstruction (Table I). Values of TLC and static lung compliance in the patients were more variable, but TLC was often above 130% of the predicted value and eight patients had values of static lung compliance which were greater than those found in any of the normal subjects.

Relation between total airways conductance and lung volume. In all patients the conductance-volume points were displaced to higher lung volumes than in the normal subjects (Fig. 4). As a result specific airways conductance (SG_{aw}) at FRC (obtained by dividing the value of conductance at FRC by the value of FRC in liters) was abnormal in all the patients (Table I). In addition, in 14 of the 17 patients the value of conductance at FRC was less than 0.4 liter/s/cm H_2O, which is usually taken as the lower limit of normal. In the remaining three patients the absolute value of conductance was in the normal range and the abnormality in specific conductance was entirely due to the increase in FRC.

Routine measurements of airways conductance in patients with airflow obstruction are often made at a volume above FRC measured during quiet breathing, since lung volume tends to increase at the onset of the panting maneuver. When the present patients were asked to pant after breathing quietly in the normal tidal range, the average lung volume at which conductance was measured was 0.4 liter greater than FRC and conductance averaged 0.08 liter/s/cm H_2O greater than the value at FRC. In Fig. 4 the open circles indicate the results obtained when patients were asked to pant after a normal tidal breathing pattern and without any deliberate attempt to change lung volume. In the Table, values of conductance at the actual FRC have been recorded.

In most patients the conductance-volume slope had a large intercept on the volume axis. As a result specific conductance in the patients will not be independent of the volume at which it is measured, but will increase with increase in lung volume.

Relation between total airways conductance (at low flows) and lung recoil pressures. There was considerable variation in the relation between conductance and P_{st}(L) in the patients, with a nearly 10-fold difference between the highest and lowest $\Delta G_{aw}/\Delta P_{st}$(L) slopes (Table, Fig. 5). In seven of the patients these slopes fell within the range obtained in our normal subjects; in these patients the abnormalities in conductance shown in Fig. 4 could be attributed to a reduction in lung recoil pressure at a given lung volume. In contrast, we assume that the patients with low $\Delta G_{aw}/\Delta P_{st}$(L) slopes have intrinsic disease of the airway wall or lumen. We were interested in whether there were differences in the dynamic performance of the lungs of patients with normal and abnormal $\Delta G_{aw}/\Delta P_{st}$(L) slopes. In subsequent figures therefore we have confined our analysis to the seven patients with normal $\Delta G_{aw}/\Delta P_{st}$(L) slopes and the six patients with the most abnormal slopes (Fig. 5), and have omitted those with intermediate abnormality. The mean FEV_1 was 1.27 liter in the patients with normal $\Delta G_{aw}/\Delta P_{st}$(L) slopes and 0.93 liter in the six patients with markedly abnormal slopes; only one of the eight patients studied with an FEV_1 of less than 1.0 liter had a normal slope. The mean expiratory static compliance in the patients with a normal $\Delta G_{aw}/\Delta P_{st}$(L) slope was 0.56 liter/cm H_2O, as compared to 0.37 liter/cm H_2O in the group with a reduced slope.

Relation between $V_{E,MAX}$ and lung recoil pressure. In all patients $V_{E,MAX}$ was reduced at any given value of lung recoil pressure. The abnormality of the maximum

