Ventilatory Mechanics and Expiratory Flow Limitation during Exercise in Normal Subjects

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Abstract We have examined the interrelationships among transpulmonary pressure, flow, and volume during exhausting exercise in 10 normal adult males. Expiratory transpulmonary pressures during exercise were compared with flow-limiting pressures measured at rest by two techniques. In no case did pressures developed during exercise exceed to an appreciable extent the flow-limiting pressures. This indicates that, during near-maximal exercise, ventilation remains efficient as judged in terms of the pressure-volume relationships of the lung. The mechanical properties of the lung do not appear to limit ventilation during exhausting exercise in normal subjects. We could find no relationship between the magnitude of transpulmonary pressure and exercise limitation. There was no evidence that lung mechanics changed during exhausting exercise in normal subjects. The two methods for estimating expiratory flow-limiting pressures, the orifice technique and the isovolume pressure–flow method, gave similar results.

INTRODUCTION

Only limited and somewhat conflicting data are available on ventilatory mechanics during exhausting exercise in normal subjects (1–4). Also, there has been no detailed evaluation of the relation of exercise pressure swings to expiratory flow-limiting pressures. We have examined in detail ventilatory mechanics at the limit of exercise tolerance, to determine whether any aspect of lung mechanics correlated with the limit of exercise tolerance, and to determine whether, during heavy exercise, normal subjects developed expiratory pressures in excess of those associated with expiratory flow limitation.

It has been shown (5) that at any given lung volume over at least the lower two-thirds of the vital capacity (VC) there exists a transpulmonary pressure (P_{TP}) beyond which further increases in pressure do not produce an increase in expiratory flow. Fig. 1 illustrates this observation. The maximal dynamic pressures developed during forced expiratory and inspiratory VC efforts form the perimeter of the plot. The static recoil curve of the lung (P_{st}) is shown for reference. The locus of pressures associated with expiratory flow limitation (P_{max}) as a function of lung inflation is given by the P_{max} line. Hyatt and Flath (6) suggested that, if positive pressures in excess of those required to produce maximal flow (defined by the P_{max} line) are developed during a breathing cycle, energy is wasted and ventilation may be termed "inefficient" during this portion of the breath. These pressures would not result in increased flow but would be associated with increased work of breathing.

We first obtained data on the volume relationships of P_{max} in normal subjects, there being only limited data on this in the literature (7, 8). We then related exercise pressure volume (P-V) loops to P_{max} values.

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METHODS

Resting studies were performed with the subject seated in a volume-displacement body plethysmograph (9) which had a frequency-amplitude response that was ±5% up to 14 cycles/sec. The box-spirometer system was pressure-corrected to give adequate phase relationships up to 8 cycles/sec. With this system, volume is measured from the spirometer attached to the box and is corrected for alveolar gas compression or rarification. P_{TP} was estimated by subtracting airway pressure from esophageal balloon pressure which was measured by a 10-cm-long thin latex balloon containing 0.8 ml of air placed in the middle third of the esophagus in a region free from artifacts. Flow ($\dot{V}$) was measured by a pneumotachograph placed just distal to the mouthpiece. Outputs from the various transducers were fed to a direct-writing recorder and also to a FM tape recorder for later playback with time reduction into an X-Y plotter.

The following data were obtained at rest: static P-V curve of the lung (10); dynamic compliance (C_{dyn}) during quiet breathing; static lung volumes, including total lung capacity (TLC), by a modification of the method of DuBois and associates (11); and P-V and flow-volume (F-V) loops during forced inspiratory and expiratory VC maneu-

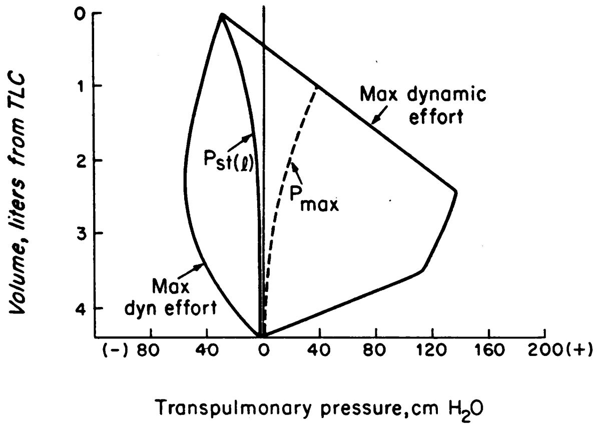


FIGURE 1 Typical pressure-volume plot for normal subject. Perimeter of plot was developed as subject performed maximally forced expiratory and inspiratory vital capacity efforts (maximum dynamic effort). Static recoil curve of lung is given by solid line P_{st} (1). Dashed line, P_{max}, gives volume locus of pressures associated with expiratory flow limitation.

vers and the maximal breathing capacity (MBC) test. In addition we estimated P_{max} by two methods. The first method consisted of measuring isovolume pressure–flow (P-$\dot{V}$) curves at various levels of lung inflation in a manner similar to that described by Hyatt, Schilder, and Fry (5). Fig. 2 illustrates four such curves. No expiratory flow maxima could be defined for the curve measured at 1 liter from TLC. The other curves have regions where it is evident that $\dot{V}$ is no longer increasing with pressure. We estimated the lowest pressure at which this occurred and took this value as equal to P_{max} for that lung volume.

