Ventilatory Mechanics and Expiratory Flow Limitation during Exercise in Patients with Obstructive Lung Disease

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ABSTRACT The interrelationships among transpulmonary pressure, flow, and volume during exhausting exercise were studied in 12 males with chronic obstructive lung disease. Expiratory pressure during exercise was compared with flow-limiting pressure (P_{max}) measured at rest. In 11 patients, expiratory pressure during exercise exceeded P_{max}, indicating that ventilation became mechanically inefficient. P_{max} values of the patients were lower than those of normal subjects. Evidence of expiratory flow augmentation during exercise was noted in two subjects. Since 10 subjects achieved maximal expiratory flow predicted from flow-volume curves when heart rate was not maximal, we conclude that exercise capacity in most subjects was clearly limited by the deranged ventilatory apparatus. Elevations in mean intrathoracic pressure during exercise also may interfere with venous return and impose an additional limitation.

INTRODUCTION

When transpulmonary pressures during ventilation exceed those associated with expiratory flow limitation (P_{max}), ventilation becomes "inefficient" to the extent that the increased pressure does not produce increased flow but does require additional metabolic work (1, 2). Normal subjects exercised to exhaustion rarely develop transpulmonary pressures in excess of P_{max} (1). Thus, the normal person maintains a mechanically efficient pattern of ventilation under maximal exercise stress.

A number of studies have described various aspects of lung mechanics during exercise in subjects with chronic obstructive lung disease (COLD) (3–10). However, none of these studies present the interrelationships among transpulmonary pressure, flow, and volume in sufficient detail to ascertain whether these patients maintain mechanical efficiency during severe exercise.

We have quantified the simultaneous interrelationships among transpulmonary pressure, flow, and volume in a group of patients with COLD before, during, and after exhausting treadmill exercise. We determined P_{max} as a function of lung volume in these subjects and related exercise transpulmonary pressure to P_{max}.

METHODS

12 male patients with clinical, roentgenologic, and physiologic evidence of obstructive lung disease were studied (Table I). Resting studies were performed with the subject seated in a volume-displacement body plethysmograph (16), which had a frequency-amplitude response that was ±5% up to 14 cps. The box-spirometer system was pressure corrected to give adequate phase relationships up to 8 cps. All volumes reported in this study were corrected to body temperature and pressure saturated (BTPS).

Transpulmonary pressure (P) was estimated from a 10 cm long, thin, latex balloon positioned in the middle third of the esophagus in a region that was free of artifacts. Airflow ($\dot{V}$) was measured by a pneumotachograph just distal to the mouthpiece. Oral pressure was measured at the mouthpiece. Outputs from the transducers were fed to a direct-writing recorder and to a frequency-modulated tape recorder for playback, with time reduction into an x-y plotter.

The following data were obtained at rest: (*a*) static expiratory pressure-volume curve of the lung (17); (*b*) static lung volumes, including total lung capacity (TLC) by a modification of the method of DuBois, Botelho, Bedell, Marshall, and Comroe (18); (*c*) isovolume pulmonary flow resistance (R_L); and (*d*) pressure-volume (PV) and flow-volume (FV) loops during quiet breathing, forced inspiratory and expiratory vital capacity breaths (FIVC and FVC), and maximum breathing capacity (MBC).

P_{max} as a function of lung volume was estimated in all patients by two methods. The first method utilized isovolume pressure-flow (IVP$\dot{V}$) curves (19) determined at different levels of lung inflation. However, construction of IVPV curves is time consuming and difficult at lung volumes below functional residual capacity (FRC) in subjects with COLD. Thus, a second method described by Olafsson and Hyatt (1) also was employed. Briefly the procedure is as

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TABLE I

Physical Characteristics, Resting Static and Dynamic Lung Volumes, and Lung Mechanics Data in 12 Patients with Chronic Obstructive Lung Disease