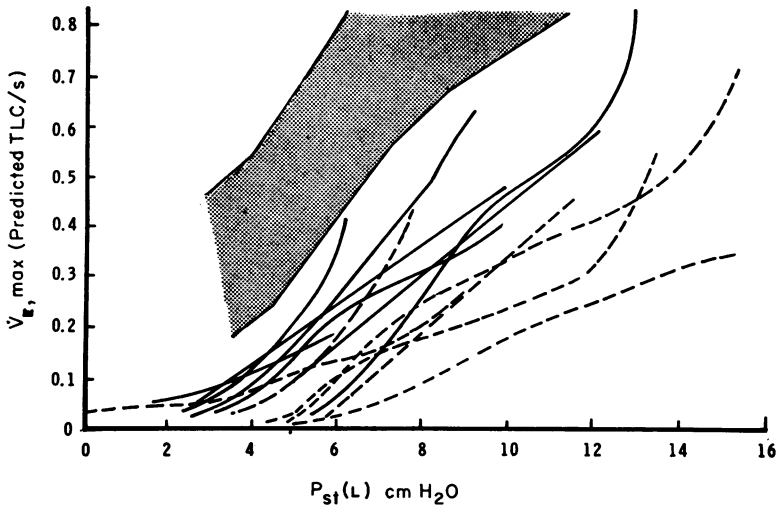

FIGURE 6 $\dot{V}_{E,MAX}$ (expressed as predicted TLC per second) plotted against lung recoil pressure. Lower part of normal range indicated by shaded area. Continuous lines indicate patients with normal $\Delta G_{aw}/\Delta P_{st}(L)$, interrupted lines those with a marked reduction in $\Delta G_{aw}/\Delta P_{st}(L)$.

flow-static recoil curves was greatest in the patients with low $\Delta G_{aw}/\Delta P_{st}(L)$ values (Fig. 6).

G_s in the normal subjects lay between 0.069 and 0.142 predicted total lung capacity/s/cm H_2O; it was below this normal range in 13 of the 17 patients. P_{tm}' was above the upper limit of our normal range (+ 1.7 cm H_2O) in 13 patients so that commonly the maximum flow-static recoil curve in the patients showed abnormalities in both slope (G_s) and intercept (P_{tm}'). However the seven patients with normal $\Delta G_{aw}/\Delta P_{st}(L)$ values had relatively little reduction in G_s. Three of these patients had values of G_s within the normal range and in three more G_s was between 0.062 and 0.068 predicted TLC/s/cm H_2O. In these seven patients the average value of G_s was 0.072 predicted TLC/s/cm H_2O compared to mean values of 0.094 in the control subjects and 0.047 in the patients with low $\Delta G_{aw}/\Delta P_{st}(L)$ values. The mean increase in P_{tm}' was slightly less in the patients with a normal $\Delta G_{aw}/\Delta P_{st}(L)$ slope (+ 2.8 cm H_2O) than in those with reduced $\Delta G_{aw}/\Delta P_{st}(L)$ slopes (+ 4.0 cm H_2O).

Relationship between total airways conductance at low flows and $\dot{V}_{E,MAX}$ *(Fig. 7).* There were considerable differences between the two groups of patients. In general those with a low $\Delta G_{aw}/\Delta P_{st}(L)$ slope had relatively good $\dot{V}_{E,MAX}$ in relation to the value of total conductance at the same lung volume, while the reverse was found in the patients with a normal $\Delta G_{aw}/\Delta P_{st}(L)$ slope.

DISCUSSION

The striking feature of the results is that in 7 of the 17 patients the observed reduction in conductance (measured at low flows) could be accounted for by the loss of lung recoil pressure. In no patient, however, was the loss of lung recoil pressure sufficient to account directly for the reduction in $\dot{V}_{E,MAX}$. This difference between static and dynamic measurements is discussed below.

Limitations in the methods. Previous workers (3) who have related airway conductance to lung recoil pressure have obtained lung recoil pressure during occlusion of the shutter at the end of each period of panting. In pilot studies we found that the scatter of such directly obtained conductance-static recoil points was at least as great as that of conductance-volume points; as our patients tolerated the repeated panting procedure better when they were required to do this without an

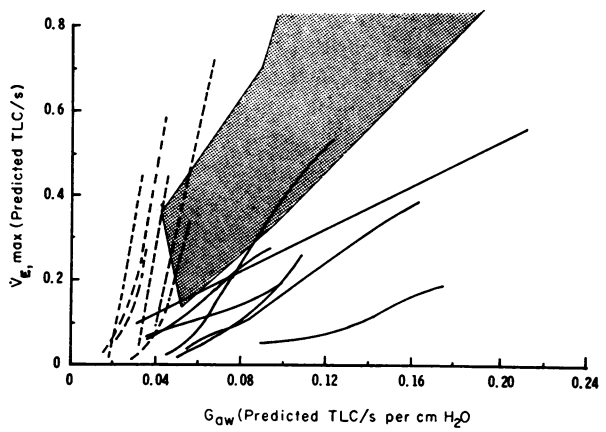

FIGURE 7 Relation between G_{aw} (measured at low flows) and $\dot{V}_{E,MAX}$. For both measurements flow rates are expressed as predicted TLC per second. The shaded area represents the lower part of the normal range. Continuous lines indicate patients with normal $\Delta G_{aw}/\Delta P_{st}(L)$, interrupted lines those with a marked reduction in $\Delta G_{aw}/\Delta P_{st}(L)$.

