THE EFFECTS OF CORONARY HEART DISEASE, BETA-BLOCKADE MEDICATIONS AND STAGE DURATION ON GRADED EXERCISE TESTING

by

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(ABSTRACT)

Controversy exists regarding the effects of beta-blocker medications on functional capacity in cardiac patients and in the effects of disease-related impairments on cardiorespiratory dynamics during exercise testing. Therefore, this study was conducted to examine the exercise responses of 26 subjects (ages 37-66 years) to a graded exercise test. Subjects were divided into three groups based on clinical status: apparently healthy (AH; N=8); cardiacs receiving beta-blockers (C-BB; N=8); cardiacs not receiving beta-blockers (C-NBB; N=10).

Variables examined included maximal and submaximal oxygen consumption ($\dot{V}O_2$), ventilation ($\dot{V}$), heart rate (HR), rate of perceived exertion (RPE), respiratory exchange ratio (RER), post-exercise blood lactic acid (HLa) and gas exchange parameters. In addition, regression analysis was employed to determine whether $\dot{V}O_2$max could be accurately predicted from treadmill grade and selected physical characteristics. Subjects performed symptom-limited maximum GXT's using a modified Balke protocol designed to extend

stage durations from 2 to 3 minutes approximately at test midpoint. Results indicated no significant differences between the two cardiac groups in maximal and submaximal $\dot{V}O_2$, $\dot{V}$, respiratory gas fractions, RPE, RER and HLa ($p>.05$). As anticipated, the AH group was significantly higher than the two cardiac groups in peak $\dot{V}O_2$, $\dot{V}$, heart rate, HLa and submaximal heart rate. The C-NBB group evidenced significantly higher heart rates ($p<.05$) than the C-BB group as well as higher submaximal RER values as compared to the AH group ($p<.05$). No significant differences between any of the groups were noted in RPE, gas exchange fractions or peak RER ($p>.05$). A linear regression model developed from this data base yielded no greater accuracy of prediction for $\dot{V}O_2$max ($p>.05$) than currently available equations. These data suggest that coronary diseased patients under beta-blocker therapy demonstrate no greater functional aerobic impairment than patients who are not medicated. Furthermore, when compared to normals, cardiacs exhibit similar O_2 uptake kinetics but lower absolute capacities.

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, , ,

, , , and

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Chapter I

INTRODUCTION

The treatment of cardiovascular disease has become a multi-billion dollar business. Over 42 million people in the U.S. have one or more forms of heart or blood vessel disease. Approximately 1 1/2 million people in the U.S. will have a heart attack this year; of those, 550,000 will die (AHA, 1984). Despite the physical, emotional and financial havoc heart disease has wreaked in the past, cardiac rehabilitation has only recently come into the limelight of public interest. The goals of rehabilitating the cardiac-diseased patient include returning that person to his "greatest physical, emotional, social, vocational and economic usefulness" (Cornett & Watson, 1984). To do this, the clinical practitioner must be able to assess the functional ability of the individual to safely re-engage in his daily activities.

The determination of functional aerobic capacity is an established evaluative and diagnostic tool that reflects the physiological efficiency of the cardiovascular system during graded exercise testing. Functional capacity is a general term often used synonymously with maximal oxygen uptake, a representative indicator of the peak level of muscular activity that an individual is capable of achieving. The upper limit of an individual's maximal cxygen consumption is

set by two physiologic capacities, namely the maximal cardiac output and the maximal arterio-venous oxygen difference (Froelicher, Thompson, Naguera, Davis, Stewart & Triebwasser, 1975). Since there is little variance in maximal arterio-venous oxygen difference among individuals, maximal oxygen consumption is thus directly relateld to maximal cardiac output and is considered the best index of aerobic work capacity, or cardiorespiratory function (Sullivan & Froelicher, 1983; Pollock, Schmidt & Jackson, 1980).

Maximal oxygen uptake ($\dot{V}O_2max$) is measured through collection and analysis of expired gas samples and pulmonary ventilation taken at various intervals of an exercise test; it is then mathematically determined from these parameters. By definition, maximal oxygen uptake is attained when no further increase in measured oxygen uptake ($\dot{V}O_2$) occurs despite further increases in metabolic demand (Mitchell & Blomqvist, 1971).

Because measurement of oxygen consumption and gas analysis can be costly in terms of equipment, time and personnel, and can be quite uncomfortable for the patient, several investigators (Balke & Ware, 1959; Bruce, Kusumi, & Hosmer, 1973) have attempted to develop regression equations that accurately predict $\dot{V}O_2max$ based on such simple variables as treadmill speed/grade combinations or total

treadmill time. Following on such concepts, Bruce, Kusumi & Hosmer (1973) have demonstrated high correlations (r=.87) between maximal treadmill time in standard, progressive protocols and the measured $\dot{V}O_2$max. Still others have used the "steady-state" concept (leveling off of $\dot{V}O_2$ at submaximal exercise stages) in varying exercise load to predict $\dot{V}O_2$max (Wyndham & Ward, 1957; Astrand & Rhyming, 1954). In clinical practice, attempts to replicate the results of these early studies and apply prediction of peak exercise capacity to larger populations have resulted in erroneous functional capacity values for some. For instance, investigators who have studied patients with cardiovascular disease have reported lower measured maximal and submaximal $\dot{V}O_2$ values when compared to their estimated values: Sullivan and McKirnan (1984) reported measured $\dot{V}O_2$ values for cardiacs 10-23% below predicted values using the original Bruce equations. Adams, Marlon and Quinn (1980) similarly reported a 20% overprediction in estimated vs measured oxygen uptake at various stages for post-MI patients. Hence, $\dot{V}O_2$ prediction equations appear to be accurate only within the context of specific populations and estimation of VO_2max for diseased populations bears further investigation.

Recent investigations by Sullivan and Froelicher (1983) and Adams et al. (1980) involving patients with coronary

heart disease demonstrating lower measured $\dot{V}O_2$ values vs estimated values suggest that these discrepancies may be attributed to functional impairment intrinsic to the diseased heart. It is possible that there is a lower dynamic oxygen transport capability for ischemic heart diseased individuals at the same relative exercise load of healthy individuals that in part accounts for these predictive errors. Other researchers further suggest a time-delay in O_2 uptake kinetics for cardiac patients that subsequently results in a greater anaerobic performance for them at the same relative exercise load that is a steady-state aerobic pace for healthy individuals (Auchincloss, Gilbert, Kuppinger, Peppi & Teperow-Putter, 1974; Sullivan & McKirnan, 1984).

Another potential factor affecting oxygen uptake kinetics in cardiac patients during exercise testing is related to the ingestion of cardio-suppressive medications. The increased use of antiarrhythmic medications since the 1960's, especially beta-adrenergic blockers, have raised many questions regarding their alteration of circulatory responses during exercise. Beta-blocker medications have the effect of reducing cardiac response to the sympathetic nervous system stimulation, resulting in a lowered heart rate, lower cardiac contractility and slower circulatory adjustment during exertion (Harrison, 1985). Recent reports

upon the effects of beta-adrenergic blocker medications on exercise performance have demonstrated that cardiac patients maintained on these medications can increase their total treadmill time without a concomitant increase in oxygen consumption (Shepherd, 1985). Hence, the medications that cardiac patients consume may be a significant factor in the problems of $\dot{V}O_2$max prediction for that population. Other reports regarding effects of beta-blockade drugs on exercise are controversial and require further investigation for resolution (Sable et al., 1982; Marsh et al., 1983; Ewey et al., 1983; McGhee et al., 1984).

Presently, research exists to suggest that a slower increase in stage increments within the graded exercise test (GXT) will provide the necessary potential for accommodation to steady-state by cardiac patients (Haskell, Savin, Oldridge & DeBusk, 1982). The standard treadmill test protocols in use today (i.e., Balke and Bruce) contain either 2 minute stages or aggressive load increments and using the presently developed nomograms for these protocols has resulted in consistent overprediction of $\dot{V}O_2$max for cardiac diseased individuals. Most recently, investigators such as Foster et al., (1984), Zohman, Young and Kattus (1983) and Haskell et al. (1982) have postulated that less aggressive, 3 minute stage increments will produce the accommodation to steady-state necessary for cardiacs to

achieve higher $\dot{V}O_2$ capacities during exercise testing and hence more accurate estimations of both submaximal and maximal VO_2 for this population may be obtained.

Statement of the Problem

This study was designed to evaluate the physiological factors influencing the $\dot{V}O_2$ responses between ischemic heart disease patients and apparently healthy individuals during graded exercise tests. Specifically, the problem addressed was the effect of stage duration and cardiodynamic medication status on GXT performance in subjects of these two classifications. A modified Balke GXT protocol was utilized in which stage duration was 2 minutes at low levels and 3 minutes at later stages for groups of cardiac and apparently healthy subjects.

Three subject groups were tested: 1) cardiac patients receiving beta-blockade medication (C-BB); 2) cardiac patients receiving no beta-blockade medication (C-NBB); and 3) apparently healthy adult fitness participants (AH). Each subject had been previously treadmill tested and had been a regular participant (72% attendance) in a cardiac rehabilitation or adult physical fitness program for at least 3 months prior to the study. Imposition of these criteria allowed for subject familiarity with treadmill exercise procedures and increased probability that medication regimes were stable at the time of testing.

Significance of Study

In the past, published and widely accepted nomograms for predicting oxygen uptake during treadmill exercise testing have proven inaccurate for cardiac-diseased individuals. Utilizing erroneous functional capacity values can be hazardous to the patient both medically and financially, with an overprediction of peak $\dot{V}O_2$ resulting in an unsafe exercise prescription as well as loss of medical insurance coverage for exercise testing/cardiac rehabilitation. The practical considerations for accurate estimation of functional capacity are thus obvious: ability to pay is often the limiting factor in outpatient cardiac rehabilitation while safety of participants is the top priority for program administrators.

This investigation sought to determine functional aerobic capacity ($\dot{V}O_2max$) in a treadmill test protocol modified to increase stage duration during standard graded exercise testing of cardiac and apparently healthy individuals. The assumption was that increased stage time would allow for complete adjustment to a $\dot{V}O_2$ steady state in the higher stages of exercise for cardiac patients, hence providing a more accurate indication of when maximal oxygen consumption is attained. This investigation also attempted to examine the effects, if any, of cardiodynamic medications (beta blockades) on the oxygen uptake kinetics of the

cardiac population. Finally, the results of this investigation intended to demonstrate a more appropriate testing protocol for use in evaluating functional capacity in heart diseased patients, perhaps generating a more accurate prediction equation for estimating $\dot{V}O_2max$ from treadmill speed/grade workloads for this population. These findings may be of particular interest to those utilizing exercise stress testing as diagnostic and prescriptive tools without the availability of gas analysis equipment to directly measure oxygen uptake.

Research Hypothesis

1. Ho: There is no significant difference in attained peak oxygen consumption between: cardiacs receiving beta-blockade medication (CBB); cardiacs not receiving beta-blockade medication (CNBB); and apparently healthy (AH) subjects.
2. Ho: There is no significant difference in final $\dot{V}O_2$ within two submaximal exercise stages of identical speeds and grades between: cardiacs receiving beta-blockade medication; cardiacs not receiving beta-blockade medication; and apparently healthy subjects.
3. Ho: There is no significant difference in the dynamics of oxygen consumption, % FEO_2, %

$FECO_2$, $\dot{V}$ or RER within a given stage of exercise between cardiacs receiving beta-blockade medication; cardiacs not receiving beta-blockade medication; and apparently healthy subjects.

4. Ho: There is no significant difference between predicted and measured $\dot{V}O_2max$ using the obtained regression equation for the three groups of cardiacs receiving beta-blockade; cardiacs not receiving beta-blockade; and apparently healthy subjects.

Delimitations

The following delimitations were imposed in this study:

1. Subjects were restricted to 26 adult male participants from the Virginia Tech Cardiac Therapy and Intervention Center.
2. Candidates included in this study had undergone at least one previous treadmill exercise test in the Virginia Tech Human Performance Laboratory, were male, and had been exercising on a regular basis (3x/week) in the program.
3. Subjects were divided into three groups according to health status (physician diagnosed): 1) coronary heart diseased patients receiving beta-blockade medication (C-BB); 2) coronary heart

diseased patients not receiving beta-blockade medication (C-NBB); and 3) apparently healthy individuals without known heart disease (AH).

4. A modified Balke treadmill exercise test was the selected protocol utilized in this study.

Limitations

The following restrictions were imposed in this study:

1. Results of this study are applicable only to adult males possessing similar health characteristics as those sampled here.
2. Results of this investigation may be applicable only to testing protocols of similar makeup.

Basic Assumptions

For the purposes of this study it was assumed that:

1. The subjects had not engaged in any prior physical activity on the day of testing.
2. The subjects had fasted for a minimum of 8 hours prior to testing.
3. The recorded gas and ventilation values were accurately synchronized and recorded.

Definitions and Symbols

APPARENTLY HEALTHY - asymptomatic, physically active persons with or without coronary heart disease risk factors.

BALKE PROTOCOL - a multistage, incremental treadmill protocol established by Balke and Ware (1959) to test

functional capacity of Air Force personnel, now used for maximal exercise stress tests.

CARDIAC POPULATION - persons with known, diagnosed heart disease, be it myocardial infarction, coronary artery disease, unstable angina or coronary artery bypass surgery.

FRACTION OF EXPIRED OXYGEN (F_EO_2) - the fraction of oxygen present in an individual's expired air.

FRACTION OF EXPIRED CARBON DIOXIDE (F_ECO_2) - the fraction of carbon dioxide present in an individual's expired air.

