Alterations in the Mechanical Properties of the Lung during Dyspnea in Chronic Obstructive Pulmonary Disease

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ABSTRACT The mechanical properties of the lungs in seven patients with chronic obstructive pulmonary disease (COPD) were measured before and during dyspnea on exertion, as well as when relief with added oxygen was obtained. Mean pulmonary dynamic compliance was 0.091 liters/cm of H_2O before dyspnea, 0.057 during dyspnea, and 0.101 liters/cm H_2O during relief. During dyspnea there was an increase in the total respiratory work (both elastic and nonelastic work) and this fell during relief with oxygen. Nonelastic resistance and respiratory rate were not significantly different during the three periods. In five similar patients a progressive increase in the instantaneous rate of change of transpulmonary pressure (dP/dt) was observed during exercise and this was markedly increased during dyspnea. These changes in dP/dt during exercise could explain the observed fall of pulmonary dynamic compliance.

INTRODUCTION

Dyspnea on exertion is a major cause of disability in patients with chronic obstructive pulmonary disease (COPD). Although many pulmonary function abnormalities have been recorded in this disease, there is little information (1) concerning the alterations in the mechanics of breathing when the patients are actually dyspneic. The purpose of this communication is to report the changes in the mechanical properties of the lungs in COPD patients walking on a treadmill. Measurements were made before the patient became dyspneic, during dyspnea, and also when relief was obtained by breathing an added oxygen-inspired gas mixture while walking continued.

METHODS

12 men with a clinical diagnosis of COPD (2) took part in the investigation. The average age was 56 yr (Table I) and all were disabled by dyspnea on exertion. None had clinical evidence of right heart failure. The preliminary pulmonary function studies consisted of spirometry, carbon monoxide steady-state diffusing capacity at rest, and estimation of mixed venous carbon dioxide tension by a rebreathing technique (Table I). All patients had marked airway obstruction, the mean forced expiratory volume–1 sec being 33% of the forced vital capacity. The mean maximum voluntary ventilation was 27.6 liters/min. The carbon monoxide–diffusing capacity was lower than predicted normal in all except patients 3, 9, and 11. The mean mixed venous carbon dioxide tension was 57 mm Hg.

Seven patients (Nos. 1–7) took part in the first phase of the investigation. On the first laboratory visit, the patient walked on the treadmill breathing room air until he felt dyspneic, at which point he pressed a switch to ring a bell. The time from the beginning of exercise to this occurrence of dyspnea was recorded as "dyspnea time." During later laboratory visits, treadmill grade and speed were adjusted so that settings could be found when the patient would become dyspneic after about 5 min of walking. On subsequent occasions, even when the patient felt dyspneic, walking was continued and, after a delay of 15–20 sec, conditions for breathing were switched to an approximately 50% oxygen mixture. Although he continued to walk, he soon experienced relief of dyspnea and, at this point, was again instructed to ring the bell. The time from the switching of added oxygen to the time of relief was recorded as "relief time." The whole procedure was repeated several times on different days until consistent "dyspnea times" (within 1 min) and "relief times" (within 30 sec) were obtained. The 15–20 sec lag period before switching to increased oxygen was provided to simulate the final test when this time would be required for recording the measurements during the actual period of dyspnea.

On the final day of the tests, an ear oximeter (3) was placed on the left ear and changes in arterial oxygen saturation were monitored continuously. Pulse rate was also continuously monitored from the cardiac pulsations which were recorded by means of an alternating current coupling from the output of the infrared channel of the oximeter. A 15 cm balloon on a polyethylene catheter was placed in the lower one-third of the esophagus. Transpulmonary pressure was measured using a differential pressure transducer (Statham PR23-20).[1] Air flow was determined by a pneumotachograph using a differential strain gauge (Statham PL-5), which signal was integrated to record tidal

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[1] Statham Instruments, Inc., Los Angeles, Calif.