esophageal balloon in place, we chose to construct our conductance-static recoil curves by drawing lines of best fit through 12–18 conductance-volume points and through 3–5 expiratory pressure-volume curves in each patient. This difference in technique does not seem to have systematically affected the results, since the $\Delta G_{aw}/\Delta P_{st}(L)$ slopes in our normal subjects are very similar to those previously reported (3). A possible source of error is that we have compared our normal subjects with patients who were considerably older. We know of no evidence as to whether the conductance-static recoil curve changes with age but we found no obvious difference in the position or the slope of the curve between the older and younger individuals in our normal series. Although the maximum flow-static recoil relationship was approximately linear in most of the normal subjects, in about a third of the patients it was curved so that the $\Delta \dot{V}_{E,MAX}/\Delta P_{st}(L)$ slope declined as static recoil pressure and lung volume were reduced. In such curves we estimated G_s from the lower part of the $\Delta \dot{V}_{E,MAX}/\Delta P_{st}(L)$ slope between 50% and 30% of the vital capacity and P_{tm}' from the intercept of this part of the $\Delta \dot{V}_{E,MAX}/\Delta P_{st}(L)$ slope, so as to derive the lowest possible values of G_s and P_{tm}'.

Significance of the conductance-static recoil plot. In 7 of the 17 patients conductance-static recoil points were within the normal range so that there was no functional evidence of intrinsic disease of the bronchi. This does not necessarily exclude the presence of anatomical changes in these airways, for the following reasons. (*a*) In diseased lungs conductance will tend to rise with increasing frequency of breathing (22) and will strictly reflect static airway dimensions only if the measurement is made at low flow rates and at a very low frequency of breathing, whereas the present measurements were made at a frequency of about 2 breaths/s. However, values of conductance at 2 cycle/s in the patients with normal conductance-static recoil relationships were greater than 0.2 liter/s/cm H_2O at FRC, and in such patients changes in conductance between frequencies of 0.3 and 2 cycle/s are small (see Figs. 6 and 9 in reference 22). Although we cannot exclude large changes in conductance at frequencies less than 0.3 cycle/s, it appears unlikely that frequency dependence of conductance played an important part in explaining the findings in the patients with normal conductance-static recoil relationships, but it will have led us to underestimate the severity of the airway disease in the patients with more abnormal values of conductance. (*b*) Even at a very low breathing frequency a total airway conductance within the normal range cannot exclude anatomical changes in the airways, because the measurement is relatively insensitive to abnormalities in the smaller airways (23), and furthermore reflects the lumped effects of all the airway generations and so might result from the combination of narrowing in some airways and increased dimensions of other airways.

In the patients with reduced $\Delta G_{aw}/\Delta P_{st}(L)$ slopes, the major factor reducing static airway dimensions was a reduction in bronchial distensibility, but in addition there was almost always some loss of recoil pressure. We were unable to distinguish whether the reduced distensibility was due to stiffening of individual airways or due to a reduction in the number of parallel airways by destruction or occlusion of the lumen.