FUNCTIONAL CAPACITY - index of maximal aerobic work capacity usually represented by maximal oxygen consumption.

GRADED EXERCISE TEST (GXT) - any continuous increment treadmill exercise test designed to stress the cardiovascular system.

HEART RATE RESERVE (HRr) - the difference between the resting heart rate and the maximal heart rate.

MAXIMAL OXYGEN CONSUMPTION ($\dot{V}O_2max$) - the maximal amount of O_2 in milliliters that can be consumed by an individual per minute.

MINUTE VOLUME OF OXYGEN UPTAKE ($\dot{V}O_2$) - the amount of oxygen in milliliters consumed by an individual per minute.

MINUTE VOLUME OF OXYGEN UPTAKE - steady state ($\dot{V}O_{2ss}$) - the levelling off of oxygen consumed by an individual per minute, usually noted in submaximal exercise at a

steady intensity.

MINUTE VENTILATION EXPIRED ($\dot{V}_E$) - the volume of air expired in one minute.

MINUTE VENTILATION INSPIRED ($\dot{V}_I$) - the volume of air inspired in one minute.

RATE OF PERCEIVED EXERTION (RPE) - a numerical representation of subjective work cost of an exercise based on the work of Borg (1970).

RESPIRATORY EXCHANGE RATIO (RER) - the ratio of volume of carbon dioxide produced per minute to the volume of oxygen uptake per minute; an indication of anaerobic metabolism.

Chapter II

LITERATURE REVIEW

The clinical assessment of functional aerobic capacity provides valuable information relative to the integrity of the oxygen transport system for both cardiac diseased and healthy individuals. This chapter examines the pertinent literature regarding physiological responses to graded treadmill exercise testing in cardiacs and healthy persons and is divided into six sections most relevant to the study described herein. The categories are as follows: a) History of Graded Exercise Testing; b) Measurement and Prediction of Oxygen Consumption; c) Prediction of Oxygen Consumption in Cardiac Patients; d) Errors in Prediction of $\dot{V}O_2$ in Treadmill Exercise Tests; e) Extraneous Factors Affecting $\dot{V}O_2max$ Assessment; and f) Effects of Beta-Adrenergic Blocker Medications on Cardiorespiratory Response to Exercise.

Graded Treadmill Exercise Testing: The Early Years

In 1938, Margaria evaluated the energy cost of walking/running on a treadmill using indirect calorimetry, i.e., measurements of oxygen consumption. Margaria (1938) demonstrated that a linear relationship existed between energy cost and speed of walking on the treadmill. Later reports by Margaria and associates (1963) suggested that the energy cost of treadmill exercise on an incline could be

estimated from the vertical component (grade) while walking or running without directly measuring the amount of oxygen consumed.

Margaria, Cerretelli, Ahgemo and Sassi in 1963 exercised two athletes at various walking and running speeds up to 22 $km \cdot hr^{-1}$ on a treadmill at grades between -20 to +15% and reported that net energy consumption per kilogram body weight was .2 $ml \cdot min^{-1}$ regardless of speed. The authors thus concluded that net energy consumption was independent of speed and related only to treadmill incline.

Dill in 1965 conducted a similar study on three subjects (two competitive runners and the author) at varying speed and grade combinations on the treadmill. At speeds below 150 $m \cdot min^{-1}$, oxygen cost was .1 $ml \cdot min^{-1}$ per $m \cdot min^{-1}$. At speeds from 150 $m \cdot min^{-1}$ to 350 $m \cdot min^{-1}$, the O_2 cost ranged from .17 $ml \cdot min^{-1}$ per $m \cdot min^{-1}$ to .2 $ml \cdot min^{-1}$. The data indicated a curvilinear relationship between speed and net oxygen consumption. From the results the authors developed an equation for estimating net oxygen consumption and concluded their results to be valid for predicting O_2 consumption for seven additional athletes who were exercised under similar conditions.

From the aforementioned early investigations, the idea evolved that clinical graded exercise testing with measurement of oxygen consumption could provide an

indication of functional aerobic capacity and thus be a valuable tool in assessing cardiovascular function. As early as 1958, Mitchell and associates suggested the need for a relatively short, standardized continuous graded exercise test with established criteria for measuring maximal VO_2. However, since direct measurement of oxygen consumption is rarely obtained in clinical evaluation settings, the value of functional capacity assessment rests upon the ability to accurately predict submaximal and maximal VO_2 responses from knowledge of speed and grade combinations (Foster, Hare, Taylor, Goldstein, Anholm & Pollock, 1984).

Measurement and Prediction of Oxygen Consumption

The first treadmill exercise test protocols were developed to obtain accurate measures of maximal oxygen uptake. Maximal oxygen consumption represents the peak exercise capacity for an individual, and was demonstrated by Astrand (1952) and Taylor, Buskirk and Henschel (1955) to be the rate of oxygen consumption at which a further increase in the grade (incline) does not call forth an addition to the level of oxygen consumption. Initially Taylor et al. (1955) used interrupted workloads to determine the maximal oxygen consumption obtained by healthy men. These tests were both strenuous and time consuming, often taking days to complete. As a consequence, more practical tests were

devised.

Balke and Ware (1959) developed a continuous treadmill protocol to test a group of Air Force personnel (n=500) and from their data concluded that duration of performance was linearly related to the $\dot{V}O_2$ attained. The authors proposed a nomogram for estimating $\dot{V}O_2max$ based on known work intensity that could be used for predicting $\dot{V}O_2max$ in settings where gas analysis equipment was unavailable. This nomogram for estimation of VO_2 was demonstrated in the following linear equation:

$$\dot{V}O_2 = \text{speed (m/min)} \times \text{body weight (kg)} \times (.073 + \text{grade}/100) \times 1.8$$

where 1.8 is the factor constituting the oxygen requirement in ml/min for 1 kilogram-meter of vertical work.

Bruce, Blackman and Jones (1963) and Bruce, Kusumi, and Hosmer (1973) took the idea of $\dot{V}O_2$ estimation one step further and developed a protocol to measure cardiovascular function in both healthy persons and cardiac diseased men. Measuring submaximal and maximal oxygen consumption in hundreds of healthy men and women and in male cardiac patients, these investigators determined that a linear relationship existed between treadmill exercise duration and $\dot{V}O_2$. From these data, they developed nomograms based on maximal treadmill time specific to the populations tested,

and specific to their (Bruce) protocol. Correlations between treadmill tolerance time and actual $\dot{V}O_2max$ were presented by the investigators as r = .91 for healthy men and r = .86 for cardiac men.

The graded exercise test thus became an established clinical tool yielding two vital indices of information: 1) the peak physical work capacity an individual could achieve; and 2) the diagnosis of coronary heart disease. The two areas were very much related, with the heart diseased individual usually functioning at a reduced capacity, and a poor functional capacity further suggesting the severity of an underlying cardiovascular disease process.

Later attempts to replicate the Balke and Bruce protocols demonstrated that the prediction of $\dot{V}O_2max$ from treadmill time was an oversimplification. For instance, a study conducted by Froelicher and Lancaster in 1974 evaluated the validity of estimating maximal oxygen consumption from the Balke test protocol. In this study, 1025 healthy Air Force men performed symptom-limited maximum exercise tests and their results were presented in two subgroups: 1) those who exercised to a heart rate of < 180 bpm; and 2) those who exercised to a heart rate of > 180 bpm. Maximal oxygen consumption for each group was linearly related to maximal time on the treadmill. Results indicated that mean $\dot{V}O_2max$ did not differ significantly between the

two groups (i.e., at maximal treadmill time of 15 minutes: (group 1) VO_2max = 33.18, SEM - ±3.70 $ml \cdot kg^{-1} \cdot min^{-1}$; (group 2) $\dot{V}O_2max$ = 34.35, SEM = ±4.40 $ml \cdot kg^{-1} \cdot min^{-1}$). Furthermore, the measured versus estimated $\dot{V}O_2max$ using the Balke nomogram demonstrated a correlation of r = .72, SEE for the regression of VO_2 on speed was 4.26 $ml \cdot kg^{-1} \cdot min^{-1}$. With an approximately 52% error variance in maximal $\dot{V}O_2$ estimation, the investigators concluded that $\dot{V}O_2max$ can differ widely among individuals for any maximal treadmill time and that this performance criterion was useful only for gross predictions of functional aerobic capacity.

In a later study, Froelicher, Brammell, Davis, Noguera, Stewart and Lancaster (1974) reported that experience alone could produce an increase in maximal treadmill performance time without a concomitant increase in $\dot{V}O_2max$. In the Froelicher et al. (1974) study, 15 healthy volunteers performed the Taylor, Balke, and Bruce protocols three times each over a period of 9 weeks. The results revealed a greater mean maximal $\dot{V}O_2$ in the Taylor protocol over the other two, but high reproducibility of $\dot{V}O_2max$ noted in all three protocols. Furthermore, there often was great variability between a given subject's $\dot{V}O_2max$ and his particular total treadmill time in any of the three protocols.

Another study by Froelicher, Thompson, Noguera, Davis,

Stewart and Triebwasser (1975) further challenged the use of treadmill time as a predictor for functional capacity. In this study, the results of 79 men exercising under the Balke protocol and 77 men exercising under the Bruce protocol indicated that the equations used for estimating maximal oxygen consumption from maximal treadmill time were inadequate except for very gross delineations. Maximal oxygen consumption linearly regressed on treadmill time, age and activity status under the Bruce protocol demonstrated a correlation of $r = .87$ (SEE = $\pm$ 4.71 $ml \cdot kg^{-1} \cdot min^{-1}$) and under the Balke protocol demonstrated a correlation of $r = .80$ (SEE = $\pm$ 3.95 $ml \cdot kg^{-1} \cdot min^{-1}$). The authors concluded that the use of the Balke and Bruce treadmill test protocols were of no preferable value over any other clinically acceptable protocol. Obviously, the error variance associated with these regression equations provides little support to the notion that treadmill performance time is a predictor of functional aerobic capacity.

Prediction of Oxygen Consumption in Cardiac Patients

More recently, researchers have attempted to evaluate the use of standard treadmill test protocols to assess the functional capacity of cardiac diseased populations. A study by Adams, Marlon, and Quinn (1980) was directed toward prediction of $\dot{V}O_2max$ in a group of 65 cardiac patients. The treadmill test protocol used was a modified Bruce technique,

as standardized by the Wake Forest Cardiac Rehabilitation Center. The investigators compared measured versus predicted $\dot{V}O_2$ values using the published prediction equations established by the American College of Sports Medicine (ACSM, 1980). The data indicated that 80% of the patients failed to achieve either their predicted workload or their predicted maximal oxygen consumption under the ACSM equations. Furthermore, the investigators demonstrated that these equations overpredicted the actual exercise capacity of the cardiac patients by approximately 20%. Adams et al. (1980) concluded that using speed and grade to predict maximal $\dot{V}O_2$ resulted in consistent overestimation of the exercise capacity of cardiac patients.

In a similar study, Singer (1983) evaluated the ACSM formulas as well. The equations were developed for use with any standard exercise test protocol to predict maximal oxygen consumption (classified in METS) from speed and grade combinations on the treadmill. Singer (1983) divided 60 subjects into groups of fit (FIT), unfit (UNFIT), medicated cardiac patients (BB) and non-medicated cardiac patients (NBB). Medicated versus non-medicated referred only to the use or non-use of beta-blockade substances. Results of the investigation demonstrated that ACSM formulas significantly overestimated VO_2max in all groups; mean error in METS were as follows: 1.8 (FIT); 2.9 (UNFIT); 3.1 (BB); and 3.2

(NBB). Singer (1983) concluded that use of the ACSM equations results in overestimation of the exercise capacity of both healthy and cardiac diseased individuals with a greater margin of error demonstrated in the cardiac group.

Another study conducted by Foster, Jackson, Pollock, Taylor, Hare, Sennett, Rod, Sarvar and Schmidt (1984) evaluated the validity of several published equations for predicting treadmill performance in cardiacs. Twenty-five cardiac patients and 12 healthy volunteers were tested for submaximal and maximal $\dot{V}O_2$ using the Bruce protocol. The results indicated that using the Bruce equations developed for normal subjects to predict $\dot{V}O_2$ in cardiacs resulted in submaximal $\dot{V}O_2$ measures that did not differ significantly from predicted values; however, maximal $\dot{V}O_2$ values were consistently overpredicted (7% - 15%). The authors concluded that accurate submaximal $\dot{V}O_2$ estimation was critically dependent upon the use of equations that are appropriately specific to the population being tested. In the Foster et al. (1984) study, the correlation between predicted and measured values for healthy subjects was estimated to be r=.84. This correlation indicates an error variance of approximately 30% that is not accounted for by the predictor variables, an error level that can have serious implications for clinical evaluation and exercise prescription therapy in cardiovascular diseased patients.

Foster et al. (1984) further suggested that a combination of the several different population-specific equations may permit a more accurate, single generalized equation useful for predicting functional capacity for a wide range of populations.

To address this latter concept, Foster, Hare, Taylor, Goldstein, Anholm and Pollock (1984) evaluated the responses of 230 males to the Bruce exercise test protocol. The sample included cardiac patients, apparently healthy individuals, and athletes. After familiarization with the treadmill, 200 subjects performed a symptom-limited maximal exercise test with oxygen consumption measured directly. From the data collected, the authors predicted $\dot{V}O_2$max for 30 subjects using a multi-factorial regression equation combined from several of the standard equations. They then evaluated accuracy of prediction against actual measured values and reported a correlation of r = .96. They concluded that their simplified regression equation provided a more accurate evaluation of functional capacity than currently used population-specific equations.