The second method is illustrated in Fig. 3. It consists of having the subject inhale to TLC and then exhale forcefully through an orifice placed at the end of the breathing system. If the orifice offers a significant resistance, it initially limits expiratory flow and the major pressure drop occurs across the orifice (P_{ao}). However, a lung volume will be reached at which the lung becomes flow limiting. At this point, indicated by the arrows in Fig. 3, P_{TP} increases rapidly and both $\dot{V}$ and P_{ao} decrease. The P_{TP} at this point is taken as P_{max} for that lung volume. Note that esophageal pressure relative to atmosphere (P_E) remains relatively high throughout the effort. The gradually increasing $\dot{V}$ and P_{ao} in Fig. 3 reflect gradually increasing effort by the subject during this particular breath as evidenced by the high but increasing P_E. By varying the orifice size between 3 and 15 mm in diameter, it was possible to obtain rather quickly 8–10 values of P_{max} at various lung volumes, particularly at volumes below functional residual capacity (FRC) where it is difficult to obtain satisfactory isovolume (P-$\dot{V}$) curves. Fig. 4 illustrates that decreasing the orifice size leads to development of flow limitation at decreasing levels of lung inflation.

Fig. 4 presents simultaneous F-V and P-V curves obtained during forced expiration through three orifices of different sizes. The forced expiratory vital capacity breath (FVC) is shown on the F-V plot for reference. It can be seen from curve *B*, for example, that flow is fairly constant and less than the maximal flow defined by the FVC line until more than 4.5 liters has been exhaled. At this volume, expiratory flow limitation occurs and flow decreases. Simultaneously, the P-V representation of effort *B* shows that P_{TP} increases rapidly at this volume. We estimate that our measurements of P_{max} by both techniques are accurate to within ±3 cm H_2O for all except the highest lung volumes.

After these resting measurements the subject stood at rest on a treadmill and breathed through a low-resistance valve (12), the ports of which were connected by large-bore tubing to the body box (with a 500 liter bag placed in it) which now served as a bag-in-box system (9). Pneumotachographs were placed in both the inspiratory and expiratory lines between the valve and the box. P_{TP} was measured

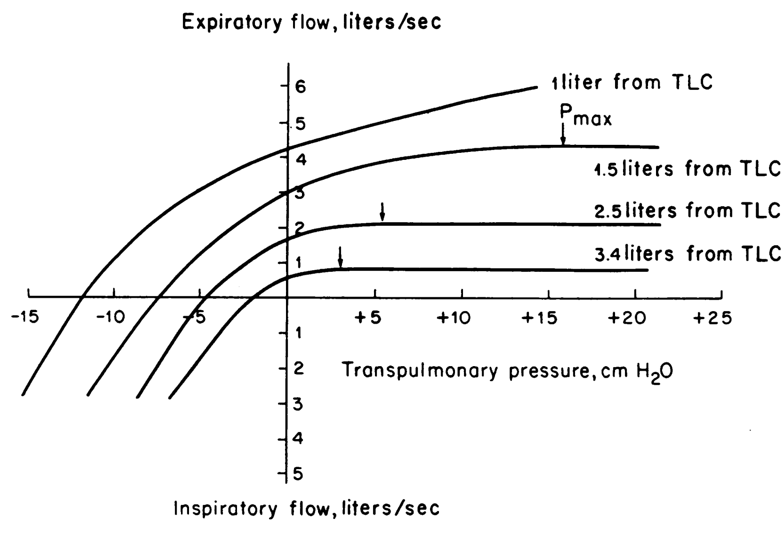


FIGURE 2 Isovolume pressure-flow curves for normal subject. Volume at which each curve was measured is given in liters from total lung capacity (TLC). Arrows indicate pressures (P_{max}) estimated to occur at expiratory flow limitation. Expiratory flow limitation could not be developed at 1 liter from total lung capacity.

as before, and volume was recorded from the box spirometer. With this arrangement, P_{TP} and $\dot{V}$ were in phase. Volume lagged behind $\dot{V}$ and P_{TP} by 10 msec at the highest respiratory frequencies encountered. This time lag was corrected for by playing the P_{TP} and $\dot{V}$ signals from the tape recorder through an operational amplifier with a RC network in the feedback loop before making X-Y plots. This circuit had linear phase relationships out to 15 cycles/sec and a maximal decrease in output amplitude of 4%, which was corrected for. The MBC and several inspiratory and expiratory FVC efforts were recorded. Next, the subject performed a series of expiratory VC breaths of varying effort from which the maximal expiratory F-V curve, as described by Hyatt and associates (5), was constructed.. The F-V curve obtained in this manner corrects in large part for artifacts due to gas compression (13). P_{st} at full inflation and C_{dyn} during quiet breathing were measured.

The subject then walked on the treadmill, at a 10° inclination, at a speed of 3.5–4.0 mph. The subject was instructed to signal with a buzzer when he first noted being winded or short of breath. A second signal was given when he felt he could only continue for approximately a minute longer. A third signal indicated when he was exhausted, and the treadmill was stopped. P_{TP} was measured continuously throughout exercise as was heart rate from a telemetered electrocardiogram. At the second signal we began continuous recording of volume and flow, both on the direct writer and on tape. At the termination of exercise the subject inhaled to TLC several times. 6 of the 10 subjects then immediately performed two FVC maneuvers for comparison to the control efforts. The last 10 breaths of exercise were used for detailed analysis and were related in volume to the maximal inspirations performed at the termination of exercise. TLC was not measured during exercise, and we assumed that there was no change in TLC with exercise. The arrangement we used did not permit the simultaneous measurement of oxygen consumption.