The only previous study of the relation between conductance and $P_{st}(L)$ in patients with chronic airflow obstruction using the present method, appears to be that of Butler, Caro, Alcala, and DuBois (3). In their patients "there was less than the normal change in airways conductance from alterations of lung elastic pressure" but they do not present any further details. Jonson (24) has developed a technique of plotting total lung resistance (obtained by the esophageal balloon method) against lung recoil pressure during the course of an expiratory vital capacity maneuver. He found three patients, all with only slight impairment of FEV_1, in whom the relation between resistance and lung volume was abnormal but the resistance-lung recoil pressure relation was normal. In this method resistance was measured at an expiratory flow of 1 liter/s, which will lead to significant dynamic effects on the airways, especially in the presence of airflow obstruction, so it is probable that Jonson's technique will underestimate the number of patients with normal static airway dimensions at a standard distending pressure. Other authors have attempted to distinguish between the roles of loss of recoil pressure and of intrinsic airways disease on the basis of the value of airway resistance during quiet breathing or panting at FRC (25, 26). Only three of our seven patients with a normal conductance-static recoil curve would have been picked out by this criterion. Whether a patient with a normal conductance-static recoil curve will have an abnormal conductance at FRC will depend on whether lung recoil pressure is normal or low at FRC. A better technique would be to measure the value of $G_{aw}/P_{st}(L)$ at FRC (27), but there are advantages in making this measurement over a range of lung volumes, since Fig. 5 shows that the distinction between a normal and an abnormal conductance-static recoil slope is least obvious at low lung recoil pressures.

Significance of the maximum flow-static recoil plot. All the patients showed a greater reduction in $\dot{V}_{E,MAX}$ than could be accounted for directly by loss of lung recoil, so that all had decreased upstream conductance [absolute value of $\dot{V}_{E,MAX}$ divided by the value of $P_{st}(L)$ (5)] during forced expiration. This finding was expected in the patients with low $\Delta G_{aw}/\Delta P_{st}(L)$ slopes

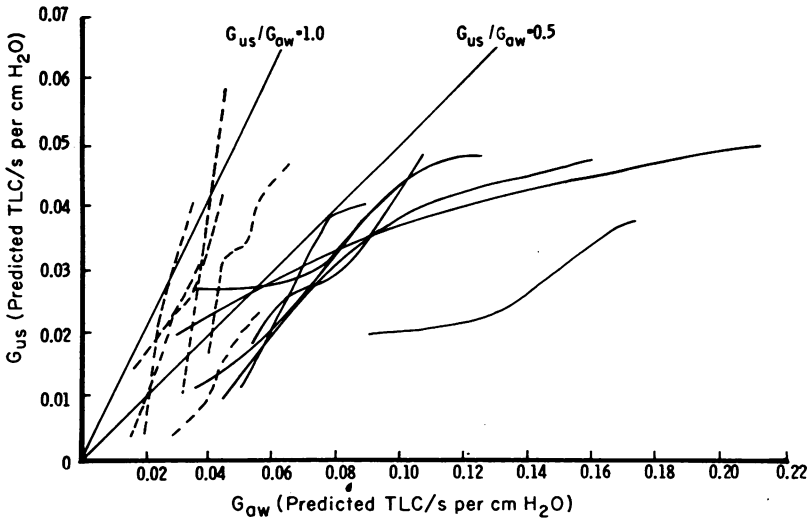

FIGURE 8 Relation between G_{aw} (measured at low flows) and G_{us}. For both measurements flow rates are expressed as predicted TLC per second. Continuous lines indicate patients with normal $\Delta G_{aw}/\Delta P_{st}(L)$, interrupted lines those with a marked reduction in $\Delta G_{aw}/\Delta P_{st}(L)$. Diagonal lines from origin indicate the line of identity between G_{aw} and G_{us} and the line where G_{aw} is twice G_{us}. Normal values of G_{us} were greater than 0.075 predicted TLC/s/cm H_2O at all lung volumes.

