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VALIDATION OF A MODIFIED ONE-STEP REBREATHING TECHNIQUE 1/1
FOR MEASURING EXE. (U) ARMY RESEARCH INST OF
ENVIRONMENTAL MEDICINE NATICK MA P C SZLYK ET AL.

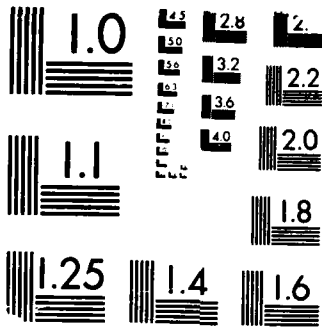
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VALIDATION OF A MODIFIED ONE-STEP REBREATHING
TECHNIQUE FOR MEASURING EXERCISE CARDIAC OUTPUT

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Running Head: Field Measures of \dot{Q}

ABSTRACT

A modification of the Farhi one-step rebreathing technique (Respir. Physiol. 28:141-159, 1976) is described for determining submaximal exercise cardiac output (\dot{Q}). Factors critical in the estimation of \dot{Q} are initial rebreathing bag volume and constant bag volume during the maneuver. By substituting a high flow rate analyzer ($500 \text{ ml} \cdot \text{min}^{-1}$) for the recommended low flow rate mass spectrometer ($60 \text{ ml} \cdot \text{min}^{-1}$), adding a recirculation circuit from the outlet of the analyzer to an inlet at the base of the rebreathing bag and reducing the length of sample tubing to the analyzer, we were able to recirculate the subject's expired gas and achieve no loss of bag volume. No statistically significant differences in estimate of cardiac output were noted between the mass spectrometer and LB-2 analyzer with recirculation circuit during submaximal cycling. Heart rate and oxygen uptake were highly correlated with cardiac output and agreed well with the literature, irrespective of the CO_2 analyzer system used. A unique feature of our method is that the subject's tidal volume is measured prior to the maneuver and then used as the initial rebreathing bag volume. Varying the bag volume by $\pm 0.2\text{L}$ from the tidal volume had no significant effect on the estimate of cardiac output during exercise. Now quick, reliable and noninvasive measurements of cardiac output are feasible in subjects not only in the laboratory but also in the field where a mass spectrometer is not readily portable.

Index terms: Field portable, noninvasive, submaximal exercise, cardiac output, rebreathing

INTRODUCTION

Several different approaches for determining cardiac output in humans are available. To circumvent unnecessary subject risk, noninvasive approaches requiring the subject to rebreathe a gas such as acetylene or carbon dioxide (CO_2) have been developed (1, 3, 5, 8, 15). Because our research projects investigate circulatory function and fluid balance in subjects during heat/exercise stresses and military training operations, a quick, reliable and noninvasive method to determine cardiac output in both laboratory and field settings is required. The rebreathing technique developed by Farhi and coworkers (1) effectively meets this requirement. The novelty of Farhi's technique is that it requires only one-step, takes less than 30 seconds for each maneuver, can be repeated at 1-2 minute intervals, and is accurate and reproducible. One drawback to the prescribed methodology and initially a major obstacle in our laboratory, was the requirement for a low flow rate (40-60 $\text{ml}\cdot\text{min}^{-1}$) CO_2 analyzer or mass spectrometer for sampling CO_2 at the mouth without significant loss of bag volume during the rebreathing maneuver. A standard CO_2 analyzer such as the Beckman, Sensormedics or Electrochemistry with sampling rates of 500 $\text{ml}\cdot\text{min}^{-1}$ was not recommended because it draws off more than eight times the sample of a mass spectrometer.

The purpose of this article is 1) to describe the recirculation circuit which was configured for using the Farhi et al. (1) one-step rebreathing technique with a high flow rate analyzer (Beckman LB-2 CO_2 analyzer) and 2) to provide validation of this recirculation circuit for measuring cardiac output during submaximal exercise.