10 healthy, relatively sedentary male subjects with no history or evidence of cardiopulmonary disease were studied (Table I). Routine pulmonary function studies gave normal results in all subjects. Subjects 6 and 7 were nonsmokers, subject 3 was an ex-smoker, subjects 1, 2, 5, 9, and 10 smoked pipes, subject 8 smoked cigars, and subject 4 smoked 15 cigarettes daily for 28 yr.

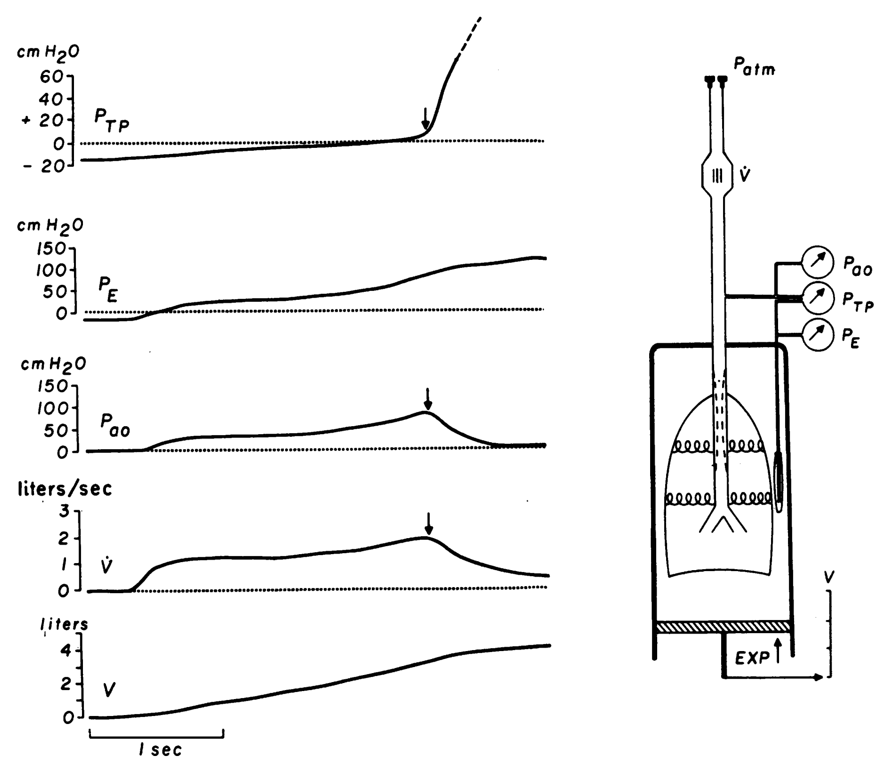


FIGURE 3 Method of estimating P_{max} by orifice technique. (Right) diagrammatic representation of method. Patient sits in volume-displacement body plethysmograph and makes forced expiratory vital capacity effort. Orifice of desired size is placed at end of breathing tube. Pleural pressure estimated by esophageal balloon. P_E is esophageal pressure relative to atmospheric pressure (P_{atm}). P_{TP} is transpulmonary pressure (esophageal pressure minus oral pressure). P_{ao} is oral pressure relative to P_{atm}. Body box records volume expired (V) and pneumotachograph records flow ($\dot{V}$). (Left) record of variables during forced expiratory VC breath through an orifice. P_{ao} gives the pressure drop across the orifice. Flow limitation is taken to occur at volume, flow, and pressures indicated by arrows. See text for further discussion.