but not in those with normal $\Delta G_{aw}/\Delta P_{st}(L)$ slopes. Previously Duffell, Marcus, and Ingram (28) have described normal maximum flow-static recoil relationships in about half of a series of patients with chronic airflow obstruction, and more recently Black, Hyatt, and Stubbs (29) have reported similar findings in patients in whom the airflow obstruction was associated with α_1-antitrypsin deficiency. α_1-antitrypsin levels were measured and found to be normal in three of the present seven patients with a normal $\Delta G_{aw}/\Delta P_{st}(L)$ slope while none of the remaining four patients showed any of the characteristic clinical features (early onset of disability, strong family history, or predominantly basal emphysema) that suggest α_1-antitrypsin deficiency. Although our failure to find patients with completely normal maximum flow-static recoil relationships could therefore be explained, if α_1-antitrypsin deficiency was particularly associated with uncomplicated emphysema, we believe the explanation may be that we studied patients with more advanced disease. The group of patients with normal maximum flow-static recoil curves studied by Duffell et al. (28) had an average forced expiratory volume in 0.75 s of 1.44 liter, while two of the four patients found to have normal maximum flow-static recoil relationships by Black et al. (29) had a maximum breathing capacity within normal limits. Outside the present series we have observed patients with radiological evidence of emphysema and considerable reduction in $P_{st}(L)$ (but without α_1-antitrypsin deficiency) in whom $\dot{V}_{E,MAX}$-$P_{st}(L)$ curves were completely normal. In these subjects, however, expiratory flow limitation and the disability were relatively slight.

We have considered two possible explanations for our findings that the patients in whom conductance was reduced in proportion to loss of static recoil showed a disproportionate reduction in $\dot{V}_{E,MAX}$. First, it may be that an abnormality of smaller airways, present in both static and dynamic conditions, is detected by measurements of maximum flow but not by measuring G_{aw}. Second, all airway dimensions may truly be normal under static conditions but airways contributing to G_{us} may show enhanced dynamic changes on forced expiration. In distinguishing these two possibilities it is useful to compare values of G_{aw} with those for G_{us} on forced expiration at the same lung volume. In patients with severe intrinsic airways disease, narrowing of airways of less than 2 mm diameter is responsible for most of the reduction in G_{aw} (23). So in these patients, increased frictional losses in small airways will be the dominant factor in determining the values of both G_{aw} and G_{us} and these values might be expected to be similar. In fact a close relationship between G_{aw} and G_{us} was found in patients with low values of $\Delta G_{aw}/\Delta P_{st}(L)$, although G_{aw} was somewhat higher than G_{us} (Fig. 8). In part this difference arises because G_{aw} may have been overestimated by use of the panting maneuver in these patients. In contrast, the patients with normal values of $\Delta G_{aw}/\Delta P_{st}(L)$, although they had values of upstream conductance similar to those found in the patients with low $\Delta G_{aw}/\Delta P_{st}(L)$ slopes, had much higher values of