$\dot{V}O_2$ Prediction Error in Treadmill Exercise Tests

Because of the difficulties associated with accurate $\dot{V}O_2$ prediction in cardiacs using the more popular treadmill test protocols (i.e., Bruce and Balke) several investigators have attempted to identify and correct the factors

responsible for overestimation of oxygen consumption in these diseased populations. It has been demonstrated that cardiacs exhibit lower maximal $\dot{V}O_2$ measures than normals and are also observed to have higher submaximal respiratory exchange ratios ("RER" values) for given exercise loads (Haskell et al., 1982; Sullivan & McKirnan, 1984; Linarsson et al., 1974). These characteristics indicate a greater net energy cost and presence of anaerobic metabolism to maintain a given exercise intensity.

Haskell, Savin, Oldridge and DeBusk (1982) in an attempt to isolate the factors influencing $\dot{V}O_2$ estimation in myocardial infarction patients tested two groups of men (similar clinical status) at 3 and 11 weeks post-MI. One group was tested under a "standard" modified Balke protocol (3 $m \cdot h^{-1}$ with 2.5% grade increment stages every 3 minutes); a second group was tested under an "accelerated" version of the same protocol (3 $m \cdot h^{-1}$ with 5% grade increment stages every 3 minutes). Measured vs estimated values were not significantly different for either group at 3 weeks, nor for group 1 at 11 weeks. However, under the accelerated protocol for group 2 at 11 weeks, estimated $\dot{V}O_2max$ values were significantly higher than those actually measured (30.8 vs 27.7 $ml \cdot kg^{-1} \cdot min^{-1}$). Haskell et al. (1982) attributed the significant difference in measured vs estimated $\dot{V}O_2$ values to a delay in the oxygen transport system secondary

to functional myocardial impairment suffered by the patients after their MI's. In addition, the investigators noted elevated respiratory exchange ratios in the accelerated vs standard protocol (RER = 1.09 vs 1.01) suggesting that anaerobic mechanisms were more strongly evident under the accelerated protocol.

In a study conducted by Sullivan and McKirnan (1984), 12 post-myocardial infarct and 12 healthy subjects underwent a modified Bruce protocol treadmill test (3-minute warm-up stage at $1.7 m \cdot h^{-1}/5\%$ grade) to determine maximal oxygen consumption. The results indicated: 1) a significantly lower mean VO_2 for cardiac patients in the first four stages of the test (1.0 vs 6.2 $ml \cdot kg^{-1} \cdot min^{-1}$); 2) a significantly higher RER value for cardiacs by stage III of the test (.81 vs .93); and 3) a significantly lower predicted max $\dot{V}O_2$ for the post-MI patients when derived from the normal subjects' data. The authors suggested that slower oxygen uptake kinetics are prevalent in cardiacs due to their myocardial damage; consequently the O_2 deficit is increased at any standard exercise load and the result in such patients is an increased anaerobic metabolism to compensate for the oxygen deficit.

The delayed oxygen uptake kinetics of cardiac diseased individuals may be a direct result of their decreased rate of delivery of oxygenated blood reaching the working

muscular system (Wasserman, Van Kessel, & Burton, 1967; Linarsson, Karlsson, Fragraesis & Saltin, 1974). Reduced oxygen transport is often the limiting factor in an exercise situation for patients with cardiovascular disease; consequently, a verifiable maximal oxygen uptake capacity cannot be obtained (Wasserman & Whipp, 1975).

Roberts, Sullivan, Froelicher, Genter and Myers in 1984 investigated the oxygen uptake kinetics of normal subjects and cardiac patients utilizing a modified Balke test protocol (initial stage at 2 $m \cdot h^{-1}$/0% grade; a second stage at 3.3 mph and grade increments of 5% every 2 minutes thereafter). The investigators found that below the anaerobic threshold, $\dot{V}O_2$ values were similar between the two groups. At exercise loads above the anaerobic threshold, however, cardiac patients exhibited functional capacities approximately 1 MET (3.5 $ml \cdot kg^{-1} \cdot min^{-1}$) lower than the normal subjects. These results appear to corroborate the findings of Wasserman and Whipp (1975) who have noted an increased amount of time needed to achieve a steady-state $\dot{V}O_2$ above the anaerobic threshold. Hence, the already depressed ability of heart patients to supply oxygen to exercising muscles is reflected in their lower $\dot{V}O_2$ values. Roberts and associates (1984) also developed regression equations for predicting $\dot{V}O_2$ from treadmill time. Their correlation coefficients were r=.93 and r=.85 for normals

and cardiacs, respectively. The authors suggested that population-specific regression equations were essential due to the population differences in oxygen uptake kinetics surrounding the anaerobic threshold and concluded that the use of standard exercise test loads for individuals or populations must be dependent upon the rate at which oxygen uptake reaches a cardiorespiratory steady-state.

Zohman, Young, and Kattus (1983), having recognized the possibility of impaired oxygen uptake kinetics in cardiacs, devised a progressive walking treadmill test protocol to assess submaximal oxygen consumption patterns in cardiacs. The protocol has been tested on over 40,000 persons in the last 15 years without incidence of cardiovascular accident and utilizes stages of 3 minutes duration. The grade is held constant in the early stages at 10% and speed is increased at .5 mph every 3 minutes to physiological maximum for subject. Once 4 $m \cdot h^{-1}$ is reached, the grade is increased 4% every stage to maintain the walking protocol. Hence, the rate of increase in metabolic demand per minute for this protocol is less than the protocols described earlier in the foregoing pages. Zohman et al. (1983) conducted their study using this 3-minute protocol on 131 individuals separated into four clinical groups: normal; post-MI; coronary artery diseased (CAD); and probable CAD risk (atypical chest discomfort plus equivocal or

inconclusive exercise test results). Measures of submaximal $\dot{V}O_2$ were obtained and no significant differences in $\dot{V}O_2$ values at various stages (which were dependent on clinical status) were noted. These data suggest that if diseased patients are allowed a greater time period to achieve steady-state with a less aggressive protocol, their $\dot{V}O_2$ levels will resemble those of healthy subjects for the same speed/grade combinations. The investigators concluded that their protocol allowed for diagnostic testing and accurate exercise prescription for CAD diseased individuals and suggested that perhaps the traditional protocols may not be the most efficient for obtaining accurate graded exercise testing data.

Perhaps a major limitation associated with attempting prediction of maximal oxygen uptake in cardiac and healthy populations is the assumption that $\dot{V}O_2$ is linearly related to total treadmill time within specific protocols. The recent investigation by Foster et al. (1984) examining 230 males tested under the Bruce exercise test protocol suggests that a curvilinear approach to evaluating $\dot{V}O_2$max estimation with respect to treadmill exercise time would be more appropriate. The investigators developed regression models on a validation sample of 200 cardiac-diseased and apparently healthy subjects using the Bruce protocol and tested the accuracy of the regression models against an

independent sample of 30 clinically matched subjects. Simultaneously, the investigators examined the population-specific linear Bruce (1973) equations. Using age, health status, activity status, and treadmill time as predictor variables, cubic model multiple regression equations were obtained that demonstrated a curvilinear relationship between treadmill tolerance time and $\dot{V}O_2max$; r = .97 (SEE = ±3.5 $ml \cdot kg^{-1} \cdot min^{-1}$). A generalized equation utilizing all significant predictor variables presented a correlation between predicted and measured $\dot{V}O_2max$ of r=.96 (SEE = ±3.6 $ml \cdot kg^{-1} \cdot min^{-1}$). The new regression models developed by Foster et al. (1984) demonstrated greater correlation and lower standard errors of prediction than the population-specific equations developed by Bruce and associates (1973). Foster et al. (1984) thus concluded that due to subject variability in exercise stress testing (i.e., clinical status, age, sex, stage duration and increment increase) a curvilinear and generalized multiple regression equation provides a more simplified and utilitarian approach to estimating functional capacity during graded exercise testing for all populations. However, Foster et al. themselves have noted that all of the studies recommending a curvilinear approach to prediction of $\dot{V}O_2max$ have utilized the more aggressive Bruce test protocol resulting in stage increments of > 1 MET and infer that this factor explains

the observed variation in $\dot{V}O_2$max linear response.

It is evident from these most recent studies evaluating the widely-utilizedted treadmill test protocols that more accurate methods of predicting functional capacity must be developed if clinical laboratories continue to exclude gas analysis during their evaluations of cardiac patients. Perhaps more importantly, precise understanding of the metabolic and cardiorespiratory processes specific to cardiacs that produce their inefficiencies during exercise is essential if safe and effective rehabilitation prescriptions for physical training are to be delivered.

Extraneous Factors Influencing $\dot{V}O_2$ Assessment

Although the area of quality control in exercise testing has not been thoroughly addressed in the literature, it is important to provide both reliable and valid data in exercise evaluations. Quality control refers to the appropriate administration of both technical and procedural aspects of the GXT to prevent confounding influences upon resultant data. The identified areas of concern include: maintenance and calibration of gas analyzers; measurement and operation of testing devices; environmental influences; habituation to exercise; and hand-rail support.

1) Calibration and maintenance of gas analyzers. Cotes and Woolmer (1962) conducted one of the first documented evaluations of quality control in gas analysis. The authors

investigated 27 British laboratories for accuracy in gas analysis. They circulated cylinders of gas containing oxygen, carbon dioxide and nitrogen and utilized Haldane and micro-Scholander equipment to demonstrate variations in gas content of ±3% for O_2 and ±2% for CO_2 among the labs, an insignificant difference.

Jones and Kane in 1979 as part of a comprehensive study of quality control of multiple testing facilities analyzed the long-term variability in expired gas analysis among four laboratories. The investigators noted variations in O_2 and CO_2 content as large as ±10% of the actual concentrations. Jones and Kane (1979) identified several problem areas within the laboratories that accounted for the errors. Most importantly, the accuracy of analysis depended on well analyzed/calibrated initial gas mixtures. Secondarily, other errors were recognized: too infrequent calibration, too long and too wide sampling catheters, different tube sampling at different sites and leaks in the tubing circuit. Jones and Kane (1979) suggested that quality of testing cannot be assumed but must be dependent upon established control techniques carefully incorporated into the testing protocol itself.

2) Measurement and Operation of Testing Devices. The study by Jones and Kane (1979) further examined the long and short-term variability of testing measurements. The

investigators standardized a cycle ergometer exercise protocol and obtained data for short-term and long-term variabilities within one laboratory as well as for long-term variability among the four laboratories. The parameters examined were HR, $\dot{V}O_2$, $\dot{V}CO_2$, and $\dot{V}_E$. The short-term study consisted of testing 9 females, five consecutive days, at the same time each day. Data collection at 200, 400, 600 and 800 $kpm \cdot min^{-1}$ demonstrated insignificant variation ($p>.05$) within subjects on repeated testing. The long-term variability analysis consisted of three subjects tested nine times each, once per year for 5 years. Variability in measurements at all power outputs was not significantly different ($p>.05$).

The data for between-lab variability were obtained as described earlier and demonstrated significant variation over the within-laboratory analysis. Measurement variabilities were: $\dot{V}O_2 \pm$ 10.9% and HR± 5.5%. One laboratory in particular contributed to the error rate and when excluded, the variability rates dropped to: $\dot{V}O_2 \pm$ 5.6; $\dot{V}CO_2 \pm$ 8.44; $V_E \pm$ 8.2% and HR± 4.6%. From these results Jones and Kane (1979) noted that a systematic error of 100 $kpm \cdot min^{-1}$ in ergometer calibration seriously affected oxygen consumption data and suggested that periodic calibration of testing ergometers is crucial to accurate measurement results.

Similarly, the American Heart Association (1979a) has published standards for use of exercise ergometers (specifically bicycles and treadmills) in exercise testing. The Association states that all exercise equipment capable of administering progressive, incremental workloads be accurate. Bicycle ergometers must be mechanically or electrically braked, calibrated and serviced monthly. Treadmills should be power-drive and capable of maintaining speeds at various elevations for a variety of weight ranges (children to adults >100 kg). Calibration for speed and grade elevation should occur monthly.

3) Environmental Influences. Environmental conditions can affect exercise response parameters and include such factors as external ambient temperature, internal body temperature, humidity and meal ingestion prior to exercise. Most laboratory conditions are controlled and the American Heart Association has again recommended standards for these testing conditions. The recommendations are for temperatures between 20-23°C (68-79°F) and humidity below 60% and are based on research demonstrating increased changes in S-T segment and dysrhythmias at increased temperatures (23-25°C) and humidity (> 60%), respectively (AHA, 1979b). Davis and Convertino (1975) have also noted the presence of an increased heart rate response during increased temperature and humidity.

Additional evidence confirms the effects of external temperatures on exercise. Rowell, Marx, Bruce, Conn, and Kusumi in 1966 demonstrated significant reductions in cardiac output, stroke volume and central blood volume in 10 unacclimatized men at high ambient temperatures (43.3°C). Heart rate was significantly elevated as well and although no significant decrements in oxygen consumption were noted, the duration of time in which it could be achieved was markedly shortened. The authors concluded that detrimental effects of increased temperature do occur: a reduction in work capacity as manifested by a failure in cardiac output and a redistribution of central blood flow to supply the exercising muscles.

These results support earlier work by Rowell and colleagues (1965) who noted similar findings in $\dot{V}O_2max$, but that a significantly greater quantity (20%) of blood was diverted away from the hepatic-splanchnic system during exercise at elevated temperatures.

Internal body temperature can affect exercise response as well. Froelicher et al. (1974a) in their comparison of three testing protocols noted that the longer duration test protocols of Bruce (1963) and Balke (1959) vs the interrupted Taylor (1955) protocol elicited higher body temperatures. The investigators (1974) hypothesized that this increased heat load increased the blood flow to the

skin, lowering the a-v O_2 difference and ultimately, the $\dot{V}O_2max$.