	Patient											
	1	2	3	4	5	6	7	8	9	10	11	12
Age, *yr*	39	28	51	67	28	55	52	36	38	39	45	35
Height, *cm*	164	185	175	170	175	172	173	178	170	173	178	191
Vital capacity, *liters*												
Observed	2.3	6.1	3.6	3.1	3.9	3.0	4.1	3.2	3.8	3.7	3.7	2.6
Predicted (11)	4.1	5.4	4.1	3.6	4.9	4.0	4.0	4.8	4.4	4.5	4.5	5.4
Total lung capacity (TLC), *liters*												
Observed	8.0	10.8	8.1	10.0	9.5	5.8	9.2	10.1	7.1	8.5	8.0	8.5
Predicted (12)	5.2	7.5	6.3	5.8	6.3	6.0	6.1	6.7	5.8	6.1	6.7	8.2
Maximum breathing capacity, *liters/min*												
Observed	33	68	44	35	59	83	56	40	47	74	80	36
Predicted (13)	114	150	124	94	145	105	114	134	122	123	141	130
P_{st} at TLC,* *cm H_2O*												
Observed	−8.6	−8.0	−11.7	−8.0	−11.5	−18.0	−9.7	−8.0	−16.0	−13.0	−14.0	−12.0
Predicted (mean) (14)	−34.1	−38.4	−25.5	−21.1	−38.4	−25.5	−25.5	−34.1	−34.1	−34.1	−29.8	−34.1
(−1 SE‡)	−24.2	−28.5	−15.6	−11.3	−28.5	−15.6	−15.6	−24.2	−24.2	−24.2	−19.9	−24.2
R_L,* *cm H_2O/liters per sec*												
Observed	12.5	2.8	4.4	9.9	4.7	2.4	3.8	7.0	3.2	3.6	3.3	5.5
Predicted§	1.4	1.3	1.7	1.1	1.4	2.3	1.4	1.2	2.1	1.7	1.9	1.4
MMF,* *liters/sec*												
Observed	0.4	1.0	0.7	0.3	0.4	0.7	0.5	0.4	0.6	0.8	0.6	0.3
Predicted (15)	3.8	4.4	3.2	2.4	4.4	3.0	3.1	3.9	3.9	3.8	3.5	4.0

* P_{st} at TLC, maximal static recoil of the lung; R_L, isovolume pulmonary flow resistance; MMF, maximum midexpiratory flow.

‡ Standard error of the mean.

§ Predicted from relationship: R_L = 9.4 divided by thoracic gas volume (liters).

follows: the patient is seated in the body plethysmograph, and the volume, flow, oral pressure, esophageal to atmospheric, and transpulmonary pressures are recorded. Orifices of different sizes, ranging from 3 to 15 mm, are positioned distal to the flow meter. After a maximal inspiration, the patient performs a forced vital capacity (FVC) maneuver through the orifice. Initially, the orifice limits flow, and the major pressure decrease is across the orifice. Esophageal pressure is high, but transpulmonary pressure is low and increases slowly. As exhalation continues, the airways narrow, and resistance increases. This continues until the airways themselves limit flow, and the major pressure decrease occurs within the lung. At this point, transpulmonary pressure increases rapidly as oral pressure and flow decrease. The transpulmonary pressure at this point is taken as P_{max} for that particular volume. By varying the orifice size, we were able to define P_{max} values at different lung volumes. The two methods agreed well, and we were able to establish P_{max} as a function of lung volume for each patient (Figs. 1 and 2).

For the exercise portion of the study, the patient stood on a motor-driven treadmill inclined to 10° and breathed through a low resistance valve (20) connected by large-bore tubing to the body box that contained a 500 liter balloon and served as a bag-in-box system (16). Inspiratory and expiratory flows were measured separately from pneumotachographs. Transpulmonary pressure was recorded as before, and volume was measured by the box spirometer. Time lags were corrected in a manner previously described (1).

With the patient standing, several FIVC and FVC breaths were recorded. Next, the subject performed a series of expiratory vital capacity breaths of varied effort, from which a composite maximal expiratory FV curve was constructed. This composite curve corrects in large part for