total conductance, which were usually two to three times the values of G_{us} at the same lung volume (Fig. 8). Since in the patients with normal $\Delta G_{aw}/\Delta P_{st}(L)$ slopes there would be less tendency to overestimate conductance by making the measurement during rapid panting, we postulate that these large differences arose either because increased dimensions of large airways offset the effects of small-airway narrowing on G_{aw} or because there were enhanced dynamic changes in airways contributing to G_{us} on forced expiration. Although the major bronchi may be slightly larger in patients with emphysema than in normal subjects (30), the functional significance of this change is doubtful since the conductance of central airways (those with an internal diameter greater than 2 mm) was definitely above the normal range in only one of seven emphysematous lungs studied at necropsy (23). We believe it is more likely that the large differences between G_{aw} and G_{us} were due to enhanced dynamic changes in the airways. Although such changes are most obvious in the major extrapulmonary airways, lateral pressures in all the intrapulmonary airways on expiration are less than alveolar pressure so that even the most peripheral airways tend to be narrower than during breath-holding at the same lung volume. If the effective compliance of upstream airways is increased this could lead to enhanced dynamic changes during forced expiration. Further analysis of maximum flow-static recoil curves in terms of the $\Delta \dot{V}_{E,MAX}/\Delta P_{st}(L)$ slope over the range 70%–30% of the vital capacity (G_s) and of the intercept of this slope on the static recoil axis (P_{tm}') supports the presence of a dynamic effect in these patients. G_s was within or just below the normal range in six of the seven patients with normal conductance-static recoil curves, while P_{tm}' was increased to a mean value of + 2.8 cm H_2O compared to the value of − 1.3 cm H_2O in our ten normal subjects (Table I). Hence most of the abnormality in maximum flow-static recoil curves in these patients was due to parallel displacement of maximum flow points to higher values of static recoil, a change which is compatible with enhanced collapsibility of flow-limiting airways (6). This analysis is open to criticism in that it assumes that values of G_s and P_{tm}' are independent of lung volume so that the relation between maximum flow and static recoil can be described in terms of a slope and intercept. Although in some of the present patients this relationship was notably curvilinear, this was not the case in those patients who had a normal relation between conductance and $P_{st}(L)$ (Fig. 7). Other studies have shown examples of nearly linear maximum flow-static recoil curves with normal slopes but with an intercept at positive values of $P_{st}(L)$ in patients with a clinical diagnosis of emphysema (28, 29, 31). A positive P_{tm}' implies that airways were limiting flow when lateral airway pressure was greater than extra-airway pressure. We cannot explain this finding; increases in P_{tm}' have previously been described in asthma and have been attributed to increase in the active tension of bronchial smooth muscle (6), but this is unlikely to explain the results in chronic airflow obstruction. Obviously there is a need for a more direct assessment of dynamic airway changes than is provided by analysis of maximum flow-static recoil curves; nevertheless both the large discrepancies between G_{aw} and G_{us} and the tendency to an increase in P_{tm}' without reduction in G_s are most easily explained by enhanced airway collapsibility of airways at, or on the alveolar side of, the flow-limiting segment. Several other studies have indicated that dynamic factors are important in the airflow obstruction of emphysema. In the middle of the vital capacity $\dot{V}_{E,MAX}$ may be less than a fifth of the value of maximum inspiratory flow at the same lung volume (32). Compliance of lobar bronchi on forced expiration has been shown to be increased in emphysematous patients compared to normal subjects (33); this abnormalitity may be explained by atrophic changes in the airways, which have been shown to involve lobar and segmental bronchi and several divisions of the bronchi beyond segmental bronchi (34), implying that alterations in airway compliance in emphysema may be equally extensive.

Previously the value of P_{tm}' in normal subjects had been estimated as between − 5 and − 10 cm H_2O (6). In the present normal subjects, the value of P_{tm}', derived directly from maximum flow-static recoil curves, was − 0.8 cm H_2O, which agrees closely with the value of − 1.3 cm H_2O found by Permutt and Hyatt ([31] and personal communication). As P_{tm}' is so close to zero, the two analyses of $\dot{V}_{E,MAX}$ set out in Eq. 1 and 2 above will not differ significantly in normal subjects.

Role of extrabronchial factors in chronic airflow obstruction. In 1951 Dayman (2) attempted to define the roles of intrinsic disease of the airway and of loss of airway-distending forces in patients with severe airflow obstruction. He suggested that in some forms of emphysema, "intrinsic obstruction of the airways may be slight or even absent." The present results confirm that in some patients with chronic airflow obstruction there is no evidence of intrinsic obstruction during breathing at low flow rates. In general these were not the most severely disabled patients although they often had large increases in static lung compliance. In these patients maximum flow was reduced out of proportion to the reduction in $P_{st}(L)$, implying there must have been in addition either fixed intrinsic disease of the airways (which for some reason was not detected by measurements of G_{aw}) or abnormal dynamic changes in the airways. We have argued above that this reduction in maximum flow could be explained by enhanced collapsibility of flow-

limiting airways or airways on the alveolar side of the flow-limiting segment. Although enhanced collapsibility of extrapulmonary airways presumably indicates a change in the airway wall itself, this is not necessarily the case for intrapulmonary airways where enhanced collapsibility might also be due to loss of airway support by lung tissue. Hence in the patients with a normal relation between conductance and $P_{st}(L)$ even the results on forced expiration could be due to loss of extrabronchial support as originally proposed by Dayman (2). In most of the severest cases of chronic airflow obstruction, however, there must be an abnormality in either the position or the slope of the maximum flow-static recoil relationship, since recoil pressures are rarely reduced below about one-third of the expected values, while maximum flows may be reduced to one-tenth or less of expected values. In advanced disease there is probably both intrinsic airways disease and loss of airway distending forces. A reduced conductance at a standard $P_{st}(L)$ was found in all the lungs studied at necropsy by Hogg, Macklem, and Thurlbeck (23), while all but one of the patients in the present series had some reduction in lung recoil pressure. We suspect that loss of airway-distending forces commonly contributes to chronic airflow obstruction but is rarely the sole cause of the severest disability.