Patricia C. Szlyk: Research Physiologist

APPARATUS DESCRIPTION

The apparatus configuration during a breathing maneuver is shown in Fig. 1. A modified 15 gauge stainless steel hypodermic needle permanently affixed to the common port of the T-shaped Collins valve served as the sampling inlet of the LB-2 CO₂ analyzer. A mouthpiece (Vacumed, large adult with bite-block) was also attached to one of the remaining ports. A "V" shaped aluminum bar was inserted into the apex of the bag to assist in gas mixing and to prevent premature collapse of the bag. To prevent loss of bag volume, analyzed gas was returned to the rebreathing anesthesia bag via a recirculation circuit.

This recirculation circuit interposed between the LB-2 CO₂ analyzer and the anesthesia bag consisted of the following: a small Y-tube (Kartell, 4 mm diameter) was mounted into the nipple at the base of the anesthesia bag. The other two openings of this tube were connected to a 3-way stopcock (Nalgene Labware, 4 mm diameter) and to a one-way quick connect fitting (Swagelock). During the rebreathing maneuver, this 3-way stopcock was connected to a 1.2 m length of Tygon tubing (ID 3/16", OD 5/16") which is connected to the exhaust port of the LB-2 CO₂ analyzer. To optimize recirculation time, the length of the tubing extending from the sampling inlet on the CO₂ sensor head to the analyzer pump was reduced from 4.6 m to 1.7 m. The total length of all sampling and recirculating tubing was 2.9 m during exercise.

Tracings of mouth CO₂ concentration during rebreathing were recorded on a Hewlett Packard (model 7004B) X,Y plotter connected to the analog output of the LB-2 CO₂ analyzer. The tracings were digitized with an Altek (ACT23-1-RP1) digitizing table and controller (AC40-4888-DKF). Cardiac output (Q) was computed using a Hewlett Packard (HP 9000 series 300) micro-computer. The BASIC language program used for analysis of the tracings is based on the theory and assumptions proposed by Farhi et al. (1).

SYSTEM EVALUATION

Six physically fit and active subjects (5 males; 1 female) participated under written informed consent. Physical characteristics for the individuals are: (means \pm SEM) age = 32 ± 3 yr; weight = 75.9 ± 6.5 kg; height = 181 ± 4 cm. Maximal oxygen consumption ($\dot{V}O_{2\max}$) was assessed while the subjects performed exhaustive graded exercise on a Collins Pedalmate cycle ergometer (average $\dot{V}O_{2\max} = 3.74 \pm 0.29$ L \cdot min $^{-1}$). During the max test and all subsequent trials, expired gases were collected using an online system. Following the max test, subjects performed two exercise protocols on nonconsecutive days.

The "day 1" protocol was designed to compare values of cardiac output (\dot{Q}) measured with the rebreathing technique using the Beckman LB-2 analyzer with recirculation circuit (flow rate = 500 ml \cdot min $^{-1}$) to those obtained with a mass spectrometer (Perkin Elmer model MGA-1100) (flow rate = 40-60 ml \cdot min $^{-1}$). Each of six (6) subjects pedaled at each of four (4) target work loads (25%, 40%, 55%, and 70% of $\dot{V}O_{2\max}$) for fifteen minutes. Steady state oxygen uptake ($\dot{V}O_2$) was measured five minutes into each work load, and was used to confirm the $\dot{V}O_{2\max}$. During this interval, average tidal volume (V_T) was measured for use as the rebreathing bag volume. During the next 8-12 minutes of bicycling at each work level, four (4) estimates of \dot{Q} were obtained with a 2 minute recovery period between measures. The first and the last estimates were obtained from the mass spectrometer and the intermediate measures of \dot{Q} were generated by the Beckman LB-2 CO $_2$ analyzer. $\dot{V}O_2$ and V_T were again assessed prior to each increase in work load. Heart rate (HR) was measured immediately before and during each rebreathing maneuver using a Hewlett Packard telemetry system.