Schvartz, Shapiro, Birnfield and Magaznik (1978) examined the relationship between $\dot{V}O_2max$, heat tolerance and rectal temperature in 21 subjects: 8 trained (T), 8 untrained (UT) and 5 heat acclimated (HA). Subjects were tested under three exercise conditions: 60 mins of exercise at a fixed load (35 W at 23°C); 60 mins of exercise at 35% $\dot{V}O_2max$ (23°C); and 3 hrs of exercise in heat (40°C db, 30°C wb). The heat acclimated group showed the best heat tolerance and lower core temperatures under the fixed exercise conditions (T = 37.6°, 37.9° and 38.2°C, HA, T and UT, respectively) and the relative exercise condition. The results demonstrated that temperature was correlated highly with $\dot{V}O_2max$ (r=-.70) and that the remaining variability was accounted for by heat acclimatization.

Ingestion of food immediately prior to acute exercise bouts has likewise been demonstrated to detrimentally affect performance. Goldstein, Redwood, Rosing, Beiser and Epstein in 1971 examined exercise responses (to bicycle ergometer) in 12 angina patients. Subjects performed symptom-limited maximal bike exercise tests in a fasted state and three hours after eating a light breakfast. Eleven of the twelve patients developed angina sooner ($\bar{X}$=13 min) after the meal. Furthermore, heart rate was significantly faster ($\bar{X}$=12

$b \cdot m^{-1}$) and arterial pressure significantly higher ($\bar{X}$=6 mmHg) post-prandial as compared to pre-prandial. The results indicated a decreased time to onset of angina due to the rate pressure product (HRxSBP) increasing at a faster rate following a meal. Goldstein et al. (1971) concluded that alterations in heart rate and blood pressure during exercise following a meal increase the myocardial oxygen requirements while reducing the ability to supply underfused regions, thus hastening the onset of ischemic pain.

Jones and Haddon in 1972 conducted a similar study with healthy subjects. Four males exercised at 30% and 60% of $\dot{V}O_2$max following a 24-hr fast, a 12-hr fast and 1-hr after a 300 kcal meal. Heart rate during exercise was not significantly different between any of the three testing trials, although resting values were higher in 3 of the 4 subjects following meal ingestion. $\dot{V}O_2$ exercise measurements were not notably altered in any of the exercise conditions, but $\dot{V}CO_2$, R, and ventilation were observed to be higher following the meal. Effects on these exercise measurements were attributed to the reduced free fatty acid (oxygen) metabolism and the resultant anaerobic state (lactate production). The authors (1972) concluded that following a large meal for normal subjects, exercise effects are a result of metabolic rather than cardiovascular alterations.

More recent studies have confirmed these findings. Foster, Costill and Fink (1979) exercised 16 subjects (8 male and 8 female) to exhaustion on a bicycle ergometer at 80% of VO_2max following ingestion of water (W), glucose (G), and a liquid meal (M). Endurance performance time was significantly reduced (19%) as a result of the glucose feeding, though no difference was found between the W and M trials. The results demonstrated impaired lipid mobilization following CHO ingestion and indicated that glucose feedings prior to exercise increases the rate of carbohydrate metabolism and thus reduces exercise performance.

4) Habituation to exercise. Previous testing experience has been demonstrated to affect physiological parameters and mechanical efficiency. Froelicher and colleagues (1974b) while investigating the responses to exercise in aircrewmen found a reduction in $\dot{V}O_2$ and heart rate at similar workloads for subjects with repeated exercise tests. The authors suggested that mechanical efficiency was improved with sequential testing practice.

Charteris and Taves in 1978 conducted a kinematic analysis of subject accommodation to treadmill walking. Using naive subjects, the investigators demonstrated that it took 15 minutes of walking to develop a fairly stable pattern. Charteris and Taves (1978) also identified two

basic processes of habituation: an initial tripping gait that consisted of faltering and regaining balance and a second process that gradually established a stable gait not significantly variant from the kinematic stride subjects exhibited during normal ground walking.

In 1980, Wall and Charteris took their examinations one step further to determine at which point habituation to treadmill walking occurred. Eighteen naive male subjects were divided into three groups based on stature differences that affect walking velocity (Charteris & Taves, 1978). Results indicated that the "tripping" gait occurred in the first 10 seconds of walking followed by a gradual acclimatization to a normal stride length. Progressively more efficient motion was still being noted 10 minutes into exercise and Wall and Charteris (1980) suggested that to obtain valid exercise test data, test measurements should not be made in the initial 10 minutes of exercise. Sullivan and Froelicher (1983) have also confirmed this process of habituation as a factor in treadmill performance; they caution attention to its presence when assessing functional capacity. The authors (1983) noted that an increase in total treadmill time during serial testing may often be a reflection of increased mechanical efficiency (through practice) rather than an increased cardiorespiratory efficiency (through conditioning).

5) Hand-Rail Support. A final area of concern in quality control of exercise tests includes the influence of hand-rail support upon oxygen consumption values. In 1980, Ragg, Murray, Karbonit and Jump tested six healthy subjects under a treadmill walking protocol with and without hand-rail support. Results indicated that while exercise duration was signficantly greater (10.2± 4.40 mins) when handrail support was allowed, significantly higher measured mean oxygen consumption and heart rates were obtained without handrail assistance. Ragg et al. (1980) further demonstrated an average over-prediction of $\dot{V}O_2$max of 17.5% with handrail support using the index of test duration. The authors concluded that unless strict adherence to testing procedures is obeyed, direct measurement of gas analysis should be the preferred method of determining safe and effective exercise prescriptions.

More recently, Haskell, Savin, Oldridge and DeBusk (1982) corroborated these findings with cardiac patients. Haskell et al. (1982) tested 12 post-myocardial infarction patients with and without handrail support and found that measured peak $\dot{V}O_2$ values were not significantly different (32.1 vs 32.7 $ml \cdot kg \cdot^{-1} \cdot min^{-1}$). However, treadmill time increased significantly with handrail support resulting in significantly greater estimated peak $\dot{V}O_2$ values (37.9 vs 31.8 $ml \cdot kg^{-1} \cdot min^{-1}$). Estimated values again overpredicted

peak performance by 19% and the authors concluded that handrail support must be eliminated to prevent inaccurate estimation of functional capacity in cardiovasculars.

Finally, Zeimetz, McNeill, Hall and Moss (1985) conducted an extensive study to quantify the effects of handrail support on exercise parameters (VO_2, HR and time to target heart rate). The authors tested 15 healthy male volunteers under various degrees (forces) of handrail support in treadmill walking. Resting the palms of one's hands on the side railings produced no significant differences in the measured parameters when compared to non-support (arms swinging freely). However, as the force of support was increased, so was the amount of observed decrease in $\dot{V}O_2$, up to 30% with a horizontal pull of 6.8 kg on the rail. Furthermore, tension of the handrail supports tended to increase with both test duration and workload imposition. Finally, the investigators demonstrated an overestimation of 31% in $\dot{V}O_2$ from Stage V using handrail support. Zeimetz et al. (1985) thus concluded that significant alterations in physiological response to treadmill exercise do occur with handrail support and they emphasize the importance of strict adherence to appropriate testing procedures to ensure valid and useful test results.

Beta-Adrenergic Blockade Medication and Exercise

A final area of concern identified in the evaluation of exercise testing in diseased populations is that of the use of cardiodynamic medications by these persons. Questions regarding the physiological effects of beta-adrenergic blocking agents on exercising individuals are difficult to answer precisely and most recently have become an area of interest to cardiac care professionals.

Receptor-specific beta-blocking drugs were introduced in the early 1960's and their use in the treatment of patients with cardiovascular disease quickly gained clinical acceptance. Beta-blockers are made pharmacologically effective through biochemical alteration of the beta receptor coupling site on cell membranes (Harrison, 1985). In the treatment of cardiovascular disease, beta-blockers have the specific action of blocking the beta-receptor site for catecholamines, primarily norepinephrine. This action results in inhibition of the heart's response to the sympathetic nervous system, a reduction in cardiac rate and contractility and hence, myocardial oxygen demand (Opie, 1985).

Adrenoreceptors such as those affecting cardiac rate and contractility are classified as beta-1 receptors; in contrast, those affecting muscular vasodilation, bronchodilation and glycogenolysis are classified as beta-2

receptors (Shepherd, 1985). Beta-blocking agents work by either antagonizing the catecholamine effects at both the beta-1 and beta-2 receptor sites (non-selectivity) or by selectively blocking only the beta-1 receptor site. In addition, some non-selective beta-blockers possess the property of intrinsic sympatheomimetic activity (ISA) which allows some metabolic beta-receptor stimulation while blocking primary receptors (Hughson, 1984).

Biochemical and Metabolic Effects During Exercise

Normal hemodynamic responses to exercise include increased heart rate, cardiac output, and blood pressure due to increased myocardial oxygen demand. These hemodynamic changes reflect the adrenergic activity (release of catecholamines) which occur in an attempt to satisfy that demand (Opie, 1985). Similarly, in the skeletal muscle, blood flow is increased to meet the rising demand for oxygen necessary to sustain activity.

To maintain the energy systems, the exercising organs tend to increase their uptake of fuels such as glucose, lactate and free-fatty acids (FFA's). The initial blood supply to the working muscles at the start of exercise is not adequate to meet the energy demands and glycogen must be catabolized to fuel the skeletal muscle system. Lactate is the major energy supply to the heart at this time (Opie, 1985). During prolonged exercise, circulating FFA's become

the major source of energy for both the heart and working muscles (Gollnick, 1977).

All of the potential effects of beta-adrenergic receptor blockades on these working systems during exercise are not known; studies of long-term beta-blockade are limited partly due to the only relatively recent interest in their clinical effects on exercise. During beta-blockade, heart rate increase is blunted and cardiac contractility and blood pressure are decreased (Opie, 1985). As a consequence, myocardial oxygen demand is decreased. This, of course, is the preferred benefit for CAD patient management. Other secondary effects of beta-blockade administration have also been demonstrated. For instance, the extraction of glucose by the heart muscle increases relative to the utilization of FFA's, thus creating an antilipolytic effect in the exercising patient (Opie & Thomas, 1976). Hypothetically, in the setting of acute infarction, this action would be effective in reducing the metabolic demand for O_2 and consequently the degree of myocardial ischemic damage that would otherwise be present (Kurien & Oliver, 1970).

Similarly, there is indirect evidence that beta-blockcade decreases the rate of glycogen breakdown in skeletal muscle as well. Kaiser and Tesch (1983) found that in subjects rich in slow-twitch muscle fibers,

administration of non-cardioselective beta-blockers resulted in greater lactate accumulation in the working muscle as compared to control conditions during peak exercise. However, the authors also suggested that there is a relatively greater suppression of lipolysis vs glycolysis during acute exercise as well. Tesch and Kaiser in 1983 noted a decrease in submaximal oxygen consumption during exercise of highly trained endurance athletes undergoing b-blockade therapy. The authors attributed the decrease to a reduced need for O_2 in the exercising muscle due to the availability of the preferred substrate (glycogen), a result of the accumulated lactate. Ironically, beta-blockade also results in higher circulating lactate levels during acute exercise. This has been theoretically attributed to the decreased uptake of lactate by exercising organs; i.e., the decreased cardiac output of the heart muscle along with the decreased lactate production in the skeletal muscle (Opie, 1985).

Obviously, there are a number of difficulties associated with identifying the effects of beta-blockade on exercise response. Acute versus prolonged exercise elicits somewhat different metabolic responses in the body, even in the absence of beta-blockade therapy. Chronic vs acute administration of beta-blockade substances confounds the issue further and B_1 vs B_2 selectivity status of the drug

presents yet a third area of complication. The following sections will attempt to examine some of these questions with regard to beta-blockade treatment during exercise training.

Effects during Exercise Training in Healthy Adults

Beta-blocker medications potentially exert two important circulatory effects with regard to exercise training: a decrease in heart rate at rest and a decrease in heart rate response to a given amount of stress (Harrison, 1985). This response consequently allows the individual to work at a given exercise demand with a reduced response by the circulatory system (i.e., decreased heart rate). However, exercise training also produces these same changes and the question arises whether the interaction of beta-blockades and exercise training interfere with each other to the extent that improvement in functional capacity is altered (Fletcher, 1985).

Attempts to address this question have presented contradictory results. For instance, an investigation by Sable, Brammell, Sheehan, Nies, Gerber and Horowitz in 1982 indicated no increase in maximal oxygen consumption following exercise training of healthy males taking beta-blockade drugs. Sable et al. (1982) randomly assigned 17 males to receive propranolol, a commonly prescribed nonselective beta-blocker, or a placebo. The propranolol

dosage, administered q.i.d., was titrated to achieve a blood level of 100 $mg \cdot ml^{-1}$ 3 hours post-administration (average total dosage = 160 to 400 mg/day). Subjects then participated in a 5 $d \cdot wk^{-1}$ aerobic exercise program (bike/walk/jog) at a training intensity of > 75% peak HR for 45 $min \cdot d^{-1}$. The results indicated no significant improvement in $\dot{V}O_2max$ after training for those receiving beta-blocker drugs (40.4 ± 1.4 to 40.9 ± .9 $ml \cdot kg^{-1} \cdot min^{-1}$) while those receiving a placebo demonstrated significant increases in $\dot{V}O_2max$ (43.6 ± 2.9 to 52.7 ± 3.2 $ml \cdot kg^{-1} \cdot min^{-1}$). Sable et al. (1982) concluded that propranolol prevented the physiological adaptations that normally occur with aerobic exercise training and that beta-adrenergic stimulation is a major physiological mechanism contributing to cardiovascular conditioning in dynamic exercise.

