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THE EFFECTS OF SUBMAXIMAL TRAINING UNDER HYPOXIC CONDITIONS UPON PERFORMANCE AT SEA LEVEL

By

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ABSTRACT

THE EFFECTS OF SUBMAXIMAL TRAINING UNDER HYPOXIC CONDITIONS UPON PERFORMANCE AT SEA LEVEL

By

Mohammed S. Sanguq

This investigation was conducted to determine the effects of hypoxic submaximal training (simulated high-altitude training) upon performance at sea level. Prime consideration was given to acid-base parameters of the arterialized blood, to oxygen consumption during exercise and recovery as indicators of efficiency in energy metabolism, and to performance time.

Eight healthy male students at Michigan State University (22-24 years of age) were used as subjects in the study. The subjects were assigned randomly to one of two treatment groups (n = 4). Group I (normoxic trained while breathing normal air (PO_2 = 152 mmHg, 20.7% O_2). Group II (hypoxic) trained while breathing air with a reduced oxygen concentration (PO_2 = 122 mmHg, 16.6% O_2).

The training consisted of one five-minute run per day on a motor-driven treadmill at 7.0 mph and zero percent grade. The treatment period lasted three weeks with four days of training during each of the first two weeks and three days of training during the final week. The training was conducted under either normoxic or hypoxic conditions as indicated earlier.

Three tests were conducted before and after the treatment period. The first was an all-out run to determine performance time. The treadmill was set at 7 mph and 8% grade, and the grade was increased 1% per minute after the first two minutes of running. The other two tests were submaximal standard runs, one under hypoxic and one under normoxic conditions. In these two tests gas collection took place during the run and during the first fifteen minutes of recovery. The Douglas bag method was used to determine the oxygen uptake during exercise, the oxygen debt, and the oxygen requirement under each condition. Blood samples were taken before and after the submaximal runs to determine PCO_2, pH, HCO_3, and BE.

The blood PCO_2 was significantly higher in the hypoxic group than in the normaxic group under hypoxic test conditions. There were no other significant differences between the two treatment groups under the two submaximal test conditions.

Comparisons of the data obtained before and after training for each group resulted in significant differences only in the performance time of the normoxic group and the oxygen debt of the normoxic group under hypoxic test conditions.

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CHAPTER I

INTRODUCTION

Research on the effects of high altitude training on physical performance began early in this century (22). However, it became intensified after the decision to hold the 1968 Olympic games in Mexico City (2,300 m above sea level). In regard to training and performance, there are at least three questions to be answered: (a) What are the effects of acute high altitude exposure on performance? (b) Does high altitude training improve or impair performance at high altitude? (c) What are the effects of high altitude training on performance at sea level?

The immediate effects of acute high altitude exposure on performance have been studied intensively (36, 40, 66, 94, 143, 149, 186, 187, 214). It is well established that hypoxia is the major problem at altitude and, therefore, aerobic performance is negatively correlated with altitude. Although the effects of altitude exposure upon anaerobic capacity have not been precisely determined, no impairments of performance have been reported in those activities which require explosive power (i. e. throwing, sprinting, jumping). On the contrary, improvements of these activities have been noticed due to other factors such as changes in air resistance and gravity.

In respect to the second question, there is general agreement in the literature that performance at altitude is enhanced in athletes who have acclimatized themselves by training at the same altitude (11,

36, 40, 66, 143, 186).

The question that has not been fully answered pertains to the effects of altitude training on performance at sea level. Enhanced performances have been reported in some studies (13, 14, 15, 62, 67, 139), but another body of literature has failed to support this observation (35, 63, 101, 107, 138, 152). Therefore, there is a demonstrated need to further investigate the effects of hypoxic training on performance at sea level.

Several studies have been conducted to determine the effects of high altitude training on maximum performance capability as measured by maximum oxygen uptake (Max. VO_2). Although the Max. VO_2 is an important factor in aerobic work, it does not furnish precise information about the economy of work and the efficiency of energy metabolism (161, 207). Astrand et al. (9) noted that a submaximal work level provides more accurate information about the subject's aerobic capacity. Thus, O_2 consumption and the degree to which a subject is able to approach Max. VO_2 for a prolonged period of time are better predictors of endurance capacity than is Max VO_2 itself (182).

At present, little is known about the changes in blood acid-base balance that occur at sea level as a result of hypoxic-submaximal training. At altitude, however, arterial P_{CO_2} and blood HCO_3 were reported to increase at rest (76, 106) and to decrease with submaximal exercise as a result of hyperventilation (107, 129, 130). Blood lactic acid has been reported to increase both at rest (80, 107) and during submaximal exercise (10, 80, 107, 112, 124, 130, 160, 195). Blood pH, however, is increased (11, 27, 124, 130). The elevation of the blood lactic acid concentration usually is believed to be a result of

insufficient O_2 supply (147, 177).

From a physiological point of view, acute exposure to altitude, even without exercise, will increase pulmonary ventilation by an increase of respiratory rate (37, 159) as a compensatory mechanism in response to hypoxia. More CO_2 may be blown off which in turn would raise the blood pH and result in slight alkalosis. It has been reported that alkalosis might reduce the aerobic metabolic capacity (116) by inhibiting the activity of cytochrome c (117) and by a decrease of conversion of lactate to glucose in the kidneys (114, 115) and liver (118).

However, with submaximal exercise at altitude, alkalosis might not be experienced because of an increased CO_2 production, and the accumulation of lactic acid in the blood pH may override the effects of compensatory hyperventilation. The blood pH may fall (11) and slight acidosis would result. It is well documented that acidosis impairs aerobic capacity (60, 71, 204). The question is: to what extent would this shift in blood acid-base balance and low PO_2 under hypoxic-submaximal training cause adaptation in the body and, therefore, affect performance at sea level?

Statement of the Problem

The purpose of this study was to determine the effects of hypoxic submaximal training (simulated high-altitude training) upon performance at sea level. Main consideration was given to acid-base parameters of the arterialized blood, to oxygen consumption during exercise and recovery as indicators of efficiency in energy metabolism, and to performance time.

Research Hypotheses

1. Hypoxic submaximal training should help to maintain the blood acid-base balance during standard exercise which is performed at sea level.
2. Hypoxic submaximal training should reduce the O_2 utilization for standard exercise which is performed at sea level.
3. Hypoxic submaximal training should prolong the performance time of subjects doing exhaustive exercise at sea level.

Research Plan

Eight healthy male students at Michigan State University, between 22 and 24 years of age, were recruited as subjects for this study. The subjects were classified as active, but not highly trained athletes. A stress test was administered to determine the subjects' ability to participate in the study.

The subjects were assigned randomly to one of two treatment groups (n = 4). Group I (normoxic) trained while breathing normal air (PO_2 = 152 mmHg, 20.7% O_2). Group II (hypoxic trained while breathing air with a reduced oxygen concentration (PO_2 = 122 mmHg, 16.6% O_2).

The training consisted of one five-minute run per day on a motor-driven treadmill at 7.0 mph and 0% grade. The training period lasted three weeks with four days of training during each of the first two weeks and three days of training during the final week. The training was conducted under either normoxic or hypoxic conditions as indicated earlier.

Three tests were conducted before and after the treatment period. The first was an all-out treadmill run to measure performance time.

The treadmill was set at 7 mph and 8% grade, and the grade was increased one percent per minute after the first two minutes of running. The other two tests were submaximal standard runs, one under hypoxic and the other under normoxic conditions. These two tests were used to determine the acid-base balance of the blood (pH, PCO_2, HCO_3, BE), the O_2 uptake during the exercise, the oxygen debt, and the oxygen requirement of each run.

Standard two-sample t-tests were used to analyze the data. The probability of making a Type I error was set at $\alpha = .10$, and two-tailed tests were used for all analyses.

Rationale for Research Plan

A 5 min., 6 mph, 0% grade treadmill protocol was used as a reproducible submaximal test for measuring economy of work. Room air was used during all recovery periods to make comparisons between the oxygen debts and the oxygen requirements of the two groups possible.

The first minute of recovery gas was excluded on the assumptions that this period of time was needed to flush the lungs of the hypoxic air mixture and that the effects on the oxygen debt calculations would be approximately the same across all treatment and test conditions.

Limitations

1. Exposure to hypoxic air (simulated high altitude) occurred only during the workout period.
2. All recovery data were collected while the subjects were breathing room air.
3. All dependent variables, except performance time, were observed under only one kind of work, at one intensity,

and one duration.

4. There was no control over the subjects' living patterns. For example, sleep, diet, and recreational activities were not regulated.
5. The results of the study cannot be generalized to other populations or sub-populations of individuals.

Definitions

1. Altitude. The term "altitude" refers to the vertical elevation above sea level. The following standard pattern has been used for altitude physiology descriptions.

Modest altitude	1,500 to 2,500 meters (4,920 to 8,200 feet)
Moderate altitude	3,000 to 3,300 meters (9,840 to 10,500 feet)
High altitude	4,000 to 5,000 meters (13,120 to 16,400 feet)
Great heights	above 5,500 meters (above 16,400 feet)

2. Submaximal Work. Physical work of less than maximal intensity or work that can be sustained chiefly by aerobic metabolism is called submaximal work. The submaximal work in this study was considered to be of moderate intensity.
3. Normoxic Air. Air with a normal PO_2 or normal oxygen content (20.9%) is said to be normoxic. In this study, the subjects breathed compressed air adjusted to the ambient pressure when exercising under normoxic conditions.

4. Room Air. Unmodified ambient air is called room air. In this study the subjects were disconnected from the compressed air system and breathed room air during recovery from exercise.
5. Hypoxic Air. Air with a low PO_2 or a low O_2 content is said to be hypoxic. The hypoxic air used in this study was a mixture of compressed N_2 and O_2. The O_2 content was reduced to 16.6 ± 0.04%.
6. O_2 Uptake. (VO_2): The volume of O_2 (STPD) that is taken in by the body from the inspired air during exercise is called O_2 uptake.
7. Oxygen Debt. (O_2D): The term oxygen debt was used in this investigation to indicate the volume of O_2 (STPD) used during the last 14 minutes of the 15-minute post-exercise recovery period.
8. Oxygen Requirement. (O_2R): The total volume of O_2 (STPD) used during the entire exercise and recovery period is called the oxygen requirement. No adjustment of volume was made for basal or resting metabolic rate.
9. Acid-Base Balance. The relative proportions of acids and alkali (H^+ and OH^- ions) in the blood and tissues determine the acid-base balance.
10. Blood pH. Blood pH is a measure of the acidity or alkalinity of the blood.
11. Standard Bicarbonate. (HCO_3): The amount of alkalizing salts as bicarbonate at PCO_2 of 40 mmHg, 38°C and completely

O_2-saturated hemoglobin that is available in the blood and body fluid for buffering is referred to as standard bicarbonate.

12. Base Excess. (BE): The base concentration of whole blood as measured by its titration to pH 7.40 at a PCO_2 of 40 mmHg is called BE. It is equal to buffer base minus normal buffer base: therefore normal BE = 0.

13. Alkalosis. A shift of the acid-base balance to the alkaline side when the alkalinity of the blood and tissues is increased (pH increased) is called alkalosis.

14. Acidosis. A shift of the acid-base balance to the acid side when the acidity of the blood and tissues is increased (pH decreased) is called acidosis.

CHAPTER II

REVIEW OF RELATED LITERATURE

This review of literature is focussed in two pertinent areas: (1) physiological adaptations to hypoxia which includes (a) immediate responses to acute hypoxic exposure and (b) physiological adaptations after prolonged altitude exposure, and (2) physiological adaptations to submaximal exercise.

Physiological Adaptations to Hypoxia

The most apparent physiological adjustments in response to hypoxic exposure at rest and during submaximal physical work are in the oxygen transportation system of the body. The primary stimulus may be the increased demand of oxygen at the tissue level, especially during exercise. Therefore, a new homeostasis for transportation of oxygen between the environment and the tissues must be reestablished.

Immediate Responses to Acute Hypoxic Exposure

Evidence has shown that the immediate responses to acute hypoxic exposure include: (a) respiratory rate is increased (37, 159), (b) minute ventilation is increased (37, 48, 101), and (c) oxygen diffusion capacity in the lungs is increased (103, 171), unchanged (195), or decreased (100, 216). From a physical point of view, a decrease of oxygen diffusion capacity in the lungs is more likely to occur since arterial PO_2 is reduced with altitude (99, 76, 215).