The "day 2" protocol was designed to investigate the effect of bag volume on the estimate of \dot{Q} obtained with the rebreathing technique using the Beckman

LB-2 analyzer and recirculation circuit. Four (4) subjects bicycled for 20 minutes at each of 2 target levels: 35% $\dot{V}O_2$ max and 55% $\dot{V}O_2$ max. After five minutes of bicycling at each work load, $\dot{V}O_2$ was measured to verify % $\dot{V}O_2$ max and V_T was assessed for dispensing bag volume. Three estimates of \dot{Q} were then obtained: one with a bag volume equal to the subjects V_T , and the other two with volumes 0.2L greater than and less than V_T . We chose to vary the bag volume by 0.2L because this volume represents about 10% of the anticipated exercise V_T and this amount of variability was reported by Prihan (11). $\dot{V}O_2$, V_T and HR were verified after duplicate measures of \dot{Q} .

Repetitive measures for each of \dot{Q} and $\dot{V}O_2$ were averaged to obtain mean values at each work level for each subject. Comparisons between analyzer systems and between bag volumes were done using ANOVA. Significance was accepted at $p < 0.05$.

RESULTS OF SYSTEM EVALUATION

Comparison of high flow rate CO₂ analyzer with recirculation circuit and low flow rate mass spectrometer

Nearly simultaneous estimates of cardiac output were determined using the two different instruments for CO₂ analysis. The relationship between cardiac output measured with the mass spectrometer and the LB-2 CO₂ analyzer with recirculation circuit was described by a regression line close to identity (Fig. 2). Cardiac output measured with the LB-2 analyzer with recirculation circuit was, on average, 0.35 L*min⁻¹ less than that measured with the low flow rate analyzer, but this difference was statistically insignificant.

Heart rate (HR), $\dot{V}O_2$ and \dot{Q} (regardless of CO₂ measuring device) all demonstrated statistically significant ($p < 0.05$) increases with increased work load (Table 1). The linear increases in heart rate and $\dot{V}O_2$ associated with

increased worklevels were highly correlated ($\dot{V}O_2 = 0.03 * HR - 1.36$, $R = 0.93$). Also, HR was highly correlated with Q irrespective of the CO_2 analyzer system used ($\dot{Q} = 0.15 * HR - 1.58$, $R = 0.86$).

The \dot{Q} and $\dot{V}O_2$ relationship generated in the present study was linear and remarkably predictable during graded cycle exercise as previously demonstrated for both treadmill and cycle exercise (2, 5, 15). Faulkner and coworkers (2) have shown that the \dot{Q} - $\dot{V}O_2$ relationship measured with a slower multiple step rebreathing method and a high flow rate CO_2 analyzer, is described by the equation: $\dot{Q} = 5.2 * \dot{V}O_2 + 5.2$. Using similar CO_2 rebreathing techniques, others have described this relationship by regression lines of $\dot{Q} = 6.2 * \dot{V}O_2 + 3.1$ (5) and $\dot{Q} = 4.96 * \dot{V}O_2 + 5.12$ (3). In the present study, we computed regression lines of $\dot{Q} = 5.2 * \dot{V}O_2 + 6.6$ and $\dot{Q} = 5.6 * \dot{V}O_2 + 6.1$ for the mass spectrometer and LB-2 analyzer with recirculation circuit, respectively (see Table 1). Because no statistical difference between the regressions for the two analyzer systems was found, data from day 1 and 2 protocols were combined and one regression of $\dot{Q} = 5.5 * \dot{V}O_2 + 5.75$, $R = 0.91$ was calculated. Our data best agrees with that of Pendergast (personal communication, Physiology Dept, SUNY at Buffalo, NY) who used the Farhi technique and observed that $\dot{Q} = 5.65 * \dot{V}O_2 + 5.0$ for a multitude of exercise regiments and with Smyth and coworkers (15) who calculated that for treadmill running, $\dot{Q} = 4.82 * \dot{V}O_2 + 6.7$ using dye-dilution and $\dot{Q} = 5.04 * \dot{V}O_2 + 4.67$ using acetylene rebreathing. Aside from Pendergast, we were unable to identify another group who generated the \dot{Q} - $\dot{V}O_2$ relationship for graded exercise using a one-step CO_2 rebreathing maneuver. The slope of the regression line in the present study agrees well with other studies (2, 3, 5, 7, 8, 15). Several possible explanations for the slightly higher intercept observed by ourselves and Smyth et al. (15) are that the subject's initial breaths during the rebreathing maneuver were either too