Marsh, Hiatt, Brammell and Horwitz conducted a similar study in 1983 with 12 healthy male volunteers. The subjects were randomly assigned to receive a placebo or propranolol (dosage = 20 or 30 mg, qid with a total of 80-120 mg/day) under a similar exercise at > 75% peak HR, 40 min/day, 5 days per week for 6 weeks. The investigators reported no significant increase in $\dot{V}O_2max$ for those receiving propranolol but an increased maximal VO_2 for those receiving a placebo.

A later study by Ewy, Wilmore, Morton, Stanforth,

Constable, Buono, Conrad, Miller, and Gatewood (1983) utilized longer training sessions and drug dosages than the aforementioned studies, and dosages more similar to those prescribed for cardiac treatment. The conflicting results did not corroborate those of the Sable and Marsh groups. Ewy et al. (1983) had randomly assigned 27 healthy male volunteers to placebo or drug groups (sotalol, 320 mg/day) and exercised them for 13 weeks (jog/run) at an intensity of 75% $\dot{V}O_2$max, 45 min•d^{-1}, 5 days•wk^{-1}. Significant pre-to-post training increases in peak $\dot{V}O_2$ were reported for both groups tested after cessation of drug therapy: Placebo (44.4 ± 6.7 vs 48.4 ± 6.1 ml•kg^{-1}•min^{-1}); beta-blocker group (43.6 ± 5.9 vs 46.8 ± 6.6 ml•kg^{-1}•min^{-1}). However, the subjects in the beta-blocked group did not show a significant gain in maximal oxygen uptake when tested post-training while still on the drugs (43.6 ± 5.9 - 43.8 ± 6.1 ml•kg^{-1}•min^{-1}). Ewy and associates (1983) concluded that central and peripheral benefits of endurance training do occur in the presence of beta-blockade but that these benefits could not be manifested while still under the acute effects of the medication.

McLeod, Kraus and Williams in 1984 similarly assigned 30 healthy subjects to drug treatment or control groups (placebo, atenolol, 100 mg/day; propranolol, 80 mg/day, b.i.d. and exercised them in a 9 week program of walking,

jogging, or cycling, 45 $min \cdot d^{-1}$, 4 $days \cdot wk^{-1}$ at an intensity of 60-85% of peak heart rate. McLeod et al. (1984) reported results similar to Ewy et al. (1983) with all three groups demonstrating significant improvement in exercise capacity following training and with post-treatment testing after cessation of drug treatment (mean improvements: in $\dot{V}O_2$peak atenolol = increase of 22 ± 6%; propranolol = increase of 13 ± 6%; placebo = 10 ± 3%). Interestingly, when tested while still under medication, patients receiving the selective beta blockers (B_1) atenolol and the placebo demonstrated improved exercise capacity while the propranolol group failed to show significant improvement. The investigators attributed the decline in performance to the fatiguing effects of the non-selective beta-blockade drug.

The results of these two investigations just cited are clearly in contradiction to the earlier findings of Sable and associates (1982) and Marsh et al. (1983). However, it should be recognized that drug type, drug dosage differences and/or variations in the training protocols confound direct comparisons.

Savin, Gordon, Steven, Kaplan, Hewitt, Harrison and Haskell (1985) recently examined the aforementioned studies for design flaws and demonstrated confounding factors such as initial subjects fitness, drug dosage level, altitude,

amount of exercise training, and questionable success of blinding the subjects to treatment assignment. Savin et al. (1985) thus have called into question the results of these recent studies on the beta blocker-training issue. Savin et al. (1985) also have reported their investigation of a closely monitored exercise training study of 39 healthy men under beta-blockade treatment. Subjects were assigned randomly in a double-blind procedure to receive propranolol, atenolol, or placebo titrated individually to minimize heart rate response to submaximal exercise (dose ranges: atenolol, 50-200 mg/day; propranolol, 160-320 mg/day). The exercise program consisted of a supervised 6 week (5 days$\cdot wk^{-1}$, 45 min$\cdot day^{-1}$) stationary cycle training program at $\geq$ 75% heart rate peak.

Savin et al. (1985) reported that peak oxygen consumption increased significantly in all three groups, both in the presence and absence of medication, as measured through direct gas analysis. Both the variables of estimated exercise capacity and duration of treadmill time increased significantly in all groups as well. The authors concluded that long-term beta-blockade treatment does not prevent development of increased exercise capacity via exercise training and that the advantage of cardio-selective beta-blockades over $beta_2$ (non-selective) drugs has not been clearly documented in the present literature.

In a more recent study, however, Wilmore, Ewy, Freund, Hartzell, Jilka, Joyner, Todd, Kinzer, and Pepin (1985) presented evidence supporting better endurance training outcomes with cardioselective blocking agents. Wilmore et al. (1985) assigned 47 healthy, sedentary males to either placebo, propranolol (160 mg/day) or atenolol (100 mg/day) treatments and administered a 15 week, 45 $min \cdot day^{-1}$, 5 $days \cdot wk^{-1}$ aerobic exercise program. Results indicated that all subjects reduced their submaximal steady-state heart rates as a consequence of training as well as increased their max $\dot{V}O_2$ (and maximal treadmill time). The $\dot{V}O_2$ peak ($ml \cdot kg^{-1} \cdot min^{-1}$) gains were: placebo, 45.4 ± 4.5 to 53.3 ± 3.2; propranolol, 42.4 ± 8.7 to 49.6 ± 8.1; and atenolol, 41.5 ± 5.6 to 49.1 ± 7.1. However, while still on medication, the atenolol group had significantly greater increases in maximal oxygen uptake and maximal treadmill time as compared to the propranolol group. The authors concluded that administration of beta-blockade does not reduce the ability of normal, healthy subjects to increase their endurance capacity, but that cardioselective blocking agents maintain a distinct advantage over non-selective ones for aiding the development of that training benefit.

Effects During Exercise Training in Cardiovascular Disease

Although the data regarding the effects of beta-adrenergic blocking agents on exercise response in healthy individuals remains controversial, even less information exists on cardiac-diseased populations. Nevertheless, physicians continue to prescribe beta-blocking agents due to their effective properties in treating angina, hypertension and coronary artery disease (Froelicher, Sullivan, Myers, & Jensen, 1985). For this reason and the fact that exercise training for the management of cardiovascular disease also continues to involve more and more such medicated patients, the study of their combined influence on patient management is of great importance.

Early investigations on the effects of beta-blockade on exercising in cardiac patients examined only acute responses to exercise. Epstein, Robinson, Kahler and Braunwald (1965) compared seven healthy male volunteers and nine cardiac patients in their responses to graded exercise treadmill testing. The subjects performed the test both under the influence of propranolol (.15 $mg \cdot k^{-1}$) and without the drug. Both the normal and cardiac groups experienced a 40% decrease in exercise endurance time as well as significant reductions in both cardiac output (-22%) and $\dot{V}O_2$ peak (-6%) while under the influence of the beta-blockade. Cardiac patients demonstrated lower absolute levels of these

parameters as well. Epstein et al. (1965) concluded that acute induction of beta-blockade impairs the circulatory response to exercise in both normal and diseased individuals.

Initially, an exercise training study by Malborg, Isaccson and Kallivroussis (1974) of coronary patients confirmed the foregoing hypothesis. Their training program, however, consisted of 2 days per week, for 18 minutes duration, for six weeks, likely to be too short to stimulate beneficial training effects. Vanhees, Fagard and Amery in 1982 reported conflicting results when they compared two groups of post-MI patients, 15 receiving beta-blockade agents (varied) and 15 receiving no agents for a notably longer training period. In their study, the subjects participated in an exercise training program for 3 months, 3 days per week, with session durations of 75 minutes at 60-80% of measured maximal exercise capacity. The beta-blocked group demonstrated improvements in $\dot{V}O_2max$ (increase of 35%) similar to that for the untreated group, leading the authors to conclude that beta-blockade treatment does not adversely affect cardiorespiratory improvements with exercise in cardiac patients. Again, however, results are limited with subjects receiving only a non-selective beta-blocker and tested only while under treatment.

More recently, Fletcher (1985) investigated the effects

of cardioselective and nonselective beta-blocking agents on endurance trained cardiac patients. Fifty subjects participated in a thrice weekly medically supervised program and received individually prescribed beta-blockade drugs. Subjects attended the exercise program with at least a 75% compliance rate and were tested prior to and immediately after 3 months of training to determine estimated functional capacity. Fletcher (1985) noted significant increases in treadmill test duration (7.5 ± 2.2 vs 9.9 ± 2.3 min) for all patients and concluded that exercise training benefits could be achieved in patients with cardiovascular disease under the presence of beta-blocking agents. These data corroborate earlier preliminary investigations which had demonstrated improved exercise capacity of cardiac patients under propranolol therapy (Dressendorfer, Smith, Gordon, & Timmis, 1984; Laslett, Paumer, Baier, Amsterdam & Foerster, 1982), but are limited in their generalizability due to the lack of direct gas analysis.

A study by Stuart, Koyal, Lundstrom, Thomas and Ellestad (1985) reported similar findings to those of Fletcher (1985) with direct gas analysis. Eight men and one woman undergoing propranolol therapy were selected to receive a training program (12-16 wk) with sessions of 30-40 min duration, 3 times per week at 75-80% peak pulse rate. Pre-to-post training measured $\dot{V}O_2max$ values were

significantly improved ($\bar{X}$ = 24.57 ± 6.34 vs 30.47 ± 4.87 $ml \cdot kg^{-1} \cdot min^{-1}$), as were other indices of cardiorespiratory fitness (i.e., heart rate, oxygen pulse, total treadmill time). The authors concluded that training benefits with exercise can be obtained under beta-blockade therapy.

Lastly, an extensive study by Froelicher et al. (1985) examined 59 male CAD patients receiving beta-blockade therapy and 69 healthy, control volunteers undergoing one year of supervised exercise training (3 $days \cdot wk^{-1}$, 45 $mins \cdot day^{-1}$, at intensity of 60-85% of $\dot{V}O_2max$). Comparisons of initial vs one year follow-up GXT demonstrated significant increases in aerobic capacity as well as treadmill hemodynamic parameters for both beta-blocker and non-beta-blocker exercising patients ($\bar{X}$% improvement in $\dot{V}O_2peak$ = 12% BB; 6.5% NBB) while non-exercising controls demonstrated decreases in $\dot{V}O_2max$ ($\bar{X}$ = -6.3% BB and -3.1% NBB). The authors thus concluded that beta-blockade therapy did not interfere with improvement in exercise training and performance, nor with other hymodynamic parameters related to exercise.

Summary

The early investigations by Margaria (1938; 1963) and Dill et al. (1965) into the measurement of oxygen consumption and energy cost in exercise provided a base upon which other researchers formulated standard incremented

exercise tests to assess aerobic work capacity of individuals. The first treadmill exercise test protocols were developed to obtain accurate measures of maximal oxygen consumption and thus peak exercise capacities for individuals (Astrand, 1952; Taylor, Buskirk & Henschel, 1955). Balke and Ware (1959) and Bruce et al. (1963) were the first to develop standard test protocols that are still in widespread use for assessment of cardiovascular function in both healthy and diseased populations. Although regression equations have been established to allow prediction of maximal $\dot{V}O_2$ using treadmill time or speed/grade, attempts to validate these equations have been unsuccessful (Froelicher et al., 1974; 1975; Foster et al., 1984).

More recently, researchers have attempted to evaluate the use of standard treadmill test protocols for $\dot{V}O_2$ prediction in cardiacs and have demonstrated significant underestimation of $\dot{V}O_2$ peak for that group when using the equations for established protocols in use today (Adams, Marlon & Quinn, 1980; Singer, 1983; Foster et al., 1984). Haskell and coworkers (1982) and Foster et al. (1984) further attempted to identify the factors present in erroneous prediction of oxygen uptake in cardiacs vs normals and noted that technical care in administering the GXT was as important a variable as myocardial impairment.

Errors in prediction have been attributed to the circulatory deficiencies of coronary diseased persons as well as to the physiological alterations of cardiac drug effects (Sullivan & Froelicher, 1983). As a result, some researchers have attempted to develop new prediction equations (Foster et al., 1984) and new test protocols for evaluation of functional aerobic capacity (Zohman et al., 1983). To date, no conclusive literature is available that accurately determines and predicts the functional aerobic capacity for all populations.

Chapter III

JOURNAL MANUSCRIPT

The Effects of Coronary Heart Disease, Beta-Blockade Medication and State Duration on Oxygen Consumption During Graded Exercise Testing

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(Beta-blockade effects on $\dot{V}O_2$ during graded exercise testing)

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The Effects of Coronary Heart Disease, Beta-Blockade Medication and Stage Duration on Oxygen Consumption During Graded Exercise Testing

by

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(ABSTRACT)

Controversy exists regarding the effects of beta-blocker medications on functional capacity in cardiac patients and in the effects of disease-related impairments on cardiorespiratory dynamics during exercise testing. Therefore, this study was conducted to examine the exercise responses of 26 subjects (ages 37-66 years) to a graded exercise test. Subjects were divided into three groups based on clinical status: apparently healthy (AH; N=8); cardiacs receiving beta-blockers (C-BB; N=8); cardiacs not receiving beta-blockers (C-NBB; N=10).

