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Evolution of inspiratory and expiratory muscle pressures during endurance exercise

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Krishnan, Bharath S., Trevor Zintel, Colm McParland, and Charles G. Gallagher. Evolution of inspiratory and expiratory muscle pressures during endurance exercise. *J. Appl. Physiol.* 88: 234–245, 2000.—We investigated the relationship between minute ventilation ($\dot{V}E$) and net respiratory muscle pressure (Pmus) throughout the breathing cycle [Total Pmus = mean Pmus,I (inspiratory) + mean Pmus,E (expiratory)] in six normal subjects performing constant-work heavy exercise (CWHE, at ~80% maximum) to exhaustion on a cycle ergometer. Pmus was calculated as the sum of chest wall pressure (elastic + resistive) and pleural pressure, and all mean Pmus variables were averaged over the total breath duration. Pmus,I was also expressed as a fraction of volume-matched, flow-corrected dynamic capacity of the inspiratory muscles ($P_{cap,I}$). $\dot{V}E$ increased significantly from 3 min to the end of CWHE and was the result of a significantly linear increase in Total Pmus ($\Delta = 43 \pm 9\%$ from 3 min to end exercise, $P < 0.005$) in all subjects ($r = 0.81–0.99$). Although mean Pmus,I during inspiratory flow increased significantly ($\Delta = 35 \pm 10\%$), postinspiratory Pmus,I fell ($\Delta = -54 \pm 10\%$) and postexpiratory expiratory activity was negligible or absent throughout CWHE. There was a greater increase in mean Pmus,E ($\Delta = 168 \pm 48\%$), which served to increase $\dot{V}E$ throughout CWHE. In five of six subjects, there were significant linear relationships between $\dot{V}E$ and mean Pmus,I ($r = 0.50–0.97$) and mean Pmus,E ($r = 0.82–0.93$) during CWHE. The subjects generated a wide range of Pmus,I/$P_{cap,I}$ values (25–80%), and mean Pmus,I/$P_{cap,I}$ increased significantly ($\Delta = 42 \pm 16\%$) and in a linear fashion ($r = 0.69–0.99$) with $\dot{V}E$ throughout CWHE. The progressive increase in $\dot{V}E$ during CWHE is due to *1*) a linear increase in Total Pmus, *2*) a linear increase in inspiratory muscle load, and *3*) a progressive fall in postinspiratory inspiratory activity. We conclude that the relationship between respiratory muscle pressure and $\dot{V}E$ during exercise is linear and not curvilinear.

endurance exercise; minute ventilation; respiratory muscle pressure; postinspiratory inspiratory activity

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THE PATTERN OF RESPIRATORY muscle recruitment and the individual contribution of the different respiratory muscle groups to ventilation at rest and during exercise have been the focus of many studies. At rest, inspiration is predominantly a result of diaphragmatic contraction (19, 27), whereas expiration is a passive process determined by the interaction of inspiratory muscle pressure decay ("expiratory braking") and the elastic characteristics of the respiratory system (2, 31, 37). It is well documented that, during mild and moderate exer-cise, other inspiratory-accessory and expiratory (abdominal) muscles are recruited to meet the increasing flow requirements (19, 20, 27). Furthermore, it has been shown that, during heavy endurance exercise [>80% maximal O_2 uptake ($\dot{V}O_{2\,max}$)], inspiratory-accessory muscles contribute more to the increase in inspiratory airflow, whereas diaphragmatic pressures plateau (22, 29). In a recent report, however, Aliverti et al. (6) showed that, although transdiaphragmatic pressure increased only modestly, the dramatic increases in the velocity of diaphragm shortening and diaphragmatic work suggest that the diaphragm behaves essentially as a flow generator, rather than as a pressure generator, at increasing exercise intensities. The authors (6) also suggested that there is an immediate increase in central drive to all respiratory muscle groups in the transition between quiet breathing and exercise and that this drive increases equally and proportionally to all muscle groups with increasing exercise intensity thereafter. The translation of this drive (into force or velocity of shortening), however, depends on the load on the specific muscle groups. For example, the increase in abdominal pressures during exercise serves to off-load the diaphragm, thus enabling a dramatic increase in its velocity of shortening (flow), with only a modest increase in its force (pressure).

Increasing expiratory muscle recruitment during exercise has been inferred from the measurement of rib cage and abdominal volume displacements (17, 19, 20) and changes in end-expiratory lung volume (23, 28) and expiratory pleural (24, 26) and/or gastric pressures (11). Recent studies in humans also indicate that although inspiratory pleural pressures plateau, expiratory pleural pressures continue to increase throughout heavy endurance exercise (24). More recently, Sliwinski et al. (38) showed that, during heavy exercise after induced global inspiratory muscle fatigue, increasing tonic and phasic abdominal muscle pressures contribute to maintain tidal volume (VT), despite reduced diaphragmatic and rib cage inspiratory muscle activity. In addition to increasing airflow, expiratory muscle activity during exercise reduces end-expiratory lung volume (EELV) (20). The resultant increase in elastic recoil combined with the relaxation of the abdominal muscles at end expiration contributes significantly to lung inflation (19). Furthermore, the persistence of abdom-

inal muscle relaxation well into inspiration has been interpreted as assisting in diaphragmatic output, while stabilizing the rib cage, thus reducing distortion (6).

During moderate prolonged exercise [e.g., <50% of maximal work rate ($\dot{W}_{max}$)], minute ventilation ($\dot{V}E$) increases initially but stabilizes soon thereafter (24). $\dot{V}E$, however, continues to increase throughout constant-work heavy exercise (CWHE, >70% $\dot{W}_{max}$) (22, 24, 25), resulting in an ever-increasing load on all the respiratory muscles. A variety of indexes, i.e., rib cage-abdominal pressure-volume (P-V) relationships (17, 19, 20, 27), electromyography (EMG) (11), and pressure (11, 17, 19, 20, 22, 24, 26, 27), have been used to assess patterns of respiratory muscle activity during exercise. Although these indexes provide for qualitative assessment, quantitative measures of net respiratory muscle pressure throughout the breathing cycle during heavy exercise have been relatively scarce. The measurement of respiratory muscle pressure (Pmus) throughout the respiratory cycle, however, provides information on the relative contributions of all the inspiratory (not just the diaphragm) and expiratory muscles to the ventilatory output of heavy exercise. Pmus measurements throughout the respiratory cycle also allow for the assessment of postinspiratory inspiratory activity (PIIA), by which inspiratory Pmus (Pmus, I) activity "brakes" the start of expiration (2, 37). Data from animal studies suggest that diaphragmatic PIIA remains the same or increases during exercise (5) or with hypercapnic ventilatory stimulation (34, 39). This study was designed to address the following issues: *1*) What is the relationship between the ventilatory output and net respiratory muscle pressure (Total Pmus) throughout the breathing cycle in humans performing CWHE to exhaustion? *2*) What is the relative contribution of inspiratory and expiratory pressures to $\dot{V}E$ during CWHE in humans? *3*) What happens to postinspiratory activity of the inspiratory muscles in humans during CWHE?

Previous studies that have examined the relationship between $\dot{V}E$ and pressure [measured as mouth pressure (Pm) at 100 ms into inspiration ($Pm_{0.1}$) (21, 28) or esophageal pressure (Pes) (40)] or their rates of change (40) during exercise have produced conflicting results. It has been suggested that the nonlinear relationship between $\dot{V}E$ and $Pm_{0.1}$ during exercise (21, 28) was due to the nonlinear increase in respiratory impedance during exercise (21). As discussed elsewhere (41), although $Pm_{0.1}$ is a useful noninvasive index of inspiratory muscle output, its interpretation during exercise is confounded by *1*) the reduction in EELV, *2*) changes in the shape of the Pmus, I waveform (16, 41), and *3*) the varying temporal difference between the start of neural and mechanical inspirations (16). Furthermore, occluded airway pressure measured at the start of inspiration does not necessarily reflect the complex interactions between inspiratory and expiratory forces throughout the breathing cycle that ultimately contribute to airflow with each breath. We have therefore examined the relationship between $\dot{V}E$ and Pmus measured throughout the respiratory cycle (Total Pmus and its components) in subjects performing CWHE.

Pmus, I at any time during exercise can be expressed in terms of the dynamic capacity ($P_{cap, I}$) of the muscles to generate that pressure. Although the demand on all the inspiratory muscles increases during heavy exercise (↑Pmus, I), the capacity to generate that pressure decreases (↓$P_{cap, I}$) with increases in lung volume (23, 26) and inspiratory flow rate (3, 23, 26). Pmus, I has therefore been measured as a fraction of volume-matched, flow-corrected $P_{cap, I}$ as an index of inspiratory muscle load during CWHE.

METHODS

Subjects

Six healthy men (average age 25 yr) with no previous history of cardiopulmonary or neuromuscular disorders were recruited and gave informed consent in writing. On a preliminary visit to the laboratory, each subject had a physical examination, an electrocardiogram (ECG), and a pulmonary function assessment. Absolute lung volumes were measured in a body box (Cardio-Pulmonary Instruments, Houston, TX). The subjects were physically active and well motivated to perform exhausting exercise; *subjects 1, 3*, and *5* exercised regularly (e.g., cycling, swimming, and weight training 3–4 times/wk), *subjects 2* and *4* took part in recreational exercise (e.g., cycling and tennis), and *subject 6* exercised infrequently. They were specifically advised to avoid any strenuous physical activity on the day of the test and to refrain from food and caffeinated drinks for 2 h before exercise testing.