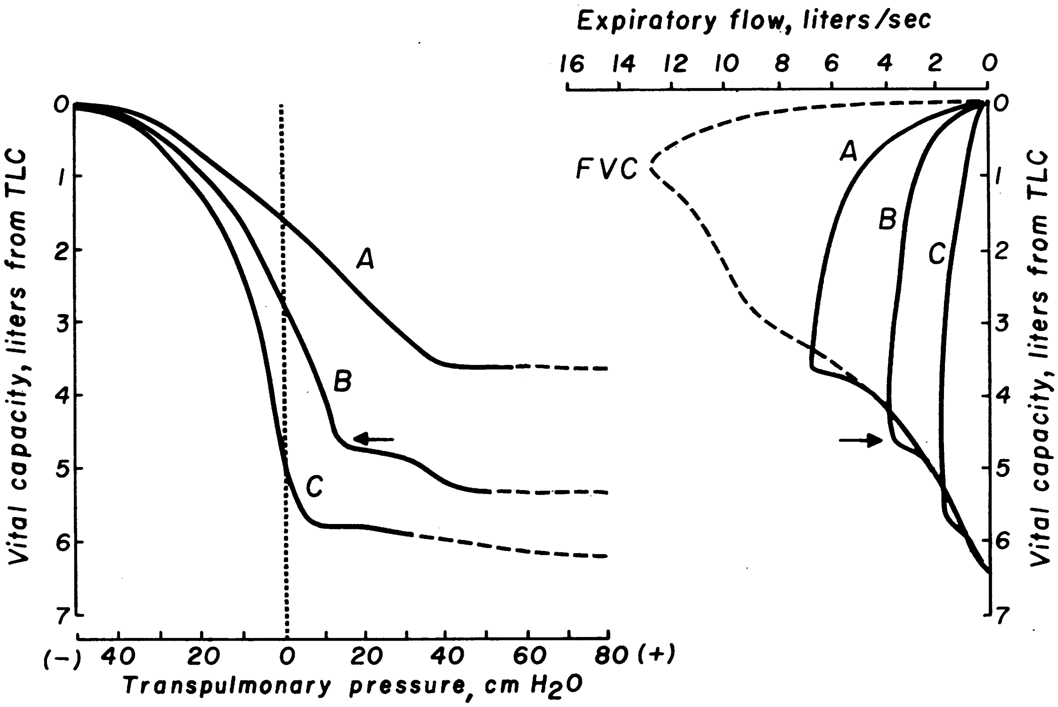


FIGURE 4 Simultaneous flow-volume (right) and pressure-volume (left) plots during forced VC expirations through three orifices of decreasing size: orifice *A*, 9 mm in diameter; *B*, 7 mm; and *C*, 5 mm. Control forced expiration (FVC) is shown on flow-volume plot. Estimated point of flow limitation is shown for orifice *B* by arrows.

RESULTS

The values of P_{max} obtained in each subject by the isovolume P-V curve and orifice techniques are plotted against volume in Fig. 5. We consistently were able to measure P_{max} at lower lung inflations by the orifice method. There was no tendency for values by one technique to differ consistently from those by the other technique. P_{max} consistently increased as lung volume in-

TABLE I
*Physical Characteristics and Resting Static and Dynamic Lung Volumes in 10 Healthy Subjects**

Parameter	Subject 1	2	3	4	5	6	7	8	9	10
Age, *yr*	29	32	55	39	41	45	28	33	26	34
Height, *cm*	188	178	176	172	178	182	171	178	175	184
Vital capacity, *liters*										
Observed	5.5	4.6	5.1	4.7	4.6	4.7	5.7	4.9	5.1	6.9
Predicted‡	5.9	5.0	4.8	4.5	5.0	5.3	4.4	5.0	4.7	5.5
Total lung capacity, *liters*										
Observed	7.1	6.5	7.2	6.2	6.2	7.1	6.6	6.9	5.9	9.1
Predicted‡	7.8	6.7	6.4	6.0	6.7	7.1	5.9	6.7	6.3	7.4
Maximum breathing capacity, *liters/min*										
Observed	191	185	180	219	181	183	150	187	203	249
Predicted§	194	177	145	160	165	166	172	176	180	182

* All volumes are at body temperature and pressure, and saturated with water vapor (BTPS).
‡ See reference 14.
§ See reference 15.