TABLE I

Physical Characteristics and Results of the Preliminary Pulmonary Function Tests

Patient	Age	Ht.	Wt.	FVC	Pred.	FEV_1	$\frac{FEV_1}{FVC}$	MVV (free)	Pred.	MMFR	D_{LCO}	Pred. D_{LCO}	$P\bar{v}_{CO_2}$
	yr	*inches*	*lb*	*liter*	%	*liter*	%	*liter/min*	%	*sec/sec*	*ml/min per mm Hg*		
1	44	65	98	2.80	75	0.65	23	24	26	0.25	10.5	17.2	57
2	58	63	134	1.75	52	0.55	31	22	24	0.20	8.7	13.5	70
3	61	66	133	2.75	79	0.75	27	27	32	0.20	14.0	13.2	55
4	59	68	102	2.00	59	0.55	28	18	21	0.10	5.8	14.2	61
5	51	68	134	3.55	94	1.65	47	50	49	0.70	9.7	16.4	61
6	54	65	102	2.65	74	1.15	43	46	52	0.50	8.3	15.1	58
7	52	66	116	2.20	61	0.70	32	24	26	0.30	11.9	15.8	50
8	35	71	151	2.85	67	1.05	37	33	26	0.40	10.9	21.1	53
9	69	67	132	1.40	41	0.50	36	15	18	0.20	11.1	11.3	49
10	59	67	152	1.95	55	0.75	38	28	28	0.30	8.6	14.0	62
11	70	69	143	2.95	85	0.90	31	28	31	0.40	13.3	11.4	54
12	65	66	96	2.10	62	0.50	24	17	22	0.20	6.7	12.1	54

Abbreviations used in tables: FEV_1, forced expiratory volume (1 sec); FVC, forced vital capacity; MMFR, maximum mid-expiratory flow rate; MVV, maximum voluntary ventilation; Pred., per cent of predicted normal; D, diffusing capacity.

volume. Minute ventilation was recorded on a 120 liter gasometer. Measurements of pulmonary dynamic compliance, nonelastic resistance, respiratory work, respiratory rate, tidal volume, minute ventilation, and pulse rate were made at the following three specific periods: (*a*) during the 3rd min of exercise (except in patient 4 when the measurements were made during the 2nd min of exercise), (*b*) when the patient became dyspneic, and (*c*) when he felt relieved of the dyspnea.

Pulmonary dynamic compliance was calculated as the ratio of tidal volume to transpulmonary pressure at the points of zero air flow. Nonelastic resistance was calculated as the ratio of transpulmonary pressure to total respiratory flow between midinspiration and midexpiration. Total work was calculated from the sums of work against the elastic forces on inspiration, plus the work done against the nonelastic forces measured from pressure volume loops.

Five patients (Nos. 8–12) took part in the second phase of the investigation. Dyspnea was similarly provoked by walking on the treadmill. Transpulmonary pressure was measured by the esophageal balloon method as described previously. A circuit was constructed to differentiate the transpulmonary pressure signal and display the first derivative (dP/dt) of transpulmonary pressure. Loops of dP/dt (on *Y* axis) against transpulmonary pressure (*X* axis) were recorded on an oscillographic recorder.

RESULTS

Phase 1. The results of measurements of respiratory rate, tidal volume, minute ventilation, arterial oxygen saturation, and pulse rate are shown, with the dyspnea and relief time, in Table II. The mean dyspnea time was 4 min 45 sec, and the mean relief time was 57 sec. There was no significant change in either respiratory rate or tidal volume at the three measurement times although minute ventilation was slightly lower with relief of dyspnea. There was also a slightly lower pulse rate with relief of dyspnea. Oxygen saturation fell by a mean 4.3% during dyspnea.

The results of the measurements of the mechanical properties of the lung are shown in Table III. There was a significant decrease in pulmonary dynamic compliance at the point of dyspnea when compared with measurements during the 3rd min of exercise. With relief from added oxygen, dynamic compliance increased significantly, becoming similar to the predyspneic values. Both total respiratory work and elastic work significantly increased during dyspnea and both variables returned to predyspneic levels following relief with added oxygen. Nonelastic work increased significantly with the onset of dyspnea but did not return to predyspneic levels at the time of relief. There was no significant change in nonelastic resistance at any of the three measurement times.

Patient 1 underwent the test on three occasions during three different admissions to the hospital. Each time, the above pattern of change in the mechanical properties occurred, but the amount of total work at the time of dyspnea varied considerably.