Variables examined included maximal and submaximal oxygen consumption ($\dot{V}O_2$), ventilation ($\dot{V}$), heart rate (HR), rate of perceived exertion (RPE), respiratory exchange ratio (RER), post-exercise blood lactic acid (HLa) and gas exchange parameters. In addition, regression analysis was employed to determine whether $\dot{V}O_2$max could be accurately predicted from treadmill grade and selected physical characteristics. Subjects performed symptom-limited maximum GXT's using a modified Balke protocol designed to extend

stage durations from 2 to 3 minutes approximately at test midpoint. Results indicated no significant differences between the two cardiac groups in maximal and submaximal $\dot{V}O_2$, $\dot{V}$, respiratory gas fractions, RPE, RER and HLa ($p>.05$). As anticipated, the AH group was significantly higher than the two cardiac groups in peak $\dot{V}O_2$, $\dot{V}$, heart rate, HLa and submaximal heart rate. The C-NBB group evidenced significantly higher heart rates ($p<.05$) than the C-BB group as well as higher submaximal RER values as compared to the AH group ($p<.05$). No significant differences between any of the groups were noted in RPE, gas exchange fractions or peak RER ($p>.05$). A linear regression model developed from this data base yielded no greater accuracy of prediction for $\dot{V}O_2$max ($p>.05$) than currently available equations. These data suggest that coronary diseased patients under beta-blocker therapy demonstrate no greater functional aerobic impairment than patients who are not medicated. Furthermore, when compared to normals, cardiacs exhibit similar O_2 uptake kinetics but lower absolute capacities.

Introduction

Graded exercise testing provides an objective measure of functional aerobic capacity, an important diagnostic and prescriptive index for assessing clinical status in both healthy and diseased individuals. Functional aerobic capacity, expressed as maximal oxygen consumption ($\dot{V}O_2max$), is a universally accepted indicator of cardio-respiratory function[1,2].

Maximal oxygen uptake, by definition, is attained when no further increase in measured $\dot{V}O_2$ occurs despite further increases in metabolic demand[3]. $\dot{V}O_2max$ can be measured directly in a laboratory setting, but because of expense, inconvenience, and time required, estimation of $\dot{V}O_2$ from speed/grade or workload (bicycle ergometer) data has become the preferred clinical approach. The nomograms of Balke and Ware[4] and Bruce, Kusumi, and Hosmer[5] were developed from treadmill performance time and have been used widely to predict functional capacity. However, recent reports[6-8] have demonstrated that these predictions result in significant misrepresentations of actual $\dot{V}O_2$ responses. Others[9,10] have demonstrated lower measured oxygen uptake values when compared to predicted values. Furthermore, it has been shown that coronary diseased patients exhibit a lower $\dot{V}O_2max$ when compared to normals at the same relative workload[11,12]. Use of prediction equations may thus result

in substantial overestimations of functional capacity in coronary diseased populations.

Some researchers have attempted to determine the factors responsible for these discrepancies among predicted vs measured $\dot{V}O_2$ values for cardiacs. Suggested theories include underlying cardiovascular pathology of the heart which results in slower oxygen uptake kinetics[4,13] in the patient as well as the potentially suppressive hemodynamic effects of cardiac medications, specifically beta-blockers[14]. Attempts to address these theories have resulted in the presentation of conflicting evidence[14-16].

Given the difficulties associated with exercise performance evaluation in coronary diseased populations, some investigators have attempted to develop more efficient methods of determining functional capacity. For instance, Foster[17] et al. have developed a multifactorial regression equation using the Bruce treadmill protocol in an attempt to more accurately predict $\dot{V}O_2$ responses at test endpoints for all populations. Bubb[18] et al. have demonstrated that a quadratic rather than linear regression best estimates $\dot{V}O_2$ prediction for both normals and cardiacs when an aggressive protocol is utilized. Zohman and associates[19] have developed a walking test protocol with extended stage durations to more accurately assess oxygen consumption in cardiacs and hence have produced more accurate estimates of

functional capacity in this population.

The present study sought to compare selected cardio-respiratory responses to a modified Balke treadmill graded exercise test protocol between cardiac and apparently healthy subjects. This investigation further attempted to assess the predictive accuracy for estimating $\dot{V}O_2$ using selected test performance variables and subject physical characteristics.

METHODS

Subjects

Twenty-six male participants in the Virginia Tech Cardiac Therapy and Intervention Center served as subjects. Each was classified into one of three groups according to health status: 1) cardiac-beta blocker medication (C-BB, n=8), documented coronary heart disease and receiving beta-blockade medication; 2) cardiac-no beta-blocker medication (C-NBB, n=10), documented coronary heart disease but not receiving beta-blockade medication; and 3) apparently healthy (AH, n=8), no medication and no documented heart disease, but at least one major AHA coronary risk factor[20]. All had been participants in an organized exercise program for at least 6 months and had received at least one prior treadmill exercise test. Subjects gave informed consent prior to participation.

Procedure

Each subject performed a symptom-limited maximum exercise test on a motor-driven treadmill using a modified Balke protocol in which stages were extended to 3 minutes approximately at the test midpoint. Individualized criteria for the point of stage extension were: an RPE ≥ 9 and a heart rate ≥ 40% of heart rate reserve as determined from the previous GXT.

The first two stages of exercise (1 min each) were provided for purposes of warm-up and differed in actual speed/grade for the cardiacs and apparently healthy groups. Beginning at Stage III (3 $m \cdot h^{-1}$/7.5% grade) all subjects were exercising at similar metabolic demands; increments of 2.5% grade continued throughout the remainder of the test. The purpose of this protocol design was to maintain a total exercise test duration of 12-15 minutes while providing a preliminary warm-up representing nearly equal fractions of the $\dot{V}O_2max$ for all subjects. Analysis of the relative energy costs (% $\dot{V}O_2peak$) during Stages I and II revealed that all three groups had indeed performed at similar metabolic demands ($p>.05$).

Heart rate was monitored electrocardiographically each minute throughout the test and during recovery; blood pressure and rate of perceived exertion (RPE) were evaluated once per stage until termination of exercise. Subjects were

encouraged to walk freely on the treadmill and were not permitted to do more than rest their hands lightly on the side handrails.

Oxygen consumption was measured by means of open circuit spirometry. Expired gases were analyzed by Beckman OM-11 or LB-2 respiratory gas analyzers calibrated immediately prior to and after each test using reference gases verified by Haldane analysis. Minute ventilation was measured using either inspired (Parkinson-Cowan P-4 dry gas meter) or expired (Hewlett-Packard 47303-A) flowmeters which were calibrated dynamically with a 3.0 L volumetric syringe. Treadmill speed and grade were calibrated once every two weeks for accuracy. Statistical procedures for data analysis included one-way ANOVA, two-way repeated measures ANOVA and stepwise regression.

RESULTS

Physical Characteristics. Physical characteristics of subjects are presented in Table 1. There were no differences among groups for age, weight, or percent body fat ($p>.05$).

Submaximal and Maximal $\dot{V}O_2$ Variables. Figure 1 presents the $\dot{V}O_2$ changes across time for Submaximal Stage IV and the final complete stage for all groups.

Insert Figure 1 about here

The AH group demonstrated significantly higher $\dot{V}O_2$ values than the two cardiac groups ($p<.05$) at both stages, with the two cardiac groups not significantly different from each other ($p>.05$). The difference between the AH group and its two cardiac counterparts were noted at all six 30-sec intervals within the two stages ($p<.05$). Mean $\dot{V}O_2$ when compared across time was significantly greater for intervals 5 and 6 (minute 3) vs intervals 1 and 2 (minute 1) at both maximal and submaximal levels ($p<.01$) for all groups. There was no significant ($p>.05$) interaction noted for group x time at either stage level.

Peak Exercise Responses. Figure 2 contains the peak $\dot{V}O_2$, $\dot{V}$, HR, RER and HLa results. The AH group had significantly greater ($p<.01$) peak $\dot{V}O_2$, $\dot{V}$, HR and HLa than the two cardiac groups with no differences noted between the two cardiac groups for peak $\dot{V}O_2$, $\dot{V}$ and HLa ($p>.05$). Cardiac patients on beta-blocker medication had relatively lower ($p<.01$) peak exercise heart rates than did the non-beta-blocker cardiac group. However, no significant differences ($p>.05$) were noted between any of the groups in rating of perceived exertion at peak exercise.

Insert Figure 2 about here

Submaximal Exercise Responses. Figure 2 also contains the submaximal end-stage $\dot{V}O_2$, $\dot{V}$, HR and RER results for Stage IV (3 $m \cdot h^{-1}$/10% grade). Stage IV was chosen for comparison due to the fact that it was the only stage in which a full 3 minute performance was completed by all subjects. Again, the AH group demonstrated significantly higher ($p<.01$) $\dot{V}O_2$, $\dot{V}$ and heart rate values over the two cardiac groups similar to peak exercise, with no differences between the two cardiac groups in $\dot{V}O_2$ and $\dot{V}$ ($p>.05$). The beta-blocker cardiac group again exhibited significantly ($p<.01$) lower heart rates at Stage IV than did the C-NBB group which in turn had significantly ($p<.01$) lower heart rates than the AH group. Submaximal RER results showed that the C-NBB group experienced a significantly ($p<.05$) higher RER than the AH group; however, the C-BB group was not significantly ($p>.05$) different from either the C-NBB or AH groups. No significant ($p>.05$) differences were noted between the three groups in RPE. End-stage $\dot{V}O_2$ values for each group were converted to fractions of peak $\dot{V}O_2$ and found to be 86.1% for the C-NBB group; 75.08% for the C-BB group; and 71.28% for the AH group, with the C-NBB group significantly higher ($p<.05$) than both the AH and C-BB groups.

Regression Analysis. Step-wise linear regression was utilized to develop a prediction equation for $\dot{V}O_2max$ for each of the groups examined. The significant predictors

identified were: highest treadmill grade achieved and age for C-BB ($p<.10$); highest treadmill grade achieved and age for C-NBB ($p<.05$); and body fat, grade, and body weight for AH ($p<.05$). Multiple correlations between $\dot{V}O_2max$ and the sets of predictors for each of these groups were r=.71, r=.80, r=.92, respectively. Regression analysis across groups revealed a multiple correlation of r=.77 for the predictor variables. The resulting prediction equation was: $\dot{V}O_2max = 1.047\ (gr) - .2747\ (age) - .132\ (bwt) + 24.587\ (sp) + 36.69$.

DISCUSSION

In this study cardiac patients receiving beta-blockers do not differ significantly from their non-medicated counterparts in response to exercise testing. Moreover, physically active cardiac patients as a group exhibit significantly lower cardiorespiratory exercise responses in treadmill testing than healthy adults. The higher $\dot{V}O_2$ values noted for the AH group both at peak and submaximal levels are consistent with previous research[11,12] demonstrating lower O_2 uptake values for cardiacs vs normals when performing equivalent exercise.

Presently, no literature exists comparing $\dot{V}O_2$ responses in treadmill testing for cardiac patients receiving beta-blockers and those not on beta-blocker medications. Here, comparisons of the ventilatory, gas exchange, and aerobic

capacity between these two groups indicated no differences at stages demanding the same energy expenditure. These data suggest that beta-blocker therapy does not hinder the cardiac patient's cardiovascular response to exercise any more than does the disease process itself. This is a question recently posed, but as yet unanswered by other researchers[1]. One important limitation in such a comparison, however, is the fact that it is often difficult in many clinical studies to precisely define the type and extent of coronary disease among patient comparison groups as well as to accurately determine the type and dosage of the cardio-active medication. This potential inequity, in turn, makes it nearly impossible to compare exercise results among groups of cardiac subjects. For instance, the cardiac populations in this study were quite variant in their medication types, dosages, and disease etiology. Various attempts by other researchers[10,19,21] to label "diseased" populations have resulted in often mixed labeling of patient groups and, probably, contributed to their equivocal findings.

The major thrust of this investigation was to determine whether increased stage duration could maximize $\dot{V}O_2$ responses for cardiacs, especially those taking beta-blockers, whereby they could achieve higher end-stage $\dot{V}O_2$ and possibly attain higher peak exercise $\dot{V}O_2$ values. In

this study , extending the stage duration to three minutes vs two did not provide a significant increase in $\dot{V}O_2$ for any of the groups. These results suggest that any CAD- or drug-induced suppression of circulatory dynamics that may have affected the C-BB or C-NBB groups here were not sufficient to reduce the $\dot{V}O_2$ response. It is possible that the sample group tested here represent a subset with the least impairment, disease and/or left-ventricular damage since they are healthy enough to participate in a cardiovascular maintenance program (i.e., achieving ≥ 5 METs capacity). Lack of uniform effects in these patients with respect to drug type and dosage and actual extent of left ventricular impairment prevent any firm conclusions on these matters.

The $\dot{V}O_2$ values did show a tendency to increase for all groups by the 3rd minute of the stage, perhaps raising some doubt as to whether a leveling of the $\dot{V}O_2$ response was achieved. Wasserman and associates[22] have found that 4-10 minutes of exercise at a constant submaximal rate is needed (depending on exercise intensity) before a steady-state VO_2 is achieved. If this is the case, obtaining an exercise steady-state in each submaximal stage and a true maximal oxygen uptake within the time frame of a single clinical treadmill test would appear to be mutually exclusive. Indeed, Hansen[23] and Buchfurer[24] et al. have recommended that a total test duration of between 8-12 minutes is

necessary for obtaining treatment-relevant data while preventing undue fatigue and stress for the patient. Hence, from their[23,24] conclusions and the findings here, stage durations of greater than 2 minutes appear to be superfluous.