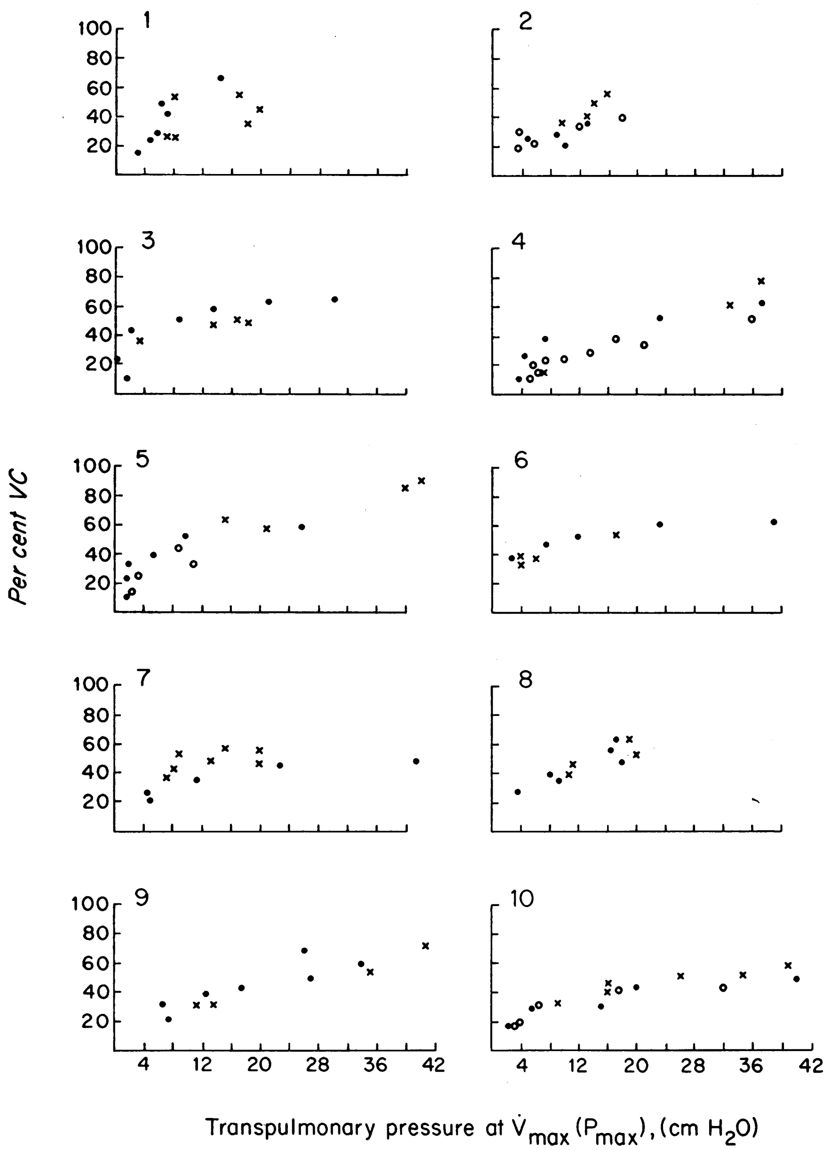


FIGURE 5 P_{max} as estimated by isovolume pressure-flow (PV̇) technique (x) and by orifice technique (at time of exercise study represented by solid circles and repeat runs represented by open circles). P_{max} plotted as a function of percentage of observed VC. Repeat estimates of P_{max} obtained at following times after original study: subject 2, 4 months; subject 4, 2 months; subject 5, 7 months; subject 10, 3 months.

creased. P_{max} as a function of volume was measured at least twice in four subjects and the values were consistent with the original measurments. As a further test of the validity of our estimates of P_{max} we plotted the flow corresponding to P_{max} against the corresponding volume. The resulting F-V curve was found to agree closely with the F-V plot of the FVC obtained in the box.

In Fig. 6 we present the mean values and standard deviations of P_{max} for all subjects as a function of both VC and TLC. P_{max} varied from + 2.0 cm H_2O at 10% of VC to + 40 cm H_2O near TLC.

Table II summarizes pertinent data obtained just before the cessation of exercise. On the average the subjects exercised for 7.2 min. The average heart rate of 180 beats/min indicates that a high level of exercise was achieved. In all instances, maximal heart rate was reached at least 30 sec before exercise was terminated.

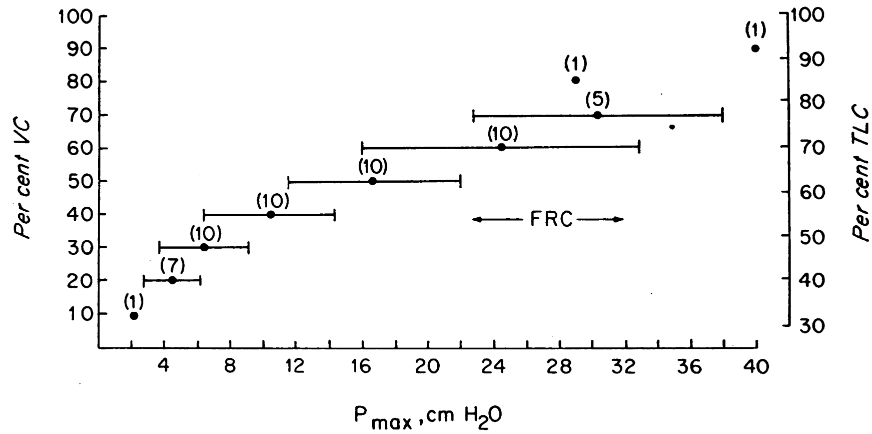


FIGURE 6 Mean values (●) and standard deviations of P_{max} plotted as percentages of observed VC (left) and observed total lung capacity (right). Numbers in parenthesis indicate numbers of subjects contributing to each value. Mean functional residual capacity (FRC) for group is indicated.

Average minute ventilation was 120 liters/min which was 64% of the MBC. We were unable to relate the P_{TP} swings to the onset of dyspnea as signaled by the subject. At the time of the second signal, when the subject was reaching the end of his exercise tolerance and was definitely winded, the average pressure swing was from -29 to $+5$ cm H_2O. At the end of exercise, an average of 70 sec later, when all subjects were breathless, the swing was from -30 to $+6$ cm H_2O. The maximal changes in P_{TP} were often achieved in a given individual well before the second signal. Thus, we did not find a clearly defined level of negative pressure at which shortness of breath was perceived, as has been suggested in the literature (3), but we did not pursue this question in detail.