Note added in proof. Since this paper was submitted, an analysis of the relation between total pulmonary conductance (obtained by a similar method to that used by Jonson [24]) and static lung recoil pressure has been published by H. J. H. Colebatch, K. E. Finucane, and M. M. Smith. (1973. Pulmonary conductance and elastic recoil relationships in asthma and emphysema. *J. Appl. Physiol.*, **34**: 143). These authors found that in patients with emphysema but without cough and sputum the relationship between expiratory conductance and lung recoil pressure during a single slow expiration was similar to that in normal subjects, and that in normal subjects the slope of this relationship did not change with advancing age. These results support our argument that the normal conductance-static recoil relationship found in some of our patients is unlikely to be explained by the respiratory frequency at which we measured airways conductance.

ACKNOWLEDGMENTS

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REFERENCES

1. Christie, R. V. 1934. The elastic properties of the emphysematous lung and their clinical significance. *J. Clin. Invest.* **13**: 295.
2. Dayman, H. 1951. Mechanics of airflow in health and emphysema. *J. Clin. Invest.* **30**: 1175.
3. Butler, J., C. G. Caro, R. Alcala, and A. B. DuBois. 1960. Physiological factors affecting airway resistance in normal subjects and in patients with obstructive respiratory disease. *J. Clin. Invest.* **39**: 584.
4. Mead, J., T. Takishima, and D. Leith. 1970. Stress distribution in lungs: a model of pulmonary elasticity. *J. Appl. Physiol.* **28**: 596.
5. Mead, J., J. M. Turner, P. T. Macklem, and J. B. Little. 1967. Significance of the relationship between lung recoil and maximal expiratory flow. *J. Appl. Physiol.* **22**: 95.
6. Pride, N. B., S. Permutt, R. L. Riley, and B. Bromberger-Barnea. 1967. Determinants of maximal expiratory flow from the lungs. *J. Appl. Physiol.* **23**: 646.
7. Leaver, D. G., A. E. Tattersfield, and N. B. Pride. 1971. Factors contributing to airflow obstruction in patients with chronic bronchitis and emphysema. *Bull. Physio-Pathol. Respir.* **7**: 479.
8. Fry, D. L., and R. E. Hyatt. 1960. Pulmonary mechanics: a unified analysis of the relationship between pressure, volume and gas flow in the lungs of normal and diseased subjects. *Am. J. Med.* **29**: 672.
9. Macklem, P. T., and N. J. Wilson. 1965. Measurement of intrabronchial pressure in man. *J. Appl. Physiol.* **20**: 653.
10. Stubbs, S. E., and R. E. Hyatt. 1972. Effects of increased lung recoil pressure on maximal expiratory flow in normal subjects. *J. Appl. Physiol.* **32**: 325.
11. Hyatt, R. E., and R. E. Flath. 1966. Influence of lung parenchyma on pressure—diameter behaviour of dog bronchi. *J. Appl. Physiol.* **21**: 1448.
12. Hughes, J. M. B., F. G. Hoppin, Jr., and J. Mead. 1972. Effect of lung inflation on bronchial length and diameter in excised lungs. *J. Appl. Physiol.* **32**: 25.
13. Macklem, P. T., R. G. Fraser, and W. G. Brown. 1965. Bronchial pressure measurements in emphysema and bronchitis. *J. Clin. Invest.* **44**: 897.
14. DuBois, A. B., S. Y. Botelho, and J. H. Comroe, Jr. 1956. A new method for measuring airway resistance in man using a body plethysmograph: values in normal subjects and in patients with respiratory disease. *J. Clin. Invest.* **35**: 327.
15. DuBois, A. B., S. Y. Botelho, G. N. Bedell, R. Marshall, and J. H. Comroe, Jr. 1956. A rapid plethysmographic method for measuring thoracic gas volume: a comparison with a nitrogen washout method for measuring functional residual capacity in normal subjects. *J. Clin. Invest.* **35**: 322.
16. Mead, J. 1960. Volume displacement body plethysmograph for respiratory measurements in human subjects. *J. Appl. Physiol.* **15**: 736.
17. Hyatt, R. E., D. P. Schilder, and D. L. Fry. 1958. Relationship between maximum expiratory flow and degree of lung inflation. *J. Appl. Physiol.* **13**: 331.
18. Milic-Emili, J., J. Mead, J. M. Turner, and E. M. Glauser. 1964. Improved technique for estimating pleural pressure from esophageal balloons. *J. Appl. Physiol.* **19**: 207.
19. Burrows, B., C. M. Fletcher, B. E. Heard, N. L. Jones, and J. S. Wootliff. 1966. The emphysematous and bronchial types of chronic airways obstruction. *Lancet.* **1**: 830.
20. Cotes, J. E. 1968. Lung function. Blackwell Scientific Publications Ltd., Oxford. 376, 380.
21. Zapletal, A., E. K. Motoyama, K. P. Van de Woestijne, V. R. Hunt, and A. Bouhuys. 1969. Maximum expiratory flow-volume curves and airway conductance in children and adolescents. *J. Appl. Physiol.* **26**: 308.
22. Grimby, G., T. Takishima, W. Graham, P. Macklem,