Although the peak exercise capacity results obtained here are consistent with the available literature[5-10] that demonstrates lower absolute $\dot{V}O_2$max capacity for cardiac diseased individuals, the present data do not completely support the published research[19,21,25] which suggests that accommodation time during exercise is crucial to obtaining valid data. Indeed, Zohman and associates[19] reported no differences in $\dot{V}O_2$ between cardiacs and healthy counterparts at submaximal exercise stages when a 3 minute stage protocol was used. The results reported herein, however, indicated that the healthy subjects were consistently higher than cardiacs in $\dot{V}O_2$ at all time intervals, regardless of stage. However, subject groups of Zohman[19] et al. demonstrated great homogeneity of response, with little variation in mean $\dot{V}O_2$ values (at 3/10%, SEM values ranged between = ± 1.05 to ± 1.0 $ml \cdot kg^{-1} \cdot min^{-1}$). As data in Figure 1 indicate, the AH and C-BB subjects in this study evidenced a much wider range of variability at that stage and at max stage, indicating that perhaps the third minute is of consequence for certain subjects.

Other Exercise Responses.

Attained heart rates were significantly different between all three groups tested (AH>C-NBB>C-BB). This finding was expected and consistent with the available literature[26-28] describing the blunting effects of beta-blocking drugs on heart rate and the reduced chronotropic capacity of cardiac patients during exercise testing.

Comparative results for groups for peak and submaximal ventilation were similar to those of $\dot{V}O_2$max, indicating that the reduced exercise capacity of cardiacs is related to but not necessary caused by a reduced pulmonary ventilation.

No significant differences ($p>.05$) between the three groups were noted here in RPE at test termination or at Stage IV, with the mean RPE test endpoint at 16 for all subjects. Although this finding is lower than the typical ceiling values of 19 or greater reported by other investigators[29,30] testing similar subject groups, other criteria (i.e., peak RER and HLa) indicated that subjects exercised to maximal endpoint.

Results of the two peak indices of anaerobiosis appear, at first consideration, to be incongruous. The post exercise blood lactic acid of the AH group was significantly higher than the two cardiac groups, while no differences in respiratory exchange ratio between the three groups were found. These results are in agreement with the values

reported by Sullivan and McKirnan[9] who compared similar groups of normals and post-MI patients. Although blood lactate values in this study were significantly lower for cardiacs, all groups showed evidence of substantial anaerobiosis as reflected in the $\dot{V}CO_2$ in excess of $\dot{V}O_2$ (RER $\geq$ 1.1). The differences across groups in lactate may reflect the varying abilities of subjects to recruit fast twitch motor units in later test stages (where anaerobic demands are increasing) and a reduced ability to promote lactate removal from the circulating blood pool. Furthermore, the lower peak lactate values observed in the cardiac group may simply be a reflection of deconditioning rather than impaired circulatory adjustment. The significantly higher submaximal RER noted for the C-NBB subjects as compared to the AH group supports the findings of Sullivan and McKirnan[9] who observed significantly higher submaximal RER's in post-MI patients vs normals.

Chalmers and associates[31] noted that cardiac subjects demonstrated the earlier appearance of an anaerobic metabolic state relative to workload experienced when compared to normals. The authors[31] have suggested that this metabolic state is a reflection of the severity of cardiac impairment. The results reported here are conflicting. The cardiacs on beta-blocker medication demonstrated RER's at submaximal exercise similar to the AH subjects, while the C-

NBB group was signifantly higher. Furthermore, the C-NBB group was exercising at a significantly higher percentage of $\dot{V}O_2$max (85%) than either the AH (71%) or C-BB (75%). Since submaximal lactate samples were not obtained and the groups were not exercising at equivalent intensities, inferences cannot be drawn about degree of anaerobiosis. Recent research[32,33] suggests that the presence of beta-blockade suppresses glycolysis as well as promotes lactate accumulation within the exercising tissues, possibly explaining the C-BB group exhibiting submaximal RER's similar to the AH group.

Prediction Equations for Peak $\dot{V}O_2$.

Multiple correlation coefficients between $\dot{V}O_2$ and sets of various predictor variables observed in this study were no more precise than previously developed equations[4,5,20]. The results of recent investigations[17,18,34] evaluating VO_2 prediction have utilized different test protocols, different predictor variables and although yielding higher multiple correlation coefficients, recommended non-linear regression models. Moreover, those protocols (i.e., Bruce) were designed with relatively greater metabolic increments between stages likely producing the non-linear response curve[17]. This study confirms earlier reports[9,35,36] revealing the presence of prediction error for CHD patients. For all practical purposes, such prediction equations here are best

utilized only with the populations from which they were developed. The small sample size of this investigation makes generalizability of the equations herein improbable and likely contributes signficantly to the error variance associated with the correlations. In recent years, the error variance for predicting oxygen uptake in cardiacs has not been much improved over the currently identified ±20% range[25]. Overestimation of functional capacity thus provides an inaccurate foundation for certain safety-related clinical decisions, e.g., exercise prescriptions at an excessive intensity. The error variance associated with the equations developed here (24.3% for cardiacs; 40% across all groups) serve only to emphasize the implications of such decisions. Consequently, direct measurement of exercise $\dot{V}O_2$ data is still recommended whenever possible and if not available, extreme caution is advised when determining exercise prescriptions for cardiacs based on predictions of functional capacity from graded exercise tests.

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Table and Figure Captions

Table 1. Descriptive Data for Subjects

Figure 1. Dynamics of mean, maximal and submaximal $\dot{V}O_2$ values across stage time for all groups.

Figure 2. Mean values for groups at maximal test end point and end-stage submaximal Stage IV.

* denotes mean scores significantly different from each other at the .05 level; + denotes mean scores significantly different from each other at the .05 level.

TABLE I

PHYSICAL CHARACTERISTICS OF SUBJECTS*

	Experimental Group			
Variable	AH	C-NBB	C-BB	Total
N	8	8	10	26
Age (yr)	47.8 ± 9.9	60.4 ±6.3	55.6 ± 8.2	55.7 ± 9.0
Wt (kg)	88.8 ±13.5	80.6 ±8.4	93.3 ±20.3	87.0 ±14.9
B Fat (%)	21.4 ± 4.9	19.9 ±5.6	22.2 ± 4.3	21.1 ± 4.9

* Values are means ± standard deviations.
N = number of subjects; WT = weight; BFat = predicted body fat (based on Skinfold equations).

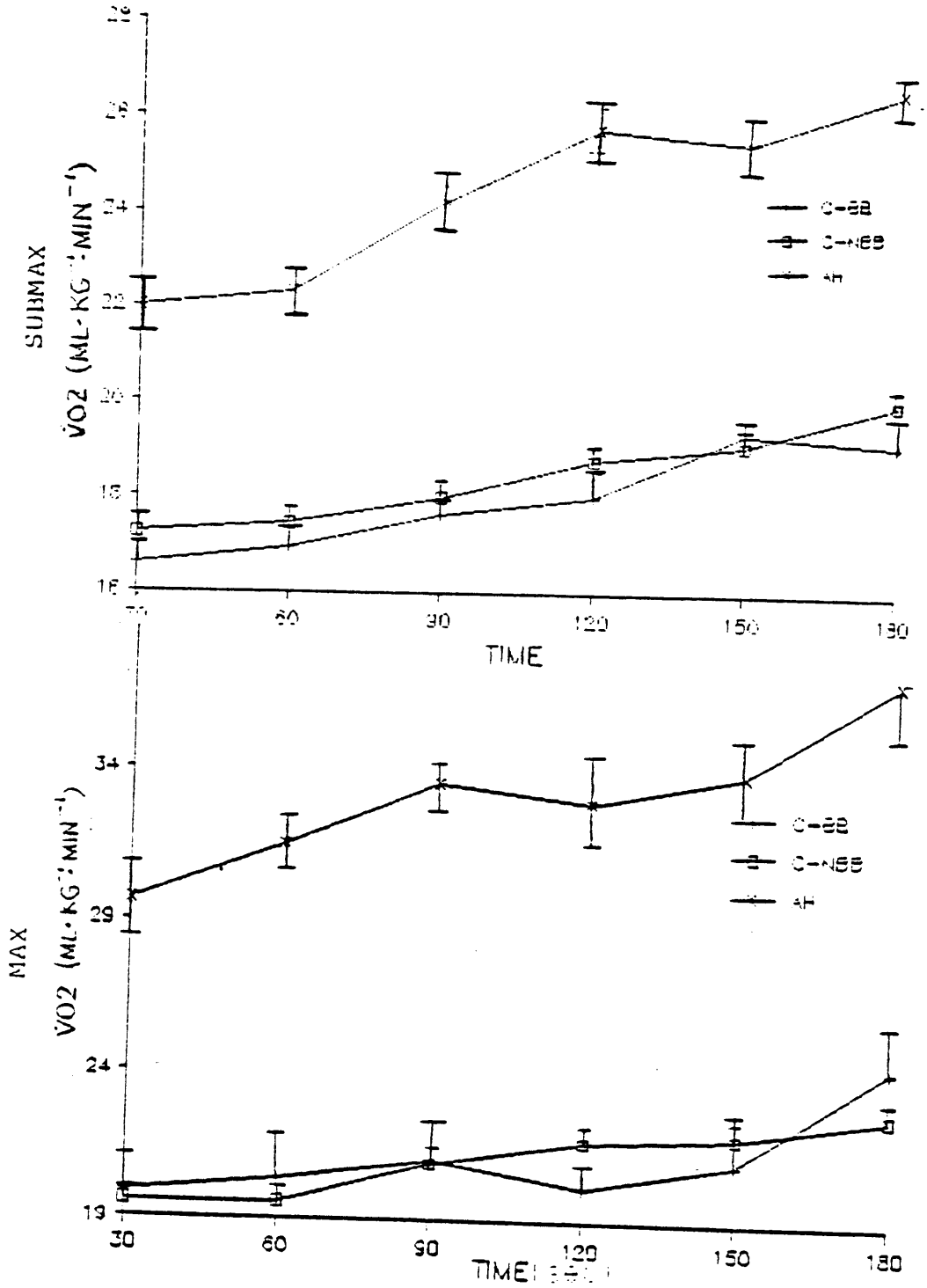
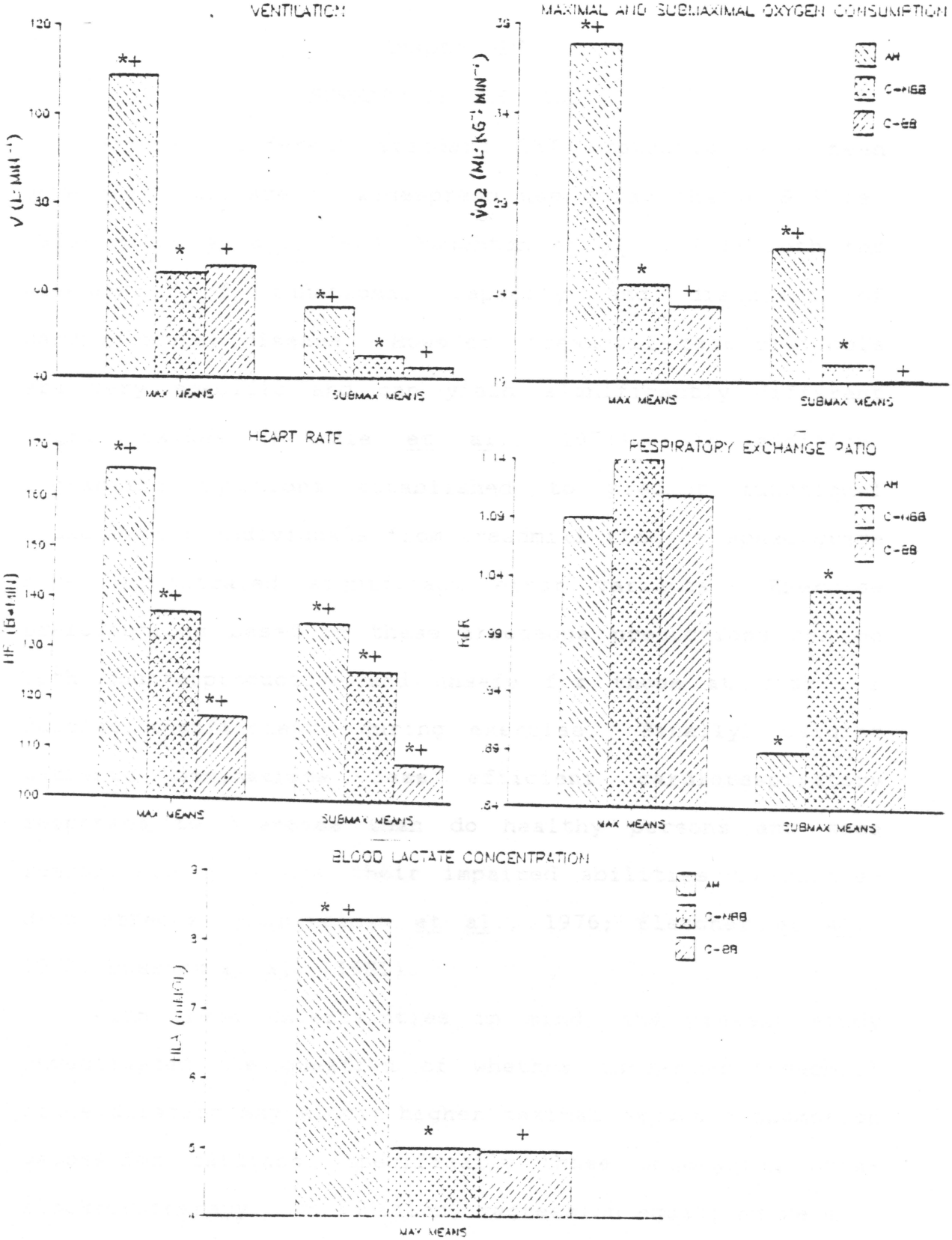


FIGURE 1. Mean $\dot{V}O_2$ values across time for submaximal and maximal exercise.