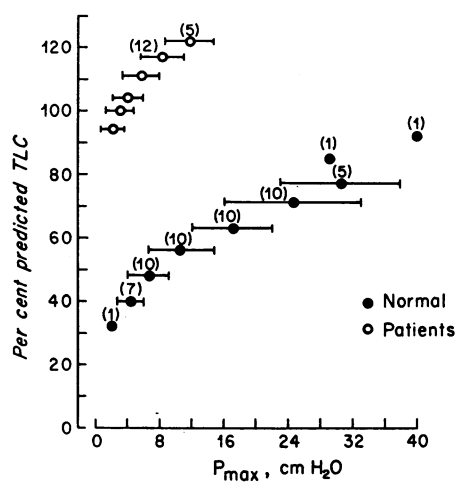
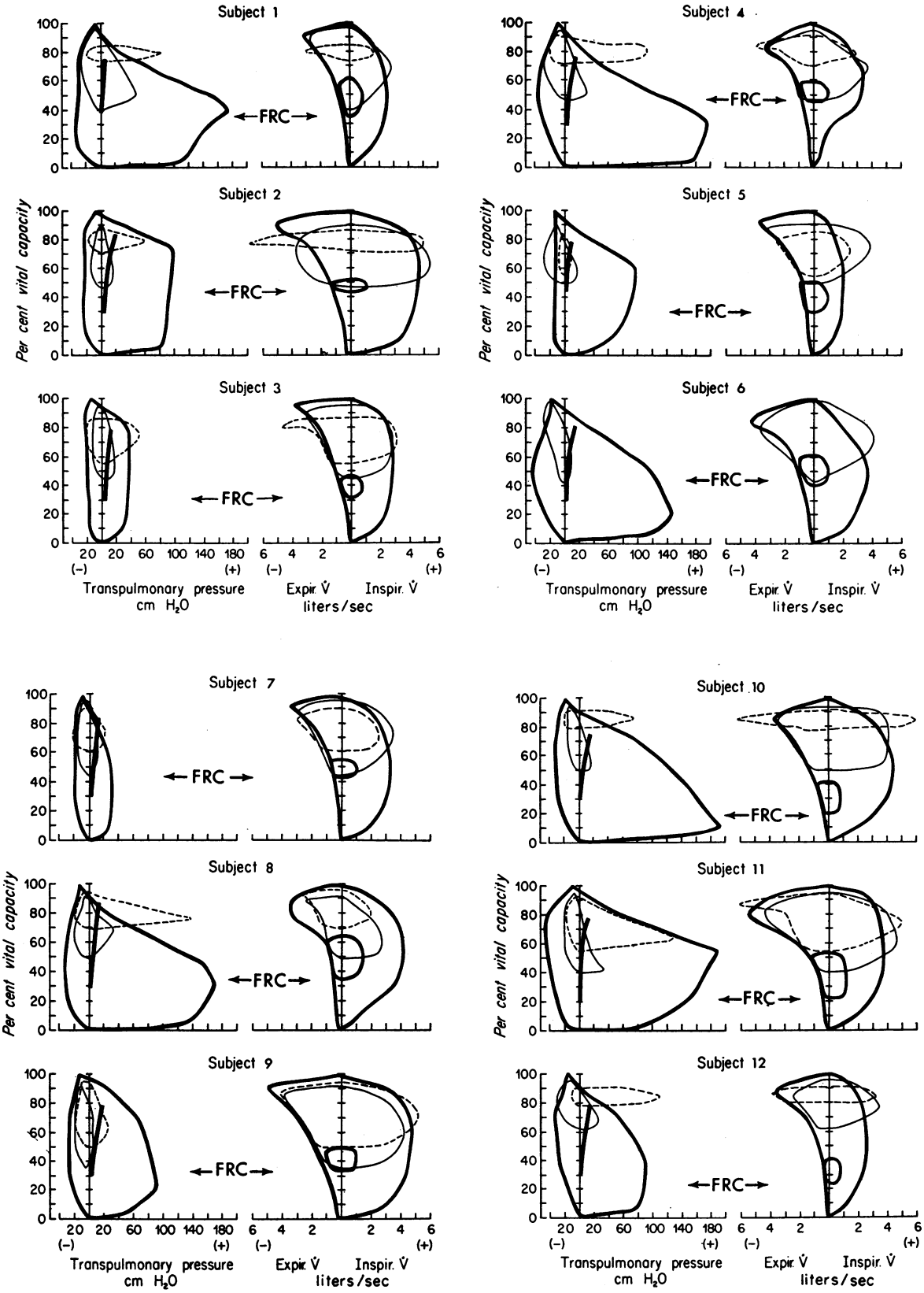


FIGURE 1 Transpulmonary pressure associated with expiratory flow limitation (P_{max}) as a function of per cent predicted total lung capacity for the 12 patients in this study and 10 normal subjects previously reported (1). Horizontal bars indicate ±1 SD. Numbers of subjects contributing to each point is given in parentheses. 12 subjects contributed to each patient point except the highest value to which five contributed.


Subject 1
Subject 4
Subject 2
Subject 5
Subject 3
Subject 6
Subject 7
Subject 10
Subject 8
Subject 11
Subject 9
Subject 12
FRC
Per cent vital capacity
100
80
60
40
20
0
20 20 60 100 140 180
(−) (+)
6 4 2
(−)
2 4 6
(+)
Transpulmonary pressure
cm H2O
Expir. V̇ Inspir. V̇
liters/sec

artifacts due to gas compression (21). These composite curves were used to construct the maximal expiratory FV loop in Fig. 2. The FIVC effort in the box was used to describe maximal inspiratory events for both the FV and PV plots. The box FVC was also used for the PV plot. The MBC loops in Fig. 2 were obtained from the resting study.