Equipment

Exercise tests were performed on an electrically braked cycle ergometer (model 18070, Godart). Subjects wore nose-clips and breathed through a mouthpiece. Inspiratory and expiratory flows ($\dot{V}$) were measured separately using two pneumotachograph-transducer (Fleisch no. 3 and Validyne MP45, ±2 cmH₂O) assemblies on either side of a two-way nonrebreathing valve (model K271, Vacumed). The response of this system was linear over the range of flows measured, and the resistance of the inspiratory and expiratory limbs of the breathing circuit was <1.0 cmH₂O·l⁻¹·s at flow rates up to 6 l/s. The individual flow signals (inspiratory and expiratory) were monitored on a breath-by-breath basis for zero drift (18) and were integrated electronically (Gould) to provide biphasic $\dot{V}$ and volume (V) throughout exercise. The expiratory pneumotachograph was heated. Respired gases (O₂ and CO₂) were monitored by a mass spectrometer calibrated with two standard gas mixtures of known composition. ECG and heart rate (HR) were recorded continuously using standard chest leads. Intrapleural pressure (Ppl) was measured with an esophageal balloon-catheter system connected to a pressure transducer by standard techniques (33). The balloon was carefully positioned in the esophagus, where the best Ppl signal was obtained (most negative at end expiration and with the least cardiogenic artifacts) (33), and its position and gas volume were checked before and after exercise. An occlusion test was performed before and after exercise, as described elsewhere (9). Ppl and Pm were measured with Validyne MP45 transducers and calibrated against a water manometer at the start of each test. All signals ($\dot{V}$, V, Ppl, Pm, ECG, HR, O₂, and CO₂) were recorded continuously on an eight-channel strip-chart recorder (model 8000, Gould), sampled (at 100 Hz), and digitized. Minute-by-minute exercise data were then analyzed on a microcomputer.

Maximal Incremental Exercise

At least 3–5 days before CWHE, each subject performed an incremental exercise test to volitional maximum. Exercise began at 50 W after 2 min of breathing at rest. The workload was then raised incrementally (25 W/min) until the subject was unable to continue exercise. $\dot{V}O_{2max}$ was calculated from the minute of the last completed workload ($\dot{W}_{max}$).

Chest wall mechanics. Static elastic recoil of the chest wall (Pw,el) and inspiratory muscle strength ($P_{max,I}$) were measured in all subjects on a separate occasion. Care was taken to obtain the measurements in a position identical to that assumed on the cycle ergometer during exercise. Two methods were used to measure Pw,el (see below), and reproducible measurements of Pw,el were available from at least one method in each subject. In normal subjects, the results obtained by both techniques have been shown to be equivalent (14).

Relaxation technique. The subjects were trained to relax against an occluded airway after full inspiration to total lung capacity (TLC), as described previously (35). The occlusion was then released in a stepwise fashion, during which the subject expired passively through a flow resistor. Relaxation pressures (Ppl) were obtained during occlusion, at various lung volumes below TLC. That the subject was relaxed was confirmed by observing the Ppl signal for a steady plateau (without artifacts) that was reproducible at each volume step. The maneuver was repeated several times, and only the relaxed, reproducible data were used to construct the chest wall P-V relationship (Fig. 1).

Weighted spirometry. A modification of the weighted-spirometry technique (13, 14) was employed. A special loading-unloading device (25) was used to apply static positive airway pressures and was connected to a closed breathing system that had a regulated 100% O_2 supply and a CO_2 absorber on the expiratory limb. All the subjects were encouraged to breathe normally and relax their respiratory muscles at end expiration. The subject was seated comfortably and breathed on the apparatus for 3–5 min until the inspired O_2 concentration stabilized at 21% and EELV was stable. With the subject thus relaxed, static airway pressures (1–8 cmH$_2$O) were applied at 2-min intervals. The changes in the baseline EELV
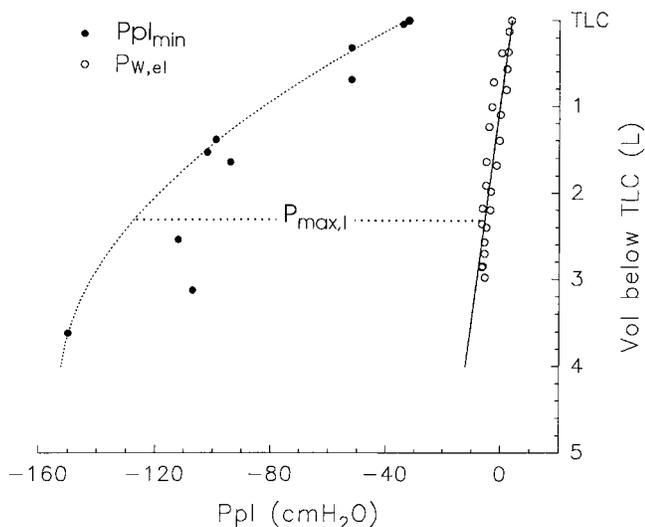

Fig. 1. Static chest wall recoil (Pw,el) and most negative inspiratory pleural pressure (Ppl$_{min}$) at various lung volumes (vol) below total lung capacity (TLC) in 1 subject. Inspiratory muscle strength ($P_{max,I}$) was measured as Pw,el − Ppl$_{min}$ at that lung volume. $P_{max,I}$ was further corrected to derive dynamic capacity of inspiratory muscles to generate pressure ($P_{cap,I}$) at a given lung volume and flow rate.

Table 1. *Subject characteristics and exercise performance data*

Subj No.	Age, yr	Height, m	Maximal Incremental Exercise		Constant-Work Heavy Exercise		
			Peak $\dot{V}O_2$		Workload		Duration, min
			ml·kg^{-1}·min^{-1}	%Predicted	W	%$\dot{W}_{max}$	
1	25	1.70	54	119	310	83	12.9
2	26	1.75	49	118	190	76	9.8
3	23	1.84	54	120	290	89	17.5
4	27	1.81	47	103	280	80	9.8
5	23	1.80	42	91	280	80	12.5
6	25	1.87	41	96	210	76	21.4
Mean	24.8	1.80	48	108	260	81	14.0

$\dot{V}O_2$, O_2 uptake; $\dot{W}_{max}$, maximal incremental work rate.

(ΔV) and Ppl at end expiration (ΔPpl) were measured at each pressure step. That the subject was relaxed was confirmed by the breath-by-breath reproducibility (during several breaths) of the end-expiratory Ppl values at each pressure step. The chest wall P-V relationship was then constructed using Ppl measured at functional residual capacity and the slope of the ΔV-ΔPpl relationship.

Inspiratory muscle strength. The subject was instructed to exert maximal inspiratory efforts against an occluded airway at various lung volumes from TLC down to residual volume. The most negative Ppl (Ppl$_{min}$) was measured during these efforts. Ppl displayed on an oscilloscope served as visual feedback to the subject to maximize his efforts. Lung volume at each step was corrected for decompression and a Ppl$_{min}$-V curve was then constructed in each subject (Fig. 1).

CWHE

While seated on the cycle ergometer, each subject was first trained to make inspiratory capacity (IC) maneuvers. This was followed by 2 min of quiet breathing and a short warm-up exercise (50 W for 2 min). The subject was then alerted, and the workload was abruptly raised to the predetermined level (~80% $\dot{W}_{max}$; Table 1). The subject used speedometer feedback to pedal at 50–70 rpm against this workload until exhaustion. At the end of every 2 min during CWHE, each subject was instructed to inhale to TLC and hold his breath, with glottis open, for 1 s (IC maneuver). The validity of these IC maneuvers (full inspiration to TLC) was ensured by one investigator who monitored lung volume and Ppl (Ppl$_{IC}$) throughout each exercise test.