Phase 2. The results of the second phase of the study are shown in Table IV. In patients 8, 9, and 10 there was a gradual and progressive increase in the instantaneous rate of change of transpulmonary pressure (dP/dt), more marked during dyspnea on exertion. There was also a significant decrease in dP/dt with relief with added oxygen in the inspired gas mixture. Patients 11 and 12 immediately become dyspneic on exertion and this was accompanied by a marked increase in dP/dt. It will be noted that in these two patients the resting dP/dt was already increased even at rest.

TABLE II

*Ventilatory Results during the Three Periods**

Patient	Dyspnea time	Relief time	Respiratory rate			Tidal volume			Minute ventilation			Pulse rate			Fall in SaO_2
			A	B	C	A	B	C	A	B	C	A	B	C	
	sec	*sec*	*min*			*ml*			*liter/min*			*min*			%
1	320.0	90.0		27.0	20.0		880.0	975.0		23.8	19.5				3.5
1	450.0	42.0	19.0	18.0	16.0	1026.0	1200.0	1100.0	19.5	21.0	17.7	140.0	150.0	130.0	3.8
1	264.0	40.0	23.0	28.0	27.0	828.0	794.0	834.0	19.0	22.2	22.5	150.0	165.0	150.0	13.1
2	212.0	41.0		28.0	24.0		589.0	629.0		16.2	15.1				7.0
3	480.0	60.0	18.0	25.0	21.0	1300.0	1196.0	1176.0	23.4	29.9	24.7	112.0	116.0	112.0	2.0
4	120.0	56.0	18.0‡	24.0	23.0	723.0‡	575.0	646.0	13.0‡	13.8	14.9	114.0‡	120.0	116.0	4.8
5	280.0	55.0	21.0	20.0	25.0	1346.0	1307.0	1011.0	28.8	26.1	25.3	108.0	120.0	108.0	2.2
6	405.0	75.0	32.0	36.0	38.0	1050.0	1081.0	782.0	33.6	38.9	29.7	120.0	150.0	135.0	6.2
7	150.0	55.0	30.0	44.0	28.0	899.0	768.0	924.0	27.0	33.8	25.9	120.0	120.0	120.0	1.1
Mean	285.0	57.0	23.0	28.0	25.0	1066.0	990.0	895.0	24.1	26.5§	21.9	119.0	129.0§	120.0	4.3
SEM difference			2.3	2.5		43.0	67.0		1.5	1.4		4.3	3.1		

* A, during 3rd min of exercise; B, during dyspnea; and C, during O_2 relief.
‡ During 2nd min of exercise.
§ $P < 0.05$ (between B and C).

DISCUSSION

It is known that during exercise the work of breathing in patients with chronic obstructive pulmonary disease (COPD) is considerably increased. The present study demonstrates that total respiratory work and its two components, elastic and nonelastic work, are increased at the point of dyspnea by almost a mean 50%, when compared with the work of breathing during exercise but before the onset of dyspnea. Although there might be a direct correlation between dyspnea and increased work of breathing, Campbell and Howell (4) suggested that a neural basis for the translation of increased work into the sensation of distressed breathing is difficult to explain or envisage. It also seemed unlikely that there would be a critical level of work load at which the sensation of dyspnea would be experienced, as this level of respiratory work load could be related to many factors, such as the individual's state of health, cardiovascular status, and muscle state. In the present investigation, the patients experienced dyspnea at various work loads and, even for a given individual, for example patient 1, dyspnea was experienced at very different levels of respiratory work on separate investigations performed on different hospital admissions.

By observing the changing pressure-volume loops on the oscilloscope, it became apparent that one could predict when the patient would become dyspneic. The fall in

