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Methodological considerations related to the use of the carbon dioxide rebreathing method for the determination of cardiac output

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METHODOLOGICAL CONSIDERATIONS RELATED TO THE USE OF THE CARBON DIOXIDE REBREATHING METHOD FOR THE DETERMINATION OF CARDIAC OUTPUT

By

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Methodological Considerations Related to the Use of the Carbon Dioxide Rebreathing Method for the Determination of Cardiac Output

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This study investigated certain methodological considerations related to the use of the carbon dioxide (CO_2) rebreathing method for the determination of cardiac output. Ten male subjects, faculty and students from the University of Montana, were tested to determine their cardiac outputs at three different oxygen uptakes ($\dot{V}O_2$). The indirect Fick principle was used to determine cardiac output. Subjects exercised on a bicycle ergometer at three separate $\dot{V}O_2$'s. Subjects rebreathed three different mixtures of CO_2 in oxygen (O_2) gas in order to obtain suitable lung-rebreathing system equilibrium patterns. The intent of this aspect of the investigation was to determine if each concentration of CO_2 placed in the external rebreathing system corresponded to a different $\dot{V}O_2$ and if these $\dot{V}O_2$'s were different from those reported in the literature. In a smaller investigation, three subjects were tested in both low and moderate altitude sites, Madison, Wisconsin, and Missoula, Montana, respectively. This was performed to determine if altitude affected the relationship between the $\dot{V}O_2$ and the concentration of CO_2 placed in the external rebreathing system. Subjects exercised on a bicycle ergometer at three different workloads and rebreathed different mixtures of CO_2 in O_2 gas.

An analysis of the data indicated that the mean $\dot{V}O_2$'s for all subjects tested in Missoula, Montana, for a given concentration of CO_2 rebreathed, were significantly different from one another. Each concentration of CO_2 corresponded to a different $\dot{V}O_2$. These values were recommended for use when estimating the concentration of CO_2 to be placed in the rebreathing system for a given workload. This relationship appeared to be different from that reported in the literature. Much lower workloads were found to be associated with a given concentration of CO_2. Also, it was determined that the cardiac output values generated by the method used in this study appeared to be as valid and reliable as those reported in the literature. In a smaller investigation (N = 3), an analysis of the data showed that the mean $\dot{V}O_2$'s needed to obtain suitable equilibrium rebreathing patterns for a given concentration of CO_2 were higher in Madison, Wisconsin.

It was concluded that the three different concentrations of CO_2 used in this study were associated with three distinctly different $\dot{V}O_2$'s. This relationship was different from that reported in the literature. Lower $\dot{V}O_2$'s, for a given CO_2 concentration, were found in Missoula, Montana, in order to obtain suitable equilibrium rebreathing patterns. The cardiac output values generated were found to be reliable and valid and compared well with values reported in the literature. In the smaller sample (N = 3), lower $\dot{V}O_2$'s were found in the moderate altitude site (Missoula) than for the low altitude site (Madison) for the same concentration of CO_2.

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INTRODUCTION

Endurance athletes must possess highly developed systems to take in, transport, and utilize oxygen in order to perform near maximal efforts for prolonged periods of time. For research in exercise physiology, the assessment of an athlete's aerobic response to exercise is important. Various tests exist to determine the functional characteristics of the systems to take in and utilize oxygen. Often, the assessment of an athlete's ability to transport oxygen, a function of the cardiovascular system, is important to identify the nature of the cardiovascular response to exercise. During exercise, an athlete's cardiac output, the amount of blood pumped per minute by the heart, is important in determining the amount of oxygenated blood reaching the tissues. This is an important factor in the ability to give a near maximal performance. Without adequate transport of oxygen, performance can suffer. The determination, therefore, of an athlete's cardiac output can be used to assess the functional characteristics of his cardiovascular system. This information can be used to expand the understanding of the cardiovascular response to exercise and can be applied to perhaps improve an individual's performance in sport.

Cardiac output can be determined by a number of methods: right heart catheterization, dye dilution (6), thermodilution (20), and gas rebreathing, e.g., carbon dioxide (8), or nitrous oxide (2) are examples of a few techniques. The majority of these methods are either invasive or too costly to be appropriate for use in exercise studies. The carbon dioxide (CO_2) rebreathing method, however, is a non-invasive, inexpensive method that can be performed in a short period of time by trained personnel.

The CO_2 rebreathing method determines cardiac output using the indirect Fick equation (8):

Cardiac Output = CO_2 production/venoarterial CO_2 difference

Carbon dioxide parameters are substituted for oxygen parameters in the calculation of cardiac output by the indirect Fick method. Carbon dioxide production ($\dot{V}CO_2$) is determined during normal, steady-state exercise. Arterial and mixed venous CO_2 contents are used to estimate the venoarterial CO_2 difference. Arterial CO_2 content is estimated from end-tidal gas analysis. The mixed venous CO_2 content is estimated with a rebreathing technique using from 6% to 15% CO_2 in oxygen (O_2).

During the rebreathing procedure, the experimenter attempts to match the CO_2 concentration arriving in the blood at the lungs of the exercising subject with the CO_2 gas concentration placed in an external rebreathing system. If an appropriate gas concentration is chosen a gradient for net diffusion of CO_2 between the blood and lungs will not exist and equilibrium will occur. In order to minimize the number of trials necessary to obtain equilibrium in the rebreathing system, Jones and Rebuck (11) have developed a table which allows the prediction of the concentration of CO_2 gas to be placed in the rebreathing system based upon two parameters: O_2 uptake and end-tidal CO_2 levels (see Table 1). In preliminary work these recommendations have been found to

Table 1

Suggested Initial Bag Concentrations to Obtain Rebreathing Equilibriums

O_2 Uptake (L·min-1)	End-Tidal PCO_2 (mm Hg)	Bag CO_2 Concentration (%)
1.0	40	11.5
	30	10.5
1.5	40	12.0
	30	11.0
2.2	40	13.0
	30	12.0
3.0	40	14.0
	30	13.0

Source: Jones, N.L., Campbell, E.J.M., Edwards, R.H.T., and Robertson, E.G. Clinical Exercise Testing. Philadelphia: W.B. Saunders, 1975, page 94.

be inappropriate--much lower oxygen uptakes, for a given concentration of CO_2, than those recommended by Jones and Rebuck are required to obtain suitable equilibrium patterns. The characterization of the oxygen uptakes associated with equilibrium-causing CO_2 concentrations, for Missoula, Montana, needs to be performed. This information can be used in a fashion similar to the data of Jones and Rebuck to expedite the process of rebreathing equilibrium attainment.

In order to obtain a possible explanation for the departure from the recommendations of Jones and Rebuck, a letter was written to Jones and his comments on these preliminary findings were requested. In a reply, the comment was made that the source of departure from his recommendations resulted from the fact that subjects with abnormal lung function characteristics were tested. While this recommendation might have some validity, certain principles involved in the rebreathing equilibrium could be effected by altitude. This could offer a more complete explanation for the departure from Jones' and Rebuck's guidelines.

The CO_2 rebreathing principle for the determination of cardiac output is based, in part, on the concentration of CO_2 as measured under certain conditions. The standard nomenclature used to refer to gas concentrations is the partial pressure the gas exerts, which is related to its concentration (percentage) in the system being considered (6). Partial pressure is calculated by the following equation:

$$\text{Partial Pressure of a gas} = (\text{Barometric pressure}) \times (\%\ \text{concentration})$$

From this equation it can be seen that if the same concentration of gas is used at locations where there is a difference in barometric pressure, differences in partial pressure will result. For example, at sea level, where barometric pressure is 760 mm Hg, a 10% CO_2 gas mixture will exert a partial pressure (PCO_2) of 76 mm Hg. At 3200 feet, where barometric pressure is lower (680 mm Hg) the PCO_2 falls to 68 mm Hg. Table 1 was constructed from experimentation at a location, Hamilton, Ontario, where the barometric pressure is very close to that at sea level. When the recommendations of this table are used at an altitude of 3200 feet (Missoula) a much lower PCO_2 is exerted due to the differences in barometric pressure between the two altitudes. This difference in PCO_2 between Hamilton, Ontario, and Missoula, Montana, is small, but, should be sufficient to explain the need for lower oxygen uptakes in order to obtain equilibriums at the same concentration of CO_2. In trying to match similar PCO_2's at the lung, it seems reasonable that a decreased CO_2 production by the body, resulting from a lower oxygen uptake, would be required. To assess this possibility directly, oxygen uptakes for a given concentration of CO_2 were determined in low and moderate altitude sites: Madison, Wisconsin, and Missoula, Montana, respectively.

The fact that lower workloads are required to obtain suitable equilibriums could affect the validity and reliability of the cardiac outputs obtained at this altitude. It does not require an extremely high workload before the concentration of CO_2 to obtain equilibrium exceeds the linearity of the analyzer. The Beckman's LB-2 analyzer is reported to be a linear analyzer over the range of CO_2 concentrations from 0% to 10% (3). Missoula's altitude requires the use of gas concentrations which often exceed the limit of the assured linearity of the analyzer. The specific performance characteristics of each analyzer are not included with each unit. The verification, therefore, of the linearity and point of departure from linearity of the analyzer is important in establishing the validity and reliability of the cardiac outputs calculated by this method when high concentrations of CO_2 are used.

Statement of the Problem

The purpose of this investigation was to examine certain methodological concerns related to the use of the CO_2 rebreathing method for the determination of cardiac output. To characterize the oxygen uptake for a given concentration of CO_2 and to determine the effects of altitude on the method, the following hypotheses were constructed:

1. There will be no difference in the oxygen uptake (workload) required to obtain suitable equilibriums for the concentrations of CO_2 gas available in Missoula, Montana.

2. There will be no difference in the workloads recommended by Jones (see Table 1, page 3) and those required to obtain suitable rebreathing equilibriums in Missoula, Montana, for similar concentrations of CO_2.

3. There will be no difference in the workloads required to obtain rebreathing equilibriums at similar CO_2 concentrations between the low altitude site, Madison, Wisconsin, and the moderate altitude site, Missoula, Montana.

Delimitations

This study involved an investigation of the equilibrium rebreathing patterns in 18 to 35 year old males. Generalizations, therefore, resulting from this study will apply to the male age bracket sharing characteristics with those tested.

Limitations

The following limitations exist in this study:

1. The calibration of the CO_2 and O_2 analyzers in low and moderate altitudes was not performed by the same calibration gas. The calibration gases used in both locations, however, were verified by repeated Scholander analyses.

2. The testing performed in Missoula, Montana, and Madison, Wisconsin, involved repeated testing on a very small number of subjects (N = 3).

Assumptions

The following principles were assumed in the determination of equilibrium rebreathing patterns and maximal aerobic power ($\dot{V}O_2$ max):

1. The Beckman Metabolic Measurement Carts used in low and moderate altitudes would produce the same equilibrium values for each subject if the machines could be used simultaneously at the same location.

2. Subjects gave a maximal effort in the determination of maximal aerobic power.

Chapter 2

METHODOLOGY

Subject Selection

Ten male volunteers between the ages of 18 and 35 were solicited from the population of University of Montana students and faculty. The invitations to participate were done during Spring Quarter, 1982. A subset of this group (N = 3) was also tested at a low altitude site, Madison, Wisconsin. All subjects were required to sign an informed consent form approved by the University of Montana Human Subjects Committee (see Appendix A).

Testing Procedure

Subjects were scheduled to report to the lab at a specific time and were requested not to eat or perform any strenuous lower body exercise two to three hours before the test. The physical characteristics of the ten subjects were determined: age, height, and weight (see Table 2). The subjects were familiarized with all testing protocols prior to any test (see Appendix B). Initially, all subjects were to be tested to determine their $\dot{V}O_2$ max using a bicycle ergometer (Monark). The protocol, recommended by Faria, was used in this study (18).