Data Analysis

For each minute of exercise, the computer counted and labeled all valid breaths (except those interrupted by swallowing, cough, and after IC maneuvers, <5–6/min). The onset and end of inspiratory and expiratory $\dot{V}$ were identified. The computer then calculated inspiratory (TI), expiratory (TE), and total breath (TT) durations for each breath. V_T was obtained by digital integration of expiratory flow to calculate $\dot{V}E$. The computer also derived (by interpolation) the average time course of all signals (e.g., $\dot{V}$ and Ppl) at 1% intervals of TI and TE. The time course of Pmus (Fig. 2) throughout the respiratory cycle was then calculated using previously described techniques (12, 16, 32, 42) for each minute of exercise

$$Pmus = Pw,el + Pw,res - Ppl \qquad (1)$$

where Pw,el and Pw,res are the pressures required to overcome the elastic and resistive forces across the chest wall,

A

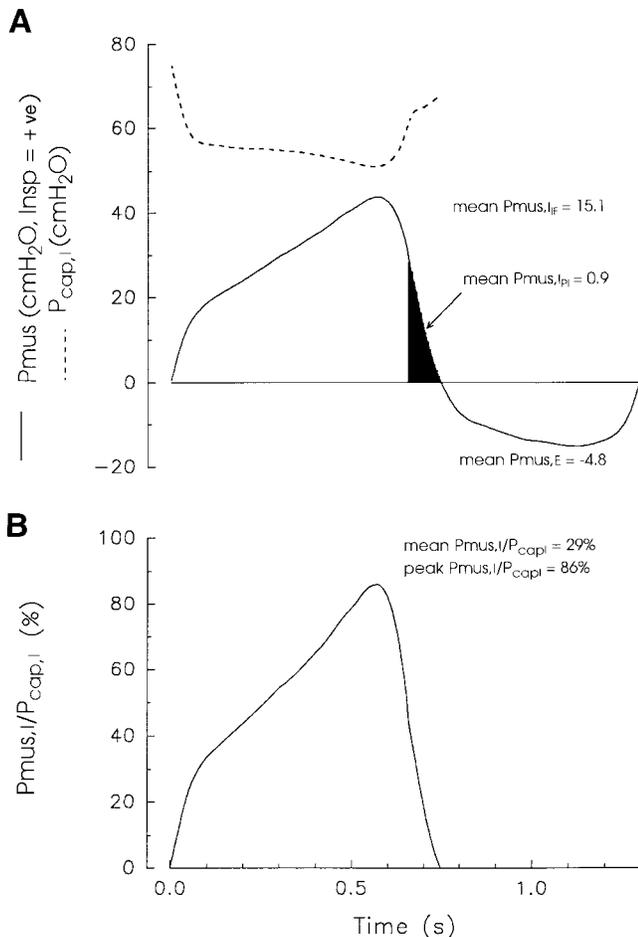**B**

Fig. 2. *A*: respiratory muscle pressure (Pmus) throughout the breath during exercise in 1 subject. Inspiratory Pmus (Pmus, I) is positive, and expiratory Pmus (Pmus, E) is negative. $P_{cap,I}$ at matched lung volume and flow rate and at each point within the breath during which Pmus is inspiratory (positive: +ve) is also shown. Pmus, I during inspiratory flow (Pmus, IF) and postinspiratory inspiratory activity (Pmus, IPI, shaded region) are clearly demarcated. *B*: time course of Pmus, I/$P_{cap,I}$ (%) ratio during the breath. All mean values are averaged over total respiratory cycle (see *Data Analysis*).

respectively, and Ppl is pleural pressure. It should be emphasized that Pmus and its components change throughout the respiratory cycle (Fig. 2). Pw, el at each point in time was derived from instantaneous lung volume and that subject's chest wall P-V curve. Pw, res was calculated from

$$Pw, res = \dot{V} \cdot Rw \qquad (2)$$

where $\dot{V}$ is flow at that time (positive during inspiration and negative during expiration) and Rw is chest wall resistance. A value of 1.0 cmH$_2$O·l^{-1}·s was used for Rw, inasmuch as this is the normal value of Rw for subjects of this age, and there is very little variation between results of different studies (7, 8). By this technique, inspiratory pressures (Pmus, I) are positive and expiratory pressures (Pmus, E) are negative (Fig. 2).

The method used to calculate Pmus, I and Pmus, E for each minute of CWHE is illustrated in Fig. 2. Mean Pmus, I was calculated as the area of the positive segment of the Pmus waveform averaged over TT

$$mean\ Pmus, I = \frac{1}{T_T} \int Pmus, I \qquad (3)$$

Pmus, I throughout each breath was subdivided into its component parts: Pmus, I during mechanical inspiration (during inspiratory flow, Pmus, I$_{IF}$) and Pmus, I persisting during the initial part of expiration (PIIA, Pmus, I$_{PI}$; Fig. 2, shaded area). Mean Pmus, I$_{IF}$ was then calculated as

$$mean\ Pmus, I_{IF} = \frac{1}{T_T} \int Pmus, I_{IF} \qquad (4)$$

and mean Pmus, I$_{PI}$ was calculated as

$$mean\ Pmus, I_{PI} = \frac{1}{T_T} \int Pmus, I_{PI} \qquad (5)$$

and mean Pmus, E (negative Pmus) was similarly averaged over TT

$$mean\ Pmus, E = \frac{1}{T_T} \int Pmus, E \qquad (6)$$

The net pressure generated by all the respiratory muscles, averaged over the respiratory cycle (Total Pmus) is the "sum" of average inspiratory and expiratory (absolute value) muscle pressures

$$Total\ Pmus = mean\ Pmus, I - mean\ Pmus, E \qquad (7)$$

Pmus, I at each point in time was expressed as a fraction of that subject's capacity ($P_{cap,I}$) to generate Pmus, I at the same lung volume and flow rate. First, to calculate $P_{max,I}$ corrected for lung volume, the measured Pw, el and Ppl$_{min}$ data for each subject were analyzed graphically. Only maximal inspiratory efforts were taken into account, and a second-order polynomial was used to fit the outer envelope of the Ppl$_{min}$-V relationship (Fig. 1). All submaximal efforts therefore lay within this curve, and these measurements were discarded. In each subject, static volume-matched $P_{max,I}$ on a breath-by-breath basis was then derived digitally, as the horizontal distance between the Pw, el and Ppl$_{min}$ curves at each lung volume increment, at all points when Pmus was inspiratory (positive Pmus; Fig. 2)

$$P_{max,I} = Pw, el - Ppl_{min} \qquad (8)$$

The force-generating capacity of the inspiratory muscles declines with increasing velocities of muscle shortening (3), and this has been shown to correlate with increases in flow rates (36). It has been shown that, at any given lung volume, $P_{max,I}$ falls by ~5% for every 1 l/s increase in flow rate (23, 26). Each subject's capacity ($P_{cap,I}$) to generate PmusI at any lung volume and for a given flow rate was therefore calculated as

$$P_{cap,I} = P_{max,I} \cdot (1 - 0.05 \cdot inspiratory\ flow\ rate) \qquad (9)$$

Figure 2*A* shows $P_{cap,I}$ throughout inspiration in one subject. As shown in Fig. 2*B*, Pmus, I was then represented as a fraction (%) of $P_{cap,I}$ at the same lung volume and flow rate, at each point in time during which Pmus was positive, for each breath. Like the other Pmus variables, mean Pmus, I/$P_{cap,I}$ (%) values were averaged over TT

$$mean\ Pmus, I/P_{cap,I}\ (\%) = \frac{1}{T_T} \int Pmus, I/P_{cap,I}\ (\%) \qquad (10)$$

For all the ventilatory and Pmus variables, statistical comparisons between the 3rd min of CWHE and end-exercise values were made using a paired *t*-test, and $P < 0.05$ was accepted as significant. The relationships between $\dot{V}_E$ and Pmus variables were examined graphically and analyzed

with regression analyses. A straight-line and a second-order polynomial function were used to fit each of the data sets in each subject to determine whether any of the $\dot{V}_E$-Pmus relationships were linear or curvilinear. A t-test (ANOVA) was then used to determine whether the β-coefficients of the quadratic equation provided a significantly better fit than a linear equation. Data are presented as means ± SE unless indicated otherwise.

RESULTS

The subjects were moderately fit ($108 \pm 5\%$ predicted $\dot{V}_{O_2 max}$) and completed all exercise tests to exhaustion. In the CWHE test the subjects exercised for 14 min on average at a mean work rate of 260 W ($81 \pm 2\%$ $\dot{W}_{max}$). Although dyspnea at end exercise was described as "moderate" or "heavy," exercise cessation was attributed to leg fatigue by each subject. Table 1 summarizes subject characteristics and exercise performance data.

Table 2 summarizes the average changes (Δ%) in metabolic rate, HR, and other ventilatory variables from 3 min to the end of CWHE. Consistent with data from previous studies of CWHE (22, 24, 25), $\dot{V}_E$ and HR increased significantly throughout exercise. End-exercise O_2 uptake, HR, and $\dot{V}_E$ values were similar to those at the end of maximal incremental exercise (Table 2).

The temporal courses of $\dot{V}_E$, end-tidal P_{CO_2} ($P_{ET_{CO_2}}$), and lung volumes during CWHE are illustrated in Fig. 3. $\dot{V}_E$ (Fig. 3A) increased rapidly at the start of exercise and continued to increase throughout CWHE. All the increase in $\dot{V}_E$ ($\Delta = 60 \pm 9\%$, $P < 0.005$) from 3 min to end exercise was due to a significant increase in breathing frequency ($\Delta = 64 \pm 6\%$, $P < 0.005$). After an initial increase at the start of exercise, V_T did not increase further during CWHE; V_T decreased slightly with increasing exercise time in three subjects, similar to previous reports (24), but this fall from 3 min to the end of CWHE (ΔV_T; Table 2) was not statistically significant. The $\dot{V}_E$ drift of CWHE was associated with a progressive fall in $P_{ET_{CO_2}}$ (Fig. 3B), which was signifi-

Fig. 3. Minute ventilation ($\dot{V}_E$; A), end-tidal P_{CO_2} ($P_{ET_{CO_2}}$; B), and lung volume (%TLC; C) during exercise. EILV and EELV, end-inspiratory and end-expiratory lung volume; V_T, tidal volume. Values are group means ± SE ($n = 6$) at 10% increments of exercise time.

cant: from 40.0 ± 0.8 Torr at 3 min to 29.2 ± 1.0 Torr at end exercise ($P < 0.005$).