The patient then walked on the treadmill at a speed of from 1 to 3 miles per hour, depending on his exercise tolerance. A buzzer, which also served as an event marker, was positioned adjacent to the patient's hand. The patient was instructed to push the buzzer when he first perceived shortness of breath. A second signal was requested when the patient was nearly exhausted, and a third signal indicated the treadmill was to be stopped because of intolerable dyspnea. During the entire exercise period, the pressures and electrocardiograms were recorded. At the second signal, we began continuous recording of volume and flow. As soon as the treadmill was stopped, the patient inhaled to total capacity twice and performed two FVC breaths for comparison with preexercise efforts. The last 5–10 breaths of exercise were used for detailed analysis and were related in volume to the maximal inspirations performed at the termination of exercise. An average loop constructed from these breaths appears in Fig. 2. TLC was not measured during exercise nor was oxygen consumption quantified.

RESULTS

Of the 12 subjects of this study, 10 had resting reductions in VC, and 11 had elevations of TLC (Table I). For the group, TLC averaged 136% of predicted value, MBC 44% of predicted value, maximum midexpiratory flow (MMF) 16% of predicted value, and R_L 374% of predicted value. The RV/TLC ratio for the group was 0.58. In all cases, static lung recoil at TLC was reduced.

Estimates of P_{max} by the IVP$\dot{V}$ curve and orifice techniques showed good agreement, similar to that reported for normal subjects (1). Fig. 1 presents P_{max} as a function of per cent predicted TLC for the entire group and compares the patients with the normal subjects previously studied (1). P_{max} as a function of per cent observed VC is given for each subject in Fig. 2. The P_{max}-volume lines in Fig. 2 are a visual best fit to an average of nine data points (range 4–13) for each subject.

Pertinent data measured during the last 10–30 sec of exercise are tabulated in Table II, and mean values from the previous study of normals (1) are included for comparison. On the average, the patients exercised 4.3 min, with a range of 0.3–16.5 min. The highest heart rate achieved was 175 beats/min with the average of 146 being well below that of the normal subjects. Respiratory frequencies were similar in the two groups, and although the exercise tidal volume (V_T) of the patients was less than the normals, it nevertheless comprised 47% of the VC. The exercise ventilation ($\dot{V}_E$) of 57 liters/min averaged 110% of the control resting MBC. $\dot{V}_E$ averaged 85% of the MBC measured at a different time after bronchodilator therapy. In contrast, $\dot{V}_E$ averaged only 64% of MBC in the normal group. Peak-to-peak transpulmonary pressures were greater in the patient group with expiratory pressures showing the greatest difference.

The interrelations among P, $\dot{V}$, and V are given in Fig. 2. A MBC breath could not be obtained in subject 6 because of persistent esophageal spasm. For the sake of clarity, tidal breathing is shown on the FV plots only.

On the FV plots, the inspiratory limb of the exercise loop is seen to exceed the FIVC maneuver over at least a third of the V_T in subjects 1, 2, 5–7, 10–12. Only in subjects 5, 6, and 12 was this associated with pressures more negative than those developed during the FIVC breath. During the MBC, only rarely did inspiratory $\dot{V}$ exceed the forced effort $\dot{V}$, and in no case was pressure more negative during the MBC than during the FIVC breath. In subjects 2 and 6, the expiratory limb of the exercise loop crossed the resting maximal expiratory flow envelope to a striking degree and did so to a much lesser extent in subjects 3 and 7. In subjects 8 and 12, the expiratory limb was below the maximal $\dot{V}$ envelope. In the other six subjects, expiratory $\dot{V}$ during exercise followed the maximal $\dot{V}$ loop almost precisely. Transient high peaks of expiratory flow during the MBC are seen in subjects 2, 3, 10, and 11.

The effects of exercise and MBC breathing on FRC are demonstrated in these plots. In no case did exercise FRC decrease below resting FRC (indicated by arrows of Fig. 2). Resting FRC averaged 35% of VC, and exercise FRC averaged 47% of VC. End expiratory level during MBC breathing averaged 65% of VC.

From the PV plots, it can be seen that subjects 3 and 7 did not develop expiratory pressures in excess of 40 cm H_2O during the FVC breath. The other subjects developed considerably greater pressures. Subjects 3, 5, and 7 had rather low inspiratory pressures during forced inspiration.