During exercise, pulmonary circulation is markedly increased and the blood circulates through the pulmonary capillaries more rapidly than at rest. Gaseous exchange is not a problem under these conditions at sea level. However, with the reduced arterial PO_2 at high altitude, it has been reported that oxygen diffusion capacity may be decreased (100, 216). As a result, the amount of oxygen transported to the working muscles is reduced for a given cardiac output. In some cases, the reduced O_2 saturation may be compensated for by an increased cardiac output (7, 83, 108, 144, 195).

There is fairly good agreement that heart rate is increased at rest and during submaximal work at altitude (29, 48, 124). Reports on stroke volume, however, are not consistent (56, 100, 140, 144, 153, 169, 184, 197). It would seem that any increase in cardiac output is produced mainly by an increase in heart rate (106, 197). On the other hand, decreased cardiac output during submaximal work at 3000 m altitude and decreased HR following swimming exertion at altitude have been reported (12, 55).

Acute hypoxic exposure also causes some adaptations in the blood. Blood hematocrit and relative hemoglobin concentration were reported to increase (100, 106, 142, 170, 197, 200). It is believed that these changes can be attributed to a slight decrease in plasma volume and to an increased kidney secretion of erythropoeitin, a powerful stimulant for red blood cell production (173, 197, 200). Oxygen carrying capacity of the blood, therefore, is enhanced due to these changes both at rest and during moderate exercise (100, 142, 197). Increases of blood constituents, such as blood glucose and potassium, also have been

reported (87, 134, 198).

The adjustments in circulation under hypoxic exposure have not yet been understood completely, especially during exercise. However, a circulatory shunt at tissue level was suggested (16) and shown by Feldman (86) and others (3). Reports of vasodilation in muscle are available (38, 54, 193). There is a shift in the oxyhemoglobin dissociation curve toward the right (11, 197, 206). Also, shifting of the extracellular fluid into the intracellular compartment and retention of Na^{+}, Ca^{++}, Mg^{++}, and K^{+} were noticed (44).

In regard to the changes in acid-base balance at altitude, an increase of arterial PCO_2 and blood HCO_3 reported at rest (76, 106). During submaximal exercise the PCO_2 (107, 129, 130) and the HCO_3 were decreased (130) due to hyperventilation (130). Although lactate concentration has been shown to increase at rest (80, 193) and during submaximal exercise (10, 80, 107, 112, 124, 130, 160, 195), the blood pH is increased under both conditions (11, 27, 124, 130).

There is an increase in oxygen uptake (VO_2) at rest (75, 102, 132, 151, 201). With moderate exercise an increase (28, 48, 124, 130), no change (6, 47, 85, 101, 189), and even a decrease (56, 151, 203) in VO_2 were reported. The conflicting results in VO_2 during moderate exercise cannot be explained at present. Further controversy comes from reports on the oxygen requirement during exercise under hypoxic conditions. No change (89), a decrease (56, 120, 151, 203), and an increase (47, 78) in the oxygen requirement for a given exercise at altitude have been shown. Further research in this area obviously is needed.

The respiratory quotient (RQ) was shown to be increased during exercise under hypoxic conditions (29, 48, 88, 130, 151). This increment in RQ may be a result of hyperventilation (130) (increased CO_2 exhalation) and/or a result of increased carbohydrate metabolism at altitude (48).

The hormonal responses to acute hypoxic exposure have been studied. An increase in urinary catecholamines was reported at rest (23, 42, 146) and during submaximal exercise (45). Factors other than hypoxia, however, might affect the catecholamine level as was pointed out by Becker (23) and Antel (4). Free fatty acids (130, 198), plasma glucose, cortisol and serum growth hormones also were reported to increase (198). On the other hand, a 50% decrease in the blood insulin level was noted during exercise under hypoxic as compared to normoxic conditions (198). These hormonal changes have been suggested by Sutton (198) to favor fat mobilization and enhanced hepatic gluconeogenisis during submaximal hypoxic exercise.

In regard to submaximal performance, it has been reported that a relatively long time is needed to reach steady state (29). This may be due, in part, to the reduced capacity for endurance work in acute hypoxia that was reported by Consolazio (47).

Physiological Adaptations after Prolonged Altitude Exposure

Acclimatization to high altitude may occur under two circumstances. So-called "natural acclimatization" is referred to as those physiological characteristics found among people who reside in high altitude all their lives; whereas, "gained acclimatization" consists

of those physiological changes that are attained by sea level residents who move to high altitudes. The following review of literature is focussed on the second type of acclimatization. It should be pointed out that acclimatization to altitude occurs gradually and the time needed for acclimatization depends upon the altitude and the individual. However, complete acclimatization or "steady state" has not been found even in subjects who have been at altitude for prolonged periods of time (126).

An increase of ventilation at rest and submaximal exercise is continued after initial exposure to altitude (29, 158, 159). A new level of pulmonary ventilation, higher than the value observed at initial exposure, may be attained (11).

Both an increase (65, 103) and no change (64, 215) in diffusing capacity in the lungs have been observed. It is believed that any increased diffusing capacity that does occur is the result of a better perfusion in the pulmonary capillaries and the elevated ventilation (196).

Cardiac output gradually decreases and returns to sea-level values (140, 181, 212) or even slightly lower (140) at rest and during submaximal exercise. Reduction in cardiac output during submaximal exercise might be attributed to a decrease in heart rate (17, 85, 211) and/or to a decrease in stroke volume (11).

The red blood cell count and the hemoglobin concentration are increased by prolonged altitude exposure (127, 189, 211). The increase of red blood cell production results in an elevated hematocrit (43, 61). In addition, a shift of the oxygen dissociation curve (23, 206, 215)

and an increase of 2,3-diphosphoglycerate (11) resulting from altitude acclimatization suggest a possible mechanism for increased availability of oxygen to the working muscles. This might explain the improvement in aerobic work which was reported by Saltin (178) and others (17, 145, 189).

Adaptations at the tissue level also occur during prolonged altitude exposure. Improved efficiency of oxygen utilization was observed by Barbashova (19). This improved efficiency might be due to an increase of myoglobin content in the muscle cell (5, 172), an increase of oxiditive enzyme activity (19, 172), and/or an increase of capillarization in the muscle (210). An increase of capillarization would reduce the oxygen diffusion distance (11, 90). Supporting data on improved oxygen utilization also come from Duckworth's work (77) in which a lower oxygen consumption in isolated diaphragm muscle exposed to hypoxia was observed.

It is difficult to explain the increased pulmonary ventilation observed after prolonged altitude exposure since the initially elevated PCO_2 (106, 128, 196) and alkaline reserve (11, 76, 106, 128, 196) are decreased with acclimatization. In addition, the blood pH decreases to its normal value (11, 128, 196), and a decrease of the blood lactate level following exercise has been reported (29, 70, 145, 165, 205).

The mechanism by which lactic acid is decreased might be explained in connection with the action of the catacholamines. The secretion of catacholamines is increased under hypoxia (23, 93). It is well established that epinephrine has great glycogenolytic effects in liver and muscle cells. However, epinephrine also may cause glycogenisis

particularly in liver cells. Therefore, large amounts of blood lactate may be taken up by the liver to be converted to glucose (51, 52, 53). Glycogenolysis also takes place and an increased supply of blood glucose becomes available for the muscles during exercise (25, 41). Based on this possibility, Tillman (203) suggested that lactate production does not decrease, but that the lower blood lactate level under hypoxia may be due to an increased secretion of catecholamines.

Another striking fact is that a reduced oxygen consumption during submaximal exercise has been reported after hypoxic training (29, 56, 160). For example, Tillman (203) observed that his hypoxic-trained subjects used less oxygen for a standard submaximal exercise when breathing hypoxic air (16.6% oxygen) than when breathing normoxic air. On the other hand, increased oxygen intake has been observed during hypoxic training (29, 57, 85). Billing (29) suggested that the effects of the intensity of the exercise and the altitude may be interrelated. He observed that oxygen intake did not change with altitude when the intensity of exercise was at 2.2 L. O_2/min. However, a lower oxygen intake value was found when the intensity of exercise was at 2.5 L. O_2/min.

The possible lower oxygen consumption during a given submaximal exercise may indicate either an improved oxidative capacity with altitude adaptation (17, 145, 165, 178) or an increased contribution of anaerobic energy metabolism with little change in the phosphagan component (21). Therefore, from the data of Billing (29) and Bason (21), altitude adaptation may result in an increase of O_2 debt capacity. However, reduction in O_2 debt capacity with acclimatization to altitude also has been observed (50).

It is well known that the total hemoglobin concentration is increased with altitude acclimatization (100, 106, 170, 197). Hemoglobin has a function other than the transportation of O_2. It is a powerful buffer in the body. In regard to exercise energy metabolism under hypoxia, anaerobic glycolysis may be stimulated and lactate formation is in fact increased. However, due to the effects of catecholamines and hemoglobin, more lactate may be taken up by the liver and more H^+ could be buffered. The contribution of anaerobic metabolism in the total energy production is therefore increased (21). The reported lower O_2 consumption during a submaximal exercise after altitude acclimatization may be the result of the readjustment of energy metabolism in the body.

Physiological Adaptations to Submaximal Exercise

Exercise tends to disturb the homeostasis of the body. A series of biochemical, physiological and anatomical changes takes place in the body in order to re-establish a new level of homeostasis as a result of physical training. Once this new level of homeostasis is achieved, the body will function better and less strain will be imposed on the body for any given amount of physical work.

Many of the physiological adaptations of the body to submaximal exercise are well established in the literature (11). However, there still are numerous areas that are not completely understood. This might be due to the fact that the effects of submaximal exercise are interrelated with many other factors such as: (a) intrinsic characteristics of the subjects (e. g., age, sex, hormonal regulation, nutritional status, heredity, muscle fiber composition, degree of motivation,

physical capacity, etc.) and (b) extrinsic conditions (e. g., environment, time of day, etc.). Therefore, the following literature is intended to present a summary of the well-known adaptations to exercise rather than a search for the mechanisms of the adaptations.

Cardiorespiratory adjustments are marked by a quicker increase of heart rate (HR) and stroke volume (SV) at the beginning of exercise, but the absolute HR will be lower for a given submaximal work load (91, 179, 180, 185). The cardiac output (Q) however, may be unchanged (150) or may be even slightly decreased (3, 81) for a given exercise. Also, resting HR is decreased (92) while SV is increased (157). Cardiac hypertrophy on the left side also has been noticed (157, 162, 176).

Respiratory rate is increased at the onset of exercise (11), while a reduced total ventilation has been reported with training (208, 209). Pulmonary diffusing capacity has been reported to be either increased (18) or unchanged (79).

Total blood volume and total hemoglobin concentration are increased with training (136, 164). It seems to be beneficial for a trained individual to have a higher total hemoglobin content in the blood since this may increase the potential oxygen carrying capacity.

It is well established that muscle capillarization is increased after submaximal training (113, 166, 182). However, blood flow to working muscles for a given work load is decreased (98, 120, 137).

A reduced oxygen consumption for a given workload also has been reported (11, 208, 209). This decline of oxygen cost with training may reflect a gain in efficiency of energy metabolism as a result of a series of changes at the tissue level. For example, the myoglobin content (164), the number and size of the mitichondria (97, 121, 135),

and the concentration and activity of a series of aerobic enzymes in the Kreb's Cycle (20, 24, 121) are all increased with training.

In regard to substrate utilization, it is well known that training will result in an increase of fat metabolism during exercise (105, 156). A reduction of RQ during exercise may reflect this shift in substrate utilization (32, 208, 209). Along the same line, there are reports that indicate glycogen concentration is increased in the muscle (25, 26, 152) and plasma triglycerides are lower after a period of submaximal training (30, 31).

Regarding hormonal responses, blood catecholamine levels are increased during exercise (105), but they are normalized rapidly during recovery (105). With training, blood catecholamine levels gradually decline during a given exercise (213). Glycogen is increased (33, 105), but insulin is decreased during work (109). The lower-than-normal insulin level during exercise has been proposed to be the result of an inhibitation by the action of epinephrine since insulin secretion by the human pancreas is virtually shut off during an infusion of epinephrine (167). This effect may be explained as the result of a direct inhibitory action of epinephrine on the beta cells.

However, it is well known that epinephrine will activate phosphorylase (58, 59) and thus facilitate glycogenolysis in both the liver and the muscles (52, 53). As a result, glucose is released from the liver into the circulation. Also, the fact that insulin in the plasma remains depressed for a much longer time after exercise than do catecholamines speaks against the hypothesis that catecholamines are the inhibators for insulin during exercise. An inhibitation of insulin

secretion might appear to be a problem for glucose transportation across the muscle cell membrane during exercise. However, it has been reported that glucose uptake by the muscle cells during exercise does not necessarily need the presence of insulin (46, 96, 168, 217). A substance with a similar effect has been postulated to be released by the contracting muscle tissue (95). Growth hormone also has been reported to be increased during submaximal exercise (109, 199) as is Cortisol (109, 199). So it seems that the adjustment of the endocrine system during submaximal exercise is to help the body establish a new level of homeostasis as was suggested by Hartley et al. (109).