Figure 3 also describes the average time course of the limits of exercise V_T throughout CWHE. End-expiratory lung volume was derived from measured IC (EELV = TLC − IC). TLC was assumed to be constant during CWHE, for it has been shown that TLC remains unchanged during incremental and endurance exercise in normal subjects (30, 42). The IC measurements were validated by the reproducibility of Ppl values at the end of a full inspiration (Ppl_{IC}). Ppl_{IC} did not change significantly during CWHE: -38 ± 4 cmH$_2$O at rest, -40 ± 5 cmH$_2$O at 50% exercise duration, and -37 ± 4 cmH$_2$O at end exercise. End-inspiratory lung volume (EILV) was derived as the sum of V_T and EELV. As Fig. 3C illustrates, most of the changes in the limits of exercise V_T occurred at the start of heavy exercise; after the first 3 min, EELV and EILV remained essentially stable throughout CWHE. EELV decreased significantly at the start of exercise: from 3.52 ± 0.26 liters ($53 \pm 2\%$ TLC) at rest to 3.01 ± 0.27 liters ($45 \pm 3\%$ TLC) at 3 min ($P < 0.05$). EILV increased significantly at the start of exercise, from 4.38 ± 0.36 liters ($65 \pm 3\%$ TLC)

Table 2. *Ventilatory variables during heavy exercise*

Variable	3rd Minute	End Exercise	Δ%
$\dot{V}_{O_2}$, l/min	3.16 ± 0.3 (84)	3.63 ± 0.2 (97)	$16 \pm 5^*$
HR, min^{-1}	149 ± 2 (86)	180 ± 3 (103)	20 ± 1†
$\dot{V}_E$, l/min	87.8 ± 6.7 (60)	141.6 ± 15.5 (95)	60 ± 9†
V_T, l	2.61 ± 0.1	2.56 ± 0.2	-3 ± 5
f, breaths/min	33.5 ± 2.2	55.4 ± 5.3	64 ± 6†
T_I/T_T	0.50 ± 0.01	0.50 ± 0.01	0.3 ± 3
$P_{ET_{CO_2}}$, Torr	40.0 ± 0.8	29.2 ± 1.0	-27 ± 2†
EELV, %TLC	44.8 ± 2.6	46.9 ± 1.1	6.5 ± 6.9
EILV, %TLC	84.5 ± 1.8	85.5 ± 2.5	1.4 ± 4.0

Values are means ± SE; numbers in parentheses represent percentage of peak values during maximal incremental exercise. Δ%, difference expressed as percentage of 3rd-min values; $\dot{V}_E$, minute ventilation; V_T, tidal volume; HR, heart rate; f, breathing frequency; T_I/T_T, inspiratory duty cycle; $P_{ET_{CO_2}}$, end-tidal P_{CO_2}; EELV and EILV, end-expiratory and end-inspiratory lung volumes, respectively; TLC, total lung capacity. * $P < 0.05$; † $P < 0.005$ (paired 2-tailed t-test).
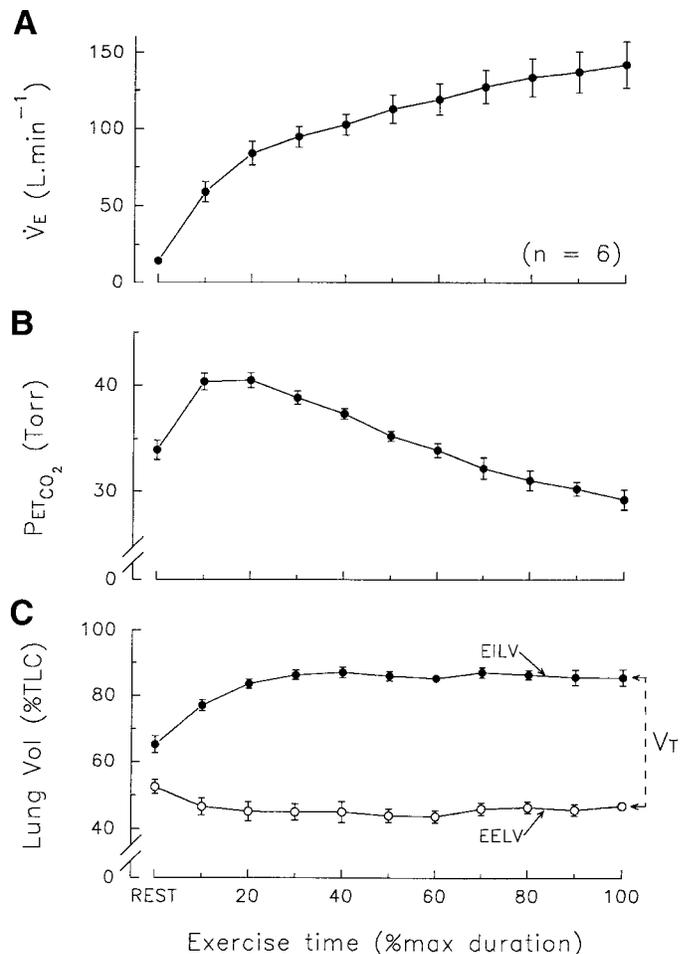
at rest to 5.62 ± 0.26 liters ($84 \pm 2\%$ TLC) at 3 min ($P < 0.05$), but did not change significantly thereafter.

Table 3 summarizes the changes in respiratory mechanics from 3 min to the end of exercise. With the significant (and equal) increases in inspiratory (Δmean $\dot{V}_I = 1.77 \pm 0.31$ l/s, $P < 0.005$) and expiratory (Δmean $\dot{V}_E = 1.80 \pm 0.37$ l/s, $P < 0.005$) flows during CWHE, Ppl (peak and mean values) during inspiration increased significantly. However, there was a greater increase in peak expiratory Ppl (Ppl,E), and this increase in Ppl,E (>4 times) was significant ($P < 0.005$). Inspiratory and expiratory lung resistances (RL,I and RL,E, respectively) at 1.0 liter above EELV were calculated using the subtraction technique of Mead and Whittenberger (32). RL,I and RL,E increased from 3 min to the end of CWHE, and as shown in earlier studies (16), RL,E was greater than RL,I in five of six subjects during CWHE. The increase in RL,E from 3 min to the end of CWHE was significant ($P = 0.048$). However, this greater increase in RL,E could not be attributed to a greater increase in mean expiratory flow, because, as shown in Table 2, TI/TT remained unchanged (at 0.5) from 3 min until the end of CWHE. Table 3 also shows that dynamic lung compliance increased slightly from 3 min to the end of CWHE in five of six subjects. However, these changes were small (24%) and not statistically significant.

Pmus data at 3 min and at end exercise are summarized in Table 4. Figure 4 illustrates the Pmus waveforms at 3 min and at end exercise in each subject. Pmus,I is positive, and Pmus,E is negative. Four of six subjects showed an increase in peak and mean Pmus,I from 3 min to end exercise; however, *subjects 2 and 6* showed little or no change in peak Pmus,I and a slight fall in mean Pmus,I from 3 min to end exercise. These two subjects (*2 and 6*, Fig. 4) displayed substantial Pmus,I$_{PI}$ at 3 min (23 and 17% of Total Pmus,I, respectively), but not at the end of CWHE. Although Pmus,I$_{PI}$ fell significantly from 14% of net Pmus,I at 3 min to 4% of net Pmus,I at end exercise (Table 4), Pmus,I$_{IF}$ increased significantly from 11.2 ± 1.1 cmH$_2$O at 3 min to 15.2 ± 1.8 cmH$_2$O at end exercise (Table 4).

Figure 4 also shows the changes in Pmus,I waveform with the increasing levels during exercise. The shape of Pmus,I changed significantly; i.e., the Pmus,I waveform became increasingly concave toward the time axis. The ratio (%) of Pmus,I at 50% of the rising duration of positive Pmus to peak Pmus,I was calcu-

Table 3. *Respiratory mechanics during heavy exercise*

Variable	3rd Minute	End Exercise	Δ
Ppl,I, cmH$_2$O			
Peak	-24.1 ± 2.2	-30.3 ± 3.4	$6.2 \pm 2.2*$
Mean	-19.7 ± 1.8	-25.9 ± 3.0	$6.2 \pm 1.8*$
Peak Ppl,E, cmH$_2$O	2.7 ± 1.3	14.0 ± 1.5	$11.3 \pm 1.8\dagger$
RL,I, cmH$_2$O$\cdot$l$^{-1}\cdot$s	1.97 ± 0.36	2.26 ± 0.24	0.29 ± 0.27
RL,E, cmH$_2$O$\cdot$l$^{-1}\cdot$s	3.16 ± 0.23	3.89 ± 0.35	$0.74 \pm 0.28*$
Cdyn, l/cmH$_2$O	0.18 ± 0.02	0.23 ± 0.04	0.05 ± 0.02

Values are means $\pm$ SE. Ppl, pleural pressure; I, inspiration; E, expiration; RL, pulmonary resistance at 1.0 liter above EELV; Cdyn, dynamic compliance. *$P < 0.05$; †$P < 0.005$ (paired 2-tailed *t*-test).