Subjects began pedalling at a rate of 80 revolutions per minute, as monitored by a metronome (Seiko SQM-357), against a light resistance for a period of two minutes. The workload increased 480 kpm every two minutes during the initial stages of the test and 240 kpm every two

Table 2

Physical Characteristics of Subjects

Subject	Age (years)	Height (cm)	Weight (kg)	$\dot{V}O_2$ Max ($ml \cdot kg^{-1} \cdot min^{-1}$)
G.A.	20	182.9	79.5	59.7
T.C.	27	177.8	70.0	
J.H.	30	177.8	77.3	58.0
P.L.	22	175.3	64.5	
K.M.	20	177.8	75.5	54.2
J.N.	25	188.0	77.3	56.6
B.S.	18	185.4	65,9	
M.S.	25	175.3	68.6	57.5
J.W.	32	190.5	86.4	
R.W.	34	172.7	68.6	55.0
Mean	25	180.4	73.4	56.3[a]

[a]Mean calculated from data obtained on six subjects

minutes as the subject approached his maximum. The test was terminated when the subject was no longer able to continue or when further increases in workload did not yield further increases in O_2 consumption. The test lasted approximately eight to ten minutes.

This information was used to obtain the relative workloads used in the cardiac output studies on each subject. Subjects exercised at 30%, 50%, and 60% of $\dot{V}O_2$ max and performed CO_2 rebreathings. These relative workloads were used as a starting point from which adjustments in the workload could be made in order to obtain suitable equilibrium patterns for a given concentration of CO_2. Cardiac output trials on the first two subjects (J.N., and M.S.) revealed that the workloads called for by 30%, 50%, and 60% of $\dot{V}O_2$ max, were too high for the concentrations of CO_2 available in Missoula; suitable equilibrium patterns could not be obtained for these workloads. Subjects needed to work at lower levels than those generated by the above percentages of $\dot{V}O_2$ max. An examination of the data revealed that absolute oxygen uptakes of .50, .80, and 1.0 $L \cdot min^{-1}$ would be more appropriate as starting points for the cardiac output trials. The use of absolute oxygen uptakes eliminated the need to perform a test to determine the $\dot{V}O_2$ max on the remaining subjects. The $\dot{V}O_2$ max data reported in Table 2 are only presented to provide further information on the physical characteristics of the subjects. (Of the eight subjects remaining in the study to be tested after this decision was made, four of these subjects requested a maximum test performed for personal reasons. Their data are also included).

During the $\dot{V}O_2$ max test, expired gas was analyzed using a Beckman Metabolic Measurement Cart. Calibration of the unit was performed with reference gases--verified by repeated Scholander analyses--

before and after each testing session. Oxygen uptake and other respiratory measures were determined every minute during the tests. The electrocardiogram was monitored by chest electrodes (CM-5) and heart rates recorded on a stress testing monitor (Avionics 2900B).

Cardiac Output

The CO_2 rebreathing equilibrium method used in this study has been shown to be a valid and reliable method for determining cardiac output. The method, in its present form, has come from work done by Collier (4) and later by Jones and his coworkers (8,9,10,11,12,13,14).

Several studies have compared the cardiac outputs calculated by CO_2 rebreathing with criterion methods for the determination of cardiac output. Muiesan and his coworkers (16) found, in 17 normal subjects, a correlation of .97 between the cardiac outputs determined by CO_2 rebreathing and direct O_2 Fick methods. In a similar comparison, Wigle and associates (21) obtained a correlation of .80, in 11 patients who exercised on a bicycle ergometer, for the cardiac outputs calculated by both methods. When comparing the cardiac outputs obtained from CO_2 rebreathing and dye dilution methods, he obtained a correlation of .75. In a report comparing the automated methods used in this study (Beckman) with a hand calculated version (McMaster) Kane and others (14) found a correlation of .97 between the cardiac outputs calculated, in both sick and healthy individuals, by the Beckman and McMaster methods.

The reliability of the CO_2 rebreathing method has also been examined. In work done on 10 normal subjects, mean age 20.9 years, Zeidifard (22) found the reliability of the cardiac output values obtained from CO_2 rebreathing to be similar to the results obtained from studies using direct (invasive) methods. In a similar study, van Herwaarden and others (7) came to the same conclusions. Wigle (21) found that all cardiac outputs calculated for a similar workload, using the CO_2 rebreathing method, were within ten percent of the average value.

Cardiac Output Testing Protocol Used in This Study. Subjects exercised at three different workloads yielding oxygen uptakes of .50, .80, and 1.0 $L \cdot min^{-1}$. These different workloads were generated by increasing the resistance against which the subject pedalled on the bicycle ergometer. Subjects rebreathed a CO_2 in O_2 mixture ranging from 10% to 15%. The concentration of CO_2 placed in the rebreathing system yielding equilibrium at each workload was determined by trial and error. Slight adjustments in the workload were performed to improve the quality of the rebreathing curve obtained for a given concentration of CO_2.

Subjects exercised three to five minutes on the bicycle ergometer. Resistance and pedalling frequency were adjusted during this time to attain a workload of either .50, .80, or 1.0 $L \cdot min^{-1}$. Before performing a CO_2 rebreathing, the existence of steady state exercise was identified. Steady state exercise is the condition "where the O_2 uptake equals the O_2 requirement of the tissues (1)." Once steady state had been obtained, end-tidal CO_2 concentrations were also examined to further verify the attainment of steady state. If end-tidal values were erratic, exercise was kept at the present workload until they stabilized. Once stable, the rebreathing procedure began.

Several procedures were performed during the time period when end-tidal CO_2 values were examined:

1. Any gas remaining in the anesthesia bag was removed by

suction.

2. The five liter anesthesia bag was filled with a volume of CO_2/O_2 gas. The volume of gas was estimated at approximately 1½ times the subject's tidal volume and delivered using a tank regulator that had been calibrated to deliver 80 mls/second.

3. The following concentrations of CO_2 were placed in a non-randomized order into the rebreathing bag. Each gas was used with a separate workload: 12.8% for .50 $L \cdot min^{-1}$, 13.8% for .80 $L \cdot min^{-1}$, and 15.1% for 1.0 $L \cdot min^{-1}$.

Having completed these tasks, the Beckman was moved into the Auto 3 mode of operation and the following procedures executed:

1. The large diameter hose (see Figure 1) was removed from the three-way, non-rebreathing valve to prevent high concentrations of gas from entering the Beckman's mixing chamber upon completion of the rebreathing procedure.

2. A metronome was set at a cadence of 60 beats per minute. The subject coordinated each inhale/exhale with a beat of the metronome to give a breathing rate of 30 breaths per minute (8).

3. After the subject made a slightly prolonged exhale, a three-way slider valve was used to allow the subject to rebreathe from the anesthesia bag. The subject was encouraged to maintain the breathing rate of 30 breaths per minute during the rebreathing procedure. After 10 to 20 seconds the procedure was terminated.

4. The subject was returned to breathing room air. Exercise was terminated and the subject was allowed to rest for two to three minutes. If a suitable equilibrium curve was not obtained, the workload was adjusted in the proper direction and the experiment repeated. Once

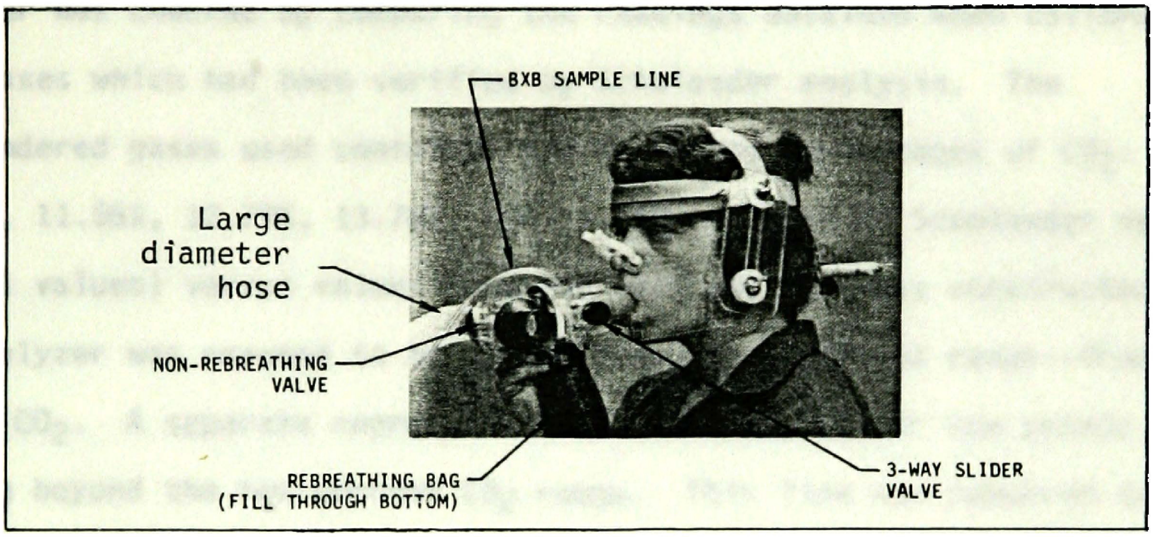

Figure 1

Headgear Worn During Cardiac Output Determinations satisfactory equilibrium was obtained, a second trial was performed at that workload. Subjects repeated the procedure to complete the rebreathing procedure at all three workloads.

Calibration of the Beckman LB-2 Analyzer

The response characteristics of the Beckman LB-2 analyzer were determined in the range of CO_2 concentrations exceeding ten percent. The analyzer was checked by comparing the readings obtained when calibrated with gases which had been verified by Scholander analysis. The Scholandered gases used contained the following percentages of CO_2: 10.20%, 11.58%, 12.79%, 13.78%, and 15.13%. A plot of Scholander values (Actual values) versus values recorded from the LB-2 was constructed. The analyzer was assumed to be linear over its specified range--from 0% to 10% CO_2. A separate regression line was computed for the points falling beyond the ten percent CO_2 range. This line was compared to the standard correction factor applied when CO_2 concentrations exceed ten percent--incorporated into the computer program used during the rebreathing procedure (3):

$$FCO_2 = ((FrawCO_2 - .10) \times .13) + FrawCO_2$$

Rebreathing Equilibrium Interpretation

The following criterion, developed from a review of the literature, were used to interpret the curves obtained during the rebreathing procedure. Various equilibration patterns can be obtained during rebreathing (8) (see Figure 2).

1. Curve A: The initial concentration of CO_2 placed in the rebreathing system was too low. The body is evolving CO_2 into the

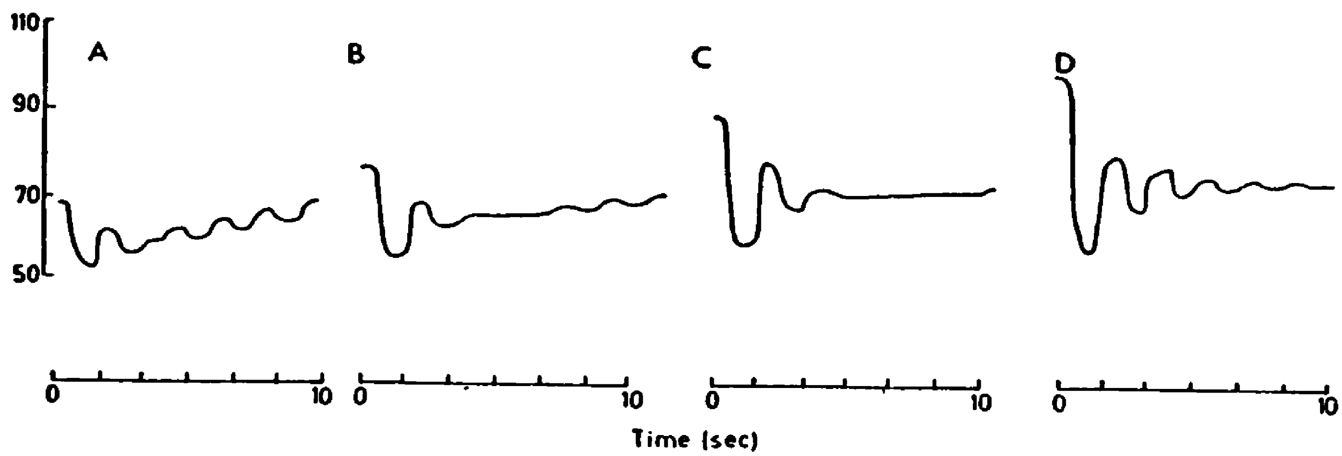

Figure 2

Various Equilibrium Patterns Obtainable During Rebreathing

Source: Jones, N.L., Campbell, E.J.M., Edwards, R.H.T., and Robertson, D.G. Clinical Exercise Testing. Philadelphia: W.B. Saunders, 1975, page 96.

system thus accounting for the rise in CO_2 concentration with time.