CHAPTER III

RESEARCH METHODS

The methods and procedures described in this chapter were used to investigate the effects of hypoxic submaximal training (breathing low PO_2 air) upon performance at sea level. Main consideration was given to performance time, blood acid-base balance, and O_2 consumption during exercise and recovery as estimators of the efficiency of energy metabolism and economy of work.

Research Design

A true experimental design, with two independent comparison groups, was used in this study. The analysis included both pre- and post-treatment data as is shown in Figure 3.1:

	Hypoxia n = 4	Normoxia n = 4
pre-treatment	T_1	T_1
post-treatment	T_2	T_2

Figure 3.1. Research Design

The experiment was conducted as a single-blind study. The subjects did not know their treatment groups during the course of the investigation.

Subjects

Eight healthy male students at Michigan State University were used as subjects in this study. The subjects were classified as active but not highly trained athletes. Their physical and physiological characteristics are given in Table 3.1.

TABLE 3.1

SUBJECT CHARACTERISTICS

Subjects	Age in Yrs	Height in cm	Weight in Kg	Max HR bpm	Max VO_2 ml/Kg/min.	fat %
JB	20	176.8	68.8	192	72.63	13.5
KC	22	189.0	82.4	191	65.63	12.5
DH	20	155.4	70.0	186	64.62	11.5
PP	22	155.8	89.4	190	49.42	20.5
SH	27	192.0	97.2	181	47.94	19.5
JS	18	173.7	71.8	183	52.56	15.5
DS	18	176.8	70.2	195	68.05	13.0
TM	18	182.9	81.6	192	66.59	12.0

Prior to the start of the study, an informed consent statement was obtained from each potential subject (See appendix A) and a modified Bruce protocol (34) was administered as a stress test to determine each individual's ability to participate in the study. In addition, weight, height, age, pre-run heart rate, and blood pressure were taken. Electrodes[1] then were placed in a single biopolar V_5 electrocardiograph

[1]Disposable 3M Red Dot Monitoring Electrod-Minnesota Mining Co., 3M Center, St. Paul, Minnesota 55101.

configuration[2] (see Figure 3.2), and each subject was stress tested under the following conditions:

Level I -- 3.4 mph, 12% grade, 3 minutes

Level II -- 4.2 mph, 12% grade, 3 minutes

Level III -- 6.0 mph, 12% grade, 1.5 minutes

Recovery -- 3 minutes (standing)

During and immediately after each level, the following data were collected:

Heart Rate: Recorded at the end of each minute of exercise and recovery.

Blood Pressure: Recorded at the end of each level.

ECG: Recorded at the end of each level (5-6 second strip).

The following criteria were used to eliminate potential subjects (82):

1. Systolic blood pressure over 220 mmHg.
2. Diastolic blood pressure over 110 mmHg.
3. Depression of the ST-segment of the ECG greater than 2 mm.
4. Premature ventricular contractions (PVC's) in pairs or with increasing frequency.

The eight subjects whose physical condition qualified them to participate in the study were assigned randomly to one of two treatment groups (n = 4). Group I (normoxic) was trained while breathing normal air (PO_2 = 152 mmHg, 20.7% O_2). Group II (hypoxic) was trained while breathing air with a reduced oxygen concentration (PO_2 = 122 mmHg, 16.6% O_2).

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[2]Cambridge 3030 EKG, Cambridge Instrument Co. Inc., 73 Spring Street, Ossining, New York 10562.

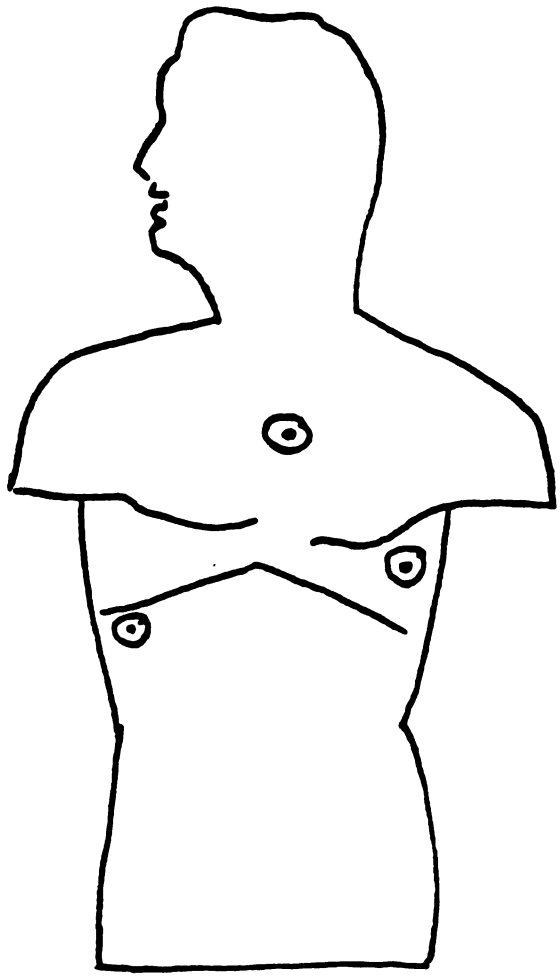

Figure 3.2. Electrode Placement.

Prior to the training period, anthropometric measurements were taken to characterize the subjects. These measurements included height (cm), weight (kg), and biceps, triceps, subscapular, and superailiac skinfolds (mm). Percent body fat was estimated from the skinfold measurements by the method of Durnin (79). The physical characteristics of the subjects are given in Table 3.1. All subjects were asked not to change their activity patterns during the course of the study.

Treatment Procedures

Although a prolonged treatment period might be necessary to demonstrate all the effects of hypoxic training, the eleven-day training period described by Tillman (203) was used in this study since it had been shown to be effective with two treatment groups similar to those used in this study. The training period was carried out over three consecutive weeks with four days in each of the first two weeks and only three days in the last week. Each subject ran eight times under either normoxic or hypoxic conditions as indicated earlier. The training was conducted on a motor-driven treadmill at 7.0 mph and 0% grade.

The schedule was set so that each subject could arrive at the research laboratory ten minutes prior to his exercise session. Barometric pressure, temperature, relative humidity, and body weight were taken each day. The subject was seated on a chair on the treadmill and heart rate was determined by palpation of the radial artery for ten seconds. Meanwhile, a reservoir balloon was filled with hypoxic air for a hypoxic subject and with normoxic air for a normoxic subject (see appendix B). This procedure was used to keep the subject from knowing his treatment group. The subject then stood up beside the

treadmill, the chair was removed, and a Collins' Triple "J" valve was placed in the subject's mouth.

After the subject was prepared, the treadmill was started, and the signal "Ready . . . set . . . go" was given. The subject then ran for five minutes.

At the end of the run, a ten-second heart rate was taken while the subject was still standing. Subsequently, recovery heart rates were taken at the end of each minute for five minutes while the subject was seated on a chair.

Gas Mixtures

The procedures described by Tillman (203) were used to prepare the hypoxic air for this study. Compressed air and nitrogen were mixed together in a SCUBA tank in such a way that the percentage of oxygen in the mixture was 16.60 ± 0.04%. This concentration of O_2 resulted in a PO_2 of 120 mmHg (STPD) which is similar to the PO_2 found in the ambient air of Mexico City (2,300 m) where the 1968 Olympic games were held. The percentage of N_2 in the mixture is considered to be biologically safe (203).

The normoxic air was prepared by filling a SCUBA tank with compressed air in the room adjacent to the laboratory. Both the normoxic and the hypoxic air mixtures were reduced to ambient pressure, moistened, and warmed by the techniques of Tillman (203) before they reached the subject (see appendix B).

Testing Procedures

The following three tests were conducted before and after the training period:

Performance Time Test. An all-out multilevel treadmill run was used to determine performance time. Each subject came to the laboratory dressed in tennis shoes and track shorts. Barometric pressure, temperature, and relative humidity were recorded. The subject was weighed and a pre-run blood sample was taken. ECG electrodes were placed. The subject then warmed up in his own manner (usually about five minutes of running at 6 mph and 0% grade). Since the run was to be terminated by exhaustion, a protective harness was used. The subject put on a head-piece which held a low-resistance Collins' Triple "J" valve through which the prepared air was inspired and expired air was collected. The treadmill was set at 7 mph, 8% grade, and the grade was increased 1% per minute after the first two minutes of running. With the signal "Ready . . . set . . . go," the subject ran until he indicated exhaustion by raising a hand and/or by grasping the iron railing of the treadmill. The treadmill then was turned off immediately. Two people on the sides supported the subject who straddled the treadmill until it stopped. The harness was removed and the subject was helped to a chair placed on the treadmill. The following data were collected:

Performance Time:	Recorded in minutes and seconds from the time the subject started running until the treadmill was turned off.
Heart Rate:	Taken at 30-second intervals during exercise and at 1, 2, 3, 4, 5, 7, 9, 12, and 15 minutes during recovery.
Gas Collection:	Obtained at 30-second intervals during exercise and at 1, 2, 3, 5, 7, 9, 12, and 15 minutes during recovery.

Submaximal Run Tests. Two submaximal run tests, one under hypoxic (H) and the other under normoxic (N) conditions were conducted. Standard laboratory procedures described earlier were used. After the warm-up, the Collins' Triple "J" valve was placed in the mouth. The subject then ran for five minutes at 7 mph, 0% grade under one of the predetermined conditions (H or N). During and immediately after the run, the following data were collected:

Gas Collection:	Obtained at 30-second intervals during exercise and 1, 2, 3, 4, 5, 7, 9, 12, and 15 minutes during recovery.
Blood Sample:	Taken at the fifth minute of recovery for the determination of PCO_2, pH, BE, and HCO_3.
Heart Rate:	Taken at 30-second intervals during exercise and at 30 seconds, 12, 15 minutes of recovery.
Respiratory Frequency:	Observed each minute (10 second strip during exercise) and at 1, 2, 3, 4, 5, 7, 9, 12, and 15 minutes during recovery.

Acid-base Balance

One hundred and twenty microliters (mml) of arterialized capillary blood were drawn from a pre-warmed, cleaned, and dry finger tip in a heparanized capillary tube (appendix C). This blood sample was used to determine the subject's acid-base status; i.e., pH, PCO_2, HCO_3, and BE were determined. The pH and PCO_2 were measured directly by a Radiometer pH 72 and a Radiometer Microtonometer.[1] BE and HCO_3 were calculated by the Siggarrd-Anderson Alignment Nomogram using the Astrup Equilibration Method (12, 190, 191, 192).

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[1]Radiometer, 72 Emdrupuei, Copenhagen NJ, Denmark.

Performance Time

An electrical digital stopwatch, accurate to 1/10 second was used manually to record the performance time.

O_2 utilization

The expired air during exercise was collected by the standard Douglas bag method (49) using a low-pressure Otis-McKerrow valve. A minimum hose length between the subject and the collection bag was used. The percentages of O_2 and CO_2 were measured by a Beckman Model E_2 oxygen analyzer and a Beckman Model LB15A Carbon Dioxide analyzer.[2] The volume of air in the bag was determined using an American-Meter Company Dry Gas Meter (Model DTM-11)[3] STPD using the gas temperature and the barometric pressure recorded during measurement. All gas analyzers and recording equipment were calibrated daily and, usually, before each run. Helium was used to determine the zero points of the analyzers. Temperature, barometric pressure, and a known standard gas sample (17.78% O_2 and 4.311 CO_2) were used to calibrate the analyzers. The O_2 uptake during exercise, oxygen debt, and oxygen requirement were calculated using the method described in Consolazio, Johnson and Pecora (49) (appendix D).

Statistical Analyses

Two procedures were used to detect statistically significant differences in the several dependent variables. Dependent-sample t-tests

[2]Beckman Instruments Inc., 3900 River Road, Siller Park, Illinois.

[3]Singer, American Meter Company, 13500 Philmont Avenue, Philadelphia, Pennsylvania.

for before (T1) to after (T2) analyses within each group and independent sample t-tests to compare the gain scores of the two groups under the two environmental conditions.

The probability of making a type I statistical error was set at $\alpha = .10$ for all analyses. The calculations were made by a CDC 6500 computer at the Computer Center of Michigan State University.