Table 4. *Pmus during heavy exercise*

Variable	3rd Minute	End Exercise	$\Delta\%$
Peak Pmus,I, cmH$_2$O	33.0 ± 1.8	39.8 ± 3.8	21 ± 10
Peak Pmus,E, cmH$_2$O	-12.8 ± 1.9	-22.3 ± 1.9	$90 \pm 28*$
Mean Pmus,I, cmH$_2$O	12.9 ± 1.0	15.8 ± 1.9	22 ± 10
Mean Pmus,E, cmH$_2$O	-3.0 ± 0.5	-6.9 ± 0.5	$168 \pm 48\dagger$
Total Pmus, cmH$_2$O	15.9 ± 1.3	22.7 ± 2.1	$43 \pm 9\dagger$
Peak Pmus,I/P$_{cap,I}$, %	50.2 ± 5.0	71.4 ± 11.1	44 ± 18
Mean Pmus,I/P$_{cap,I}$, %	17.8 ± 2.0	25.4 ± 4.3	$42 \pm 16*$
Mean Pmus,I$_{IF}$, cmH$_2$O	11.2 ± 1.1 (86)	15.2 ± 1.8 (96)	$35 \pm 10*$
Mean Pmus,I$_{PI}$, cmH$_2$O	1.7 ± 0.2 (14)	0.7 ± 0.1 (4)	$-54 \pm 10*$
TPmus,I$_{PI}$			
%TE	33.5 ± 4.4	15.3 ± 0.8	$-49 \pm 9*$
%TT	16.9 ± 2.6	7.6 ± 0.4	$-48 \pm 10*$

Values are means $\pm$ SE; values in parentheses represent percentage of mean net inspiratory muscle pressure (Pmus,I). $\Delta\%$, difference expressed as percentage of 3rd-min values; Pmus, respiratory muscle pressure; Pmus, E, expiratory muscle pressure; Total Pmus, mean Pmus,I $-$ mean Pmus,E; P$_{cap,I}$, dynamic (volume-matched and flow-corrected) inspiratory muscle capacity; Pmus,I$_{IF}$, Pmus,I during inspiratory flow; Pmus,I$_{PI}$, postinspiratory Pmus,I; TPmus,I$_{PI}$, duration of postinspiratory inspiratory activity; TE and TT, expiratory and total breath durations, respectively. Mean Pmus,I and mean Pmus,E were averaged over TT. *$P < 0.05$; †$P < 0.005$ (paired *t*-test).
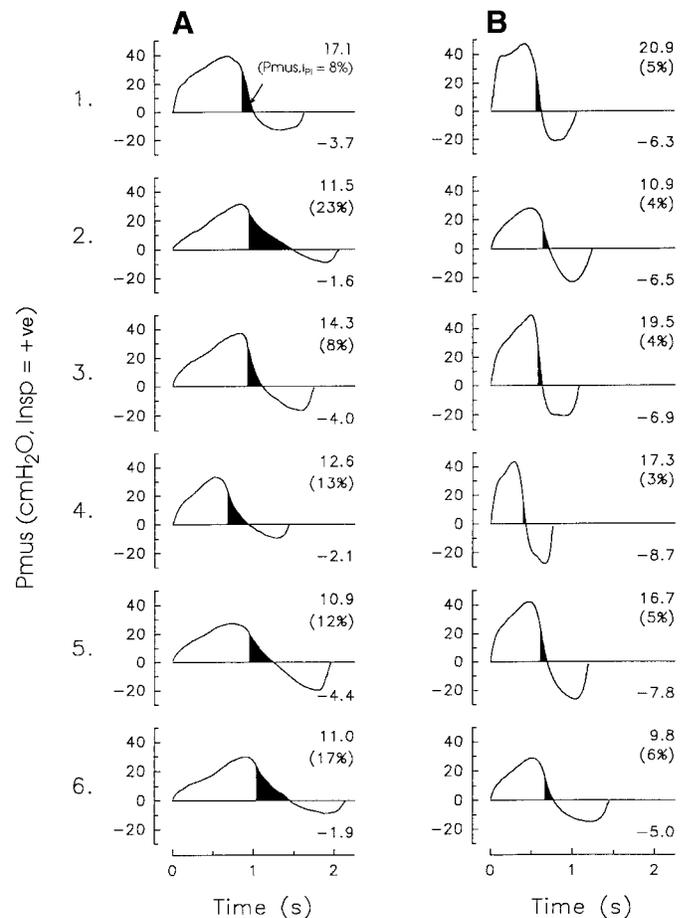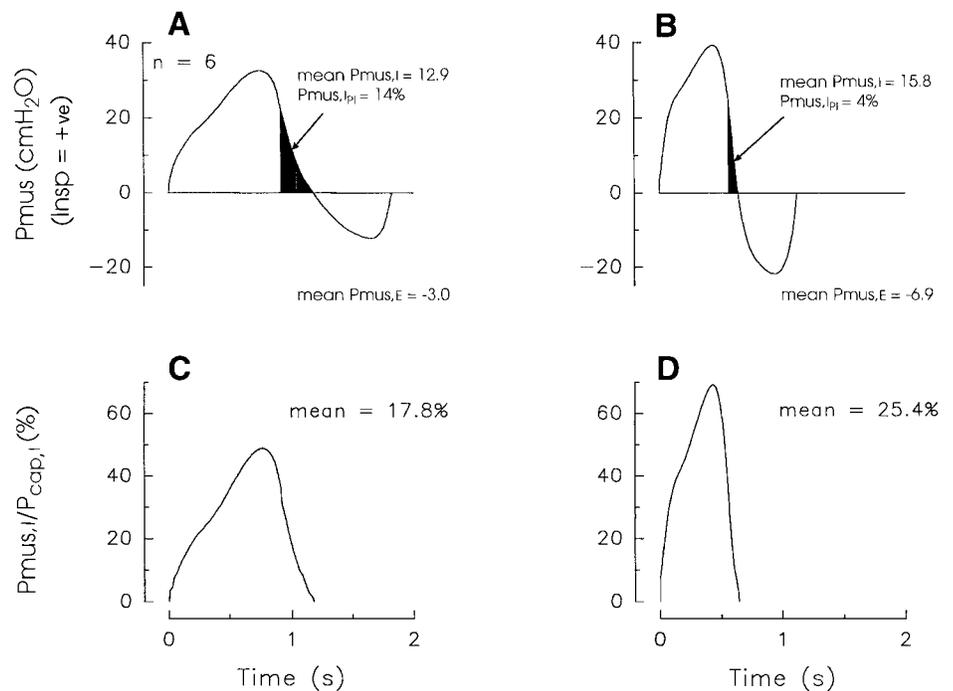

Fig. 4. Pmus at 3 min (*A*) and at end exercise (*B*) in each subject (identified by numbers at *left*). Pmus,I is positive, and Pmus,E is negative. Shaded segment of Pmus,I waveform is Pmus,I$_{PI}$. Mean Pmus,I and mean Pmus,E are averaged over respiratory cycle. Values in parentheses represent fractional contribution of Pmus,I$_{PI}$ to Total Pmus,I.

Fig. 5. Group mean Pmus and Pmus,I/$P_{cap,I}$ (%) at 3 min (*A* and *C*) and at end exercise (*B* and *D*). Pmus,I is positive, and Pmus,E is negative. Shaded region of Pmus waveform is Pmus,IPI. Fractional contribution of Pmus,IPI to Total Pmus,I is indicated. Mean values are averaged over respiratory cycle.

lated as an index of the shape of Pmus,I. This index increased significantly ($P < 0.01$) from 62 ± 3% at 3 min to 74 ± 3% at end exercise. Although there was some variation in the increase in Pmus,I among subjects, Fig. 4 shows that peak and mean expiratory pressures (Pmus,E) increased consistently from 3 min to end exercise in all subjects. Mean Pmus,E increased significantly from 3.0 ± 0.5 cmH₂O at 3 min to 6.9 ± 0.5 cmH₂O at end exercise ($\Delta = 168 ± 48\%$, $P < 0.005$; Table 4). This increase in Pmus,E resulted in a doubling of the mean Pmus,E-to-mean Pmus,I ratio from 3 min (23%) to end exercise (46%).

We wished to determine whether the greater increase in expiratory muscle pressures in these subjects was "excess pressure" resulting from expiratory flow limitation during CWHE. As maximal V̇-V measurements were not included in the study protocol, tidal V̇-V data from the last minutes of exercise were analyzed in each subject. Data from 3 min and 1 min before end exercise and at end exercise revealed that inspiratory and expiratory flows continued to increase until end exercise. That these subjects increased their expiratory flow rates at the same lung volume suggests that expiratory flow limitation did not occur, on the average. This is also supported by the observation that EELV did not change over the last 3 min of CWHE (Fig. 3). Because it was still possible that individual subjects might have had flow limitation, V̇-V data in each subject were examined. Five of six subjects continued to increase expiratory flow rates over the last few minutes of exercise, but one subject did not do so over the last minute of exercise. Therefore, expiratory flow limitation may have been present in this one subject but was unlikely in the other five subjects.