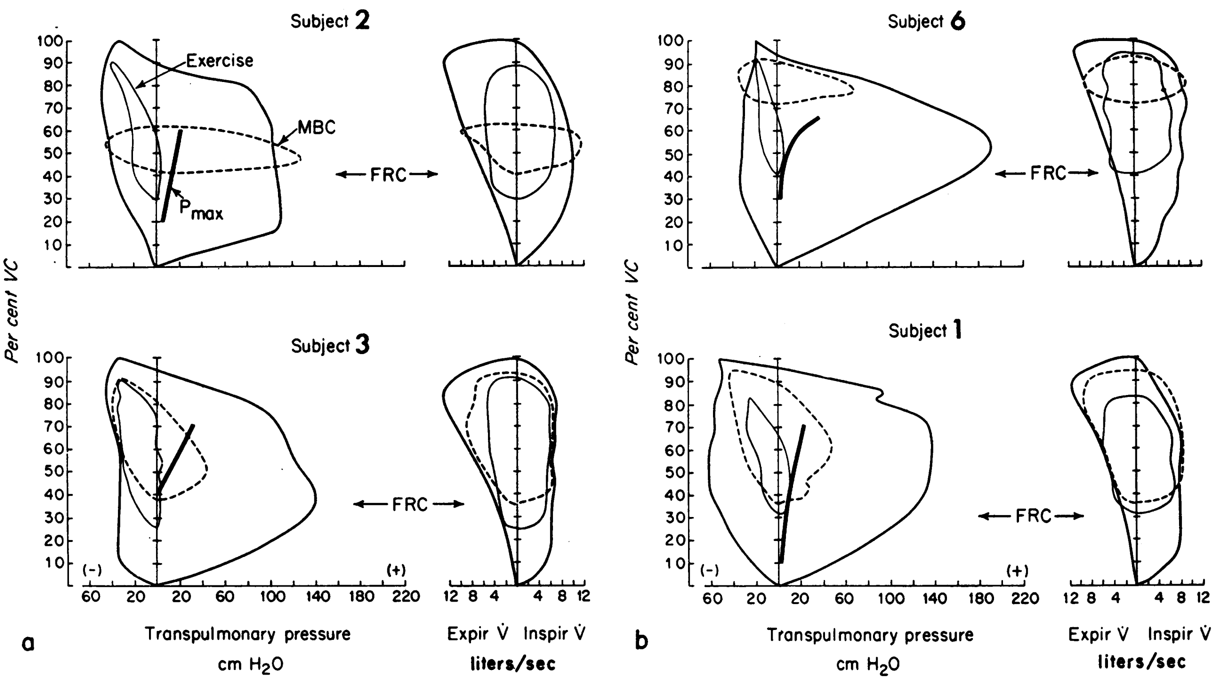
Fig. 7 presents pertinent interrelations among pressure, flow, and volume for each subject. Subject 8 consistently developed esophageal spasm during the inspiratory FVC breath and no inspiratory P-V loop was obtained. The P-V exercise and MBC loops are the same as those depicted on the F-V diagram. The exercise loop in one subject (subject 9) was discarded for technical reasons.

Only in subject 5 does the exercise loop cross the maximal expiratory $\dot{V}$ limb of the F-V plot over a large portion of the breath. The probable explanation for this is that the subject's true maximal expiratory F-V curve was not achieved by the graded VC efforts. As will be discussed, it seems unlikely that there was a change in lung mechanics leading to higher flows at these lung volumes, but this possibility cannot be totally excluded. The inspiratory MBC loops exceed the inspiratory FV loop in several subjects. This generally occurs when more negative pressures were developed during

TABLE II
*Cardiorespiratory Data Immediately Before Cessation of Exercise**

Parameter	Subject									
	1	2	3	4	5	6	7	8	9	10
Heart rate, *beats/min*	183	180	171	162	189	187	186	180	183	175
Respiratory frequency, *breaths/min*	39	47	33	47	51	49	45	36	35	25
V_T, *liters*	3.8	2.8	3.3	2.5	2.3	2.4	2.7	2.7	2.6	4.2
% VC	51	61	65	53	50	52	48	55	50	61
$\dot{V}_E$, *liters/min*	122	132	116	122	134	132	136	103	93	110
$\dot{V}_E$/MBC	0.64	0.71	0.64	0.56	0.74	0.72	0.91	0.55	0.46	0.44
Peak-to-peak pressure, *cm H_2O*‡	−25 to +11	−44 to +3	−35 to +5	−20 to +9	−34 to +9	−21 to +6	−20 to +5	−19 to +3	-§	−52 to 0

V_T, tidal volume; VC, vital capacity; MBC, maximum breathing capacity.
* All volumes are at body temperature and pressure, and saturated with water vapor (BTPS).
‡ Most negative inspiratory and most positive expiratory pressures occurring during an average breath.
§ Record during exercise not satisfactory.