2. Curve B. Transient equilibrium between the lungs, blood, and rebreathing system. This pattern indicates a transient equilibrium between alveolar gas and the rebreathing system, but, not with the blood.

3. Curve C: Ideal Equilibrium. The lack of change of slope of the line beginning at approximately five seconds identifies equilibrium between the rebreathing bag, blood, and lungs. Ideal equilibrium should occur within three to five breaths.

4. Curve D: The initial concentration of CO_2 placed in the rebreathing system was too high. It isn't possible to obtain equilibrium before recirculation of the gas within the body occurs.

Any curve which did not share characteristics with those described under Curve C above was not defined as a suitable equilibrium for the purposes of this study.

Calculation of Equilibriums at a Lower Altitude

In a smaller sample (N = 3), a subset of the sample tested in Missoula, the identical rebreathing experiments were repeated at the Biodynamics Laboratory, University of Wisconsin, Madison. The purpose of this testing was to verify the effect of altitude on the percentage of CO_2 gas needed to obtain an equilibrium at a given workload. Madison, Wisconsin, is at an altitude approximately 2500 feet below Missoula, Montana.

The same procedures performed in Missoula were carried out in Madison. Subjects followed similar pre-test habits in both Missoula and Madison. Testing in both sites was done at the same time of day.

Statistical Treatments

To characterize the oxygen uptakes associated with a given equilibrium-causing concentration of CO_2, the data were analyzed to determine the mean oxygen uptakes for all subjects tested in Missoula across all concentrations of CO_2 used: 12.8%, 13.8%, and 15.1%. A one-way analysis of variance for repeated measures was used to determine if the mean $\dot{V}O_2$ for each concentration of CO_2 (treatment) were all estimates of a common population mean using the repeated measures program available in the Biomedical Data Processing (BMDP) package (19). A comparison between pairs of means was performed using the methods outlined by Keppel (15).

To determine whether the workloads needed to obtain equilibrium for a given concentration of CO_2 in Missoula, Montana were different from the guidelines of Jones, a subjective comparison was made regarding the magnitude of the difference between these values.

Descriptive statistics were used to characterize the data obtained on three subjects tested in both altitude locations: Madison, Wisconsin, and Missoula, Montana. The mean differences between oxygen uptakes in both altitude locations, for a given concentration of CO_2, were determined.

Chapter 3

RESULTS AND DISCUSSION

Mean $\dot{V}O_2$ for a Given Concentration of CO_2

The results of the repeated cardiac output trials for all subjects can be found in Appendix C. In order to minimize the number of trials necessary to obtain a suitable equilibrium pattern, the data were analyzed to determine if the mean workloads for all subjects across all concentrations of CO_2 used were different from one another.

The mean oxygen consumption, mean of two trials, was determined for nearly all subjects. Only one trial was performed on the following subjects: G.A., K.M., J.W., and P.L., for the following percentages of CO_2: 12.8%, 12.8%, 13.8%, and 15.1%, respectively. These single values were used in the one-way analysis of variance (ANOVA) for repeated measures. The means and standard deviations for these data can be found in Table 3. ANOVA for repeated measures revealed that these means were not all estimates of a common population mean. The results of this analysis are shown in Table 4. A significant F value of 26.02 ($p < .05$) was obtained.

Having identified that the mean $\dot{V}O_2$'s for a given concentration of CO_2 were not estimates of a common population mean, a post hoc analysis was performed to determine which mean-differences were significant. When performing post hoc analyses, the appropriate error term must be used. Keppel (15) suggests that the use of the overall error term is inappropriate when comparing individual means during post hoc analyses:

Table 3

Mean Workloads for a Given Concentration of CO_2[a]

Concentration of CO_2 (%)	Mean $\dot{V}O_2$ ($L \cdot min^{-1}$) (SD)[b]
12.8	.640 (.241)
13.8	.965 (.377)
15.1	1.351 (.408)

[a]Data on all subjects collected in Missoula, Montana, (N = 10)

[b]Standard deviation

Table 4

ANOVA for Repeated Measures for $\dot{V}O_2$ and % CO_2 Data

Source	SS	df	MS	F
$\dot{V}O_2$	2.537	2	1.269	26.02[a]
Subject	2.420	9	.269	
$\dot{V}O_2$ x Subject	.878	18	.049	

[a] $p < .05$

Treatment x Subject interaction differs with each comparison of means being made. An error term specific to the comparison of means should be determined. The procedures recommended by Keppel were followed when comparisons between pairs of means were performed. The results of these comparisons can be found in Table 5.

In comparisons involving mean $\dot{V}O_2$'s for all different combinations of gases significant F values were obtained in all cases. Therefore, it was concluded that the mean workload differences were statistically significant at $\alpha = .05$.

Comparison of Workload Differences

The mean oxygen uptakes, and the CO_2 values associated with them, obtained in Missoula, were compared to Jones' data. A summary of this comparison can be found in Table 6. Because of the limited number of comparisons possible, only trends in the data were examined. Though identical concentrations of CO_2 were not used in both studies, the values were close enough to allow for comparison.

The oxygen uptakes, for each concentration of CO_2 used, were much higher in Jones' data than the values obtained in this study. There appeared to be a difference of approximately 1.5 to 2.0 $L \cdot min^{-1}$ in the oxygen uptakes for a given concentration of CO_2.

Altitude Study

A subset of three subjects (J.N., M.S., and R.W.) were tested in both low and moderate altitude sites to determine the effect of altitude on the workload needed to obtained a suitable equilibrium for a given concentration of CO_2. The raw data for these experiments can be found in Appendixes D and E. For the three concentrations of CO_2 which were used,

Table 5

Post hoc Comparison of Mean Workloads

Workload 1 versus Workload 2

Source	SS	df	MS	F
$\dot{V}O_2$	.531	1	.531	10.78[a]
Subject	1.352	9	.150	
$\dot{V}O_2$ x Subject	.444	9	.049	

Workload 2 versus Workload 3

Source	SS	df	MS	F
$\dot{V}O_2$	.741	1	.741	11.01[a]
Subject	2.172	9	.241	
$\dot{V}O_2$ x Subject	.606	9	.067	

Workload 1 versus Workload 3

Source	SS	df	MS	F
$\dot{V}O_2$	2.528	1	2.528	88.07[a]
Subject	1.671	9	.196	
$\dot{V}O_2$ x Subject	.259	9	.029	

[a] $p < .05$

Table 6

Workload Differences Between Jones' and Obtained Values

Jones		Missoula	
% CO_2 (%)	$\dot{V}O_2$ ($L \cdot min^{-1}$)	% CO_2 (%)	$\dot{V}O_2$ ($L \cdot min^{-1}$)
13.0	2.2	12.8	.64
14.0	3.0	13.8	.97
*	*	15.1	1.35

*No data available for comparison

12.8%, 13.8%, and 15.1%, a greater oxygen consumption, e.g. a higher workload, was required in Madison, Wisconsin. The mean difference in the workloads for the two altitudes ranged from .20 to .24 $L \cdot min^{-1}$ (see Table 7). For a given percentage of CO_2 a higher workload was required in Madison to obtain a suitable equilibrium.

Calibration of the Beckman LB-2 CO_2 Analyzer

Missoula. The high concentrations of CO_2 which are often used in Missoula during cardiac output trials exceed the limit of the linearity of the LB-2 analyzer. To create a correction factor to increase the validity of the Beckman generated CO_2 values, the response of the analyzer used at the University of Montana was determined beyond the ten percent CO_2 range. Five separate gas mixtures, verified by repeated Scholander analyses, ranging in concentration from 10.20% to 15.13%, were analyzed by the Beckman and its output recorded (see Table 8). Only five CO_2 in O_2 mixtures were available for use in this study. The difference in readings between the Actual CO_2 values and the Beckman CO_2 values ranged from 1.20% to 1.43% The Beckman values were higher in all cases. The mean value of the difference was 1.31% CO_2.

Linear regression analysis was used to construct a line of best fit for these data. This equation was considered as a possible correction factor to adjust the Beckman CO_2 values obtained when the concentration of CO_2 exceeded ten percent. The following regression equation was used to construct a plot for the Missoula LB-2 analyzer (see Figure 3):

$$\text{Actual } CO_2 = 1.03 \text{ Beckman } CO_2 - 1.78 \quad R^2 = .99$$

Table 7

Effect of Altitude on $\dot{V}O_2$ for a Given Concentration of CO_2[a]

% CO_2 Tank (%)	Mean $\dot{V}O_2$--Madison ($L \cdot min^{-1}$) (SD)[b]	Mean $\dot{V}O_2$--Missoula ($L \cdot min^{-1}$) (SD)	Mean Difference ($L \cdot min^{-1}$)
12.8	.78 (.04)	.58 (.15)	.20
13.8	.99 (.05)	.79 (.12)	.20
15.1	1.47 (.16)	1.23 (.34)	.24

[a]Values represent mean scores in the same three subjects tested in both locations.

[b]Standard deviation

Table 8

Actual Versus Beckman CO_2 Concentrations for LB-2 Analyzer Used In Missoula (N = 5)

Actual Value (%)	Beckman Value (%)	Difference (B - A) (%)
10.20	11.63	1.43
11.58	12.94	1.36
12.79	13.99	1.20
13.78	15.06	1.28
15.13	16.40	1.27