Figure 5 illustrates the average ($n = 6$) Pmus data at 3 min and at end exercise. Pmus,I is positive, and

Pmus,E is negative. As in Fig. 4, group mean Pmus,I, mean Pmus,E, and Pmus,IPI (%Pmus,I) are given. Peak and mean Pmus,I increased from 3 min to end exercise, but these increases (>20%) failed to reach statistical significance ($P = 0.07$). Pmus,E increased significantly from 3 min to end exercise; in relative terms, this increase (168 ± 48%) was significantly greater than that observed with mean Pmus,I. However, as Table 4 reveals, the increase in Pmus,E in absolute terms (~4 cmH₂O) is identical to the increase in Pmus,IIF. The increase in mean Pmus,I from 3 min to the end of CWHE was smaller as a result of the significant fall in Pmus,IPI during CWHE (also see below). Pmus,IPI fell significantly from 3 min to the end of CWHE.

As outlined in METHODS, Pmus,I was expressed as a fraction of Pmus during a maximal inspiratory maneuver ($P_{cap,I}$) at the same lung volume and flow rate. Average Pmus,I/$P_{cap,I}$ (%) throughout inspiration at 3 min and at end exercise is also shown in Fig. 5. The subjects generated a wide range of Pmus,I/$P_{cap,I}$ values: peak Pmus,I/$P_{cap,I}$ ranged from 25 to 80% and increased from 3 min (50 ± 5%) to end exercise (71 ± 11%). This increase, however ($\Delta = 44 ± 18\%$; Table 4), failed to reach statistical significance ($P = 0.055$). Mean Pmus,I/$P_{cap,I}$ averaged over the respiratory cycle is the tension-time index[1] of the inspiratory muscles. This index

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[1] Tension-time index of diaphragm (TTdi) has been defined (10) as the product of the ratio of mean diaphragmatic pressure (mean Pdi) to maximal diaphragmatic pressure (Pdi$_{max}$) and the inspiratory duty cycle (TI/TT): (mean Pdi/Pdi$_{max}$) × (TI/TT). Mean Pmus,I/$P_{cap,I}$ (%) represents the tension-time index of all the inspiratory muscles, inasmuch as it is the product of mean Pmus,I expressed as a fraction of $P_{cap,I}$ at the same volume and flow rate and the inspiratory duty cycle; thus (mean Pmus,I/$P_{cap,I}$) × (t/TT) ≈ (1/TT) × $\int_0^t$(Pmus,I/$P_{cap,I}$) (where t is neural inspiration, including PIIA).

increased significantly from $17.8 \pm 2.0\%$ at 3 min to $25.4 \pm 4.3\%$ at end exercise ($P < 0.05$; Table 4). Figure 5 also highlights the dynamic variations in the shape and intensity of the Pmus and $Pmus,I/P_{cap,I}$ waveforms throughout the respiratory cycle.

The decrease in PIIA with increasing $\dot{V}E$ throughout CWHE is summarized in Fig. 6. Group mean duration of PIIA ($TPmus,_{IPI}$) at matched levels during CWHE is shown as a fraction of TE and TT. $TPmus,_{IPI}$ fell progressively with increasing levels throughout CWHE; the values at end exercise were less than one-half of those at the start of exercise. $TPmus,_{IPI}$ decreased significantly ($P < 0.05$; Table 4) from 3 min ($33.5 \pm 4.4\%$ TE and $16.9 \pm 2.6\%$ TT) to end exercise ($15.3 \pm 0.8\%$ TE and $7.6 \pm 0.4\%$ TT). Although the postinspiratory activity of the inspiratory muscles was significant throughout CWHE, postexpiratory activity of the expiratory muscles [$Pmus,E$ persisting during the period of inspiratory flow ($TPmus,_{EPE}$)] was negligible in these subjects (1.3 ± 0.8 and $0.2 \pm 0.2\%$ TI at 3 min and end exercise, respectively). Postexpiratory $Pmus,E$ activity similarly was negligible (0.6 ± 0.5 and $0.03 \pm 0.03\%$ mean $Pmus,E$ at 3 min and end exercise, respectively).

The results of regression analyses between $\dot{V}E$ and various Pmus variables during CWHE are presented in Figs. 7 and 8. Figure 7 illustrates mean $Pmus,I$-$\dot{V}E$ and mean $Pmus,E$-$\dot{V}E$ relationships in each subject. Except in *subject 4*, it is evident that mean $Pmus,I$ and mean $Pmus,E$ increase in a linear fashion with increasing $\dot{V}E$ during CWHE. However, the correlation coefficient for a linear regression of mean $Pmus,I$ and mean $Pmus,E$ with $\dot{V}E$ in *subject 4* was significantly high ($r = 0.91$, $P < 0.05$, in both cases). Although mean $Pmus,I$ and mean $Pmus,E$ increased linearly with increasing $\dot{V}E$ throughout CWHE, there was considerable variation in the slopes (range $0.065–0.135$ $cmH_2O \cdot l^{-1} \cdot min$) and correlation coefficients (range $0.50–0.97$) of the mean $\dot{V}E$-$Pmus,I$ relationship. However, the $\dot{V}E$-$Pmus,E$ relationship during CWHE in these subjects was more consistent, with less variable slopes (range $0.051–$
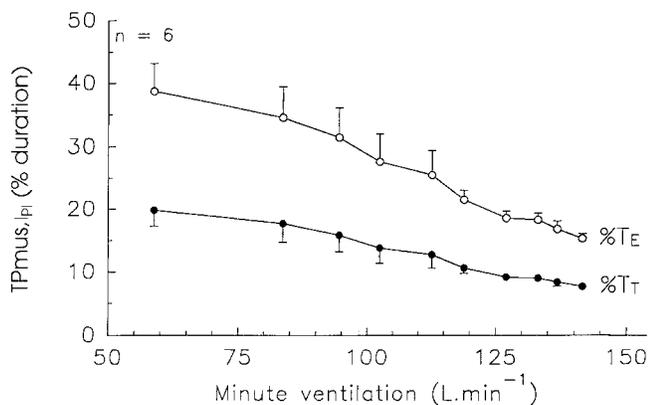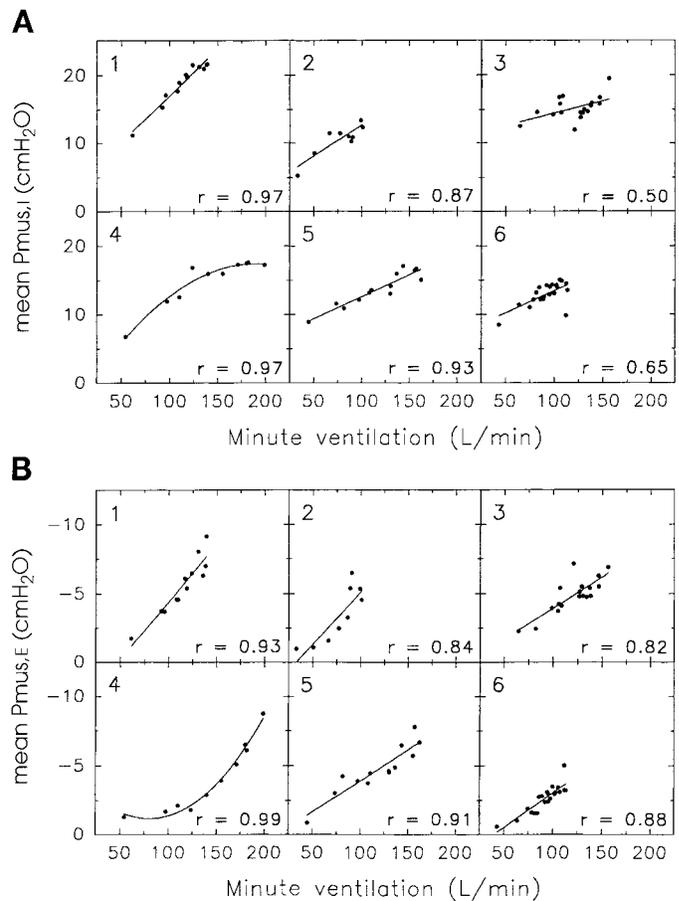
Fig. 7. Relationship between minute ventilation and mean $Pmus,I$ (*A*) and minute ventilation and mean $Pmus,E$ (*B*) in each subject (identified by numbers at *top left*) during heavy exercise. Relationship between minute ventilation and mean $Pmus,I$ and mean $Pmus,E$ is linear, except in *subject 4*.

0.083 $cmH_2O \cdot l^{-1} \cdot min$) and correlation coefficients (range $0.82–0.93$).

In contrast to the variability observed in the $\dot{V}E$-mean $Pmus,I$ and $\dot{V}E$-mean $Pmus,E$ relationships, the relationship between the net respiratory muscle pressure throughout the breathing cycle (Total Pmus) and $\dot{V}E$ was highly linear. In each subject, the $\dot{V}E$-Total Pmus correlation coefficient was significantly greater than the individual's $\dot{V}E$-$Pmus,I$ or $\dot{V}E$-$Pmus,E$ correlation coefficient. The slopes of this relation averaged 0.136 ± 0.020 $cmH_2O \cdot l^{-1} \cdot min$ ($P < 0.0001$, range $0.081–0.219$). Only in *subject 6*, however, was this relationship improved slightly with nonlinear regression ($r = 0.92$ and $r = 0.90$ with 2nd-order and linear regressions, respectively). Total Pmus increased significantly ($P < 0.005$) from 3 min to end exercise ($\Delta = 43 \pm 9\%$; Table 4). Figure 8*A* summarizes the group mean $\dot{V}E$-Total Pmus relationship (average of data at 10% increments of exercise duration) during CWHE in these subjects.