rapid or too slow, the subject's last expired breath prior to rebreathing was beyond functional residual capacity, the subject's ability and confidence in performing the maneuver would have benefited from additional practice, or the subjects were above average physical fitness. Since we discarded unsatisfactory trials, the higher intercept in the present investigation is, most probably, a combination of training in technique, subject confidence and subject fitness. The fact that values of \dot{Q} generated using the LB-2 CO₂ analyzer were not significantly different from the mass spectrometer data provides solid evidence that our estimates of \dot{Q} are valid.

Comparison of varying bag volumes on cardiac output measured using the LB-2 analyzer with recirculation circuit

Farhi et al. (1) emphasized the importance of the rebreathing bag volume being nearly equivalent to the subject's V_T . A unique feature of our methodology is that we first measure the subject's V_T and then use this volume as the initial bag volume. Moreover, we verified V_T during all $\dot{V}O_2$ collections. Table 2 depicts the range of V_T , average V_T and modal V_T obtained during all $\dot{V}O_2$ collections. While V_T varied breath to breath (4,6) the usual variation was about 0.4L or $\pm 0.2L$. Of more importance is that neither our mode nor average V_T at each work level was significantly different from the initial measure of V_T which was used as the rebreathing bag volume.

No significant differences in our estimate of exercise \dot{Q} were noted when bag volume was altered by $\pm 0.2L$ (Fig. 3). The \dot{Q} obtained with bag volumes equal to $V_T + 0.2L$ was $1.1 \text{ L} \cdot \text{min}^{-1}$ greater than the line of identity at low output ($\dot{Q} = 5 \text{ L} \cdot \text{min}^{-1}$) and $1.0 \text{ L} \cdot \text{min}^{-1}$ less than the line of identity at high output ($\dot{Q} = 20 \text{ L} \cdot \text{min}^{-1}$). When bag volume was $V_T - 0.2L$, estimates of exercise \dot{Q} were uniformly lower by $1.0 \text{ L} \cdot \text{min}^{-1}$. Directional trends in exercise \dot{Q} were not observed when bag volumes were altered by $0.2L$.

By substituting a high flow rate analyzer (Beckman LB-2 CO₂ analyzer) for the mass spectrometer, reducing the length of the sampling tubing on the LB-2 analyzer and then adding a recirculation circuit from the exhaust output of the analyzer to an inlet at the base of the rebreathing bag, we were able to recirculate the subject's expired gases and achieve no loss of bag volume. Because of the strong agreement between values of \dot{Q} determined using the LB-2 CO₂ analyzer with recirculation circuit and the low flow rate mass spectrometer, and the excellent agreement with the values of \dot{Q} reported in the literature, we conclude that our modification of the Farhi technique is a valid means of determining \dot{Q} during submaximal work. We recommend that subjects attend several practice trials prior to data collection and a minimum of 2 repetitive measures be taken to insure reproducibility. Measures for \dot{Q} can now be performed quickly, repetitively and reliably in individuals working under a variety of environmental conditions in both the laboratory and field settings.

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DISCLAIMERS

The views, opinions and findings contained in this report are those of the authors and should not be construed as official Department of the Army policy, position, or decision, unless so designated by other authorizing documentation.

Human subjects participated in this study after giving their informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on use of volunteers in research.

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FIGURE LEGENDS

Figure 1. Apparatus configuration. Pump lines are denoted by solid lines and electrical connections via dashed lines.

Figure 2. Comparison of cardiac output (\dot{Q}) measured with low flow analyzer (MASS SPEC) and high flow rate analyzer (LB-2) with recirculation circuit. Solid line represents line of identity.