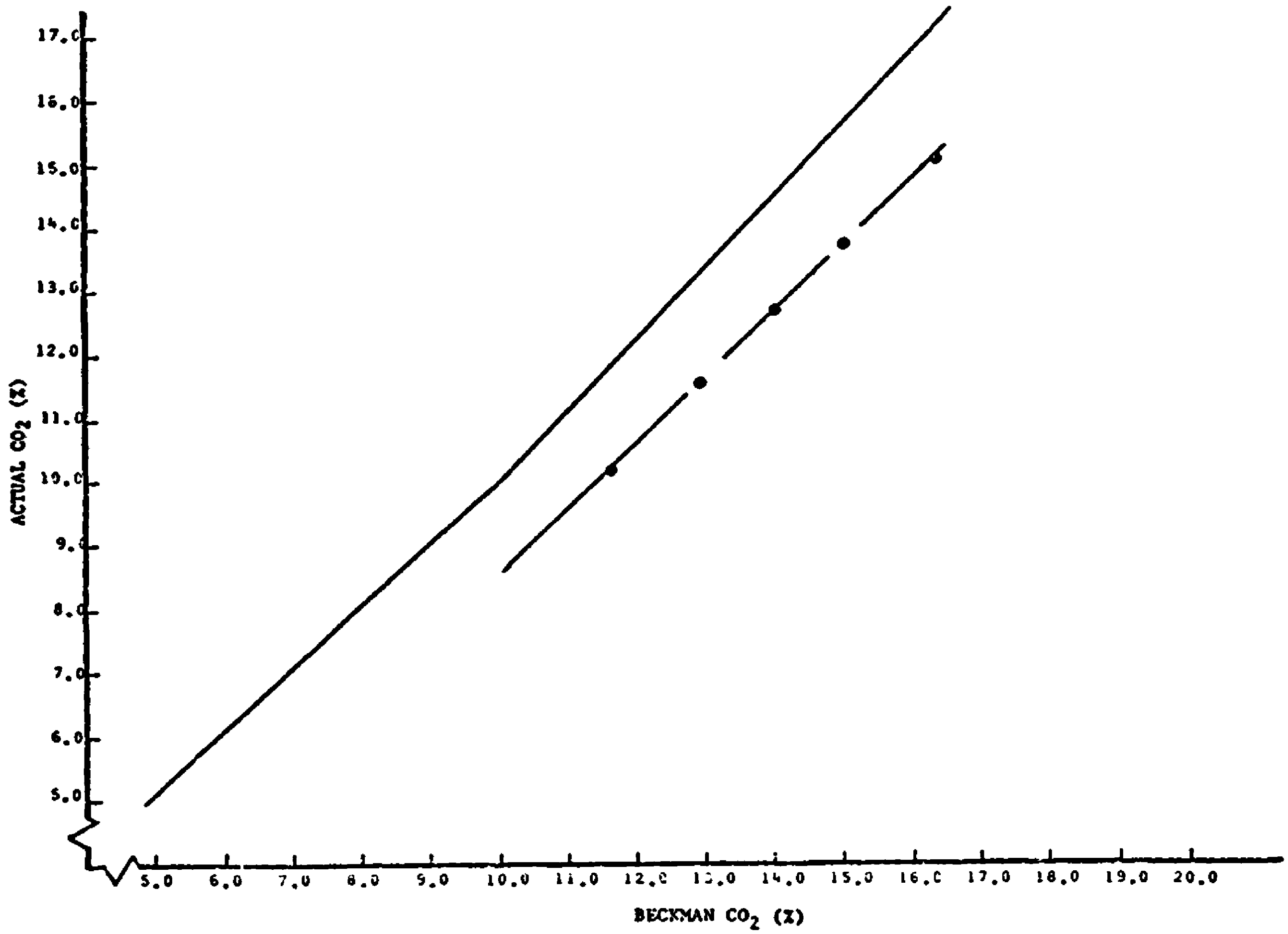

Figure 3

Beckman Versus Actual CO_2 Values for Missoula's LB-2 CO_2 Analyzer. Beckman Calibration Curve (————), Regression line for Missoula's analyzer (—— ——).

Figure 3 also depicts the calibration line which Beckman assumes, on the average, describes the behavior of the LB-2 analyzer. For the purposes of this study, similar assumptions were made regarding this line.

A subjective analysis of the two lines depicted in Figure 3 tends to suggest that a drastically different correction factor, in comparison to the average Beckman factor, was obtained. It was possible that the regression equation developed for the Missoula analyzer was valid, hence, implementation of this correction factor would be recommended. However, knowledge of the behavior of other LB-2 analyzers and of Beckman's quality procedures suggested that the difference between the correction factor obtained for Missoula's analyzer and Beckman's average correction factor was perhaps a function of something other than the behavior of the response of the analyzer. It was perhaps related to the chemical analyses done on the gases used to calibrate the Missoula analyzer. Difficulties associated with the Scholander analyses of high concentrations of CO_2 could have led to a systematic error in the values obtained. Based upon these considerations, and the observation that the Missoula analyzer had always generated valid CO_2 data, the decision was made not to implement this correction factor for the Missoula analyzer, the average Beckman correction factor was assumed to be appropriate.

Madison. The response of the Beckman LB-2 CO_2 analyzer used in Madison, Wisconsin, was provided by personnel from the Biodynamics Lab, University of Wisconsin, Madison (see Figure 4). This line was constructed from the comparison of Actual CO_2 values, verified by repeated Scholander analyses of gas mixtures, and Beckman CO_2 readings using gases ranging from 10% to 15% CO_2. The recommendation was made, by the

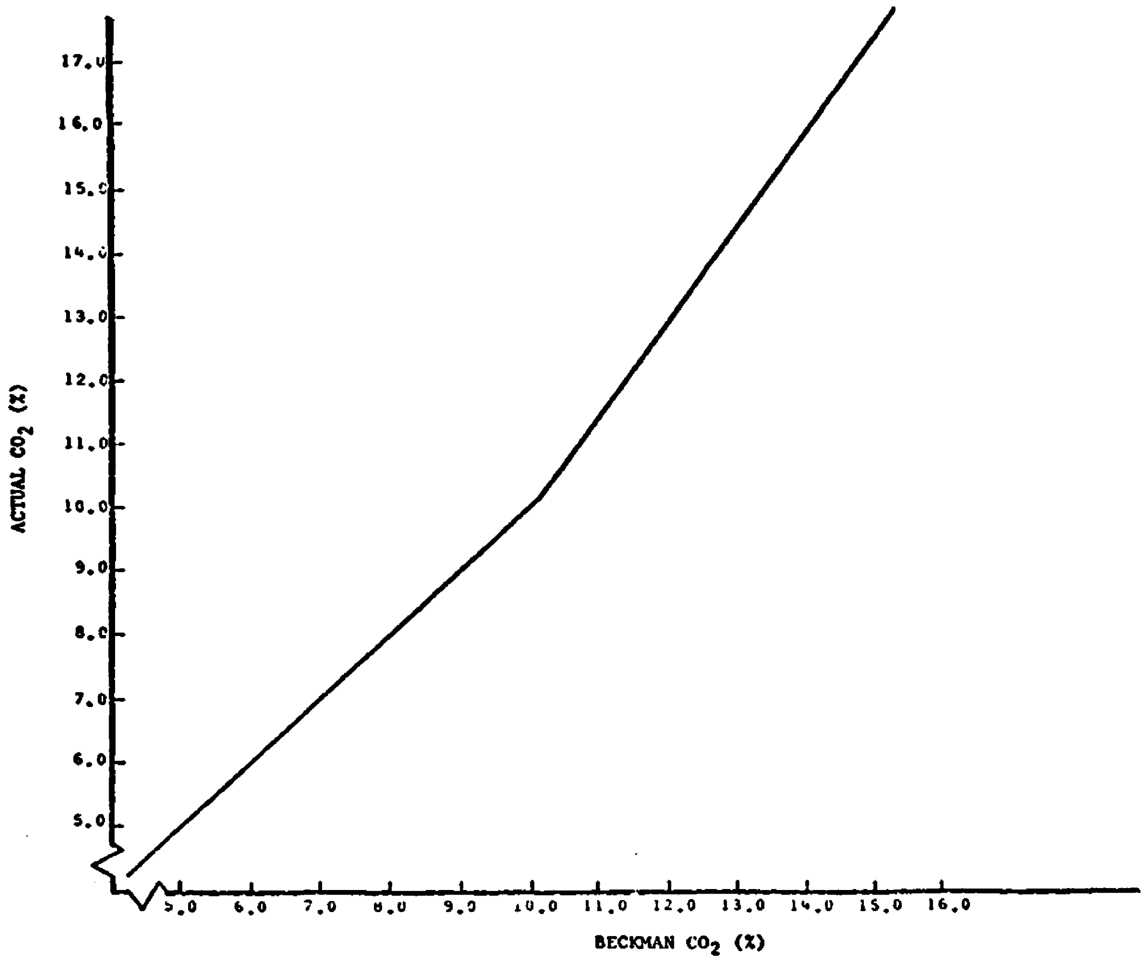

Figure 4

Beckman Versus Actual CO_2 Calibration Line for the LB-2 Analyzer Used in Madison, Wisconsin.

Biodynamics Lab technician, that this line be used to correct CO_2 values when raw CO_2 concentrations exceeded ten percent.

Cardiac Output Determinations

The data obtained using the CO_2 rebreathing method, was used to calculate cardiac output values for each subject. An analysis of these values and how they compare to values reported in the literature can help to establish the validity and reliability of the data obtained in Missoula.

Missoula (N = 10). The cardiac output values obtained in this study were used to construct regression lines to determine the relationship between oxygen uptake and cardiac output. This is a conventional approach to the treatment of these types of data. This analysis was performed on all subjects for each of the three separate concentrations of CO_2 used in this study. The subjects were not grouped into one large regression equation because the line resulting from this procedure would be inappropriate. There would be a lack of independence between data points. The same subject would have data points for three different workloads. For all of the concentrations of CO_2, the mean of each subject's trial values was used. Mean oxygen uptake and cardiac output values were regressed. In those cases where only one data point existed per trial, this value was used in the regression analysis. The following regression equations were calculated:

Concentration of CO_2		
12.8%	Cardiac Output = $5.09\dot{V}O_2 + 3.21$	$r = .82$
13.8%	Cardiac Output = $5.83\dot{V}O_2 + 2.28$	$r = .94$

Concentration of CO_2

15.1% Cardiac Output = $4.47\dot{V}O_2 + 3.64$ $r = .92$

A graphical presentation of these data can be found in Figure 5.

The reliability of the CO_2 rebreathing method was determined by comparing the relationship between each individual's scores and their mean scores for a given concentration of CO_2 (see Figure 6). As the workload exceeded .80 $L \cdot min^{-1}$, all cardiac output determinations were within six percent of the individual's mean scores.

Madison (N = 3). The cardiac output values determined for the subjects tested in Madison, Wisconsin, are presented in Figure 7. Means and standard deviations are presented. Data for the same subjects collected in Missoula are presented in the same figure for comparison. For nearly all subjects, the cardiac output values obtained in Madison, Wisconsin, were lower than those obtained in Missoula, Montana.

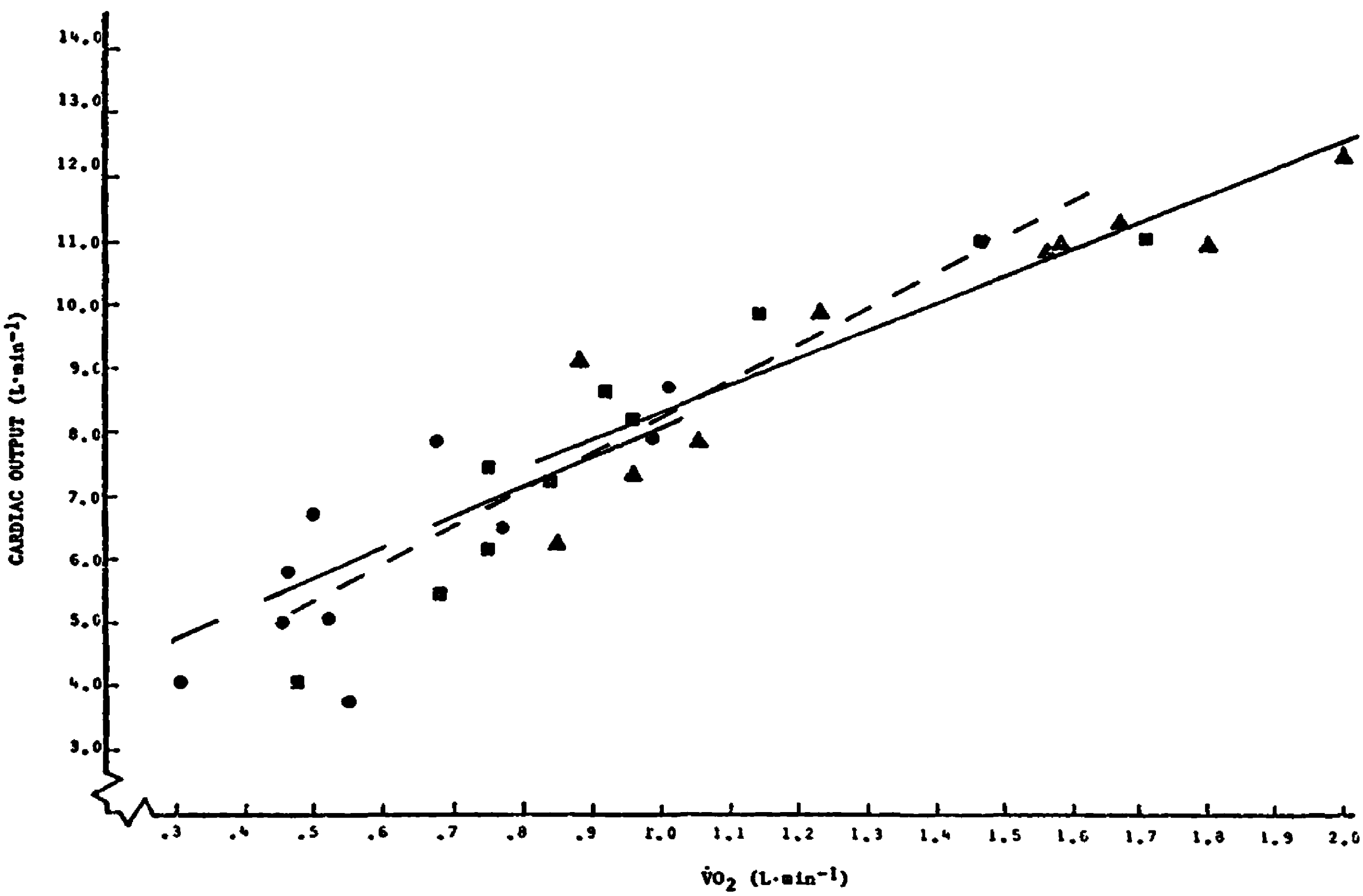

Figure 5

Mean $\dot{V}O_2$ and Cardiac Output Values for all Subjects. Three regression lines were calculated from three different conditions on the same subjects. N = 10 for each separate equation.
(●) 12.8% CO_2 — -, (■) 13.8% CO_2 - -, (▲) 15.1% CO_2 ——