FIGURE 2 Composite flow-volume (FV) (right curves in each panel) and pressure-volume (PV) (left curves in each panel) plots for each patient. Volume plotted as percentage of observed vital capacity. On FV plots, expiratory limb of large loop (heavy line) was constructed from graded VC efforts while subject was standing at rest on the treadmill. Inspiratory limb obtained from FIVC effort. Small heavy loop on FV plot represents tidal breathing. On PV plots large loop (heavy line) was obtained during forced expiratory and inspiratory VC efforts. Short, thick line on PV plots gives locus of P_{max} values. On both plots, thin loop is average of final exercise breaths while dashed loop represents average MBC breath. Position of standing, rest FRC is indicated. No MBC loop obtained on subject 6.

TABLE II

Data at Maximal Exercise Immediately before Cessation of

	Patients					
	1	2	3	4	5	6
Heart rate, *beats/min*	140	175	128	148	168	120
Respiratory frequency, *breaths/min*	60	42	20	38	28	36
V_T,* *liters*	1.27	2.56	1.74	1.44	1.54	1.64
% VC	56	42	49	46	40	54
$\dot{V}_E$,* *liters/min*	51	82	40	54	56	53
$\dot{V}_E$/MBC* (control)	1.55	1.21	0.91	1.54	0.95	0.64
(Rx)‡	1.11	0.98	0.60	1.04	0.81	0.48
Peak pressure, *cm* H_2O						
Inspiratory	−28	−15	−14	−31	−28	−29
Expiratory	+48	+16	+17	+31	+20	+9

* V_T, exercise tidal volume; V_E, exercise ventilation; MBC, maximum breathing capacity.

‡ MBC measured immediately after bronchodilator aerosol given.

The PV loops during exercise are of considerable interest. In only subject 9 did the expiratory loop fail to cross the P_{max}-volume line, whereas in seven subjects (subjects 1, 3, 4, 5, 8, 11, and 12), the degree of crossing was considerable. In the two subjects (subjects 2 and 6) whose expiratory $\dot{V}$ with exercise exceeded the maximal $\dot{V}$ envelope to a large extent, the degree of crossing the P_{max} line was not considerable. It is not clear why these two subjects developed flows in excess of those predicted from the maximal expiratory FV loop. A decrease in flow resistance or a decrease in effective compliance may have occurred during exercise. Conversely, increases in resistance or compliance, or both, might be the basis for the failure of the exercise loops in subjects 8 and 12 to reach the maximal $\dot{V}$ envelope. The IVP$\dot{V}$ curves in these latter two subjects did not show a decrease in flow at pressures in excess of P_{max}, so "negative effort dependence" (22) was not the explanation of their submaximal flow in the face of pressures in excess of P_{max}.

In all except subject 5, the expiratory pressures during the MBC exceeded those developed during exercise. Indeed, in subjects 1, 4, 8, 10, and 12, the expiratory MBC pressures exceeded those during the FVC maneuver by a considerable amount. This contrasts with our experience in normals (1), in whom the MBC rarely exceeded the maximal dynamic expiratory pressure.

DISCUSSION

In this study, it was first necessary to add to the limited data in the literature (23, 24) on the pressures associated with expiratory flow limitation (P_{max}) in COLD. When one compares P_{max} as a function of predicted TLC in patients with that in normals (Fig. 1), the patients' mechanical handicap is apparent. Dynamic compression and flow limitation occur at low pressures in these patients. The elevated airway resistance in COLD dictates that these pressures will be reached at much lower flows than in normal persons. Indeed, as has been pointed out in several studies, expiratory flow limitation in such patients may occur during resting ventilation (4, 25, 26). The cause of the low (that is, less positive) P_{max} values in COLD is not clear. Several factors may be operative. Loss of lung recoil in itself results in airways being at a smaller diameter at any given volume. As lung volume decreases in the normal so does P_{max} (1, 24). Hence, loss of recoil would have the same effect as lowering lung volume, and P_{max} would be expected to be low on this basis. The results of Park, Goldring, Shim, and Williams with papain-induced emphysema are consistent with this mechanism (27). In addition, certain patients with COLD had increased compressibility of the airways (28–30), which would favor a reduction in P_{max}.