and J. Mead. 1968. Frequency dependence of flow resistance in patients with obstructive lung disease. *J. Clin. Invest.* **47**: 1455.
23. Hogg, J. C., P. T. Macklem, and W. M. Thurlbeck. 1968. Site and nature of airway obstruction in chronic obstructive lung disease. *N. Engl. J. Med.* **278**: 1355.
24. Jonson, B. 1970. Pulmonary mechanics in patients with pulmonary disease, studied with the flow regulator method. *Scand. J. Clin. Lab. Invest.* **25**: 375.
25. Stevens, P. M., B. F. Orman, and G. Graves. 1969. Contributions of lung recoil and airway resistance to forced expiratory flow limitation. *Am. Rev. Respir. Dis.* **100**: 54.
26. Penman, R. W. B., R. P. O'Neill, and L. Begley. 1970. Lung elastic recoil and airway resistance as factors limiting forced expiratory flow. *Amer. Rev. Respir. Dis.* **101**: 528.
27. Desmeules, M., R. Peslin, C. Saraiva, H. Uffholtz, and P. Sadoul. 1971. Propriétés statiques et dynamiques pulmonaires dans la bronchite chronique et l'emphysème. *Bull. Physio-pathol. Respir.* **7**: 395.
28. Duffell, G. M., J. H. Marcus, and R. H. Ingram, Jr. 1970. Limitation of expiratory flow in chronic obstructive pulmonary disease. Relation of clinical characteristics, pathophysiological type, and mechanisms. *Ann. Intern. Med.* **72**: 365.
29. Black, L. F., R. E. Hyatt, and S. E. Stubbs. 1972. Mechanism of expiratory airflow limitation in chronic obstructive pulmonary disease associated with α_1-antitrypsin deficiency. *Am. Rev. Respir. Dis.* **105**: 891.
30. Fraser, R. G. 1961. Measurements of the calibre of human bronchi in three phases of respiration by cinebronchography. *J. Can. Assoc. Radiol.* **12**: 102.
31. Permutt, S., and R. E. Hyatt. 1971. Analysis of isovolume pressure-flow curves in normal subjects and patients with airways obstruction. *Bull. Physio-path. Respir.* **7**: 475.
32. Jordanoglou, J., and N. B. Pride. 1968. A comparison of maximum inspiratory and expiratory flow in health and in lung disease. *Thorax.* **23**: 38.
33. Macklem, P. T., R. G. Fraser, and D. V. Bates. 1963. Bronchial pressures and dimensions in health and obstructive airway disease. *J. Appl. Physiol.* **18**: 699.
34. Wright, R. R. 1960. Bronchial atrophy and collapse in chronic obstructive pulmonary emphysema. *Am. J. Pathol.* **37**: 63.