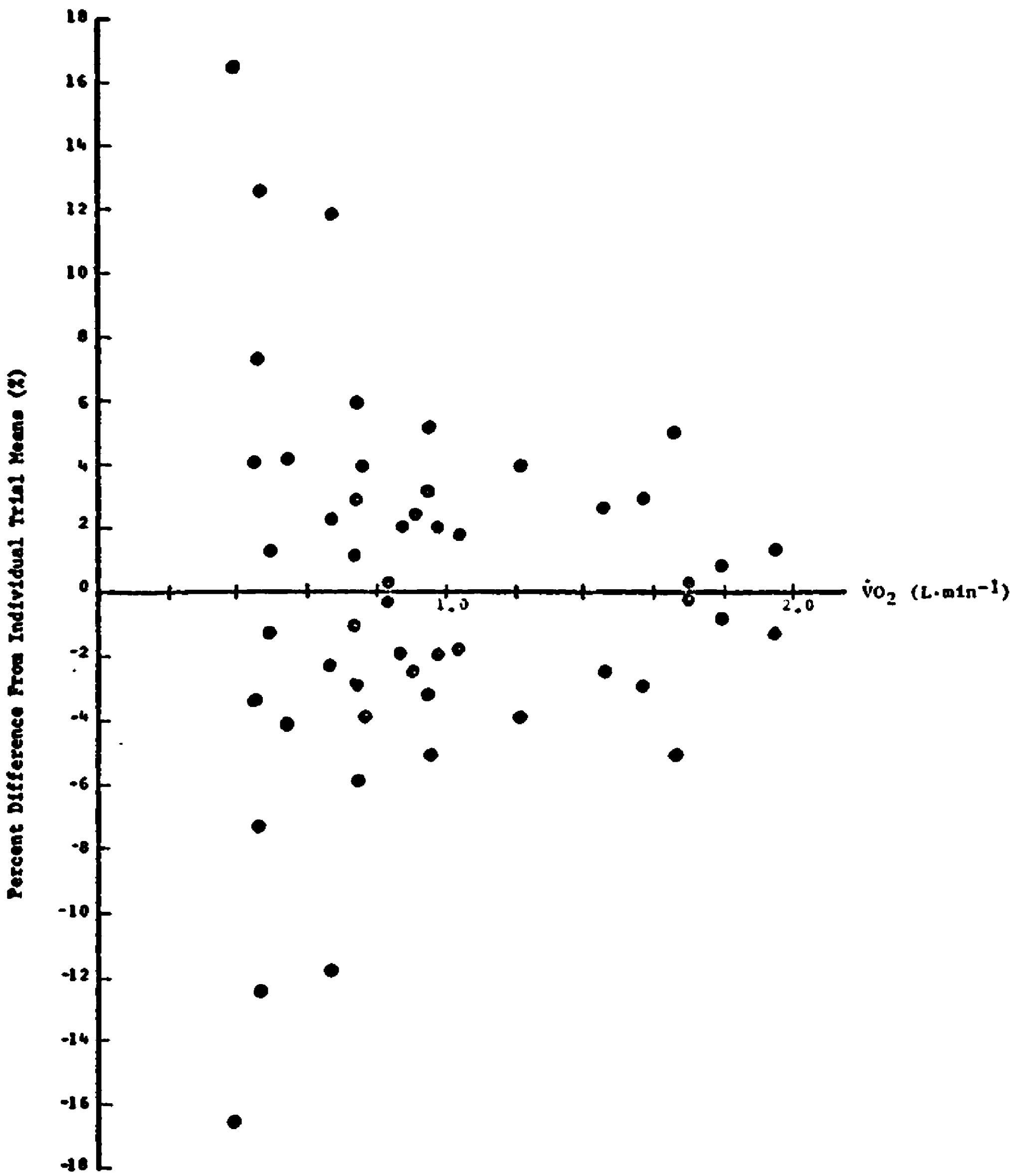

Figure 6

Percent differences between trial scores and mean trial values for all paired trials on all subjects. Data represents 10 subjects tested under three conditions.

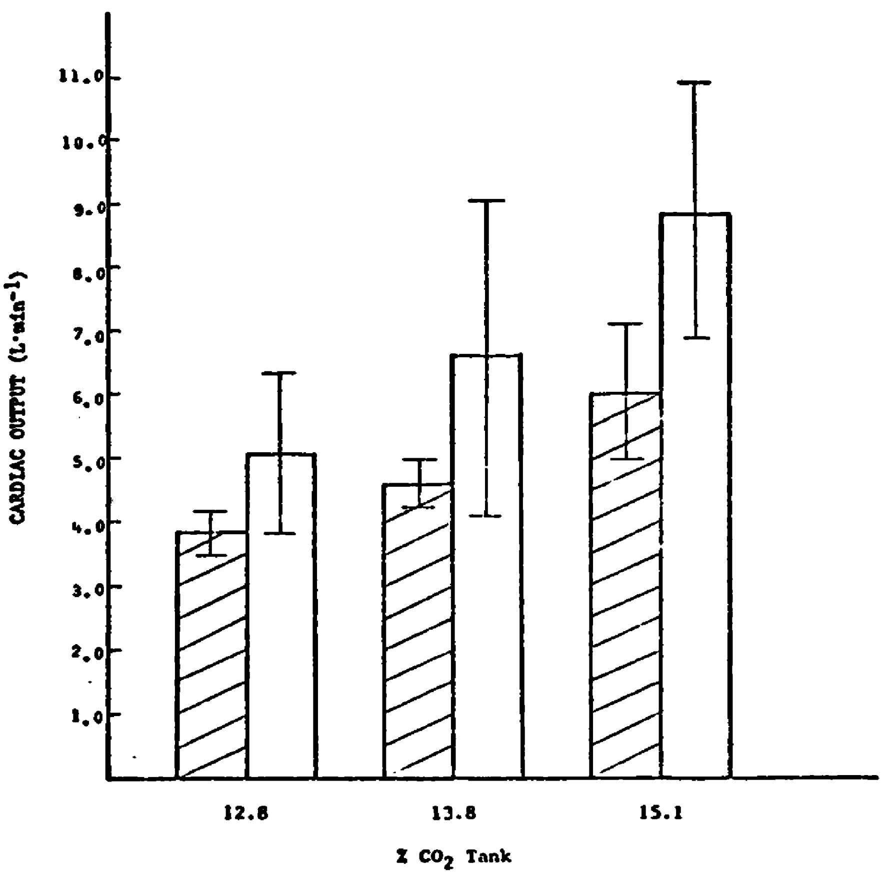

Figure 7

Mean Cardiac output values (± 1 S.D.) for repeated trials on three subjects. The same subjects were tested in both altitude locations.
▨ Madison, □ Missoula.

Discussion

Very little literature is available regarding the relationship between a given oxygen uptake ($\dot{V}O_2$) and the percentage of CO_2 to be placed in the rebreathing system in order to obtain a suitable equilibrium. The work of Jones and Rebuck (11) is the only available information in this area. In Missoula, these guidelines were found to underestimate the concentration of CO_2 necessary to obtain equilibrium for a given workload. In order to expedite the process for obtaining valid cardiac output data, hence reducing the necessity of numerous repeat trials, the characterization of the mean $\dot{V}O_2$ for a given concentration of CO_2 was necessary.

An analysis of variance for repeated measures was performed to see if the concentrations of CO_2 available in the Human Performance Lab were related to significantly different mean $\dot{V}O_2$'s within the subject population tested. A significant F value for these analyses and a subsequent finding, with post hoc analyses, that all means were different from one another, characterized the mean oxygen uptake associated with an equilibrium-causing concentration of CO_2 (see Table 9).

This information can be used as a starting point when testing a subject's cardiac output. If a determination of an individual's cardiac output, at a given oxygen uptake, is to be performed, the appropriate concentraion of CO_2 to be placed in the external rebreathing system can be obtained from Table 9. If, for example, an individual's cardiac output needs to be determined at an oxygen uptake of .64 $L \cdot min^{-1}$, a 12.8%

Table 9

Suggested Initial CO_2 Concentrations to Obtain Rebreathing Equilibriums in Missoula

O_2 Uptake ($L \cdot min^{-1}$)	Concentration of CO_2 in Bag (%)
.64	12.8
.97	13.8
1.35	15.1

concentration of CO_2 should be placed in the rebreathing system. This concentration of gas is the best estimate of the concentration that will result in the attainment of a suitable rebreathing pattern. Using these guidelines, as opposed to a random choice of workload and CO_2 concentrations, the number of repeat cardiac output trials, where adjustments are necessary to obtain a suitable rebreathing pattern, should be reduced. The data collection process, therefore, should be expedited. Many subject's lack the desires or abilities to perform repeated trials while the investigator, at random, changes both the workload and concentration of CO_2 in hopes of obtaining a suitable rebreathing equilibrium pattern.

Comparison of Workload Differences

To determine whether the workloads, for a given concentration of CO_2 were different from those recommended by Jones, at similar though not exactly the same concentrations of CO_2, a subjective comparison of these mean $\dot{V}O_2$ values was performed (see Table 6, page 24). A trend for higher workloads was observed in Jones' data. A difference of approximately 1.5 to 2.0 $L{\cdot}min^{-1}$ was observed. Much lower workloads were associated with a given concentration of CO_2 in Missoula. The implication of this is that cardiac output determinations can only be performed at $\dot{V}O_2$'s averaging less than 1.35 $L{\cdot}min^{-1}$. Greater concentrations of CO_2 were not on hand at the time of the study. The low workload for a 15% tank contradicts the recommendations made by Beckman that gas concentrations in the range between 10% to 15% CO_2 should be adequate for cardiac output determinations over a wide range of oxygen uptakes.

The source of the difference between Jones' data and the data obtained in this study is not entirely explainable. Analysis of the research design used by Jones, showed that the recommendations made from that study were based upon data collected on only six subjects. Only twelve data points were used to construct the regression equation that generated the information presented in Table 1 (see page 3). In addition to the small sample size, the same subjects were tested at multiple workloads. The data from these multiple trials was used in the regression analysis thus violating the assumption of independence between data points upon which a regression analysis is based.

Altitude Study

The testing done on three subjects in both low and moderate altitude sites, Madison, Wisconsin, and Missoula, Montana, respectively, evidenced the fact that greater oxygen uptakes were required to obtain suitable equilibrium patterns, for a given concentration of CO_2, in Madison. Though this aspect of the study was done using only three subjects, indicating the need for caution in the interpretation of this information, these findings support the rejection of the hypothesis of no difference in the workloads between the two altitude sites for a given concentration of CO_2. A possible explanation of this difference could relate to the effect of altitude on the CO_2 rebreathing method.