Figure 3. Comparison of cardiac output values (\dot{Q}) obtained with rebreathing bag volumes equivalent to tidal volume (V_T) as shown on the abscissa to those obtained with volumes equal to tidal volume plus 0.2L ($V_T + 0.2L$) depicted by the filled squares and solid line and to tidal volume minus 0.2L ($V_T - 0.2L$) shown by the open squares and dashed line. The high flow rate LB-2 analyzer with recirculation circuit was used for all measurements.

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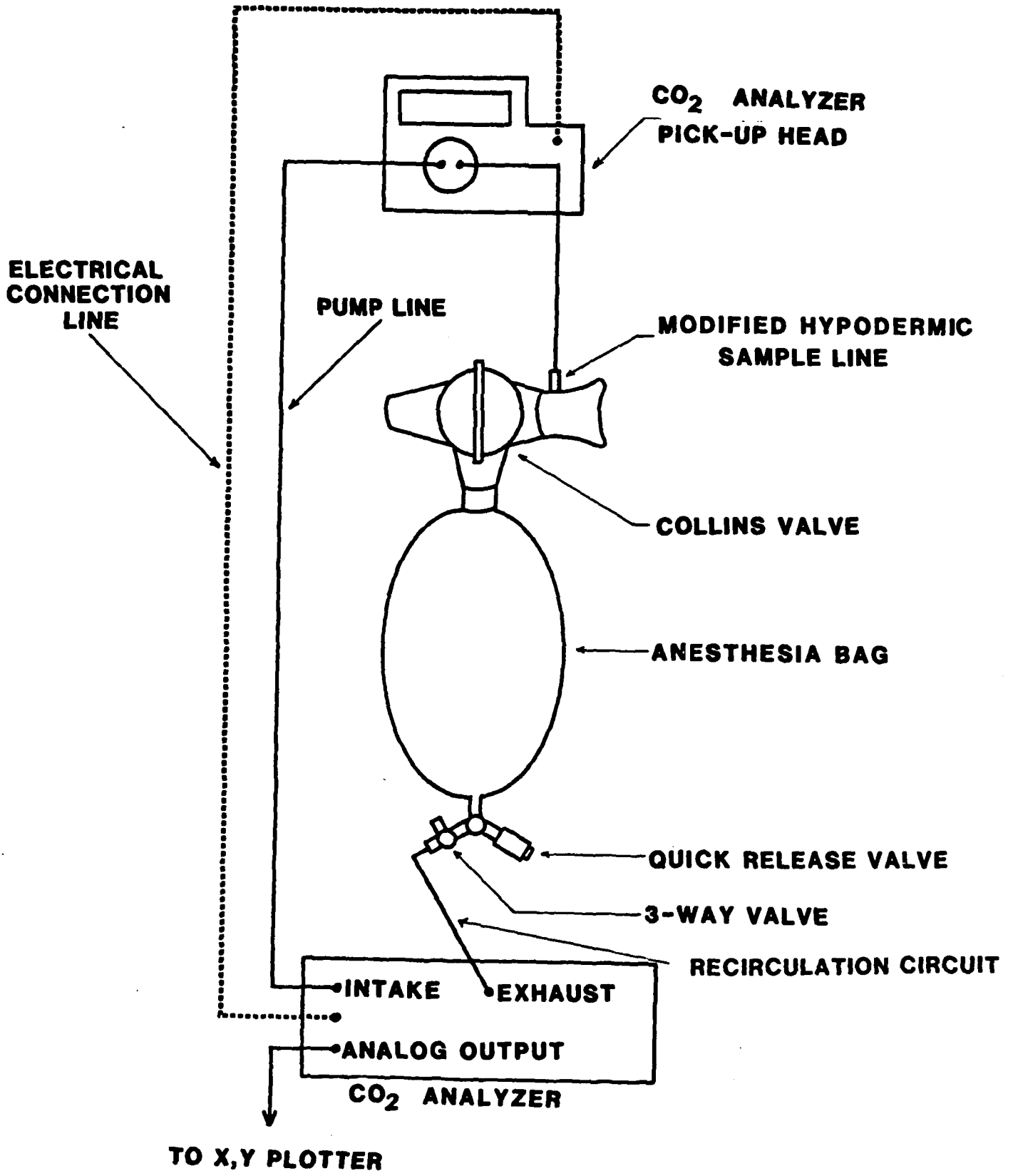