CHAPTER IV

RESULTS AND DISCUSSION

The purpose of this study was to determine the effects of hypoxic submaximal training upon performance at sea level. Consideration was given to acid-base balance parameters of arterialized blood, to oxygen utilization as an indication of efficiency in energy metabolism, and to performance time.

The data were obtained from observations of the two treatment groups (n = 4) under two test conditions: hypoxic and normoxic. Two types of comparisons were made to obtain the results: first, from prior to after training to examine the separate effects of hypoxic and normoxic training under hypoxic and normoxic test conditions; second, comparisons between the gain scores of the two groups to examine the differences resulting from the two treatments. In addition, the acid-base parameters were compared in pre-run and post-run blood samples before and after training.

Training Effects Upon Oxygen Utilization

Analysis of t-test results revealed no statistically significant differences from before to after training for the two treatment groups in oxygen uptake (VO_2) or oxygen requirement (O_2R) ($P > .10$). Likewise, the oxygen debt (O_2D) of the hypoxic group was not altered ($P > .10$). The O_2D of the normoxic group, however, was significantly decreased under hypoxic test conditions ($P \leq .10$). The results are given in

Tables 4.1 and 4.2.

The result of the analyses of gain scores in VO_2, O_2D, and O_2R, between the two training groups are shown in figures 4.1 and 4.2. There were no statistically significant differences between the two groups.

Discussion of Oxygen Utilization

Oxygen uptake during exercise (VO_2) reflects that part of the energy cost of the work that is not associated with the production of lactic acid. Therefore, VO_2 increases in proportion to the oxygen demand up to a given value known as the maximum oxygen uptake.

The individual's VO_2 during exercise is determined by several factors (131) such as respiratory rate, oxygen carrying capacity of the blood, loading of oxygen at the tissue level, and minute ventilation. These factors are known to be altered with submaximal training in a direction that serves economical transportation and utilization of oxygen (18, 98, 120, 113, 136, 164). The decline in VO_2 during submaximal exercise is a reflection of increased efficiency and economy of performance and is well established in terms of exercise physiology concepts. The effects of exercise at high altitudes upon VO_2, on the other hand, are not clear. No change (6, 47, 85, 101, 189), decreases (56, 151, 178, 203) and even increases (28, 29, 48, 124, 130, 202) in VO_2 have been reported.

The results of hypoxic and normoxic training upon VO_2 in this study are given in Tables 4.1 and 4.2 respectively. As was expected, the VO_2 was lower under hypoxic test conditions than under normoxic test conditions. Furthermore, the small sample size may have masked a tendency under normoxic test conditions for the VO_2 to be decreased

TABLE 4.1

MEANS AND STANDARD ERRORS BEFORE AND AFTER TRAINING OF O_2 UPTAKE (VO_2), O_2 DEBT (O_2D), AND OXYGEN REQUIREMENT (O_2R) UNDER HYPOXIC TEST CONDITIONS

	GROUP	BEFORE TRAINING ml/kg	AFTER TRAINING ml/kg	P
VO_2	N	188.8 ± 24.0	190.7 ± 22.4	NS*
	H	190.0 ± 35.1	192.1 ± 25.8	NS
O_2D	N	104.6 ± 5.83	97.3 ± 4.12	S**
	H	100.0 ± 6.06	102.1 ± 6.01	NS
O_2R	N	293.4 ± 16.3	288.0 ± 14.20	NS
	H	290.0 ± 23.14	294.2 ± 6.22	NS

B = Normoxic Training Group (N = 4)

H = Hypoxic Training Group (N = 4)

*Not Significant$_X$ ($P > .10$)

**Significant$_X$ ($P \leq .10$)

TABLE 4.2

MEANS AND STANDARD ERRORS BEFORE AND AFTER TRAINING OF O_2 UPTAKE (VO_2), O_2 DEBT (O_2D), AND OXYGEN REQUIREMENT (O_2R) UNDER NORMOXIC TEST CONDITIONS

	GROUP	BEFORE TRAINING ml/kg	AFTER TRAINING ml/kg	P
VO_2	N	215.1 ± 12.4	209.2 ± 8.3	NS*
	H	216.3 ± 23.5	208.4 ± 13.9	NS
O_2D	N	96.5 ± 3.92	92.4 ± 0.9	NS
	H	99.7 ± 5.10	94.9 ± 1.4	NS
O_2R	N	311.6 ± 8.84	301.6 ± 2.87	NS
	H	316.0 ± 14.86	303.2 ± 7.11	NS

N = Normoxic Training Group (N = 4)

H = Hypoxic Training Group (N = 4)

* Not Significant (P > .10)

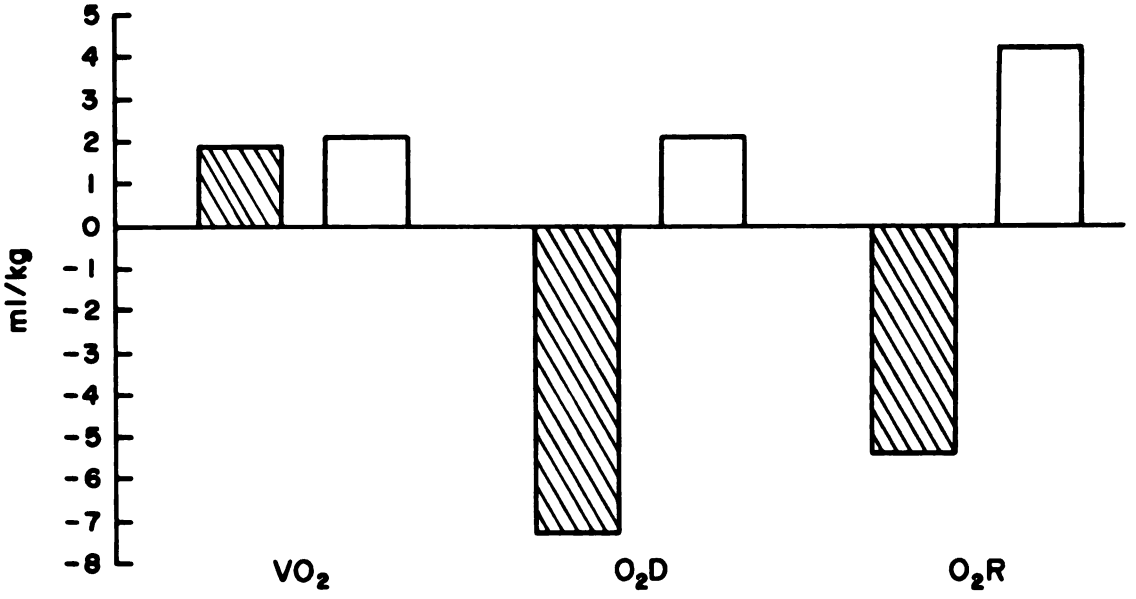


Figure 4-1— Result of the gain score comparison of the two groups in oxygen uptake (VO_2), oxygen debt (O_2D) and oxygen requirement (O_2R) under hypoxic test conditions ($p > .10$)

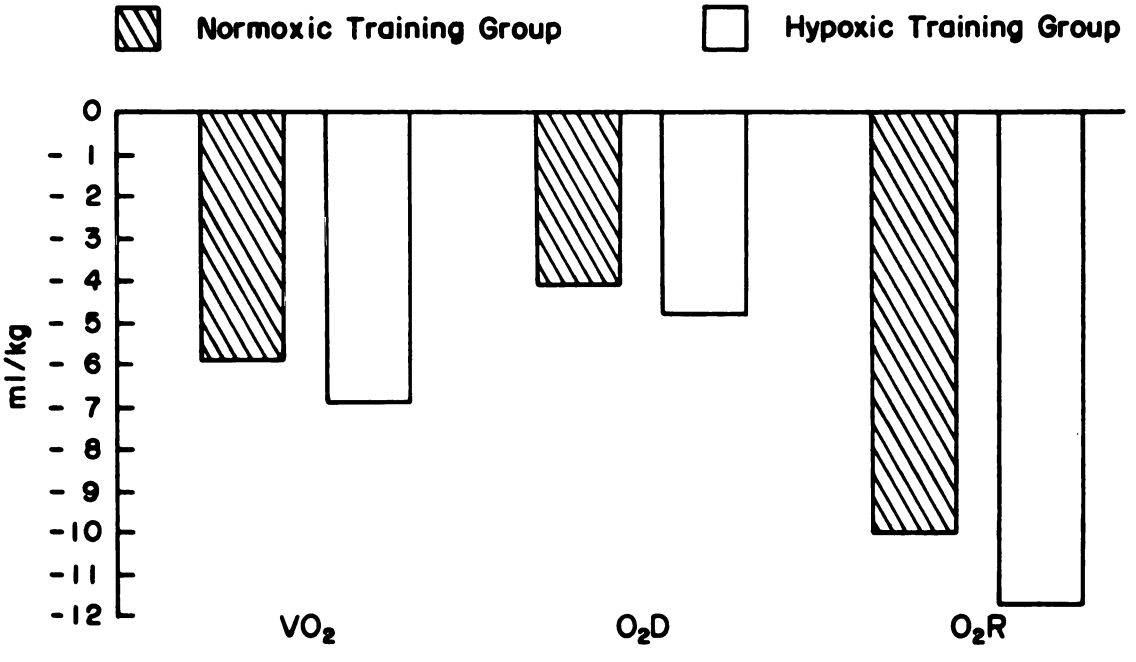


Figure 4-2 — Result of the gain score comparison of the two groups in oxygen uptake (VO_2), oxygen debt (O_2D) and oxygen requirement (O_2R) under normoxic test conditions ($p > .10$)

by both types of training. The results of this study are in agreement with data obtained by other investigations using approximately the same procedures (56, 151, 203) and with data obtained at modest altitude (122). When investigations were carried out at varying altitudes and intensities of work load, different results were obtained (29, 48, 202). The intensity of the work load seems to be an important factor in determining the VO_2 at altitude. When the intensity is low, the same or a somewhat increased VO_2 in comparison to sea level is reported (29, 48, 202). However, it has been observed that a work load which elicits a VO_2 of 2.5 l/min. or more at sea level can be accomplished with a lower VO_2 at 3800 m. altitude (29).

The comparisons between the gain scores of the two training groups under each test condition are shown in Figures 4.1 and 4.2. The results indicate that, although the two training regimens altered the VO_2 in the same direction and to approximately the same extent, performance under the two test conditions produced distinctively different effects on the VO_2. The phenomenon of a decreased VO_2 during submaximal exercise under hypoxic test conditions is not new (56, 151, 186, 178, 203). The results might lead one to think that under hypoxia subjects perform more economically and efficiently. However, this hypothesis cannot be accepted without first determining whether or not the subjects reached steady state. Furthermore, both the oxygen debt and the total oxygen requirement of the exercises must be considered.

The standard treadmill run used in this study has been shown to be appropriate for measuring the energy cost of exercise and has been employed by many researchers in the exercise physiology field (207).

Therefore, it can be assumed that all subjects did reach steady state during the run.

The O_2D that is repaid after exercise is divided into two phases or components (11, 150). The lactacid debt or fast component is the amount of oxygen used to resynthesize and restore muscle ATP and CP. This fast component reflects the oxidation delay that occurs at the beginning of exercise. The lactacid debt or slow component reflects the oxidation of the lactic acid that is accumulated during exercise beyond the steady state level. Margaria et al. (148) confirm that the fast component is the only debt present in submaximal moderate exercise. Since submaximal exercise was used in this study and the accumulation of lactic acid was negligible, the alactacid debt was of primary concern.

Submaximal normoxic training is known to decrease alactacid debt (110, 111) since training decreases the time required to reach steady state (110, 111, 122). However, an elevated O_2D is always observed during steady state exercise at high altitude (21, 29, 47, 56). The O_2D data obtained in this study are given in Tables 4.1 and 4.2 for hypoxic and normoxic test conditions respectively. In general, the results show that the O_2D was elevated under hypoxic test conditions and that the value obtained under hypoxic test conditions for the normoxic group decreased with training.

It is obvious that the lower VO_2 during exercise under hypoxic test conditions might have been repaid by a higher oxygen uptake during recovery. In fact, Cerretelli (39) observed that muscle demands an increased amount of oxygen at high altitude; however, this large

oxygen demand does not appear during exercise but during the recovery as a large repayment of O_2D. Furthermore, Astrand (11) suggested that anaerobic processes are incurred at a relatively low work load under hypoxic conditions. Unfortunately, the limitations of this study preclude the drawing of any firm conclusions with regard to O_2D. Transfer of the subjects from the hypoxic gas mixture to room air during the recovery period and not collecting the expired gas during the first minute of the recovery both are factors which may have produced spurious results in the O_2D data.