The findings obtained are consistent with that anticipated from theoretical considerations. Madison's altitude is 2500 feet lower than Missoula's. Given that barometric pressure, and partial pressure, increase when descending in altitude, the same fixed percentage gas tanks used in both testing sites exerted greater partial pressures in Madison. To obtain a suitable rebreathing pattern, which is based upon equal levels of CO_2 in both the lung and rebreathing system, the subjects were forced to work at higher levels in order to match the increased PCO_2's exerted by the tanks in Madison. This is reflected in the higher oxygen uptakes, for a given concentration of CO_2, obtained in Madison.

Cardiac Output Determinations

The methodological considerations, including the effect of altitude and the difference between literature and obtained workload and equilibrium causing CO_2 concentrations, suggested an examination of the cardiac output values obtained in this study be performed in order to verify the validity and reliability of these measures.

Missoula (N = 10). The cardiac output values obtained in this study generated regression lines that were of similar order of magnitude obtained by others doing similar work. Paterson and Cunningham (17) obtained a regression equation for the relationship of cardiac output to oxygen uptake as follows:

$$\text{Cardiac Output} = 5.63\ \dot{V}O_2 + 3.64 \qquad r = .89$$

Zeidifard (22) obtained a similar regression equation:

$$\text{Cardiac Output} = 5.82\ \dot{V}O_2 + 3.04$$

These equations compare well with the equations obtained from the data collected on the same ten repeatedly tested subjects using three different concentrations of CO_2:

$$12.8\%\ CO_2 \quad \text{Cardiac Output} = 5.09\ \dot{V}O_2 + 3.21 \qquad r = .82$$

$$13.8\%\ CO_2 \quad \text{Cardiac Output} = 5.83\ \dot{V}O_2 + 2.28 \qquad r = .94$$

$$15.1\%\ CO_2 \quad \text{Cardiac Output} = 4.47\ \dot{V}O_2 + 3.64 \qquad r = .92$$

While a statistical comparison of these regression equations with the ones obtained from the literature was not performed, a cautious generalization can be made that the subject populations and cardiac ouput values obtained were similar to data found in other studies using similar methods.

An additional fact conventionally addressed in the literature on the CO_2 method for the determination of cardiac output, is the reliability of the method. From Figure 6 it can be observed that a considerable scatter of points existed around the mean cardiac output values for each subject in the workload range below .8 $L \cdot min^{-1}$. Other investigators have found similar results (8, 21). The CO_2 rebreathing method is less accurate at the lower workloads due to the smaller value for the venoarterial CO_2 difference. This difference is more difficult to accurately determine when it is small in magnitude (8). Above the .8 $L \cdot min^{-1}$ level, nearly all of the points fall within six percent of an individual's mean values. Wigle (21) found similar results--all values were within ten percent of the mean value for each subject. The method, as it is used in Missoula, appears to be as reliable as others, doing similar work, have found.

Madison. The cardiac output data from this testing was not used to construct regression lines to determine the relationship between oxygen uptake and cardiac output due to the small sample size (N = 3). One interesting difference between the data obtained on the three subjects in Madison and in Missoula, was the dramatic difference in the cardiac output values (see Appendixes D and E). The values obtained in Madison were much lower than those obtained in Missoula (see Figure 7, page 35).

The mean values for the cardiac outputs obtained in Madison, for the three different concentrations of CO_2, were 3.85 $L \cdot min^{-1}$, 4.58 $L \cdot min^{-1}$, and 6.03 $L \cdot min^{-1}$ would suggest severe dysfunction of the cardiovascular system. Since the individuals tested were in good health while in Madison, another factor must have accounted for the low cardiac output values.

An examination of the three variables involved in the calculation of cardiac output, $\dot{V}CO_2$, $PetCO_2$, and $PbagCO_2$, provided one possible explanation for the extremely low values (see Figures 8, 9, and 10). The differences in $\dot{V}CO_2$ and $PetCO_2$ seen between the two altitude sites were consistent with the change in altitude between the two testing locations. The $PbagCO_2$ values, however, evidenced an increase which cannot be accounted for solely on the basis of the change in altitude. The greater increase in magnitude of this variable over the others involved in the calculation of cardiac output ($\dot{V}CO_2$, $PetCO_2$) and the fact that this variable is located in the denominator in the calculation of cardiac output suggests a reason why smaller cardiac output values were obtained in Madison, Wisconsin. These large $PbagCO_2$ values suggested venoarterial CO_2 differences which exceeded physiological limits. The reason for the unexpected increases in $PbagCO_2$ values was unknown and its implication in this study cannot be addressed due to the lack of sufficient information.

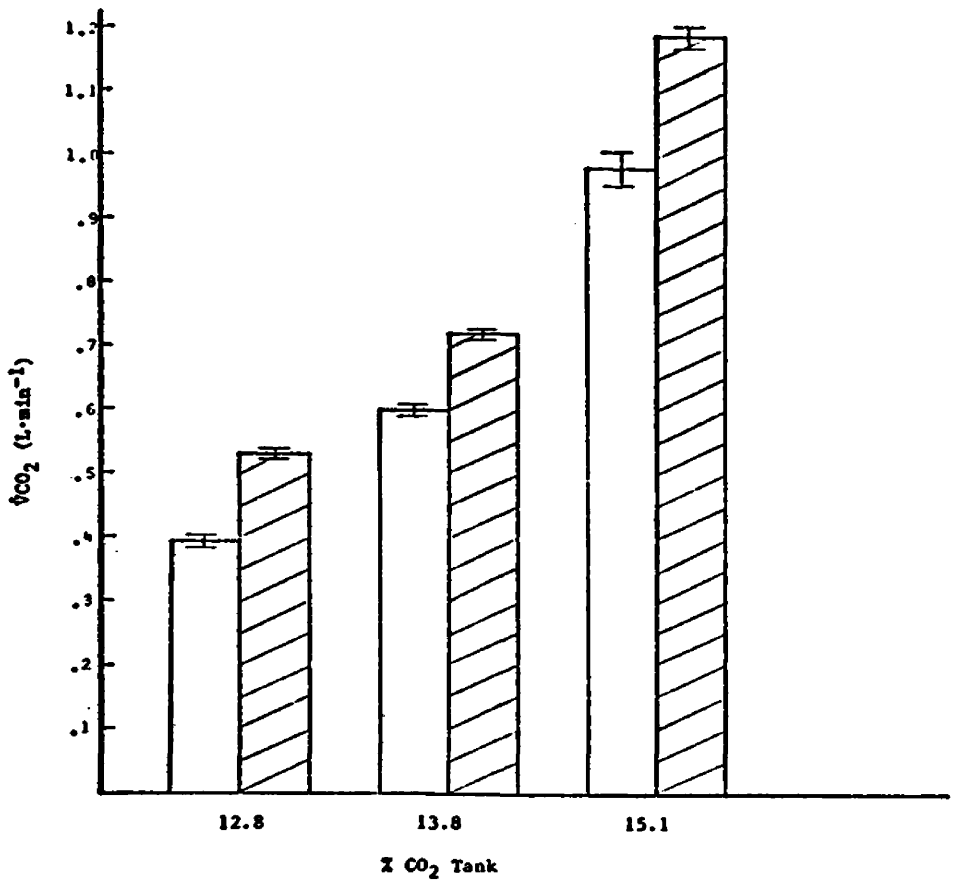

Figure 8

Mean $\dot{V}CO_2$ values (± 1 S.D.) for the same subjects tested in two altitude locations (N = 3).
Madison, Missoula.

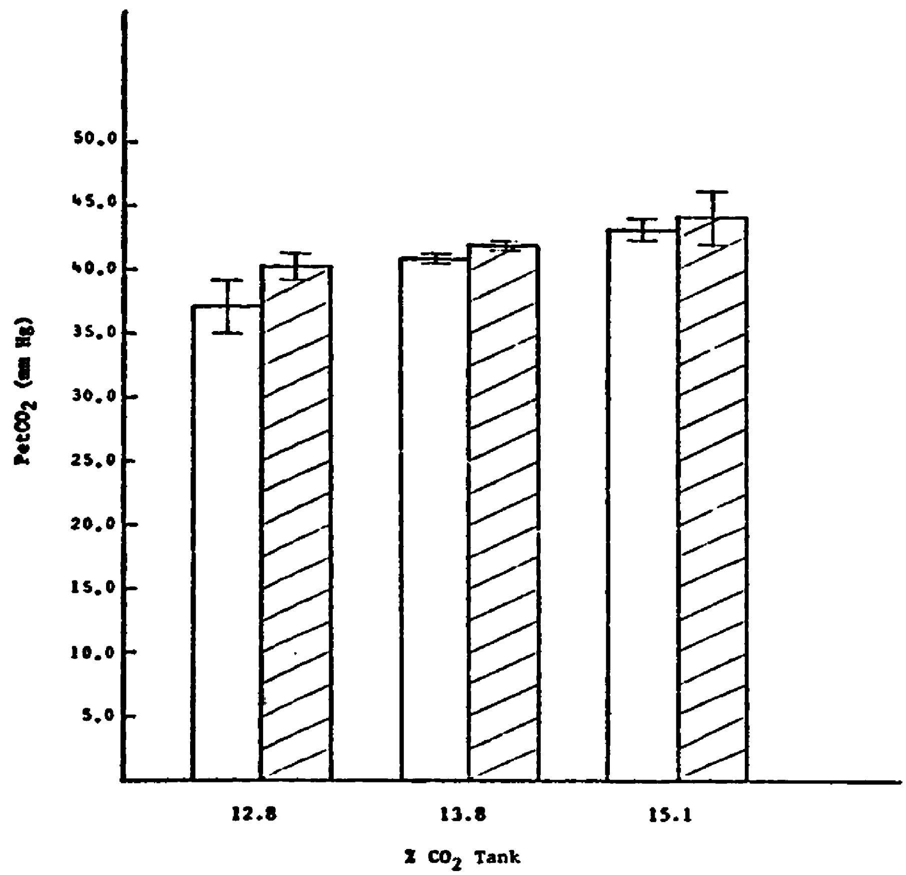

Figure 9

Mean $PetCO_2$ values (± 1 S.D.) for the same subjects tested in two altitude locations (N = 3).
▨ Madison, □ Missoula.

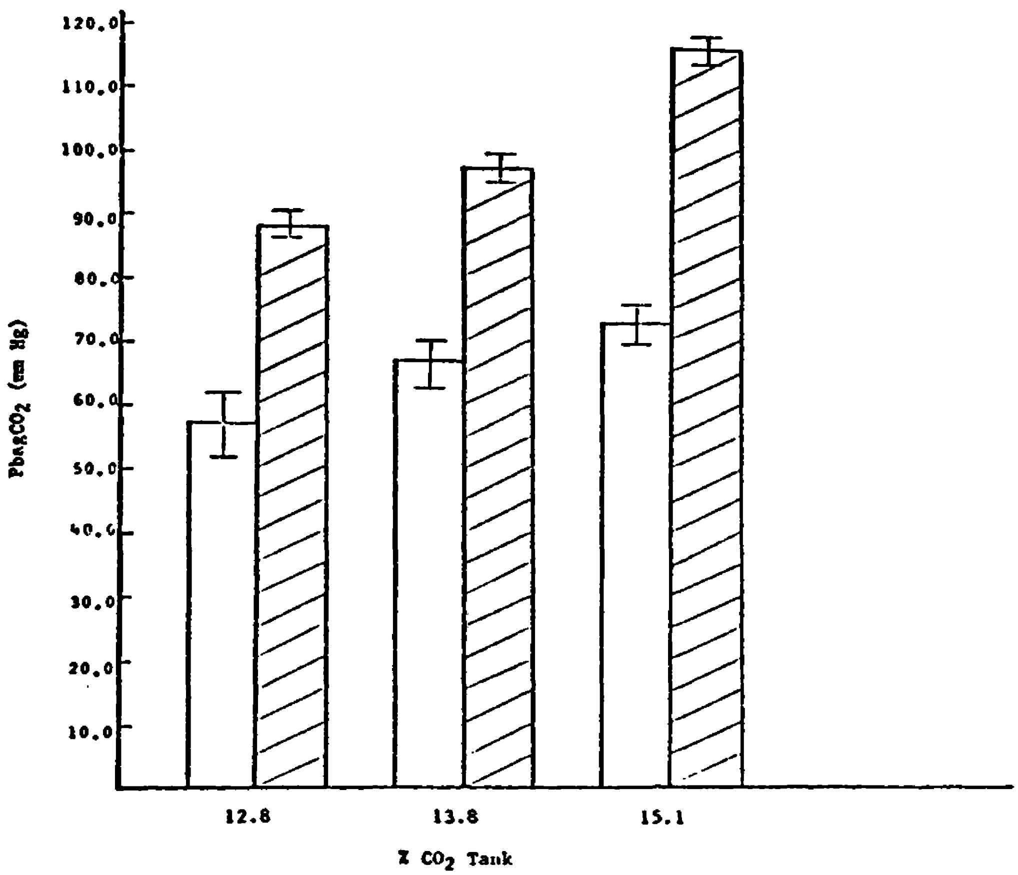

Figure 10

Mean $PbagCO_2$ values (± 1 S.D.) for the same subjects tested in two altitude locations (N = 3).
Madison, Missoula.