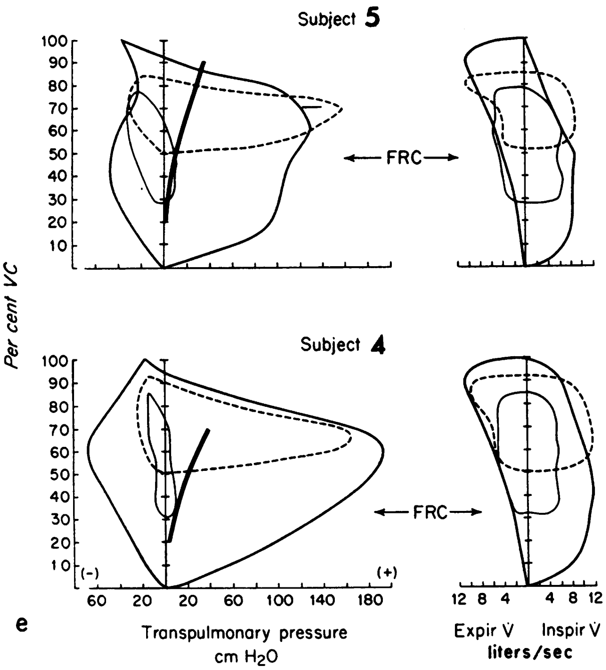
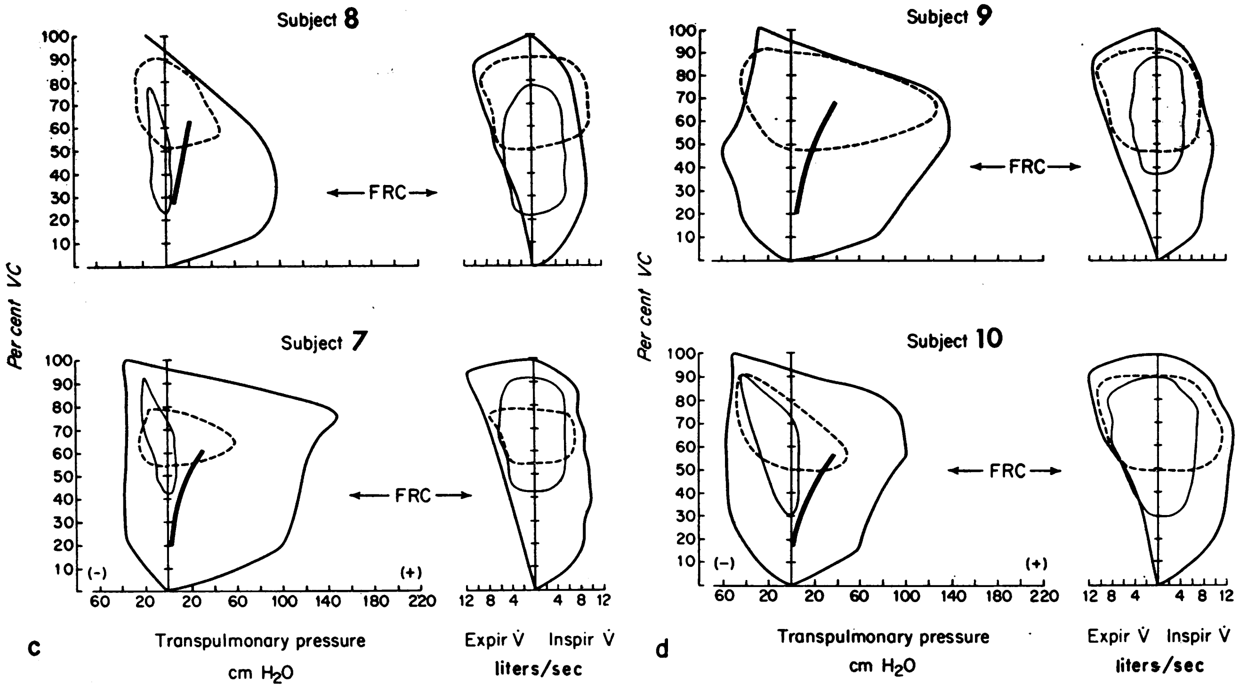


FIGURE 7 *a–e* Composite flow-volume (F-V) (right) and pressure-volume (P-V) (left) plots for each subject. Volume plotted as percentage of observed VC. On F-V plots, expiratory limb of large loop (heavy line) was constructed from graded VC efforts while subject was standing at rest on treadmill. Inspiratory limb was obtained at same time from forced inspiratory VC effort. On P-V plots, large loop (heavy line) was obtained during forced expiratory and inspiratory VC efforts. Short, thick line on P-V plots gives locus of P_{max} values (visual fit to points taken from Fig. 5). On both plots, thin loop is average of final 10 breaths of exercise. Dashed loop is one representative MBC breath. Position of standing, rest FRC is indicated for each subject. See text for further details.

the MBC than during the inspiratory VC maneuver (subjects 2 and 5). This explanation does not hold for subject 4 who was the only cigarette smoker in the group, and who has shown on other occasions a decrease in C_{dyn} with increased respiratory frequency, which may explain his behavior during the MBC. The expiratory MBC loops rarely crossed the maximal expiratory F-V loop.

The P-V plots show that, during the expiratory phase of the MBC, pressures in excess of the P_{max} line were developed. In subjects 2, 5, and 7 in particular, the associated expiratory flow is less than maximal, possibly reflecting in part a decrease in flow as pressures in excess of P_{max} are developed. It must also be recalled that these loops were recorded outside the box and some error in volume placement due to gas compression is likely



(13, 16). The exercise P-V loops are of great interest. In only one case was the expiratory portion of these breaths associated with pressures in excess of the P_{max} line. In subject 5, pressures exceeded P_{max} by a maximum of 5 cm H_2O over approximately the lower 20% of the breath.

These plots also show the relationship between the exercise tidal volume (V_T) and the various lung volume compartments. The exercise V_T averaged 55% of the VC. The increase in V_T during exercise was accomplished mainly by encroaching on the inspiratory reserve volume, although in all but three subjects there was some extension into the expiratory reserve volume (ERV), with an average of 7% of the exercise V_T extending into the ERV.

The pattern of ventilation adopted by a subject was reproducible to the extent that repeat runs in three subjects showed quite similar pressure-flow-volume interrelations.