The changes in the O_2R reflect the changes in VO_2 and O_2D discussed earlier. Tables 4.1 and 4.2 give the results of the O_2R under hypoxic and normoxic test conditions respectively. The decreased O_2R under hypoxic test conditions is in agreement with data from previous studies (56, 203). Although definite conclusions are not justified, it is possible that acute exposure to hypoxia reduced oxygen utilization and increased work efficiency. In addition, Figure 4.2 suggests that the overall effect of training, across both treatment groups, was increased economy of exercise.

The lack of significant differences in the O_2 utilization variables between the two training groups under the two test conditions might be the result of the small sample size and/or the short duration of the training period. Support for this hypothesis comes from previous work which suggests a negligible effect for a short period of work at altitude (151).

Training Effects Upon Acid-Base Parameters

Comparisons between the effects of normoxic and hypoxic training on the changes that were observed during the run in arterialized blood pH, PCO_2, HCO_3, and BE are presented in Tables 4.3 and 4.4 and in Figures 4.3 and 4.4. The only significant difference ($P \leq .10$) occurred in PCO_2 under hypoxic test conditions.

Discussion of Arterialized Blood PCO_2

The normal value of arterialized blood PCO_2 fluctuates between 38 and 42 mmHg. This value is affected by the oxidative processes in the tissues, the blood composition, and the gas exchange rate in the lungs.

During mild exercise at sea level, no important changes in PCO_2 are noticed in either athletes or normal subjects (79, 154). However, with a moderate work load, a slight fall in PCO_2 is seen until steady state is attained (270).

Changes in PCO_2 with submaximal exercise are shown in Tables 4.3 through 4.6. The decreases observed between the pre-run and the post-run values are consistent with the literature. The adaptations to the two types of training used in this study, when subjects perform under normoxic test conditions, are shown in Figure 4.4a. It is obvious from the results that the two submaximal training regimens used in this study did not differentially alter the mechanisms that control PCO_2 at sea level.

At high altitude, PCO_2 has been reported to decrease (76, 106, 107, 130). In lowland subjects who lived one week at an altitude of 3,800 m a decreased PCO_2 to 29.2 mmHg was reported (188). Clearly,

TABLE 4.3

HYPOXIC AND NORMOXIC TRAINING EFFECTS ON PRE-RUN TO POST-RUN CHANGES IN ARTERIALIZED BLOOD PCO_2, pH, HCO_3, AND BE UNDER HYPOXIC TEST CONDITIONS

		BEFORE TRAINING			AFTER TRAINING				
		PRE-RUN	POST-RUN	CHANGE DURING RUN	PRE-RUN	POST-RUN	CHANGE DURING RUN	TRAINING EFFECT	P
PCO_2	N	40.78	30.75	-10.03	41.48	30.80	-10.68	- .065	S**
mmHg	H	39.78	32,95	- 6.83	41.08	39.90	- 1.18	+5.65	
pH	N	7.415	7.352	-0.063	7.440	7.387	- 0.053	+0.010	NS*
	H	7.418	7.375	-0.043	7.423	7.395	- 0.028	+0.015	
HCO_3	N	26.20	18.35	-7.85	28.10	19.45	- 8.65	-0.80	NS
	H	25.75	19.90	-5.85	26.80	24.20	- 2.60	+3.25	
BE	N	1.50	- 7.10	-8.6	3.90	- 5.30	- 9.2	-0.60	NS
	H	1.70	- 4.45	-6.16	2.30	- .35	- 2.65	+3.51	

* Not significant ($P > .10$)

**Significant ($P \leq .10$)

TABLE 4.4

HYPOXIC AND NORMOXIC TRAINING EFFECTS ON PRE-RUN TO POST-RUN CHANGES IN ARTERIALIZED BLOOD PCO_2, pH, HCO_3, AND BE UNDER NORMOXIC TEST CONDITIONS

		BEFORE TRAINING			AFTER TRAINING				
		PRE-RUN	POST-RUN	CHANGE DURING RUN	PRE-RUN	POST-RUN	CHANGE DURING RUN	TRAINING EFFECT	P
PCO_2	N	39.98	38.9	-1.08	42.58	37.50	-5.08	-4	NS*
mmHg	H	41.00	37.7	-3.3	41.45	35.30	-6.65	-3.35	
pH	N	7.418	7.37	-0.04	7.423	7.348	- .075	-0.035	NS
	H	7.440	7.438	-0.002	7.400	7.380	- .02	-0.018	
HCO_3	N	25.90	23.20	-2.7	27.25	21.40	-5.85	-3.15	NS
mEq/l	H	28.70	24.00	-4.7	28.08	21.86	-6.22	-1.52	
BE	N	1.2	- 1.8	-2.9	2.9	- 3.6	-6.5	-3.6	NS
mEq/l	H	4.6	-0.9	-5.5	3.8	-3.3	-7.1	-1.6	

*Not significant (P > .10)

Figure 4-3. Results of hypoxic versus normoxic training upon pre-run to post-run changes in arterialized blood pH, PCO_2, HCO_3, and B.E. under hypoxic test conditions.

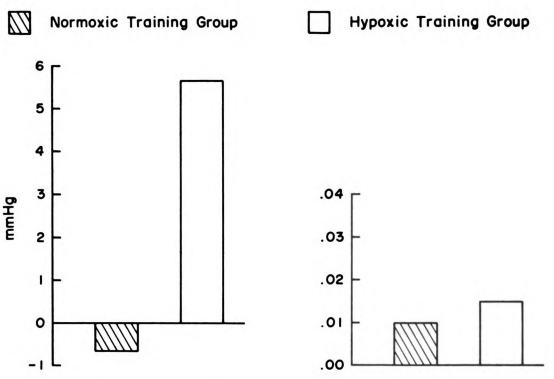


Fig. 4-3a. Results of PCO_2

Fig. 4-3b. Results of pH

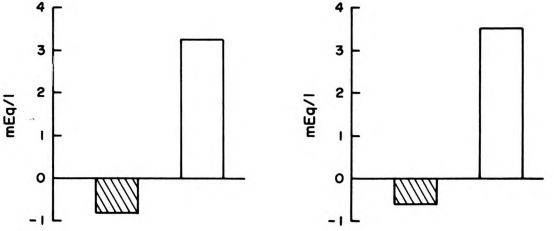


Fig. 4-3c. Results of HCO_3

Fig. 4-3d. Results of B.E.

Figure 4-4. Results of hypoxic versus normoxic training upon pre-run to post-run changes in arterialized blood pH, PCO_2, HCO_3, and B.E. under normoxic test conditions.

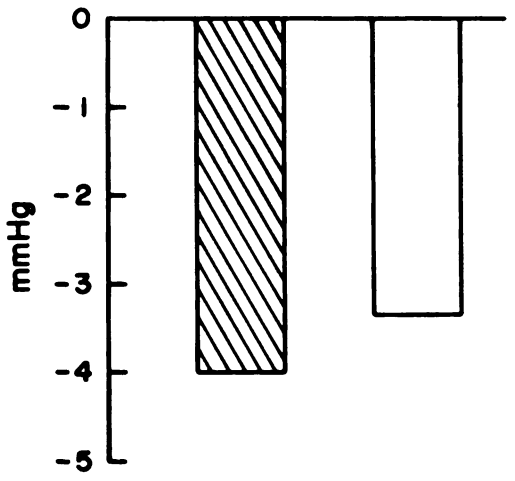


Fig. 4-4a. Results of PCO_2

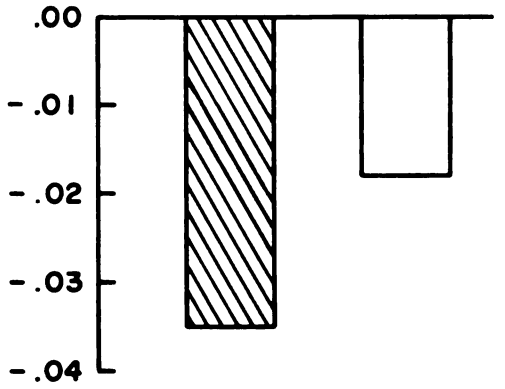


Fig. 4-4b. Results of pH

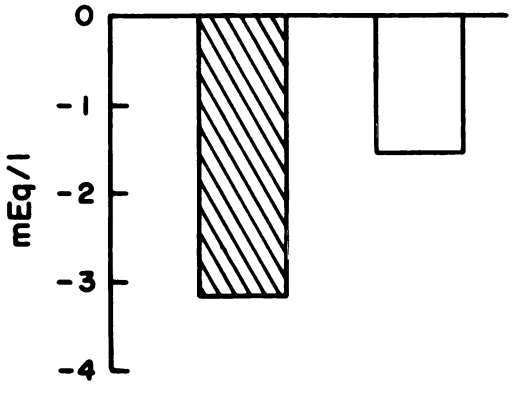


Fig. 4-4c. Results of HCO_3

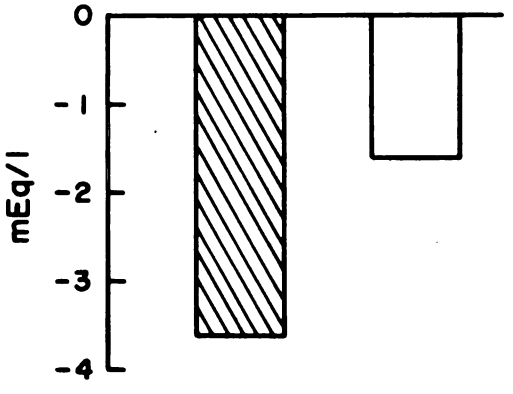


Fig. 4-4d. Results of B.E.

TABLE 4.5

MEANS AND STANDARD ERROR OF GAIN SCORES IN pH, PCO_2, HCO_3, AND BE IN PRE- AND POST-RUN DATA OBTAINED UNDER HYPOXIC TEST CONDITIONS

		PRE-RUN TESTING				POST-RUN TESTING			
		T1	T2	GAIN SCORE	P	T1	T2	GAIN SCORE	P
PCO_2 mmHg	N	40.78	41.48	+ .70 ± 2.64	NS	30.75	30.80	+.05 ± 3.84	NS*
	H	39.78	41.08	+1.30 ± .50					
pH	N	7.415	7.440	+ .025 ± .006	NS	7.352	7.387	+.035 ± .017	NS
	H	7.418	7.423	+ .005 ± .028		7.375	7.395	+.02 ± .011	
HCO_3 mEq/l	N	26.2	28.1	+1.90 ± 1.42	NS	18.35	19.45	+1.10 ± 1.73	NS
	H	25.75	26.80	+1.05 ± 1.59		19.9	24.2	+4.30 ± 1.18	
BE mEq/l	N	1.50	3.90	+2.40 ± .87	NS	- 7.10	- 5.30	+1.80 ± 1.83	NS
	H	1.70	2.30	+ .60 ± .97		- 4.45	- .35	+4.10 ± .68	

T1 = Before Training

T2 = After Training

N = Normoxic Training Group (N = 4)

H = Hypoxic Training Group (N = 4)

NS - Not Significant (P > .10)

TABLE 4.6

MEANS AND STANDARD ERROR OF GAIN SCORES IN pH, PCO_2, HCO_3, AND BE IN PRE- AND POST-RUN DATA OBTAINED UNDER NORMOXIC TEST CONDITIONS

		PRE-RUN				POST RUN			
		T1	T2	RESTING GAIN SCORE	P	T1	T2	EXERCISING GAIN SCORE	P
PCO_2	N	39.98	42.58	+2.60 ± 4.02	NS*	38.90	37.50	-1.40 ± 3.36	NS
	H	41.00	41.95	-0.95 ± 1.83		37.70	35.30	-2.40 ± 9.56	
pH	N	7.418	7.423	+ .005 ± .017	NS	7.378	7.348	- .030 ± .057	NS
	H	7.440	7.438	- .002 ± .020		7.400	7.380	- .020 ± .041	
HCO_3	N	25.90	27.25	+1.350 ± 2.41	NS	23.20	21.40	-1.80 ± 3.84	NS
mEq/l	H	28.70	28.08	- .625 ± 1.54		24.0	21.86	-2.14 ± 7.14	
BE	N	1.1	2.9	+1.85 ± 2.16	NS	-1.8	-3.6	-1.80 ± 4.30	NS
mEq/L	H	4.6	3.8	-0.80 ± 1.11		-0.9	-3.3	-2.40 ± 6.75	

T1 = Before Training

T2 = After Training

N = Normoxic Training Group (N = 4)

H = Hypoxic Training Group (N = 4)

NS = Not Significant (P > .10)

the submaximal hypoxic training used in this investigation had no such effect.