Chapter 4

SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

Summary

This study investigated the effects of altitude and other factors on the CO_2 rebreathing equilibrium method for the determination of cardiac output.

Ten male subjects exercised on a bicycle ergometer at several workloads in order to obtain suitable equilibrium rebreathing patterns for the following concentrations of CO_2 placed in the rebreathing system: 12.8%, 13.8%, and 15.1%. An analysis of variance for repeated measures was used to determine if the workloads associated with these concentrations of CO_2 were different from one another. Significant F values for comparisons between mean-differences supported this hypothesis. It was recommended that these workloads ($\dot{V}O_2$'s) be used as starting points from which to obtain suitable equilibrium rebreathing patterns for a given concentration of CO_2 placed in the rebreathing system.

There appeared to be a difference in the workload and equilibrium causing CO_2 concentration between the data obtained in Missoula and the data presented by Jones.

There appeared to be a small effect of altitude upon the concentration of CO_2 required to obtain equilibrium in the three subjects tested in two altitude locations. For a given concentration of CO_2, a higher workload was required at the lower altitude site (Madison, Wisconsin). This conclusion is cautiously made in light of the small number of subjects involved in this aspect of the investigation.

The cardiac output values obtained in this investigation compared to those reported in the literature. The method appeared to be valid. Additionally, the method appeared to be more reliable at higher exercise levels than at near resting levels.

The extremely low cardiac output values obtained in Madison, Wisconsin, seem to be due to the unexpectedly large increases in $PbagCO_2$ values which could not be accounted for solely on the basis of altitude.

Conclusions

The results of this study warrant the following conclusions:

A. Different workloads--levels of oxygen consumption--are necessary in order to obtain suitable equilibrium rebreathing patterns with the three concentrations of CO_2, 12.8%, 13.8%, and 15.1%, used in this study.

B. Lower workloads than those recommended by Jones are required to obtain suitable rebreathing equilibriums for a similar concentration of CO_2 in Missoula, Montana.

C. Lower workloads are required to obtain suitable rebreathing equilibriums for a similar concentration of CO_2 in Missoula, Montana, than in Madison, Wisconsin.

D. The cardiac outputs obtained in this study compare well to those reported in the literature. The values obtained at workloads greater than .8 $L \cdot min^{-1}$ were reliable values, falling within six percent of the individual's mean cardiac output values.

Recommendations

Based on the results of this study, the following recommendations are proposed:

A. A thorough calibration of the Beckman LB-2 CO_2 analyzer in Missoula, Montana is necessary to identify its response characteristics, especially in the range of CO_2 concentrations exceeding ten percent.

B. Larger scale studies should be conducted at different altitude sites to further investigate the effects of altitude on workload and equilibrium causing concentrations of CO_2.

C. Further study needs to be done in relation to the unexplained increases in $PbagCO_2$ values seen upon descending from an altitude of 3200 feet to an altitude of 700 feet.

D. Further study needs to be done to establish the relationship between the workload and equilibrium-causing CO_2 concentrations at levels greater than those tested in this study.

REFERENCES

1. Astrand, P.O., and Rodahl, K. Textbook of Work Physiology. New York: McGraw-Hill, Inc., 1977.

2. Becklake, M.R., Varvis, C.J., Pengelly, L.D., Kenning, S., McGregor, M., and Bates, D.V. Measurement of pulmonary blood flow during exercise using nitrous oxide. Journal of Applied Physiology, 1962, 17, 579-586.

3. Beckman Electronics Instruments Division. Clinical Exercise Testing Program: Operating Instructions. Schiller Park, Illinois: Beckman Instruments, 1980.

4. Collier, C.R. Determination of mixed venous CO_2 tensions by rebreathing. Journal of Applied Physiology, 1956, 9, 25-29.

5. Fahri, L.E., Nesarajah, M.S., Olszowka, A.J., Metildi, L.A., and Ellis, A.K. Cardiac output determination by a simple one-step rebreathing technique. Respiration Physiology, 1976, 28, 141-159.

6. Guyton, A.C. Textbook of Medical Physiology, 6th ed. Philadelphia: W.B. Saunders, 1981.

7. van Herwaarden, C.L.A., Binkhorst, R.A., Fennis, J.F.M., and van't Laar, A. Reliability of the cardiac output measurement with the indirect Fick-principle for CO_2 during exercise. Pflugers Archiv, 1980, 385, 21-23.

8. Jones, N.L., Campbell, E.J.M., Edwards, R.H.T., and Robertson, D.G. Clinical Exercise Testing. Philadelphia: W.B. Saunders, 1975.

9. Jones, N.L., Campbell, E.J.M., Edwards, R.H.T., and Wilkoff, W.G. Alveolar-to-blood PCO_2 difference during rebreathing in exercise. Journal of Applied Physiology, 1969, 27, 356-360.

10. Jones, N.L., Campbell, E.J.M., McHardy, G.J.R., Higgs, B.E., and Clode, M. The estimation of carbon dioxide pressure of mixed venous blood during exercise. Clinical Science, 1967, 32, 311-327.

11. Jones, N.L., and Rebuck, A.S. Rebreathing equilibration of CO_2 during exercise. Journal of Applied Physiology, 1973, 35, 538-541.

12. Jones, N.L., Robertson, D.G., and Kane, J.W. Difference between end-tidal and arterial PCO_2 in exercise. Journal of Applied Physiology, 1979, 47, 954-960.

13. Jones, N.L., Robertson, D.G., Kane, J.W., and Campbell, E.J.M. Effect of PCO_2 level on alveolar-arterial PCO_2 difference during exercise. Journal of Applied Physiology, 1972, 32, 782-787.

14. Kane, J.W., Jones, G., Jones, N.L., and Sutton, J.R. Beckman Metabolic Measurement Cart: Evaluation. Ambrose Cardiology Unit, McMaster University, Hamilton, Ontario, Canada, September, 1979.

15. Keppel, G. Design and Analysis, A Researcher's Handbook. Englewood Cliffs: Prentice-Hall, Inc., 1973.

16. Muiesan, G., Sorbini, C.A., Solinas, E., Grassi, V., Casucci, G., and Petz, E. Comparison of CO_2 rebreathing and direct Fick methods for determining cardiac output. Journal of Applied Physiology, 1968, 24, 424-429.

17. Paterson, D.H., and Cunningham, D.A. Comparison of methods to calculate cardiac output using the CO_2 rebreathing method. European Journal of Applied Physiology, 1976, 35, 223-230.

18. Tobin, James, Department of Health and Physical Education, University of Montana. Personal Communication. August, 1982.

19. UCLA Health Sciences Computing Facility. BMDP Manual. Berkeley: University of California Press, 1979.

20. Weisel, R.D., Berger, R.K., and Hechtman, H.B. Current concepts, measurement of cardiac output by thermodilution. New England Journal of Medicine, 1975, 292, 682.

21. Wigle, R.D., Hamilton, P.D., and Parker, J.O. Measurement of cardiac output by carbon dioxide rebreathing. Canadian Journal of Applied Sport Sciences, 1979, 4, 135-139.

22. Zeidifard, E., Silverman, M., and Godfrey, S. Reproducibility of the indirect (CO_2) Fick method for calculation of cardiac output. Journal of Applied Physiology, 1972, 33, 141-143.

APPENDIX A

Informed Consent Form

The purpose of this study is to determine my cardiac output at several workloads.

I will be requested to perform one maximal test on a bicycle ergometer. During the maximal test heart rate will be monitored using an electrocardiograph (EKG). Expired air will be collected for analysis. In addition to the above test, cardiac output will be determined using submaximal testing levels. Cardiac output will be determined using the carbon dioxide rebreathing method. I will rebreathe a carbon dioxide/ oxygen mixture for a period of 10 to 20 seconds then return to breathing room air. This procedure may cause dizziness; no other deleterious effects are known.

I will gain an understanding of my fitness for leg work. If I experience difficulty during the tests the bicycle workload or pedalling cadence will be lowered. If my EKG is or becomes abnormal the experiment will be immediately terminated and I will be referred to medical care. Carbon dioxide rebreathing will be terminated immediately if excessive discomfort is experienced.

My participation is voluntary and I am free to withdraw at any time of my own choosing. Confidentiality will be maintained in any published materials by references to me by number only.

In the event physical injury results from biomedical or behavioral research the human subject should individually seek appropriate medical treatment and shall be entitled to reimbursement or compensation with the self insurance program for Comprehensive General Liability established by the Department of Administration under authority of MCA Title 2, Chapter 9, or by the satisfaction of the claim or judgement by means provided by MCA 2-9-315. In the event of a claim for such physical injury further information may be obtained from the University Legal Counsel.

I have read and understand the above statement and wish to participate in this study.

Name_______________________________

Investigator_________________________

Date_______________________________

Before participating in this study, please answer the following questions. Mark those items that apply to you:

Yes	No	
_____	_____	Your doctor said you have heart trouble, a heart murmur, or you have had a heart attack.
_____	_____	You frequently have pains or pressure--in the left or midchest area, left neck, shoulder, or arm--during or right after you exercise.
_____	_____	You often feel faint or have spells of severe dizziness.
_____	_____	You experience extreme breathlessnesss after mild exertion.
_____	_____	Your doctor said your blood pressure was too high and is not under control. Or you don't know whether or not your blood pressure is normal.
_____	_____	Your doctor said you have bone or joint problems such as arthritis.
_____	_____	You have a family history of premature coronary artery disease.
_____	_____	You have a medical condition not mentioned here which might need special attention in an exercise program.

If you answered NO to all questions you have reasonable assurance of your suitability for this study.

If you answered YES to any question we will not be able to use you in this study.

This form has been adapted from the questionnaire contained in Exercise and Your Heart published by the U.S. Department of Health and Human Services, NIH Publication # 81-1677, May, 1981.

APPENDIX B

Instructions to the Subjects

Maximal Aerobic Power Test

During the first part of this testing session we are going to determine your maximal aerobic power ($\dot{V}O_2$ max) using a bicycle ergometer test. $\dot{V}O_2$ max is a measure of your ability to take in, transport, and utilize oxygen. The bicycle test requires a maximal effort on your part.

To help you maintain a constant pedalling rate a metronome will be set at 80 beats per minute. With each beat of the metronome one of the pedals--either right or left--should be at the top of the pedalling range.

Every two minutes the workload will be increased. The test will be terminated when you are no longer able to maintain the cadence set by the metronome. We will provide encouragement during the test and inform you as to the length of time remaining at each workload. During the final stages of the test we will ask if you have 30 seconds of effort remaining. You will signal your response by shaking you head "yes" or "no". If you need to terminate the test at any time merely stop pedalling.