Figure 8*B* also illustrates the relationship between the inspiratory muscle tension-time index [mean $Pmus,I/P_{cap,I}$ (%)] and $\dot{V}E$ and reveals that the $\dot{V}E$-mean $Pmus,I/P_{cap,I}$ relationship (shown as group mean data) was also linear during CWHE. Subjects generated a

Fig. 6. Relationship between minute ventilation and postinspiratory inspiratory activity during heavy exercise. Duration of postinspiratory inspiratory activity ($TPmus,_{IPI}$) is shown as fraction of expiratory (TE) and total breath (TT) duration. Note progressive decline in postinspiratory inspiratory activity with increasing ventilatory levels during heavy exercise. Values are group means $\pm$ SE.

Fig. 8. Relationships between minute ventilation and Total Pmus (mean Pmus, I − mean Pmus, E, *A*) and minute ventilation and inspiratory muscle tension-time index [mean Pmus, I/$P_{cap, I}$ (%), *B*] during constant-work heavy exercise. Group mean (*n* = 6) data (averaged at 10% increments of exercise duration) show a significantly linear relationship between minute ventilation and Total Pmus (*r* = 0.99, *P* < 0.0001) and minute ventilation and mean Pmus, I/$P_{cap, I}$ (*r* = 0.99, *P* < 0.0025) during heavy exercise.
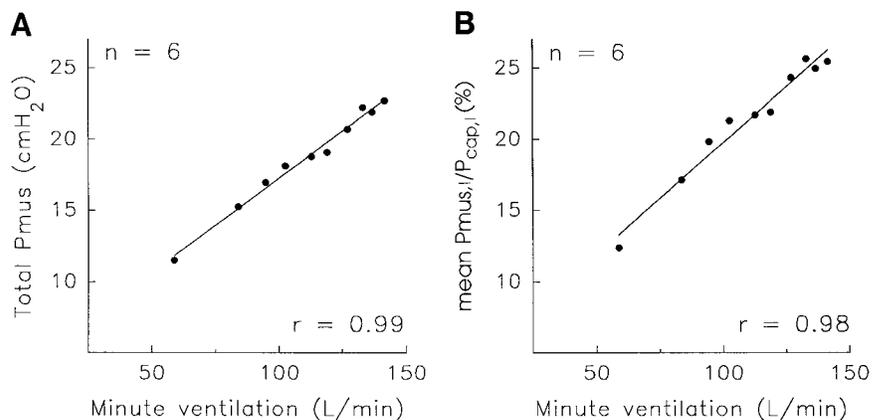
wide range (6.2–35.8%) of mean Pmus, I/$P_{cap, I}$ values during exercise, and, as Fig. 8 illustrates, mean Pmus, I/$P_{cap, I}$ was >15% for all values >75 l/min. Furthermore, the V̇E-mean Pmus, I/$P_{cap, I}$ relationship in each subject was also significantly linear (average slope 0.162 ± 0.020% · l · min^{-1}, *P* < 0.0025). In *subject 4* the correlation coefficients for the second-order and linear regressions were 0.98 and 0.97, respectively. For the V̇E-Total Pmus and V̇E-mean Pmus, I/$P_{cap, I}$ relations, the *y*-axis intercept was not significantly different from zero.

The regressions between the slopes and intercepts of the V̇E-Total Pmus and V̇E-mean Pmus, I/$P_{cap, I}$ (%) relationships (dependent variables) and respiratory system resistance (Rrs) and elastance (independent variables) during CWHE were tested. Although there were significant correlations between Rrs and the slopes of the V̇E-Total Pmus (*r* = 0.89, *P* = 0.016) and V̇E-mean Pmus, I/$P_{cap, I}$ (*r* = 0.82, *P* = 0.046) relationships in these subjects, there were no significant relationships between Rrs and any of the intercepts. Furthermore, no significant relationships were observed between respiratory system elastance and the slopes and intercepts of the V̇E-Total Pmus and V̇E-mean Pmus, I/$P_{cap, I}$ relationships in these subjects during CWHE.

DISCUSION

The results of this study designed to examine the relationship between ventilatory output and net Pmus during CWHE in humans showed that *1*) inspiratory and expiratory muscle pressures increased to meet the increasing ventilatory demands of CWHE, *2*) the relationship between the ventilatory output and the net pressure output of respiratory muscles (Total Pmus and its components) is significantly linear during CWHE, *3*) the ventilatory increase in CWHE is associated with a greater increase in expiratory than inspiratory muscle pressures, and *4*) postinspiratory (expiratory) activity of the inspiratory muscles in humans diminishes significantly with the increasing ventilatory demands of CWHE.

Critique of Methods

The validity of our assessment of changes in net Pmus during heavy exercise depends on the accuracy with which the components of Pmus (*Eq. 1*) are measured. Pes, an excellent index of changes in Ppl (33),

has been used in many studies (11, 17, 19, 24, 26, 40) and was validated before and after exercise in this study by the occlusion technique (9). In contrast to our previous work (16), Pw, el was measured in each subject by two established techniques after adequate training (see METHODS). Although the static Pw, el-V relationship is linear within the range of volume limits (35) observed in our study (EELV > 40% TLV and EILV < 90% TLC), it does not account for dynamic pressure losses due to chest wall distortion, a complex phenomenon when the dynamic P-V characteristics of chest wall (and its geometry) deviate significantly from its relaxation configuration (17, 19) as a result of increasing accessory rib cage and abdominal muscle activity during exercise. Distortive forces, although present in various degrees throughout the respiratory cycle, are most marked at VT extremes (17) (corresponding to peak pressures). Because the limits of VT (EELV and EILV) changed very little from 3 min to end exercise, it is probable that the pressure losses due to distortion, although not measured under these conditions, were similar; i.e., changes in pressure (Δ) due to chest wall distortion would have been small compared with the changes in Total Pmus.

Rw, although dependent on VT and breathing frequency in the normal range of breathing (8), tends to fall with increased frequency (0.5–2 Hz), with most of the changes (Δ ∼ 40%) occurring at the transition from 0.5 to 1 Hz (8). The change in Rw from 3 min (frequency = 34 breaths/min) to end exercise (frequency = 55 breaths/min) would therefore have been ∼0.4 cmH$_2$O · l^{-1} · s, resulting in Pw, res (*Eq. 1*) being overestimated by <1 cmH$_2$O and, in turn, mean Pmus, I and mean Pmus, E being overestimated by ∼6 and ∼16%, respectively, at end exercise. Pmus (*Eq. 1*) is therefore a valid index of respiratory muscle output during exercise in this study. Pmus, I was further expressed as a fraction (%) of the volume-matched, flow-corrected $P_{cap, I}$, and this Pmus, I/$P_{cap, I}$ (%) averaged over the respiratory cycle was used as the inspiratory muscle tension-time index (10).

Respiratory Muscle Output During Heavy Exercise

Different techniques have been used to assess the specific contributions of the different respiratory muscle

groups to the exercise ventilatory response. Measurement of thoracoabdominal P-V relationships (17, 19, 20, 27) reveal that although the diaphragm is the main muscle of inspiration at rest, significant recruitment of the inspiratory-accessory (rib cage) and the abdominal expiratory muscles contributes to the increase during exercise. However, the pattern and the magnitude of respiratory muscle activity have been shown to depend on posture and the mode of exercise (cycle ergometry vs. treadmill running) (20). Measurements of Pm (21, 28), Pes (24, 26), transdiaphragmatic pressure (11, 22, 27), and gastric pressure (11, 20, 26) also provide clear evidence of increasing inspiratory and expiratory muscle activity during exercise. Although Ppl has been used commonly as an index of net Pmus, *Eq. 1* shows that Ppl measurement by itself would underestimate respiratory muscle output, inasmuch as it does not account for static (Pw, el) and dynamic (Pw, res) pressure losses across the chest wall. Despite these limitations, Ppl measurement during exercise serves as a good qualitative index of respiratory muscle output. During incremental exercise, Leblanc et al. (26) showed progressive increases in peak inspiratory and expiratory Ppl that indicate progressive increases in inspiratory and expiratory muscle pressures. In subjects performing CWHE at 80% $\dot{V}O_{2max}$, Bye et al. (11) reported a significant increase in expiratory abdominal pressure and Ppl. More recently, Kearon et al. (24) showed that, with increasing exercise time during CWHE at >80% $\dot{W}_{max}$, although inspiratory pressures tended to plateau, there was a progressive increase in peak and end-expiratory Ppl. Johnson et al. (22) also reported a significant increase in the time integral of Pes throughout exercise with the increases in $\dot{V}E$ and inspiratory flow during heavy exercise (>85% $\dot{V}O_{2max}$). In contrast, the time integral of transdiaphragmatic pressure was shown to plateau early in exercise in their study, suggesting that the diaphragm was contributing less and the "inspiratory-accessory" muscles more to the hyperventilatory response to heavy exercise. However, these pressure measurements do not directly reflect the recruitment patterns of the diaphragm or intercostal muscle groups, inasmuch as their relative shortening and velocities of shortening are not accounted for (6). Other evidence also confirms increased inspiratory/intercostal muscle and/or reduced diaphragmatic pressures (27) during exercise; for example, Johnson et al. showed that postexercise diaphragmatic fatigue was less in the subjects in whom diaphragmatic pressure was decreased or minimal for most of heavy exercise. Similar findings have been reported in subjects performing cycle ergometer CWHE (at 80% W_{max}) to exhaustion (29).