The adaptations to the two types of training, when subjects perform under hypoxic test conditions, are shown in Figure 4.3a. The slight decrease of PCO_2 in the normoxic training group is within the normal range of values, but the significant PCO_2 change in the hypoxic training group is not understood. This increased PCO_2 might be a result of less hyperventilation during the submaximal treadmill run. The pH results in this group (to be discussed later) tend to support this hypothesis. Furthermore, hyperventilation is known to be a fast primary response to high altitude which diminishes only after 3 - 4 days of adaptation (104). However, Doll (73) observed no differences in resting PCO_2 between normal and simulated altitudes of 2,500 and 4,250 m which indicates that hyperventilation may not occur under intermittent conditions of simulated altitude. Other factors that might have contributed to increased PCO_2 in the hypoxic training group are the increased HCO_3 (see Figure 4.3c) and the increased lactic acid which often are reported during submaximal exercise at altitude (10, 80, 107, 112).

Discussion of Arterialized Blood pH

The hydrogen ion concentration (H+) in the arterial blood can be altered by many factors such as PCO_2, the buffering capacity of the blood, non-volatile acids, and the metabolic rate of the body. During exercise, in addition, pH can be influenced by the individual's physical fitness.

The slight decreases in pH noted in this study under normoxic (Table 4.4) as well as hypoxic test conditions (Table 4.3) are consistent with the literature (72, 73) and thus were expected. These slight decrements might be caused by one or more of the factors mentioned previously which are known to be affected by submaximal exercise.

The changes that occur in arterialized blood pH with submaximal performance at sea level, as a result of high altitude training, have not been reported. However, decreased pH with adaptation to high altitude has been observed (68, 112, 141, 155).

The changes in pH that occurred in this study under hypoxic and normoxic test conditions are given in Tables 4.3 and 4.4 as well as in Figures 4.3b and 4.4b. The results show that all of the changes were within the normal range of values and that there were no significant differences between the two training groups. It should be noted, however, that the two test conditions had opposite effects on blood pH. That is, both normoxic and hypoxic training reduced the pH decrease that occurred during the submaximal run under hypoxic test conditions (Table 4.3) but augmented the pH decrease that occurred during the run under normoxic test conditions (Table 4.4). The changes that took place under hypoxic test conditions are not consistent with the literature (68, 122, 141, 155). According to Missiuro (155), metabolic acid-base changes during exercise at altitude have a tendency to shift the blood pH towards acidosis. Missiuro concluded that this decrease in pH is indirect evidence of an increase in anaerobic metabolism which, in fact, is supported by the increased lactic acid production during submaximal exercise at high altitude (10, 80, 107, 112).

Another major factor which is supposed to contribute to a lower blood pH at altitude is in the increased hemoglobin concentration with altitude acclimatization (100, 106, 170, 197). Hemoglobin is known to be a powerful buffer in the body. Surprisingly, this relationship has not been reported in the literature and could be an explanation for the improvements seen in some anaerobic types of activities at high altitude.

The inconsistency between changes observed in blood pH under hypoxic test conditions in this study and the expected pH changes might be the result of different experimental approaches and methods. Factors such as the degree of hypoxia and the duration and intensity of the training program are definitely important in producing changes in blood pH. In an earlier study when subjects breathed a 15.9% O_2 mixture, which is close to the mixture used in this study, no essential effect on the arterial blood pH was noticed; whereas, the pH decreased significantly when a 12.7% O_2 mixture was used (72).

Discussion of Arterialized Blood HCO_3

The normal resting value of the standard bicarbonate (HCO_3) in arterial blood is 25 mEq/l. This value usually is constant under normal conditions, with exercise; however, HCO_3 is influenced by changes in non-volatile acids and is independent of PCO_2 (133).

At high altitude, HCO_3 decreases both at rest (76, 106, 107, 123, 150) and during submaximal exercise (106, 107, 130, 155). Under normoxic conditions, steady-state exercise causes a slight decrease in HCO_3 (133). The effect of training upon the resting value of the standard bicarbonate is still in controversy. No differences (131, 174, 175,

194) and increases (310) have been reported.

The changes observed in HCO_3 under hypoxic and normoxic test conditions in this study are given in Tables 4.3 through 4.6. The decreases observed between the pre-run and the post-run values, under the two test conditions, are in agreement with the literature. Nevertheless, it is noticeable that the HCO_3 decreased more under hypoxic test conditions than it did under normoxic conditions. The steeper decline of HCO_3 under hypoxic test conditions is understandable in view of the increased need to maintain blood pH at normal values and the increased need to buffer lactic acid (10, 80, 107, 112).

The changes that occurred in HCO_3 under hypoxic and normoxic test conditions are given in Tables 4.3 and 4.4 and in Figures 4.3c and 4.4c. The results show that all of the changes were attributable to measurement and sampling errors.

Discussion of Arterialized Blood BE

The normal value of arterial blood Base Excess (BE) is +0.05 mEq/l. Changes in BE generally are parallel to those that occur in HCO_3 during rest, exercise, and recovery in both trained and untrained subjects (133). As was expected, therefore, the changes observed in BE during this study under both hypoxic and normoxic test conditions, correspond almost exactly to the changes seen in HCO_3. The results are given in Tables 4.3 through 4.6 and in Figures 4.3 and 4.4.

Training Effects Upon Performance Time

In addition to the submaximal runs discussed previously, each subject completed an all-out treadmill run, under normoxic test conditions, before and after training. The results of the performance

times to exhaustion are given in Table 4.7. The normoxic training group achieved a significant improvement in performance time ($P \leq .10$); whereas, the hypoxic training group did not.

TABLE 4.7

MEANS AND STANDARD ERRORS OF PERFORMANCE TIME BEFORE AND AFTER TRAINING

	Before Training (min.)	After Training (min.)	P
Normoxic Group	3.3 ± .7	4.3 ± .7	S*
Hypoxic Group	4.0 ± .3	4.4 ± .4	NS*

A comparison of the gain scores in performance time achieved by the two training groups is shown in Figure 4.5. The difference between treatment groups was not statistically significant.

Discussion of Performance Time

There is almost general agreement that reduced atmospheric pressure at high altitude decreases work capacity and hence the performance time of a task carried to exhaustion (13, 19, 35, 178). On the other hand, the effects of training and acclimatization at low atmospheric pressures upon performances at sea level are not well established. Improved endurance performance upon return from altitude have been reported (13, 14, 84), but another body of literature has failed to support this observation (35, 63, 101, 138). This controversy, in fact, was the reason for studying performance time under normoxic conditions.

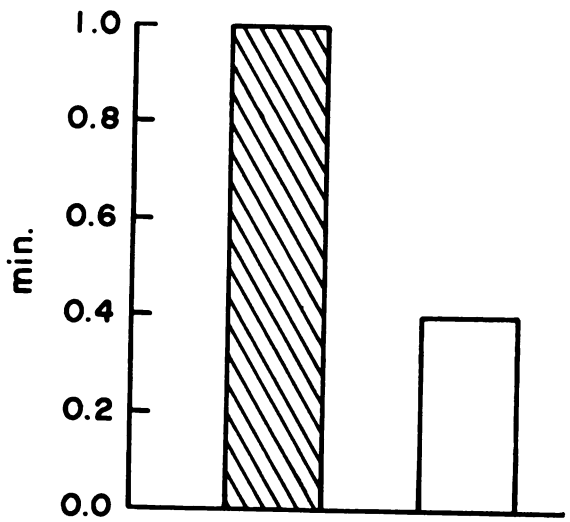


Figure 4-5. Comparison of performance time gain scores under normoxic test conditions.

Normoxic Training Group

Hypoxic Training Group

The effects of the submaximal normoxic and hypoxic training programs used in this study on performance time are given in Table 4.7. Performance time was improved in both groups. However, the change was significant only in the normoxic group. When the two groups are compared, it can be seen that the gain score of the normoxic group was one and one-half times that of the hypoxic group (Figure 4.5). These results obviously are in accord with some previous studies (35, 63, 101, 132) but contrary to others (13, 14, 84).

It is not clear why, in this study, normoxic training improved performance time more than hypoxic training. A theoretical analysis based on energy metabolism concepts would lead one to believe the opposite should have occurred. That is, endurance time is related to muscle glycogen stores and their rate of depletion as a result of anaerobic demand (25, 183). At high altitude, the reduced oxygen availability should stimulate anaerobic glycolysis at a relatively low work load (11, 147, 177). This increased rate of anaerobic glycolysis would tend to deplete the stored muscle glycogen and, therefore, should shorten performance time.

It has been suggested that two to twelve days of submaximal training at high altitude will increase the oxidative capacity of the mitochondrial enzymes and thus the anaerobic demand and the rate of glycolysis should fall (19). However, the training program in this study was quite short and the subjects were exposed to only moderate altitude conditions on an intermittent basis.

Clearly, one factor which may have contributed to the relative lack of improvement in performance time by the hypoxic training group

was their long performance time (4.0 min.) before training. Certainly this could not have been the only factor, however, because neither group achieved anything approaching a limiting value for human performance time.

CHAPTER V

SUMMARY AND CONCLUSIONS

Summary

The purpose of this study was to determine the effects of submaximal training under hypoxic conditions (simulated high-altitude training) upon performance at sea level. Prime consideration was given to acid-base parameters of arterialized blood (PCO_2, pH, HCO_3, BE), to oxygen consumption during exercise and recovery as indicators of efficiency in energy metabolism, and to performance time.

Eight healthy male students at Michigan State University (22 - 24 years of age) were used as subjects in the study. The subjects were classified as active but not highly trained athletes.

The subjects were assigned randomly to one of two treatment groups (n = 4). Group I (normoxic) trained while breathing normal air (PO_2 = 152 mmHg, 20.7% O_2). Group II (hypoxic) trained while breathing air with a reduced oxygen concentration (PO_2 = 122 mmHg, 16.6% O_2).

The training consisted of one five-minute run per day on a motor-driven treadmill at 7 mph and zero percent grade. The treatment period lasted three weeks with four days of training during each of the first two weeks and three days of training during the final week. The training was conducted under either normoxic or hypoxic conditions as indicated earlier.

Three tests were conducted before and after the treatment period. The first was an all-out run to measure performance time. The treadmill was set at 7 mph and 8% grade, and the grade was increased one percent per minute after the first two minutes of running. The other two tests were submaximal standard runs, one under hypoxic and one under normoxic conditions. In these two tests, gas collection took place during the run and during the first fifteen minutes of recovery. The Douglas bag method was used to determine the oxygen uptake during exercise, the oxygen debt, and the oxygen requirement under each condition. In addition, blood samples were taken before and after the submaximal runs to determine PCO_2, pH, HCO_3, and BE.

There was only one significant difference between the two training groups under the two submaximal test conditions. The blood PCO_2 of the normoxic group was significantly lower than that of the hypoxic group under hypoxic test conditions. Comparisons of the data obtained before and after training for each group resulted in significant differences only in the performance time of the normoxic group and the oxygen debt of the normoxic group under hypoxic test conditions.

Conclusions

1. As conducted in this study, hypoxic submaximal training (simulated high altitude) is no more effective than normoxic submaximal training in maintaining blood acid-base balance, reducing O_2 utilization, or prolonging performance time when exercise is performed under normoxic conditions.

2. Low oxygen uptakes and high oxygen debts are observed in submaximal exercise under hypoxic conditions.
3. The energy cost of submaximal exercise is reduced under hypoxic conditions.

APPENDICES

APPENDIX A

INFORMED CONSENT

I agree to serve voluntarily as a subject in an exercise physiology experiment using the following tests: all-out treadmill run; standard, moderate intensity treadmill run breathing normal and hypoxic air; a 1.5 mile run for time on an indoor track; and a matched velocity treadmill run based on the 1.5 mile performance. The battery of tests will be taken twice; at the beginning of the experiment and at the conclusion.

Furthermore, I will train on the treadmill at a standard pace (7 mph. zero percent grade) for five minutes per session, four times per week according to the conditions of the treatment group to which I am assigned to by random procedures.

I also understand that blood samples will be taken prior to and after each test run, and that expired air will be collected during and after each test.

It is my understanding that this experiment has been undertaken to further knowledge concerning the responses of individuals to simulated altitude training. The procedures have been explained to me and I understand that some physical discomfort may be experienced. I have had the opportunity to ask questions regarding the procedure and have been informed that I am free to withdraw my consent and to discontinue participation at any time. To my knowledge there are no medical reasons why I should not be able to engage in the test and training procedures described. I understand that the results of this experiment will remain anonymous unless I should release them.