All subjects but one developed positive exercise pressures that exceeded the P_{max}-volume line. This observation is of significance on two accounts. First, this indicates that ventilation has become in part mechanically inefficient because the area of the exercise PV loop beyond the P_{max} line in general represents work done on the lung that produces no increase in ventilation. An exception to this is seen in subjects 2 and 6 when some

Exercise in 12 Patients with Chronic Obstructive Lung Disease

7	8	9	10	11	12	Mean	Normal mean
124	126	168	132	162	162	146	180
28	29	27	30	39	45	35	41
2.08	1.28	2.18	1.60	1.99	0.83	1.68	2.93
51	40	57	43	54	32	47	55
56	35	66	66	78	43	57	120
1.00	0.88	1.40	1.05	0.83	1.19	1.10	0.64
0.89	0.69	0.97	0.91	0.70	1.02	0.85	—
−16	−21	−19	−16	−20	−32	−22	−30
+13	+33	+7	+17	+33	+24	+22	+6

increase in ventilation did occur, but in the other subjects the exercise FV loops do not exceed the maximal FV envelope. The second consequence of the positive pressure swings is that mean intrathoracic pressure during exercise is higher (that is, less negative) in the patient than in the normal person. This has the effect of impeding venous return and could impose a limitation to the cardiovascular response to exercise in the patients. During the last 10–20 sec of exercise in our normal subjects (1), the mean P, which closely approximates intrathoracic pressure, averaged − 10.3 cm H_2O (range − 6 to − 19), whereas in the patients with COLD, it averaged − 1.5 cm H_2O (range + 5 to − 13).

What evidence do we have that P_{max} measured at rest applies during exercise? If P_{max} became more positive during exercise, the argument regarding inefficient ventilation would be invalidated to a degree that depends on the magnitude of change. The evidence that P_{max} in normal subjects does not change during exercise has been reviewed (1). It is possible that P_{max} did become more positive in subjects 2 and 6 as exercise $\dot{V}$ exceeded resting maximal $\dot{V}$. Perhaps mild constriction of large airways occurred in these two patients and resulted in less compressible airways as suggested by the work of Olsen, Stevens, and McIlroy (31). One could speculate on other mechanisms such as changes in airway resistance or in static lung recoil, or both, but we do not have the data to answer the question. However, P_{max} may have become less positive in subjects 8 and 12 when exercise $\dot{V}$ decreased below maximal resting $\dot{V}$. Again, we can only speculate as to the cause of this apparent change. In the other eight subjects, there was no evidence that P_{max} changed appreciably. The fact that exercise FV loops did not exceed to an appreciable degree resting maximal expiratory $\dot{V}$ strongly supports this conclusion.

Does expiratory $\dot{V}$ during exercise regularly exceed maximal resting $\dot{V}$, as suggested by the study of Pierce, Luterman, Loudermilk, Blomqvist, and Johnson (4) and supported by Grimby and Stiksa (10)? Examination of Fig. 2 reveals that we encountered this phenomenon to a striking extent in only subjects 2 and 6. All other exercise FV loops were on or under the resting loop, whereas inspiratory exercise flow frequently exceeded resting maximal inspiratory flow. Only if TLC had decreased during exercise could we be in error in the placement of the exercise loops and have missed expiratory exercise flows in excess of the FV envelope. Although TLC was not measured during exercise, evidence against a decrease is that maximal static recoil of the lung (P_{st} at TLC) was not reduced at the end of exercise. The fact that contours of FV plots of FVC breaths before and immediately after exercise did not change also suggests that expiratory flow augmentation did not regularly occur. We did find an increase in peak expiratory $\dot{V}$ in eight subjects, with average peak $\dot{V}$ for the group showing an increase from 4.2 to 5.2 liters/sec. This, however, was accompanied by an increase in mean P_{st} at TLC from − 11.5 to − 15.1 cm H_2O. Therefore, a slight increase in TLC with exercise could have occurred and would