TABLE III

*Measured Mechanical Properties of the Lungs during Each of the Three Periods**

Patient	Compliance			Nonelastic resistance			Total work			Nonelastic work			Elastic work		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
	liter/cm of H_2O			*cm of H_2O/liter per sec*			*kg-m/min*			*kg-m/min*			*kg M/min*		
1		0.045	0.099		8.30	7.10		3.41	2.00		1.77	1.20		1.64	0.80
1	0.047	0.036	0.057	7.58	10.60	6.91	5.69	8.72	5.81	3.60	4.82	3.71	2.09	3.90	2.10
1	0.053	0.029	0.062	15.50	18.00	16.30	6.57	12.87	11.02	1.76	4.74	3.37	4.81	8.04	7.65
2	0.061	0.044	0.063		11.80	9.50	2.26	3.36	2.56	1.56	2.16	1.87	0.70	1.20	0.69
3	0.094	0.055	0.090				2.26	5.02	2.76	1.50	3.50	1.80	0.76	1.52	0.96
4	0.066‡	0.027	0.028	8.59‡	6.76	10.97	2.89‡	7.24	6.99	1.33‡	4.13	4.03	1.56‡	3.11	2.96
5	0.172	0.139	0.229	4.47	5.60	4.22	1.80	2.43	2.14	0.84	1.23	1.33	0.96	1.20	0.81
6	0.041	0.034	0.060	10.50	9.20	8.10	8.56	8.00	7.90	4.26	3.90	4.00	4.60	4.10	3.90
7	0.158	0.063	0.179	9.78	10.65	8.64	6.44	9.37	4.78	4.82	6.15	3.68	1.62	3.22	1.10
Mean	0.091§	0.057‖	0.101	8.18	8.56	9.10	4.27§	6.31‖	4.71	2.56§	3.70	2.92	1.76§	2.61‖	1.79
SEM difference	0.011	0.016		0.88	1.11		0.64	0.65		0.40	0.38		0.32	0.30	

* A, during 3rd min of exercise; B, during dyspnea; and C, during O_2 relief.
‡ During 2nd min of exercise.
§ $P < 0.05$ (between A and B).
‖ $P < 0.05$ (between B and C).

TABLE IV

Results of Measurements of the Instantaneous Rate of Change of Transpulmonary Pressure

Patient	Rest	Start of exercise	Before dyspnea	During dyspnea	During relief of dyspnea
			*dP/dt (cm of H_2O/sec)**		
8	12	14	32	46	14
9	13	21	—	28	21
10	13	20	24	38	32
11	18	—	—	44	—
12	21	—	—	30	—

* Maximal inspiratory values.

pulmonary dynamic compliance towards the dyspneic point was very noticeable. It also became apparent that the pattern of breathing of these patients became almost gasping in nature during dyspnea. An examination of the scalar tracings towards dyspnea suggested that the slope of transpulmonary pressure became progressively steeper on inspiration.

It was to document this aspect that the transpulmonary pressure signal was differentiated and the instantaneous rate of change or the first derivative of transpulmonary pressure (dP/dt) was recorded. It was noted that dP/dt progressively increased as the dyspnea point was approached. These changes are best demonstrated in loops of dP/dt against transpulmonary pressure (PTP) in patient 8, as shown in Fig. 1. The loops traverse a counter-clockwise direction and the inspiratory portion is approximately the first 180° of each cycle, with the remainder, during expiration. The magnitude of the transpulmonary pressures (PTP) are almost equal before and during dyspnea but dP/dt becomes markedly increased during and throughout inspiration when dyspnea occurs. The almost unchanged magnitude of expiratory dP/dt is very prominent. After relief of dyspnea, transpulmonary pressures are diminished, and dP/dt becomes markedly less. These changes occurred also in the absence of a significant increase in respiratory rate. Therefore the increase in dP/dt as the patient becomes dyspneic does not appear to be due to either an increase of respiratory rate or an increase in transpulmonary pressure but appears related to a true change in breathing pattern.

It has been shown by Young, Martin, and Hashimoto (5) that the distribution of ventilation can be altered in both normal individuals, as well as in patients with COPD. Their data have shown that inspiratory flow is an important determinant in the distribution of pulmonary ventilation and is most probably related to the distribution of resistances in the lungs. They have also stated that with increasing respiratory flow the distribution of ventilation can behave in such a manner that "the rich (small time constant units) become richer, the poor (large time constant units), poorer." The present observations of progressively increasing dP/dt's indicate an exaggeration of increasing respiratory flow and in accord with the above observations the poor or large time constant units will be discriminated against with respect to the distribution of pulmonary ventilation. Unpublished observations in this laboratory have also shown that lung models (balloons and electronic resistance-capacitance networks) will behave similarly when the first derivative of the driving pressure is increased.