To collect your expired air for analysis a nose clip will be firmly attached and you need to insert this mouthpiece firmly in your mouth. This will insure that all expired gas will be collected by the machine.

Do you have any questions? When you are ready we can begin.

Cardiac Output Determination

During this test we are going to determine the quantity of blood pumped by your heart per minute. For this test, the cadence and resistance of the bicycle will be adjusted to obtain a given workload. You will exercise three to five minutes at this workload.

During the determination of cardiac output you will be asked to rebreathe a carbon dioxide/oxygen mixture from this rebreathing bag while continuing to exercise. Once you have exercised for a sufficient period of time to reach steady state, approximately three to five minutes, we will determine your cardiac output. Just prior to the rebreathing procedure we will remove this large diameter hose from your mouthpiece assembly. After this hose has been removed be prepared to begin the rebreathing procedure.

During the rebreathing procedure you will need to breathe at a predetermined rate: 30 breaths per minute. A metronome will be turned on, just prior to rebreathing, set at 60 beats per minute. You will need to match each inhale and exhale with a beat of the metronome. Once you have achieved this breathing rate we will signal that we are going to switch you into rebreathing from the carbon dioxide/oxygen mixture. Continue to pedal and maintain the pedalling cadence to the best of your ability. Once we switch you into the rebreathing bag try to pull the entire contents of the bag in on the first breath. Continue to breathe with the metronome until we tell you to stop. The procedure will last from 10 to 20 seconds.

As before, we will need to use a noseclip and mouthpiece in order to insure that all expired gases are collected for analysis. We will attempt two trials at each workload.

Do you have any questions? When you are ready we can begin the test.

APPENDIX C

Individual Data for Missoula (N = 10)

Subject	% Tank	$\dot{V}O_2$ ($L \cdot min^{-1}$)	$\dot{V}CO_2$ ($L \cdot min^{-1}$)	RQ	$PetCO_2$ (mm Hg)	$PaCO_2$ (mm Hg)	$PbagCO_2$ (mm Hg)	$P\bar{v}CO_2$ (mm Hg)	Cardiac Output ($L \cdot min^{-1}$)
G.A.	12.8	1.10	.81	.74	39.5	38.7	65.9	61.1	8.72
T.C.		.48	.35	.72	39.4	38.9	51.9	50.4	6.87
		.51	.35	.70	40.0	39.7	53.6	51.7	6.69
J.H.		.38	.25	.65	39.6	39.9	61.3	57.6	3.37
		.41	.27	.64	38.8	39.2	54.5	52.4	4.70
P.L.		.42	.33	.80	39.5	39.9	56.9	54.2	5.38
		.49	.38	.78	39.2	39.5	56.1	53.6	6.24
K.M.		.53	.36	.68	36.4	36.8	55.4	53.1	5.01
J.N.		.78	.53	.68	39.2	38.7	60.7	57.1	6.78
		.75	.50	.67	39.3	38.9	61.6	57.8	6.27
B.S.		.63	.46	.74	37.3	37.2	54.3	52.3	6.92
		.73	.52	.72	37.5	37.2	51.9	50.4	8.79
M.S.		.57	.33	.57	35.3	35.7	60.6	57.1	3.56
		.53	.32	.62	37.6	37.9	60.9	57.3	3.87
J.W.		1.03	.68	.66	37.3	36.9	60.9	57.3	7.77
		.94	.72	.77	34.9	34.4	57.1	54.4	8.09
R.W.		.42	.31	.72	34.8	35.5	50.8	49.6	4.83
		.47	.32	.67	36.7	37.0	52.2	50.7	5.24
G.A.	13.8	1.49	1.24	.83	42.6	41.3	76.7	69.3	11.34
		1.44	1.21	.84	41.2	39.9	75.4	68.3	10.75
T.C.		.78	.57	.73	41.4	40.3	62.0	58.1	7.67
		.71	.54	.76	41.4	40.3	62.1	58.2	7.24
J.H.		.43	.29	.67	38.6	39.0	62.4	58.4	3.55
		.50	.33	.66	39.8	39.9	60.6	57.1	4.57
P.L.		.84	.70	.83	41.8	41.1	71.5	65.3	7.24
		.83	.68	.82	42.0	41.3	71.0	65.0	7.20
K.M.		1.74	1.41	.81	38.1	37.0	75.6	68.5	11.10
		1.68	1.32	.78	39.2	38.0	74.3	67.5	11.11
J.N.		.97	.72	.74	40.4	39.6	64.6	60.1	9.48
		.92	.65	.71	41.1	40.7	65.3	60.6	7.95
B.S.		.90	.65	.72	38.7	38.3	59.5	56.2	8.48
		.93	.66	.70	39.6	39.1	59.9	56.5	8.92

Subject	% Tank	$\dot{V}O_2$ (L·min^{-1})	$\dot{V}CO_2$ (L·min^{-1})	RQ	$PetCO_2$ (mm Hg)	$PaCO_2$ (mm Hg)	$PbagCO_2$ (mm Hg)	$P\bar{v}CO_2$ (mm Hg)	Cardiac Output (L·min^{-1})
M.S.	13.8	.76	.61	.80	41.5	41.0	72.6	66.2	6.09
		.74	.59	.80	41.0	40.6	69.9	64.1	6.22
J.W.		1.14	.95	.83	36.3	34.8	60.1	56.7	9.90
R.W.		.66	.50	.77	39.3	38.6	64.6	60.1	5.57
		.70	.53	.75	38.3	37.6	66.4	61.5	5.32
G.A.	15.1	1.92	1.64	.86	42.1	39.9	83.9	74.8	12.24
		1.99	1.67	.84	41.5	39.5	82.7	73.9	12.57
T.C.		.88	.69	.78	42.9	41.7	64.2	59.8	9.32
		.87	.69	.80	40.9	39.9	62.3	58.3	8.96
J.H.		.84	.59	.71	41.2	40.8	72.4	66.0	5.87
		.86	.64	.74	40.8	40.3	70.1	64.3	6.62
P.L.		1.56	1.30	.83	41.4	39.8	77.8	70.1	10.91
K.M.		1.21	.97	.80	39.0	38.1	65.4	60.7	10.28
		1.24	1.02	.82	39.2	38.1	70.2	64.4	9.49
J.N.		1.70	1.36	.80	41.6	39.3	74.8	67.8	11.95
		1.63	1.29	.79	40.8	38.9	76.3	69.0	10.78
B.S.		1.54	1.23	.80	41.0	38.2	73.4	66.8	10.65
		1.61	1.31	.82	40.9	38.1	73.3	66.7	11.32
M.S.		1.03	.83	.81	41.3	40.4	72.9	66.4	8.00
		1.07	.88	.82	40.4	39.5	75.3	68.2	7.71
J.W.		1.74	1.46	.84	38.1	35.0	74.7	67.8	10.84
		1.86	1.56	.84	38.6	34.9	77.2	69.7	11.01
R.W.		.96	.73	.76	40.4	38.9	70.6	64.7	6.97
		.96	.76	.78	40.2	39.0	68.4	63.0	7.73

APPENDIX D

Individual Data for Madison (N = 3)

Subject	% Tank	$\dot{V}O_2$ ($L \cdot min^{-1}$)	$\dot{V}CO_2$ ($L \cdot min^{-1}$)	RQ	$PetCO_2$ (mm Hg)	$PaCO_2$ (mm Hg)	$PbagCO_2$ (mm Hg)	$P\bar{v}CO_2$ (mm Hg)	Cardiac Output ($L \cdot min^{-1}$)
J.N.	12.8	.76	.55	.73	41.9	41.2	85.2	75.8	4.20
		.72	.49	.69	41.8	40.9	88.6	78.3	3.48
M.S.		.79	.50	.63	41.9	41.2	89.3	78.9	3.55
		.82	.54	.66	42.0	41.5	89.3	78.9	3.87
R.W.		.82	.59	.72	41.8	40.5	88.6	78.3	4.14
J.N.	13.8	.95	.72	.76	43.9	42.6	95.6	83.7	4.83
		.99	.72	.73	44.5	43.2	97.7	85.3	4.76
M.S.		.92	.62	.67	43.2	42.2	101.2	87.9	3.79
		1.04	.71	.69	42.9	41.5	99.1	86.3	4.38
R.W.		1.01	.79	.77	42.3	40.6	95.6	83.7	4.99
		1.04	.76	.73	42.4	40.7	97.0	84.7	4.72
J.N.	15.1	1.70	1.45	.85	47.7	44.8	117.3	100.1	7.78
		1.63	1.36	.84	46.3	43.6	119.4	101.7	6.94
M.S.		1.39	1.08	.78	42.6	40.8	113.1	97.0	5.52
		1.31	1.04	.79	42.7	40.8	112.8	97.5	5.28
R.W.		1.42	1.12	.79	41.6	39.3	117.3	100.1	5.30
		1.37	1.09	.80	44.5	42.3	120.1	102.3	5.36

APPENDIX E

Individual Data for Missoula (N = 3)

Subject	% Tank	$\dot{V}O_2$ (L·min-1)	$\dot{V}CO_2$ (L·min-1)	RQ	$PetCO_2$ (mm Hg)	$PaCO_2$ (mm Hg)	$PbagCO_2$ (mm Hg)	$P\bar{v}CO_2$ (mm Hg)	Cardiac Output (L·min-1)
J.N.	12.8	.78 .75	.53 .50	.68 .67	39.2 39.3	38.7 38.9	60.7 61.6	57.1 57.8	6.78 6.27
M.S.		.57 .53	.33 .32	.57 .62	35.3 37.6	35.7 37.9	60.6 60.9	57.1 57.3	3.56 3.87
R.W.		.42 .47	.31 .32	.72 .67	34.8 36.7	35.5 37.0	50.8 52.2	49.6 50.7	4.83 5.24
J.N.	13.8	.97 .92	.72 .65	.74 .71	40.4 41.1	39.6 40.7	64.6 65.3	60.1 60.6	8.48 7.95
M.S.		.76 .74	.61 .59	.80 .80	41.5 41.0	41.0 40.6	72.6 69.9	66.2 64.1	6.09 6.22
R.W.		.66 .70	.50 .53	.77 .75	39.3 38.3	38.6 37.6	64.6 66.4	60.1 61.5	5.57 5.32
J.N.	15.1	1.70 1.63	1.36 1.29	.80 .79	41.6 40.8	39.3 38.9	74.8 76.3	67.3 69.0	11.95 10.78
M.S.		1.03 1.07	.83 .88	.81 .82	41.3 40.4	40.4 39.5	72.9 75.3	66.4 68.2	8.00 7.71
R.W.		.96 .96	.73 .76	.76 .78	40.4 40.2	38.9 39.0	70.6 68.4	64.7 63.0	6.97 7.73

APPENDIX F

Corrections Applied to PbagCO_2 Values (Madison) N = 3

PbagCO_2 (mm Hg)	% CO_2 (%)	FrawCO_2[a] (%)	Adjusted % CO_2 (%)	Corrected PbagCO_2 (mm Hg)
81.7	11.7	11.5	12.2	85.2
84.1	12.0	11.8	12.7	88.6
85.5	12.2	11.9	12.8	89.3
85.1	12.2	11.9	12.8	89.3
83.6	12.0	11.8	12.7	88.6
89.2	12.8	12.5	13.7	95.6
90.4	13.0	12.7	14.0	97.7
93.6	13.4	13.0	14.5	101.2
92.1	13.2	12.8	14.2	99.1
91.4	13.1	12.7	14.0	95.6
90.2	12.9	12.6	13.9	97.0
105.3	15.1	14.5	16.8	117.3
106.5	15.3	14.7	17.1	119.4
101.9	14.6	14.1	16.2	113.1
102.8	14.7	14.2	16.3	113.8
105.3	15.1	14.5	16.8	117.3
107.3	15.4	14.8	17.2	120.1

[a]The following equation was used to obtain FrawCO_2:
FrawCO_2 = (% CO_2 + .013)/1.13.