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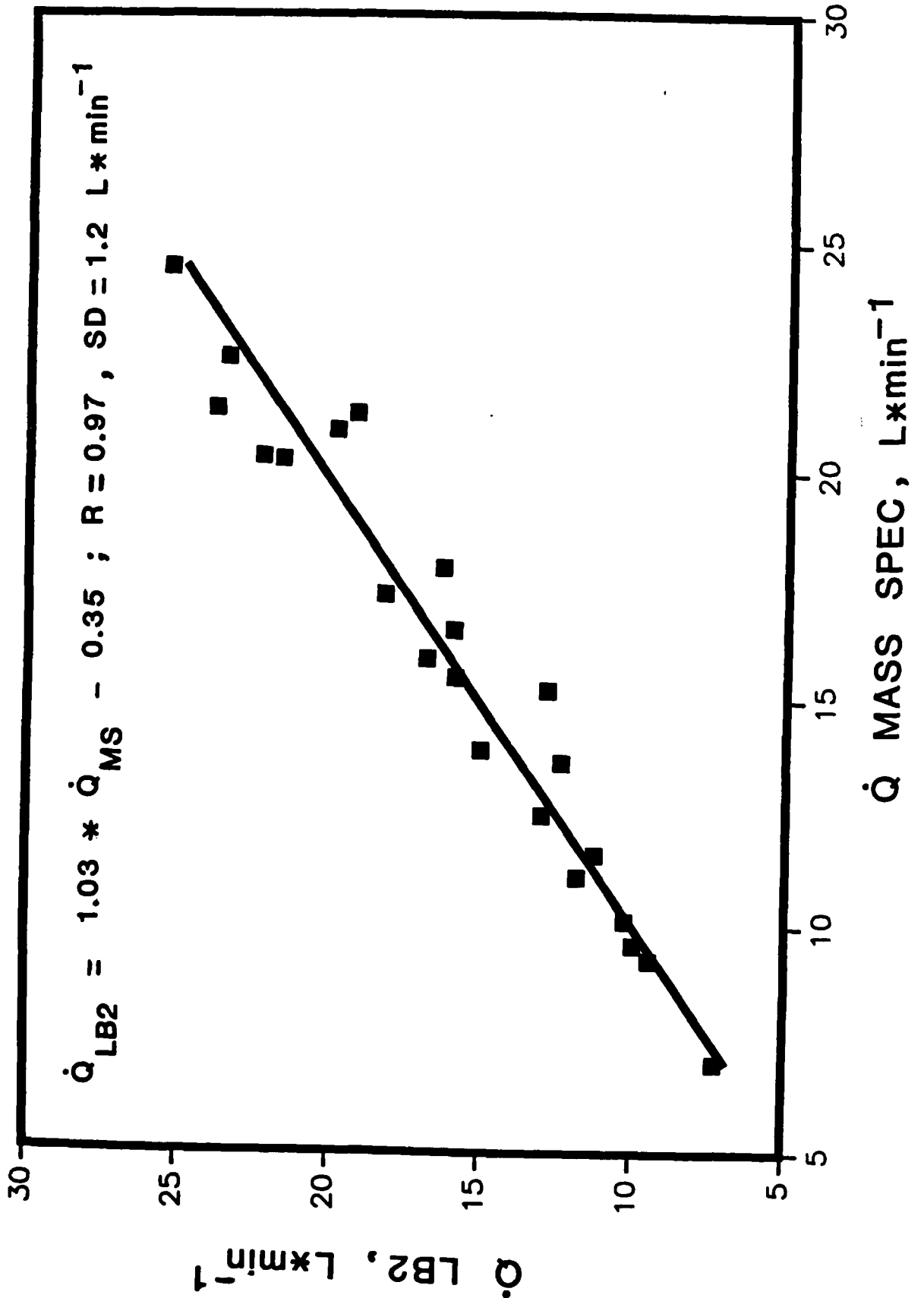