_____
Signature

_____
Date

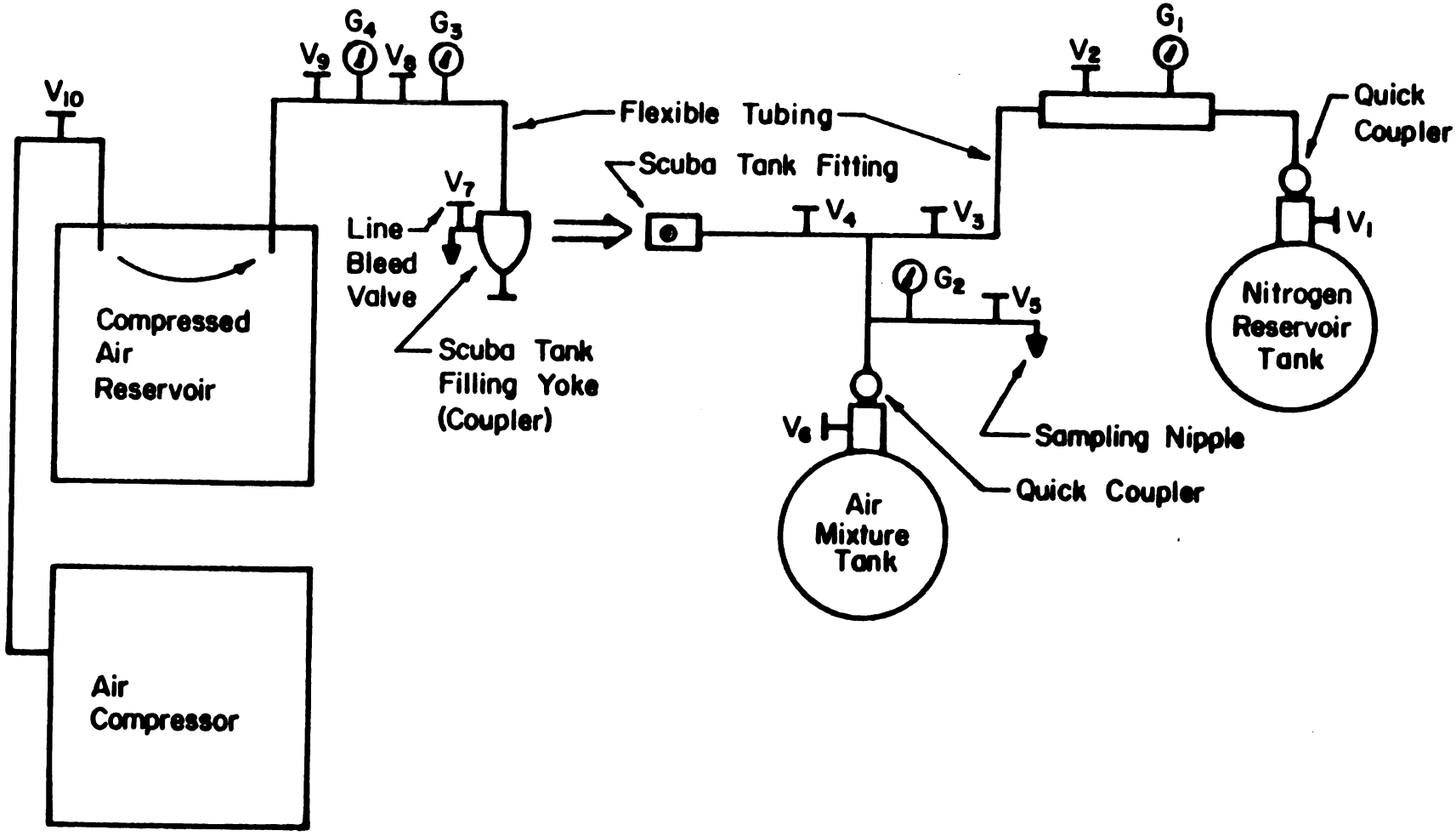
APPENDIX B

GAS MIXING APPARATUS AND PROCEDURES

For reasons of economy and certainty of adequate supply, tanks of hypoxic air needed for the study were obtained using laboratory facilities to mix compressed air with compressed nitrogen. Although an air compressor and other equipment needed for filling SCUBA tanks were already installed, it was necessary to design and assemble an apparatus for transferring compressed nitrogen from a full tank to an empty compressed gas cylinder. The schematic arrangement and essential components used for the purpose are shown in Figure B-1. Parts labeled V or G were valves or gauges, respectively. All equipment, valves, gauges and hydraulic tubing had been manufactured to handle gas and gas flow at high pressures (3000 psi) and were obtained from commercial suppliers.

General Mixing Procedures

Although temperature changes invariably accompany compression and decompression of gases, the effects of such changes on the volumes of gas being mixed were ignored. Instead, it was assumed that cooling during decompression that occurred while gas was entering the empty cylinder would be offset by heating as the cylinder became full. Mixing to specific concentrations was based solely on pressure changes until the end pressure sought was approached. At that time, a sample



SCHEMATIC DIAGRAM OF GAS MIXING APPARATUS

Figure B-1. Schematic arrangement and essential components of gas mixing apparatus

was drawn off and analyzed for oxygen content. This was always done conservatively so that more compressed air could be added to raise the oxygen content to the desired level.

As may have been inferred from the preceding statement, nitrogen was always introduced into the mixture tank first because the nitrogen pressure available in the nitrogen reservoir tank was always lower than that available in the compressed air reservoir. Since the nitrogen reservoir tank was the same size as the gas mixture tank, a point was soon reached where sufficient nitrogen had been drawn off. At that time filled mixture tank pressure also exceeded that of the nitrogen tank. Since flow direction is from high to low pressure, it would not have been possible to get more nitrogen into the mix tank. An overshoot in addition of compressed air to the mix tank would therefore result in loss of the gas mixture.

In order to obtain the greatest accuracy with the least amount of sampling trials, an end filling pressure was selected for the gas mixture tank. This was conservatively below the tank's pressure capacity (approx. 2200 psi) and below the capacity pressure of the compressed air reservoir and air compressor. It was then possible to calculate the partial pressure of nitrogen which would be needed to obtain the desired partial pressure of oxygen. Next a calculation was made of the drop in pressure of the nitrogen tank that would be needed. This was added to the partial pressure of nitrogen in compressed air to obtain the desired end partial pressure of nitrogen in the filled mixture tank. The procedure then was simply one of draining nitrogen into the mixture tank until the pressure reading in the nitrogen tank dropped

the appropriate amount. Following that step, compressed air was introduced into the mixture tank until the desired end filling pressure was reached. At that time, a sample was drawn off and analyzed. Since the tank heated up considerably during the filling, addition of compressed air was always conservative so long as the pre-determined end filling pressure was not exceeded.

Specific Mixing Procedures

With reference to the apparatus shown in Figure B-1 the specific procedures employed were as follows:

1. All valves closed. Oxygen line completely disconnected.
2. Open V_1 and read pressure in nitrogen tank on gauge G_1.
3. Open V_2, V_3 and V_6 in that order until G_1 pressure drops appropriately.
4. Close V_2 to check pressure reading. If okay, proceed. Otherwise open and close V_2 until desired reading is obtained.
5. Having sufficient nitrogen in mix tank, close V_1 and V_6. Open V_5 to bleed off line pressure completely. Then close V_2, V_3 and V_5.
6. Connect oxygen to SCUBA tank fitting. V_7 closed.
7. V_{10} closed. Open V_9 and read pressure in oxygen reservoir on G_4.
8. Open V_8, V_4 and V_6 allowing compressed air to flow into gas mixture tank until G_3 and G_2 reach desired reading.
9. Close V_6 and then V_9.
10. Open V_7 to bleed line pressure read on G_3 and G_4. Then close V_4. Compressed air supply lead can then be disconnected.

11. V_4 and V_3 closed. Open V_6. Then open V_5. Obtain sample. Close V_5.

12. Close V_6. If sample okay, open V_5 to bleed line pressure. Close V_5 and disconnect tank. If not, add additional compressed air and obtain analysis samples as before.

13. Valve V_8 and V_9 closed.

14. All valves closed. Turn on air compressor.

15. Open V_{10} to refill compressed air reservoir.

16. Open V_9 to read G_4 which shows pressure in compressed air reservoir. When full, close V_9 and V_{10}. Turn off air compressor. Open V_8 and V_7 to bleed off line pressure.

17. Close all valves.

Table B-1 shows the results of using these procedures while mixing the nine tanks of hypoxic air used in the study. End oxygen percentages and end filling pressures obtained are shown. These may be compared to the goals of 16.60% and 1900 psi.

Gas Feed Apparatus

The use of compressed gas as a source of inspired air necessitated design and construction of special gas feed apparatus. This apparatus was needed to fulfill two functions. Pressure had to be lowered to ambient levels in order to avoid forcing air into subjects' lungs. The second function needed was moisturization of the air. The moisturization was made necessary by the fact that air passing through the compressor was almost completely dried out by a desiccator. The desiccator had been built into the system to avoid problems which would result from having excess moisture in the SCUBA tanks.

TABLE B-1

HYPOXIC AIR MIXING DATA[1]

Tank Mixture No.	% O_2 (STPD)	End Filling Pressure Reached[2]
1	16.60	1902 psi
2	16.59	1951 psi
3	16.61	1921 psi
4	16.62	1903 psi
5	16.59	1951 psi
6	16.59	1966 psi
7	16.59	1967 psi
8	16.63	1894 psi
9	16.62	1953 psi

[1]Goal was to obtain 16.60% O_2 and an end of filling pressure at 1900 psi. The accuracy required for the oxygen percentage was ± 0.2%.

[2]Pressure readings given were read off of gauges at the end of filling procedures. Pressure capacity of tanks used was approximately 2500 psi.

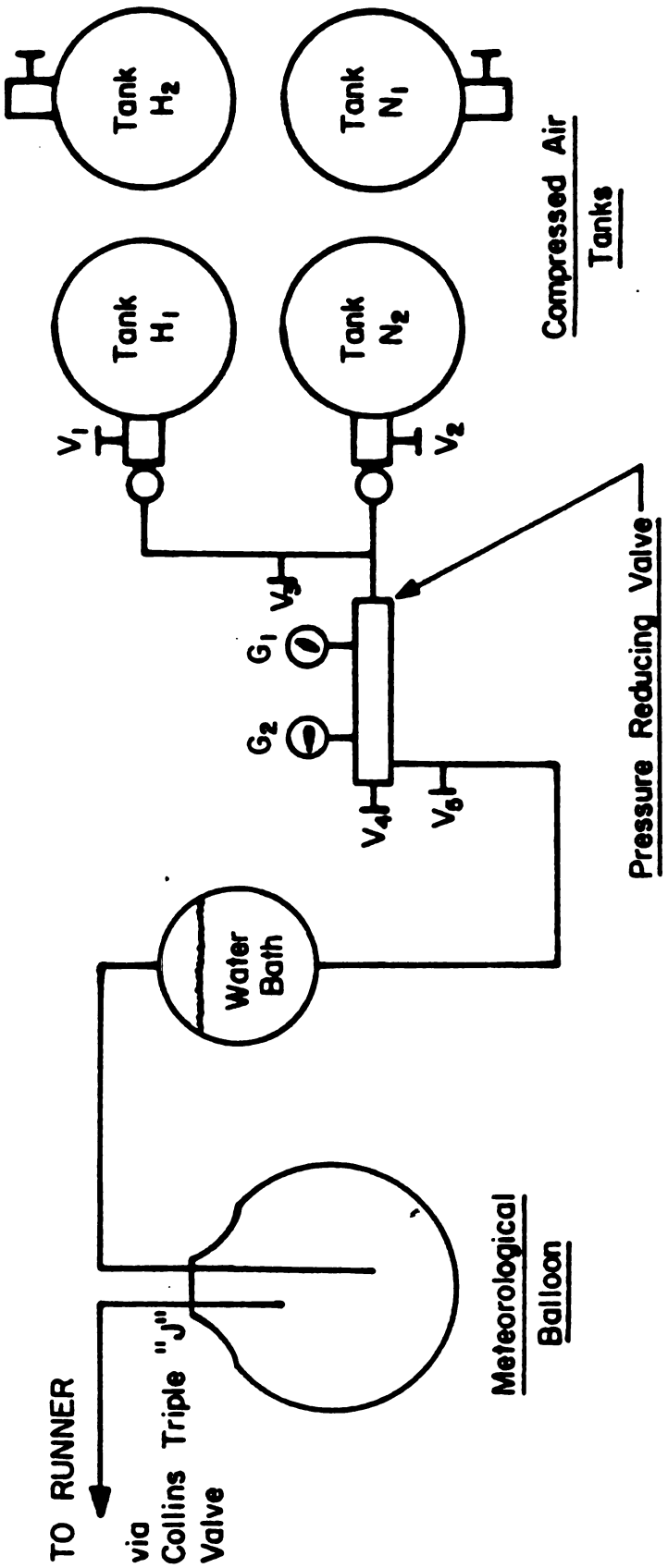
The schematic arrangement and essential components of the gas feed apparatus are shown in Figure B-2. V's indicate valves and G's indicate gauges.