It is therefore suggested that the large time-constant units would normally be participating in the distribution of pulmonary ventilation when the rate of change of transpulmonary pressure is optimal or ideal. However, when dP/dt is abnormally increased the large time constant units become poorly participating and could account for the observed fall in dynamic compliance as

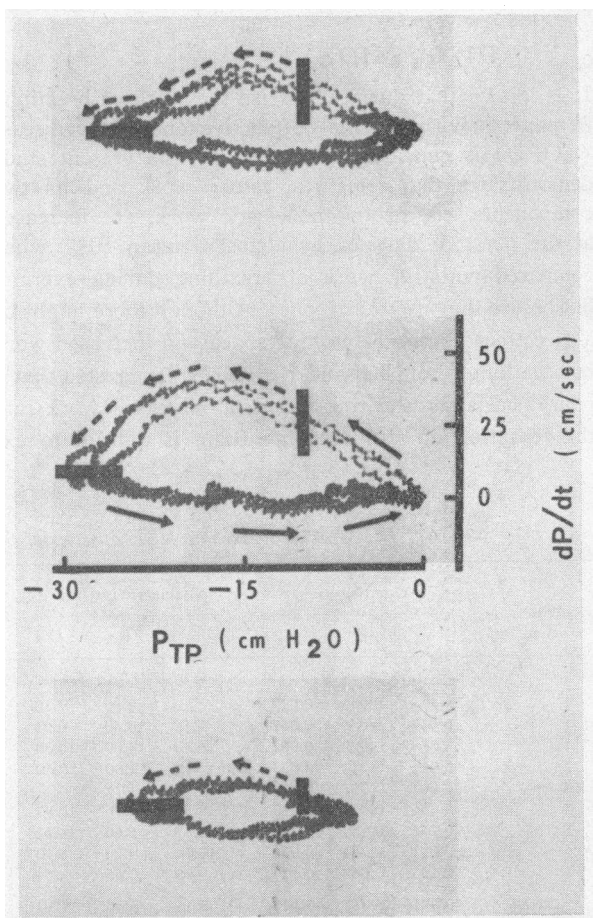

FIGURE 1 Patient J. B., 35 yr, male. Loops of dP/dt against transpulmonary pressure (PTP) before dyspnea (top), during dyspnea (middle), and after relief of dyspnea (bottom). The inspiratory portion of the loop is indicated by the arrows with the broken lines.

the tidal volume is distributed amongst fewer lung units. This is especially important when one considers that the short time constant units may be fewer than the long time constant units (6). This concept is also compatible with the basic principle proposed by Otis et al. (7) that dynamic compliance will fall with increasing respiratory rate in a lung with unequal time constant units. The rise in pulmonary dynamic compliance following oxygen breathing might be related to a decreased respiratory drive causing a less forceful inspiratory effort. This would result in a decrease in dP/dt and a more even distribution of inspired gas. As a consequence, there would be higher pulmonary dynamic compliance.

It is suggested that the observed fall in pulmonary dynamic compliance during dyspnea in patients with COPD is related to the breathing pattern, which is characterized by an increase in dP/dt. Therefore, not only are the anatomic abnormalities in these lungs important, but also the manner in which the pulmonary units are being ventilated.

Another possibility is that the changes in pulmonary dynamic compliance might be related to changes in pulmonary artery pressure during exercise. Pulmonary hypertension could have occurred in these patients as a consequence of the relatively severe exercise, the marked rise in pulmonary artery pressure (8) being brought about by a combination of hypoxia and hyperacidemia (9, 10). Reports in the literature have suggested that increased pulmonary artery pressure could cause pulmonary interstitial edema (11, 12). If pulmonary interstitial edema did occur, then this might be a contributory factor in the fall of dynamic compliance observed in the present study. The relief with oxygen breathing could be related to the subsequent fall in pulmonary artery pressure. However, this mechanism seems unlikely as dynamic compliance improved within a minute of oxygen breathing and one would expect the resolution of interstitial edema to require a longer period.

The explanation of the relief of dyspnea by oxygen breathing must be speculative. During dyspnea there was a more forceful and rapid inspiratory effort with no significant increase in effective gas exchange. Such forceful respiration probably increases the oxygen demands of the respiratory muscles (13) and in the presence of relatively decreased oxygen availability, could be a factor in the genesis of dyspnea. Giving added oxygen provides for the increased metabolic needs of the respiratory muscles. Another possibility is that the forceful and rapid inspiratory effort during dyspnea is perceived as length-tension inappropriateness. When oxygen is given the respiratory effort is less forceful and this results in possibly more appropriate length-tension relationships and the relief of the sensation of dyspnea.

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