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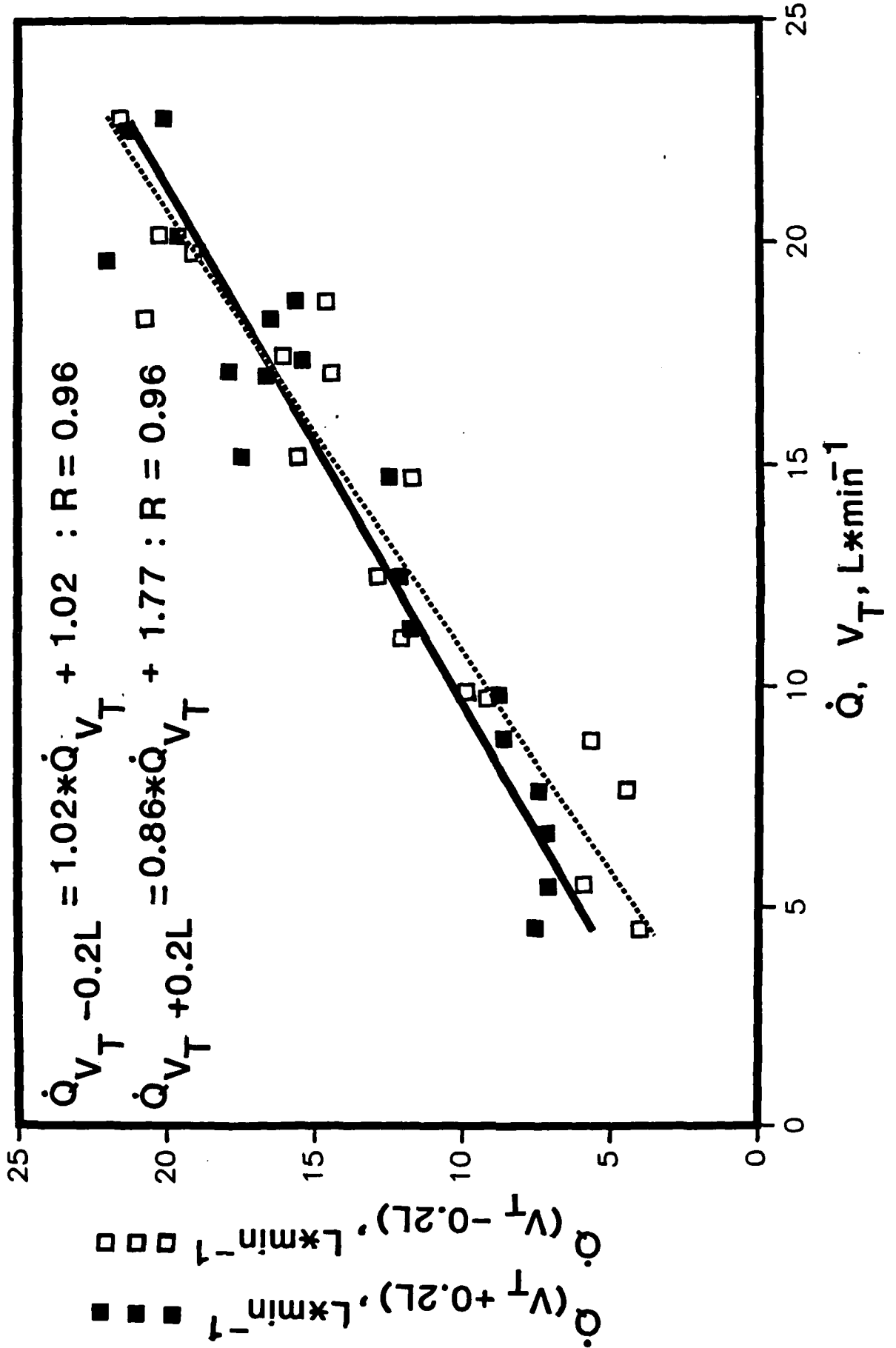