The significant and proportional increase in abdominal expiratory muscle EMG in humans during CO_2 inhalation and its persistence in early inspiration (1) indicate that these muscles contribute to inspiratory flow under augmented ventilatory conditions. EMG data from specific inspiratory and/or expiratory muscles in animals also indicate increased respiratory muscle recruitment whenever $\dot{V}E$ is increased as a result of chemical stimulation (39) or during exercise (4, 5). All the above evidence suggests that increasing inspiratory-accessory and expiratory muscle activity contribute significantly to the ventilatory response to exercise.

The technique of quantitative assessment of respiratory muscle activity throughout the breathing cycle during exercise in humans in this study is based on that of Younes and Kivinen (42). Mean Pmus, I, Pmus, E, and $\dot{V}E$ (14.0 cmH_2O, 3.0 cmH_2O, and 80.7 l/min, respectively) at the end of maximal incremental exercise in their study were very similar to those at 3 min in our study (Tables 2 and 4). Consistent with previous studies (see above), our results also showed significant inspiratory and less significant expiratory muscle pressures in early exercise (3 min; Fig. 5). However, the subsequent temporal courses of Pmus, I and Pmus, E during CWHE were quite different. Although mean Pmus, I_{IF} increased significantly (and equally as mean Pmus, E; Table 4) from 3 min to end exercise, Pmus, I_{PI} decreased throughout CWHE. In relative terms, therefore, our subjects showed a greater increase in Pmus, E than in Pmus, I from early to end exercise. Although the increase in Pmus, E and the reduction in Pmus, I_{PI} served to augment expiratory flow, increasing expiratory muscle activity served to possibly determine (and maintain) optimal EELV during exercise, thus helping the diaphragm and the other inspiratory muscles operate on a more efficient range of their length-tension relationships as well as allowing for a greater VT in the linear P-V range of the respiratory system (19, 20, 27). We interpret this progressive and significant increase in Pmus, E as "sparing" the inspiratory muscles, for the expiratory muscles take on a greater proportion of Pmus (from 19% at 3 min to 30% Total Pmus at end exercise) with increasing $\dot{V}E$. Other recent findings (38) have also shown that, during exercise after induced global inspiratory muscle fatigue, progressively increasing expiratory muscle activity significantly helps maintain the pressure generation capacity of the diaphragm and rib cage inspiratory muscles.

Studies that have examined inspiratory muscle function (inspiratory Ppl or diaphragmatic pressure) during incremental (26) or endurance exercise (24) have shown that with increasing exercise intensity, although the demand on the inspiratory muscles increases significantly, their $P_{cap,I}$ decreases progressively. As $P_{cap,I}$ varies with muscle length (lung volume) and velocity of shortening (flow rates), Pmus, $I/P_{cap,I}$ (%) was calculated as a volume-matched, flow-corrected index of inspiratory muscle contraction throughout the breath in this study. As Fig. 5 showed, Pmus, $I/P_{cap,I}$ varied throughout the breathing cycle. Tension-time indexes, which relate the force and duration of muscle contraction, have long been used to assess endurance of the respiratory muscles; a critical fatiguing value of 0.26 for the rib cage muscles (43) and 0.15 for the diaphragm (10) have been suggested. Mean Pmus, $I/P_{cap,I}$, the tension-time index of all the inspiratory muscles, was variable between subjects (Fig. 8) and averaged 17.8% at 3 min and 25.4% at end exercise. This does not by itself imply that the inspiratory muscles were fatiguing during heavy exercise, inasmuch as it is very unlikely that

there is an invariant index above which fatigue always occurs. Recent studies, however, reveal that the pressure-generating capacity of the diaphragm (22, 29) and expiratory muscle endurance (15) are significantly compromised after exercise to exhaustion. Although these studies suggest that respiratory muscle fatigue may be present during heavy exercise, there is good evidence that it does not limit exercise tolerance in humans (25, 38).

Relationship Between Ventilatory and Respiratory Muscle Outputs During Exercise

Previous studies (21, 28) of the relationship between ventilation (mechanical output) and indexes of respiratory neural output (drive) in humans, by use of $Pm_{0.1}$, suggested that the faster increase in $Pm_{0.1}$ (than of $\dot{V}E$) was due to a nonlinear increase in the "effective impedance" of the respiratory system during exercise (21). As discussed in detail elsewhere (41), $Pm_{0.1}$ measurements during exercise may not accurately reflect inspiratory drive and/or respiratory muscle output because of *1*) the increased elastic recoil due to reduction in EELV below functional residual capacity, *2*) the changes in the shape of $Pmus,I$ (Figs. 4 and 5) during exercise (16, 41), and *3*) the variability of the time difference between the onset of neural inspiration and $Pm_{0.1}$ measurement (16). The nonlinear relationship between $\dot{V}E$ and $Pm_{0.1}$, therefore, may not necessarily reflect a true nonlinear increase in respiratory impedance during exercise.

The linear relationship between $\dot{V}E$ and $Pmus$ in humans during heavy exercise shown in this study suggests that, in addition to an efficient partition of work between inspiratory and expiratory muscle groups, increases in net respiratory muscle pressure throughout the breathing cycle (Total $Pmus$) and its components (mean $Pmus,I$ and $Pmus,E$) are precisely tuned to the ventilatory need of the exercising individual. Limited data from animals performing exercise also suggest that the electrical (EMG) and mechanical (pressure) activity of inspiratory and expiratory muscles increase proportionately with exercise hyperpnea (4, 5). The higher $\dot{V}E$-Total $Pmus$ correlation (compared with $\dot{V}E$-mean $Pmus,I$ or $\dot{V}E$-mean $Pmus,E$ relationships; Fig. 7) in each subject suggests that the net pressure generated by all the respiratory muscles (not inspiratory or expiratory alone) throughout each breath is determined by the ventilatory need of the individual during heavy exercise. Furthermore, the linear relationship between $\dot{V}E$ and mean $Pmus,I/P_{cap,I}$ (%) in all these subjects indicates that the dynamic load on the inspiratory muscle load increases in direct proportion to the ventilatory need of heavy exercise. The significant positive correlations between Rrs and the slopes of $\dot{V}E$-Total $Pmus$ and $\dot{V}E$-mean $Pmus,I/P_{cap,I}$ relationships in these subjects are consistent with the idea that flow-resistive pressure losses are an increasingly important component of $Pmus$ as $\dot{V}E$ increases significantly throughout heavy exercise. However, as EILV and EELV remain relatively constant throughout CWHE

(Fig. 3), the elastic load on the respiratory muscles changes very little with increasing $\dot{V}E$.

Postinspiratory (Expiratory) Activity of the Inspiratory Muscles During Exercise

This study also provides new evidence on the persistence of inspiratory muscle activity in the first part of expiration (PIIA, $Pmus,I_{PI}$) in humans performing heavy exercise. Resting breathing in humans is predominantly an inspiratory event from a respiratory muscle point of view, and expiration is a result of passive relaxation and slowly decaying $Pmus,I$, which persists during and "brakes" expiration (2, 37). With the substantial increase in breathing frequency during CWHE, the magnitude and the rate of rise of $Pmus,I$ are increased significantly, and the increased rate of decay of $Pmus,I$ from maximal values (Figs. 4 and 5) has been shown to depend on breathing frequency in humans (2). $Pmus,I_{PI}$ persists at the high $\dot{V}E$ levels throughout exercise, however, during a smaller fraction of TE. As Fig. 6 and Table 4 show, the duration of PIIA and its magnitude at end exercise are ~50% of the values at the start of exercise. Animal studies that have examined PIIA, however, have shown that the the duration and the magnitude of changes in PIIA depend on the nature of the ventilatory stimulus. In exercising dogs, for example, the duration of PIIA remains the same, whereas there is progressive shortening of TE, resulting in a relative increase in PIIA (5). Hypoxia and hypercapnia have been shown to reduce PIIA in some studies (34) but increase PIIA in others (39). The combination of increased expiratory pressures with a progressively decreasing $Pmus,I_{PI}$ in our subjects served to augment $\dot{V}E$, which increased throughout heavy exercise.

In conclusion, this study has shown that the hyperventilatory response of CWHE is associated with progressive increases in $Pmus,I$ and $Pmus,E$ and that the relationship between $\dot{V}E$ and net $Pmus$ throughout the respiratory cycle (and its components) during heavy exercise in humans is linear. Although inspiratory muscle load increased significantly, PIIA progressively diminished during CWHE, thus resulting in a relatively greater contribution by the expiratory muscles to Total $Pmus$ throughout each breath.

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