DISCUSSION

As a first step in characterizing ventilation during exhausting exercise in normal subjects it was necessary to establish the relationship between flow-limiting P_{TP} (P_{max}) and lung volume. This was accomplished by two methods, one of which, the orifice technique, has not been used for this purpose before. We have shown that the two approaches give comparable results, with the orifice technique being less time-consuming than the isovolume P-V curve method. Hyatt and Wilcox (8) presented limited data on P_{max} as a function of lung volume. The present data extend these observations. It is evident from Figs. 5 and 6 that P_{max} varies directly with lung inflation, an observation confirmed by several recent studies (1, 7). The values of P_{max} in the present study are somewhat higher than those previously reported (8) but are similar to the limited data recently reported by Gilbert (1). We estimated P_{max} from the data of Pride, Permutt, Riley, and Bromberger-Barnea (7) and found it to be higher than in our study, but the technique used by those investigators was quite different.

We measured P_{max} at rest and related these values to events occurring during exercise. To the extent that the mechanical properties of the lung do not change appreciably in the normal subject during exhausting exercise, this is acceptable. The following observations support this assumption. Asmussen and Christensen (17) found no change in VC or TLC during exercise bouts producing minute ventilations of 80 liters/min. Dejours, Bechtel-Labrousse, Lefrançois, and Raynaud (18) detected no change in resistance and compliance during moderate degrees of exercise. Recently, Gilbert (1) reported no change in these parameters not explained by the exercise-induced hyperpnea per se. In our study there was also no conclusive evidence of decreased C_{dyn} or altered airway resistance. Comparison, in six subjects, of F-V plots of FVC maneuvers at the end of exercise with those measured before exercise revealed no consistent differences in terms of peak expiratory flow or slope of the expiratory limb of the plots. Moreover, the flows during exercise did not exceed resting maximal flows except to a minor degree in subject 5. Based on these latter findings we believe that the resting P_{max} values closely approximate those existing during strenuous exercise, a conclusion recently supported (1). Further support is seen in the exercise loops of Fig. 7. In general, when expiratory pressure is less than P_{max}, expiratory $\dot{V}$ falls short of the maximal expiratory $\dot{V}$ of the F-V plot. Conversely, when pressure equals P_{max}, expiratory $\dot{V}$ is maximal. Minor exceptions to these generalizations are seen, for example, with subject 10.

Also basic to the application of resting P_{max} data to exercise events is the assumption that TLC did not change with exercise. In four normal subjects, Asmussen and Christensen (17) found no change in TLC during moderately heavy exercise. The fact that in our study the F-V plots of forced VC maneuvers were unchanged at the end of exercise suggests that there was no significant change in TLC. We also assume that changing from sitting to standing does not alter flow-limiting pressures. This is supported by the similarity of maximal flows as a function of lung volume in the two positions(unpublished observations).

We found no correlation between negativity of P_{TP} and awareness of respiratory distress during exercise. The negative pressures recorded in these subjects are comparable to those recorded by Marshall, Stone, and Christie (3).

The major goal of this study was to relate the expiratory pressures during exercise to the pressures associated with flow limitation. It is significant that when volume is taken into account, in no subject did the exercise pressures exceed the P_{max} line by more than 5 cm H_2O. It is evident that in these normal subjects, even when exhausted, excessive positive pressures were not developed. This is beneficial both in terms of not impeding venous return and also in terms of maintaining an efficient ventilation because pressures in excess of P_{max} require an extra amount of work that does not produce an increase in ventilation. Ogilvie, Stone, and Marshall (4) reported a mean expiratory pressure of 30 cm H_2O in six normal subjects exercised to exhaustion. This finding is in marked contrast to our findings and we have no explanation for this difference.

Efficient ventilation is apparently maintained during hyperventilation resulting from high inspired CO_2 concentrations (19) but does not exist during voluntary hyperventilation, because the MBC loops rather consistently crossed the P_{max} line. In patients with chronic obstructive lung disease, Potter and Hyatt (unpublished observations) have found that expiratory pressures exceed the P_{max} line during exhausting exercise.

We do not know the basic mechanism or mechanisms by which expiratory pressures during exercise are controlled in the normal subject in such an economical fashion. Economy of ventilation occurs in normal subjects when ventilation is driven involuntarily, as by exercise to the levels encountered in this study or by carbon dioxide inhalation, but not when driven voluntarily at comparable levels of ventilation.

Our subjects had a maximal exercise ventilation that averaged 64% of the MBC (Table II), which is similar to values in the literature (20). The subject (subject 7) with the highest $\dot{V}_E$: MBC ratio had a low MBC.

There are reports that in normal subjects C_{dyn} decreases with exercise (21), does not change (18, 22, 23), or increases (24). In our study C_{dyn}, as usually measured, decreased from an average of 0.196 liters/cm H_2O to 0.129. However, these data are difficult to interpret because C_{dyn} should decrease with increasing V_T, as is predictable from the P_{st} curve (Fig. 1). C_{dyn} also decreases in some normal subjects when breathing frequency increases (25). We could explain most of the decrease we encountered on the basis of changes in lung inflation. We studied C_{dyn} in three subjects while they were rebreathing at rest from a bag initially filled with 6% CO_2 in O_2. At rates and depths of breathing similar to those occurring during the final phase of exercise, C_{dyn} decreased to values similar to those occurring during exercise. Similar findings have recently been reported (1). To the extent that high levels of inspired CO_2 do not cause a decrease in C_{dyn}, we conclude that our data are most consistent with there being no change in C_{dyn} in normal subjects during exhausting exercise.

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