TABLE 1: COMPARISON OF VALUES FOR CARDIAC OUTPUT USING THE HIGH FLOW RATE CO₂ ANALYZER WITH RECIRCULATION CIRCUIT AND THE LOW FLOW RATE ANALYZER

Subject	Target $\dot{V}O_{2\max}$	Actual $\dot{V}O_{2\max}$	$\dot{V}O_2$ (L*min ⁻¹)	HR (bpm)	\dot{Q}_{LB-2}^+ (L*min ⁻¹)	\dot{Q}_{MS}^* (L*min ⁻¹)
1	25	28	1.10	86	15.0	13.9
	40	41	1.64	100	18.2	17.3
	55	63	2.53	130	23.4	22.4
	70	82	3.28	165	25.3	24.5
2	25	28	1.02	79	10.15	10.1
	40	37	1.35	91	12.3	13.6
	55	55	2.03	110	15.8	15.5
	70	73	2.70	130	21.7	20.2
3	25	24	0.92	98	12.8	15.1
	40	35	1.36	115	15.9	16.5
	55	51	1.99	132	19.8	20.9
	70	87	3.39	162	23.8	21.3
4	25	21	0.93	85	11.2	11.55
	40	30	1.38	111	16.8	15.9
	55	56	2.53	148	22.25	20.3
5	25	26	1.03	90	9.5	9.3
	40	38	1.50	108	11.8	11.1
	55	58	2.28	136	16.3	17.9
	70	73	2.86	170	19.2	21.25
6	25	25	0.59	72	7.3	7.0
	40	33	0.79	92	9.3	9.6
	55	52	1.23	119	12.9	12.5

+ \dot{Q}_{LB-2} = cardiac output obtained with Beckman LB-2 CO₂ analyzer (flow rate=

500 ml*min⁻¹) and recirculation circuit

- * \dot{Q}_{MS} = cardiac output determined using the Perkin Elmer mass spectrometer
(low flow rate= 60 ml*min⁻¹)

TABLE 2 COMPARISON OF REBREATHING BAG VOLUME TO TIDAL VOLUMES (V_T) MEASURED AFTER MANEUVER

Sub	$\dot{V}O_{2\max}$	Rebreath ⁺ Bag Vol (L)	Range of V_T (L)	Average V_T (L) (+1SEM)	Modal V_T (L)
1	37	2.0	1.5-1.9	1.7 (0.1)	1.8
		2.2+	2.4-3.3	2.9 (0.1)	3.2
		2.4	2.5-3.0	2.8 (0.1)	2.9
	62	2.9	3.0-3.3	3.1 (0.05)	3.2
		3.1+	3.0-4.0	3.6 (0.1)	3.3
		3.3	3.0-3.2	3.3 (0.1)	3.2
4	35	1.3	1.3-1.7	1.6 (0.04)	1.6
		1.5+	1.3-1.7	1.5 (0.05)	1.5
		1.7	1.3-1.7	1.5 (0.04)	1.5
	67	1.7	1.6-1.8	1.7 (0.02)	1.7
		1.9+	1.7-2.1	1.8 (0.03)	1.8
		2.1	1.7-2.2	1.9 (0.04)	2.0
5	40	0.9	1.0-1.4	1.1 (0.04)	1.0
		1.1+	0.9-1.4	1.2 (0.05)	1.3
		1.3	0.9-1.1	1.0 (0.03)	1.1
	71	1.2	1.1-1.6	1.3 (0.03)	1.3
		1.4+	1.4-1.8	1.7 (0.05)	1.6
		1.6	1.3-1.8	1.5 (0.05)	1.3
6	24	0.8	0.5-0.9	0.8 (0.03)	0.7
		1.0+	0.9-1.3	1.0 (0.03)	1.1
		1.2	0.9-1.1	1.0 (0.02)	1.0
	45	1.0	1.0-1.7	1.3 (0.04)	1.3
		1.2+	0.9-1.6	1.2 (0.05)	1.3
		1.4	0.9-1.4	1.1 (0.04)	1.1

Rebreathing bag volume denoted by + was equivalent to initial tidal volume (V_T) measure

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