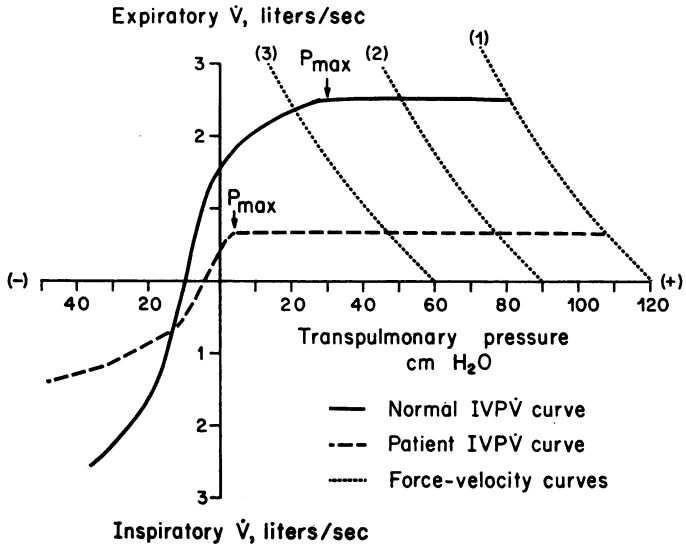


FIGURE 3 Flow plotted against transpulmonary pressure. Representative IVPV curves for a subject when normal (solid line) and when suffering from COLD (dashed line) at identical lung volumes are shown. P_{max} is indicated for both curves. The dotted curves numbered 1–3 are theoretic expiratory, isostimulus, force-velocity curves at this volume. See text for further discussion.

be consistent with increased peak flows with no change in FV slope. Alternately, a more effective contraction of expiratory muscles might have occurred to explain the increased peak flows.

What is the explanation for exercise ventilation being in excess of the MBC in six of the subjects? It is possible that the highest value of the MBC was not obtained at rest. The MBC is known to vary with rate and lung inflation (3, 25). We made no attempt by repeated trials at different frequencies or volumes to obtain a true maximum. It is of interest that Ogilvie, Stone, and Marshall (3) found that the minute volume during maximal exercise equaled the MBC produced by the subject at rest when the same breathing rate was used during exercise.

We conclude that in only two subjects were exercise expiratory flows clearly in excess of resting maximal flows. As Luterman, Pierce, Shuey, and Johnson (5) suggest, this may reflect different pressure-volume histories of the two maneuvers. Why this group (4, 5) and Grimby and Stiksa (10) so consistently found exercise flow in excess of resting maximal flow in contrast with our results is not clear as the subjects and the level of exercise achieved were rather similar. Nevertheless, the sample sizes in these studies are small, and selection may have a major role in the differences encountered. Finally, the spirometric determination of the FVC maneuver can lead to considerable volume shifts due to gas compression (21) and complicates the interpretation of the data presented by Pierce and associates (4, 5).

Several interesting differences between the patient composite plots of Fig. 2 and the previously published normal data (1) warrant comment. The inspiratory limb of the exercise FV loop in the normal subjects rarely reached the FIVC loop in contrast with the patients. The expiratory limb of the exercise FV loop also contrasted in that normals reached the maximal V̇ envelope only at low volumes. The patients' expiratory FV loop during the MBC contrasts with the normal in that it frequently showed (subjects 2, 3, 10, and 11) the high transient flows described by Takishima and associates (26). These workers suggested that this phenomenon might reflect large time-constant discrepancies between serially arranged elements. Finally, the normal subjects during exercise either maintained or lowered their FRC, whereas the patients tended to increase FRC during exercise, an observation also stressed by Grimby and Stiksa (10).

Why do patients with COLD develop excessive expiratory pressure during exercise in contrast with normal persons? It is not known how normals maintain an efficient breathing pattern during exercise. When asked to perform an MBC test, the normal person develops excessive pressures, although Ogilvie and associates (3) have made the interesting observation that if normal persons perform the MBC while emphasizing the use of inspiratory muscles they obtain the same MBC as produced voluntarily but with much lower expiratory pressures.

Admitting our ignorance in regard to the normal, we

TABLE III

Relationships between Transpulmonary Pressure and Dyspnea in 12 Patients with Chronic Obstructive Lung Disease

	Total pressure change			Peak pressure (inspiratory)			Peak pressure (expiratory)		
	Signal*			Signal*			Signal*		
Patient	1	2	3	1	2	3	1	2	3
		cm H_2O			*cm H_2O*			*cm H_2O*	
1	36	52	76	−13	−25	−28	+20	+25	+48
2	22	31	31	−15	−16	−15	+6	+15	+16
3	21	28	31	−17	−18	−14	+4	+9	+17
4	43	50	62	−23	−25	−31	+20	+25	+31
5	21	43	48	−16	−25	−28	+5	+18	+20
6	26	28	38	−24	−28	−29	−2	0	+9
7	18	20	29	−14	−16	−16	+4	+4	+13
8	36	‡	54	−18	‡	−21	+17	‡	+33
9	16	17	26	−16	−16	−19	−1	+1	+7
10	14	24	33	−12	−16	−16	+2	+8	+17
11	28	36	53	−17	−18	−20	+11	+18	+33
12	30	38	56	−23	−25	−32	+7	+13	+24
Mean	26	33	45	−17	−21	−22	+8	+12	+22

* Signal 1, dyspnea first noted; signal 2, very dyspneic, cannot continue much longer; signal 3, exhausted, stop treadmill.