In essence, this apparatus consisted of a manifold with fittings at one end for simultaneous attachment to two tanks. The other end of the manifold was connected to a gas pressure reducing valve so that gas could be released at substantially reduced pressures. Valve arrangements permitted withdrawing gas from either tank. The two gauges indicated in the drawing are both attached to the gas pressure reducing valve. G_1 shows pressure of the gas in the tank from which gas is withdrawn. Gauge G_2 shows the pressure at which the gas is released. Release pressure is adjustable by opening or closing valve V_4. Valve V_5 permitted further control over flow rates.

After passing through the reducing valve and flow rate control valve, the air entered small bore flexible tubing (1/4" I.D.) through which it was conveyed to a water bath for moisturization and warming. The moisturization and warming were considered necessary to avoid irritation of tissues in the respiratory tract.

From the water bath the air was passed into a meteorological balloon which was used to accomplish final depressurization. The flow rate was controlled such that the balloon was kept flaccid to avoid repressurization which would be generated in part by the balloon's elasticity.

Use of the meteorological balloon as the final depressurization chamber had an additional advantage in that it could literally be wrung out and milked dry of gas. This simplified the process of clearing gas from the apparatus as was done to avoid contaminating the next mixture used.



SCHEMATIC DIAGRAM OF GAS FEED APPARATUS

Figure B-2. Schematic arrangement and essential components of gas feed apparatus

APPENDIX C

BLOOD SAMPLING

Principle

It has been shown that arterialized capillary blood very closely approximates arterial blood gas composition. To insure rapid and easy flow of blood, the finger should be warmed (45°C water). The blood must be taken from the middle of rapidly forming blood drops so that the sampled blood does not make contact with atmospheric air. Heparinized capillary tubes must be used to keep the blood from clotting.

Procedure

1. The finger was warmed for about two minutes in water (approximately 45°C).
2. The finger was cleaned with alcohol and wiped dry with a sterile gauze pad.
3. The finger was lanced with a long point microlance.
4. The first drop of blood formed was wiped away and then a large pool of blood was allowed to form.
5. The capillary tube was placed in the center of the blood pool and allowed to fill via capillary action insuring that the capillary tube did not take blood from the surface of the pool.

APPENDIX D

CALCULATION OF OXYGEN UPTAKE, OXYGEN DEBT, AND OXYGEN REQUIREMENT VARIABLES

Principle

The volume of expired gases must be corrected to standard temperature pressure dry (STPD) conditions. This can be accomplished using the following STPD correction factor:

$$\text{STPD correction factor} = \frac{P_B - P_{H_2O}}{760\ (1 + .00367\ T)} \qquad (D.1)$$

where: P_B = ambient barometric pressure,

P_{H_2O} = the water vapor tension in mm Hg at the temperature of the gasometer,

T = the temperature of the gasometer in degrees Centigrade,

.0367 = 1 divided by 273 (273 is the conversion factor for converting temperature in Centigrade to Kelvin).

To simplify this computation, a line chart devised by R. C. Darling (Figure D - 1) was used. The correction factor is then multiplied by the V_E ambient temperature saturated (ATPS) in order to obtain V_E (STPD). The volume of oxygen consumed can be found by obtaining the number of ml of oxygen consumed for every 100 ml of expired gas (true O_2) and multiplying the true O_2 by V_E (STPD). Expired gas volume does not equal inspired gas volume unless the respiratory quotient (RQ) is

This figure is an example of a nomogram.

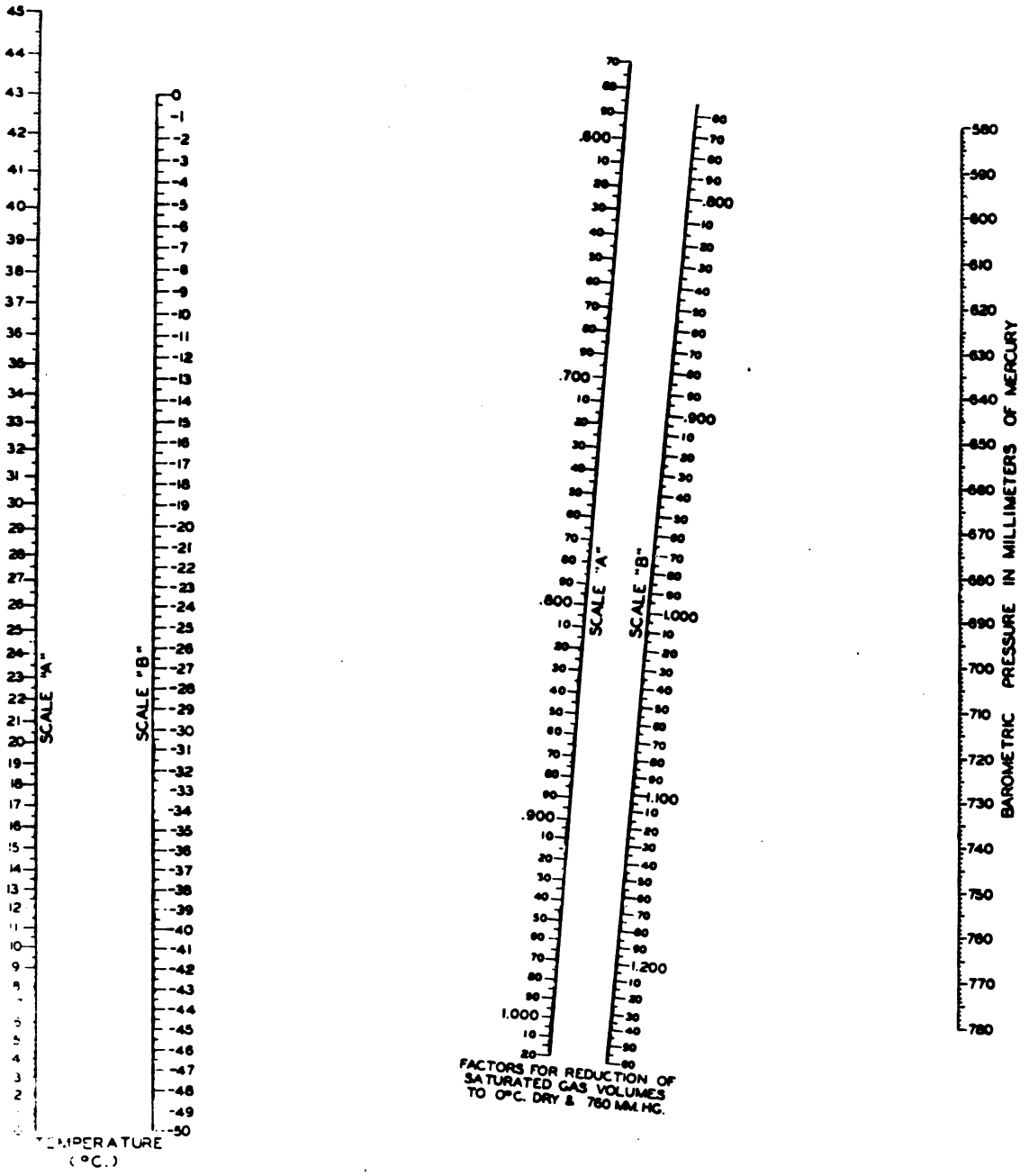


Figure D-1. Line chart for determining factors to reduce saturated gas volumes to dry volumes at 0°C and 760 mmHg

equal to 1.00. The following formula for true O_2 corrects for this difference in the inspired and expired gas volume.

TRUE O_2 = % N_2 in expired air X .265 - % O_2 in expired air. (D-2)

$$\text{Where:} \quad .265 = \frac{\%\ O_2 \text{ in ambient air}}{\%\ N_2 \text{ in ambient air}}$$

This computation can be simplified by using the line chart (Figure D-2) by Dill.

Procedure

1. An STPD correction factor was obtained for each gas collection bag using the line chart in Figure D-1.
2. The STPD correction factor was multiplied by the total gas volume for the appropriate gas collection bag.
3. True O_2 and RQ were obtained from the line chart in Figure D-2.
4. True O_2 was multiplied by corrected V_E (STPD) and divided by 100 to get the volume of O_2 consumed in each gas collection bag.
5. Oxygen intake during exercise was obtained from the sum of gas volume bags collected during five minutes of exercise.
6. Oxygen debt was obtained by the sum of oxygen intake values for all of the recovery bags in the last 14 of the 15 minutes recovery.
7. Oxygen requirement was obtained from the sum of oxygen intake during exercise and during recovery.

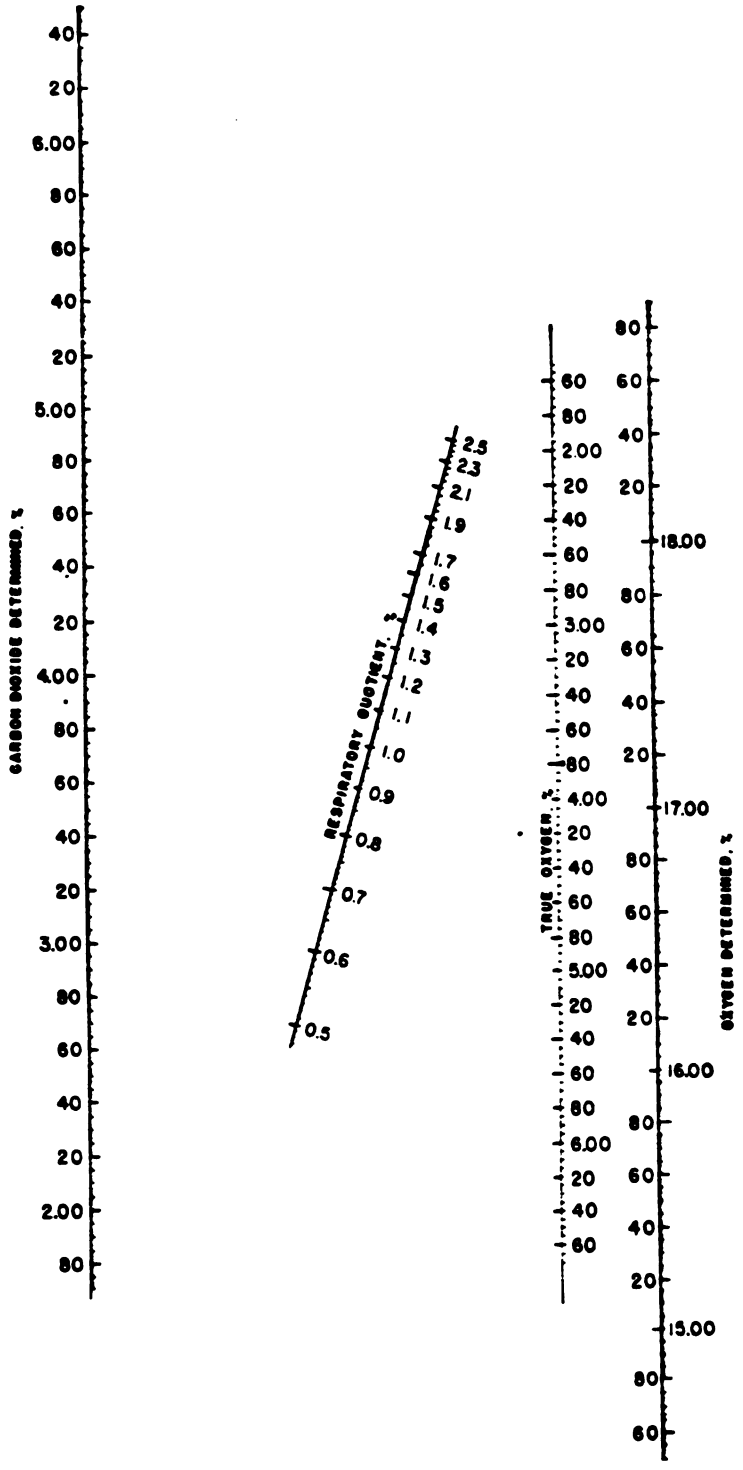


Figure D-2. Line chart for calculation RQ and true oxygen from analyses of expired air

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