* Recording technically not satisfactory.

present one possible mechanism for the increased expiratory pressures seen in our patients (Fig. 3). The solid line is an IVP$\dot{V}$ curve at 70% TLC that the patient is assumed to have possessed prior to his illness. The dashed line is an IVP$\dot{V}$ curve at the same absolute volume after COLD has developed. Note the lower P_{max} and P_{et} values (the zero flow intercepts) on this curve. The dotted lines numbered 1, 2, and 3 depict assumed isostimulus expiratory force-velocity curves measured when healthy at the same absolute lung volume.[1] Curve 1 would obtain with maximal stimulation, whereas curve 3 depicts the curve existing during maximal exercise, that is with a constant submaximal stimulus. Curve 2 represents an intermediate stimulus level. Let us assume (*a*) that the muscles and, hence, force-velocity relations are not appreciably altered by disease and (*b*) that during exercise in the disease state the same stimulus is applied to the muscle, that is, curve 3 applies. We then reason as follows: during health, the pressure developed during maximal exercise at this volume is defined by the intersection of curve 3 and the control IVP$\dot{V}$ curve, namely a pressure of + 20 cm H_2O, which is 10 cm less than P_{max}. When disease occurs, the exercise pressure at the same volume is defined by the intersection of curve 3 and the dashed IVP$\dot{V}$ curve, that is, at a pressure of + 46 cm H_2O, well above the new P_{max} value of + 4 cm H_2O. To the extent that these assumptions are valid, an increase in transpulmonary pressure is predictable as a result of the altered lung mechanics alone. If the input stimulus to the muscles were increased with disease, even higher pressures would result; for example, curve 2 might apply. A decrease in stimulus would lower the exercise pressure but not necessarily bring it to normal levels, let alone to values less than P_{max}. This is but one of a number of possible mechanisms that may be active either singly or in combination to produce excessive pressures in these patients.

Table III lists the transpulmonary pressures related to various levels of dyspnea. Total pressure swings tended to increase from the time dyspnea was first noted until exercise was stopped, but there were several exceptions. Expiratory pressure showed the greatest increase. However, in view of the variability among subjects, we do not believe that these pressures can be related in any precise manner to the perception or degree of dyspnea. Interestingly, the first indication of dyspnea (signal 1) in subjects 2, 3, 6, 7, 9, and 10 occurred be-

[1] Force-velocity curves of striated muscle show that with constant stimulation the more rapidly a muscle contracts, the less force it develops or, conversely, that the slower the contraction, the greater the force. For the respiratory system, these relationships can be presented in terms of volume flow and intrathoracic pressure (2), which for this discussion can be equated with transpulmonary pressure. Thus, on a given curve, the lower the flow, the higher the pressure developed. The intercept of the curve on the pressure axis indicates the maximal static pressure for that curve. Force-velocity (or intrathoracic pressure-flow) curves are constructed for constant levels of input stimulus and in the case of the respiratory system for constant lung volumes (2).

fore the development of expiratory pressure in excess of P_{max}, that is, presumably before significant dynamic compression. Also, the level of inspiratory pressure at the first signal was variable. Thus, it was difficult from this study to relate any mechanical event to the onset of dyspnea.

Although we were not able to measure oxygen consumption and blood lactate content during these studies, exercise in most of our subjects appeared to be limited by the ventilatory apparatus rather than by the cardiovascular system. That the cardiovascular system was not maximally stressed is suggested by the fact that heart rates averaged only 146 beats/min, and only one subject achieved a rate greater than 170. In contrast, it is evident from Fig. 2 that all subjects except 8 and 12 had achieved the maximal ventilation predicted from the resting FV loops and 11 of the 12 subjects developed inefficient ventilation with excessive expiratory pressure. The conclusion that altered mechanics of the lung-limited maximal exercise is consistent with the findings of Bouhuys and Pool (32), who noted that oxygen consumption, lactate production, and heart rate were submaximal in patients with COLD during subjectively maximal work.

Despite the rather consistent findings in this study, our small, highly selected sample suggests that these data be applied cautiously to the general population of patients with COLD. For example, subjects 2 and 8 have been subsequently found to be homozygous for α_1-antitrypsin deficiency.

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