VENTILATION
MAXIMAL AND SUBMAXIMAL OXYGEN CONSUMPTION
HEART RATE
RESPIRATORY EXCHANGE RATIO
BLOOD LACTATE CONCENTRATION
AM
C-NBB
C-BB
MAX MEANS
SUBMAX MEANS

Chapter IV

SUMMARY OF THE STUDY

Several different standard GXT protocols have been developed that are in widespread use today (Balke & Ware, 1959; Bruce et al., 1963; Naughton et al., 1973) both for assessment of functional capacity and diagnosis of cardiovascular disease. However, treadmill test protocols are very specific and can yield significantly different $\dot{V}O_2max$ values (McArdle et al., 1973). In addition, regression equations established to predict functional capacity for individuals from treadmill time or speed/grade have demonstrated significant error variance. Exercise prescriptions based on these erroneous predictions can be both counterproductive and unsafe for those at risk for cardiac insufficiency during exercise. Finally, cardiac patients demonstrate less efficient cardiorespiratory responses to exercise than do healthy persons and some researchers attribute their impaired abilities to cardiac drug effects (Auchincloss et al., 1976; Fletcher et al., 1979; Hossack et al., 1981).

With these uncertainties in mind, the present study investigated the question of whether increased treadmill stage duration may elicit higher maximal oxygen consumption values for cardiacs, specifically those undergoing beta-blockade therapy. In addition, regression equations were

developed to determine whether more accurate prediction criteria for $\dot{V}O_2$ than those currently available could be obtained.

Twenty-six male participants (ages 37-66 years) in a cardiac rehabilitation/intervention program were divided into three groups according to medical diagnosis: cardiac-medication (beta-blocker); cardiac-no beta-blocker medication; and apparently healthy. Each subject completed a maximal Balke graded exercise test protocol modified to include three minute stages during a routine program evaluation. Submaximal and maximal oxygen consumption values were recorded at 30 second intervals within each stage and compared for differences across the three groups. Additionally, between group comparisons were made for $\dot{V}$, heart rate, RPE, % $FECO_2$, % $FECO_2$, and RER at one submaximal stage and at the final stage. Immediate post-exercise blood lactates were also analyzed.

Conclusions

Based upon the findings of this study, the following conclusions are drawn:

1) The index of $\dot{V}O_2$max obtained resulted in significantly higher maximal values for apparently healthy individuals over cardiac-diseased individuals, regardless of medication status.

2) This difference in maximal attained $\dot{V}O_2$ was apparent

at all 30 second time intervals compared during the max stage for each subject group.

3) The index of submaximal final minute $\dot{V}O_2$ for Stage IV (3/10%) resulted in a significantly higher value for the AH group across all six 30 second time intervals of the stage.

4) Both at maximal and submaximal exercise stages, the ventilation of subjects rather than fractions of expired gases appeared to be the significant factor in higher attained $\dot{V}O_2$ values for AH versus cardiac subjects.

5) Under the presently used protocol, regardless of maximal or submaximal stage time, 2 minute stage durations appear to be sufficient for producing an accommodation to shift in the load of exercise. However, mean $\dot{V}O_2$ scores did have a tendency to increase with the 3rd minute of exercise producing significantly higher $\dot{V}O_2$ values over the first minute and preventing firm conclusions regarding steady-state $\dot{V}O_2$.

6) At submaximal exercise loads only the C-NBB group evidenced significantly higher values than AH subjects on the index of respiratory exchange ratio (RER). This result indicated that although cardiac patients do experience a greater degree of anaerobic metabolism for the same relative exercise load as normals, those undergoing beta-blockade treatment experience suppressed glycolytic activity and

hence exhibit RER values similar to normals.

7) The modified Balke treadmill protocol utilized did not present a useful regression equation for predicting VO_2max in the groups tested.

Recommendations for Cardiac Rehabilitation Practitioners

1) Results of this study indicated that cardiac subjects exhibited exercise response parameters similar to normal subjects but at lower absolute levels. Consequently, administration of a lower-level exercise test (i.e., load increments) is recommended for achieving optimal and safe test data in cardiac patients.

2) Results of the regression analysis of this data indicated that peak $\dot{V}O_2$ estimation is inappropriate. It is recommended that, when at all possible, testing laboratories use direct measurement of gas analysis to determine functional capacity in patients.

3) Although two-minute stage durations appeared to be sufficient for producing appropriate oxygen uptake values during the testing protocol used here, stage increments were small (<1 MET). Consequently, it is further emphasized that testing practitioners maintain slower test increment intensities in all types of protocols either through accommodation time or load to insure accurate results and to present overestimation of functional capacity.

4) It is recommended that cardiac rehabilitation

practitioners use extreme precaution when determining exercise prescription from testing data where functional capacity is estimated; overestimation and patient activity capabilities is a concern that rehabilitation practitioners can ill-afford to ignore.

Recommendations for Future Research

The following recommendations are made for future investigations:

1) One unanswered question in this investigation, especially in light of conflicting reports of others, was whether extension of stage duration resulted in accommodation to steady-state for subjects within submaximal stages. A similar study using identical protocols for AH and cardiacs and/or three minute stage durations throughout the entire test may provide more meaningful information on the $\dot{V}O_2$ kinetics of cardiac patients during exercise testing.

2) A similar study could be conducted with blood lactate measured at each stage to obtain a more conclusive understanding of the metabolic changes that occur with exercise between cardiacs receiving beta-blockers and those not on the medication. Although there were differences between the two groups at submaximal exercise in the RER, insufficient information was derived to allow conclusive judgments. Additionally, an investigation examining the

types of beta-blocker drugs used by patients could possibly help provide an even clearer understanding of the metabolic processes present in cardiacs in exercise.

3) Researchers in the field of exercise testing have questioned but not investigated thoroughly the effects of cardiodynamic medications on gas exchange during maximal and submaximal exercise. A follow-up investigation to determine whether cardiacs show changes with serial testing in the observed parameters under the protocol used here would be most appropriate to help shed light on these questions.

4) A follow-up study could also be performed to establish reliability of the protocol procedure used here and to provide a larger sampling base for the development of more accurate regression equations for $\dot{V}O_2max$ prediction in the populations studied.

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APPENDIX A

DETAILED METHODOLOGY AND DATA ANALYSIS

APPENDIX A

METHODOLOGY

Subject Screening and Selection Procedures

Twenty-six males between 37 and 66 years of age from the Virginia Tech Cardiac Therapy and Intervention Center served as subjects in this study. Subjects were recruited for the experiment during their annual or bi-annual graded exercise test (GXT) evaluation. Each subject had received at least one previous GXT in the Virginia Tech Laboratory for Exercise, Sport and Work Physiology and were familiar with testing procedures; each subject had participated in the Cardiac & Intervention program for at least 6 months.

All subjects were screened for experimental participation prior to their scheduled GXT. The subjects were assigned to one of three groups on the basis of pre-existing characteristics: cardiac/cardiodynamic medication; cardiac/no medication; or apparently healthy/no medication. The cardiac groups were identified as having previously been diagnosed with heart disease, be it myocardial infarction, coronary artery disease, or coronary bypass graft recipients as indicated by the American College of Sports Medicine Guidelines for Exercise Testing and Prescription (ACSM, 1986). Those identified as "cardiac/medication" were receiving beta-blockade drug therapy (propranolol, atenolol or timolol); those identified as "cardiac/no medication"

were receiving no beta-blockade agents. The presence of other cardiac medications were not considered for selection of experimental inclusion. "Apparently healthy" participants were identified according to standards as set forth by the American College of Sports Medicine (1986) and were asymptomatic, active persons with no known heart disease, but possessing at least one major risk factor for coronary artery disease.

All subjects were screened prior to testing for contraindications to exercise using resting blood pressure, electrocardiographic and other clinical criteria again as set forth by ACSM (1986). Descriptive data for subjects are contained in Appendix B. Prior to administration of the graded exercise test, each subject was informed of the inherent risks of the test, and each signed a written informed consent (Appendix C) acknowledging their voluntary participation in the study. Experimental procedures were reviewed and approved by the Human Subject's Committee of Virginia Polytechnic Institute and State University.

GENERAL METHOD

Instructional Procedures

Subjects were advised of the GXT protocol procedures and data measurements to be collected prior to their test session. All subjects were familiarized with the treadmill and use of respiratory collection apparatus. Prior to the

test, each subject's height, weight and body fat were recorded and procedures of the stress test were reviewed. Subjects were then informed of the requirement for venous blood lactate samples to be drawn at fingertip immediately post-exercise and each gave written informed consent for the procedure (Appendix C).

Selection of Criterion Score

The dependent measures selected for this study were individual submaximal ($\dot{V}O_2$) and maximal oxygen uptake ($\dot{V}O_2max$) as determined from pulmonary ventilation ($\dot{V}$) and expired respiratory gases (FEO_2, $FECO_2$) directly measured from subjects during the exercise tests. Other measurements recorded during the tests were: heart rate (HR); indirect blood pressure (BP; auscultation); subjective rate of perceived exertion (RPE); and the respiratory exchange ratio (RER). At 2 minutes post-exercise, blood lactate (HLa) samples were obtained via the finger-tip for rapid lactate analysis.

Experimental Procedures

Graded exercise tests were administered to all subjects during their regularly scheduled laboratory assessment as per participation in the Cardiac Therapy/Intervention Program at Virginia Tech. Prior to being tested, each subject was weighed and completed a brief questionnaire to ensure that no contraindications for participation in the

study was present (Appendix D).

Treadmill Protocol

Quinton treadmill models 24-72 and Q-55 were utilized for the graded exercise tests. A modified Balke protocol was used for all subjects: the first two stages of the protocol were considered warm-up stages and differed for the two subgroups of subjects "apparently healthy" and "cardiac." Apparently healthy subjects exercised for 1 minute in the 1st stage at 3.0 $m \cdot h^{-1}$/0% grade, while all cardiac subjects exercised at 2.0/0% grade for 1 minute 1st stage. AH subjects were advanced to a 2nd stage of 3.0/5% for 1 minute duration; cardiacs were advanced to 3.0/2.5%, 1 minute duration. Beginning with the third stage and through the end of the test, the speed/grade increments were the same for all groups. Appendix E contains the sample treadmill protocol increments utilized.

Duration of the stages were 2 minutes until predetermined criteria for stage extension to 3 minutes were met. These criteria included: a subjective RPE of ≥ 9 and a heart rate of $\geq$ 40% of the exercise heart rate reserve (HRr) as determined from each subject's previous GXT. Once a stage was extended to 3 minutes, every subsequent stage was likewise 3 minutes in duration. All subjects exercised to symptom-limited maximum levels and were supervised by a physician.

Several justifications exist for the protocol design. Three minute stage durations were not utilized for the entire test to prevent overly lengthy test durations for patients (i.e., the more fit patients) and to thus prevent test termination from leg fatigue before maximal functional capacity could be reached. Most clinicians prefer test durations of 8-12 minutes (Hansen, 1985), hence, the RPE and HRr criteria for stage duration change. This criteria was set arbitrarily, but with the pragmatic intention of beginning three minute stages at an intensity low enough to be below the anaerobic threshold (at 40-60% of $\dot{V}O_2max$) for patient accommodation. The intention here would then allow complete three minute stages at exercise prescription levels (60-85% of $\dot{V}O_2max$) while keeping test length to the minimum required time length.

Warm-up stage differences between cardiacs and AH's again attempted to remain within desired exercise test length while providing cardiacs with a lower absolute intensity level for treadmill accommodation. Foster et al. in 1984 devised similar test habituation standards for cardiacs by giving them a longer warm-up period, again the purpose of which was to provide an adjustment phase to accommodate their slower oxygen kinetic abilities.

Instrumentation and Dependent Measure Techniques

Oxygen uptake was measured during the exercise tests using open circuit spirometry technique. Each subject breathed through a Daniel's low-resistance low dead-space flutter valve with noseclips to prevent air leakage. Those subjects using the Q 24-72 treadmill had ventilation measured on the inspired side using a Parkinson-Cowan dry gas meter (PC-4). The gas meter was electrically integrated with a visual display disclosing measurement to the nearest .1 liter. Subjects tested on the Q-55 treadmill had ventilation measured on the expired side using a Hewlett-Packard pneumotach, Model 47303-A. Simultaneously, gas concentrations were determined. A Beckman OM-11 system received expired air through Aquasorb absorbant on the Q24-72 treadmill system and then transferred the O_2 content through a sensor to a recorder. Similarly, on the Q-55 system, expired air was received through an Ametek S-3A pump and recorded. Carbon dioxide analysis was determined using a Beckman LB-2 display/control with an internal pump and sensor on the Q-24-72 system and similarly, an Ametek CD 3A system on the Q-55 treadmill. These processes produced visual recordings of the fractions O_2 and CO_2 gases present, as well as ventilation frequency. All ventilation and gas exchange measures were sampled continuously throughout the tests. Visual averaging (DeBoever, 1985) and recordings of

the ventilation, FEO_2, and $FECO_2$ values were recorded every 30 seconds throughout the test. The $\dot{V}O_2$ and RER values were then obtained from the data by manually entering the sampled values into a digital MINC 11 microcomputer using a software program containing formuli for determining oxygen uptake under circuit spirometry techniques.

Gas analyzers were calibrated before and after each test with standard Haldane reference gases of 16.08/5.23% and 18.58/2.60% oxygen to carbon dioxide. The pneumotachs were calibrated after each test with 100 liter volumes of air pumped from a 3.0L volumetric syringe at pre-determined flow rates. Treadmills were calibrated once every two weeks for speed ($rev \cdot min^{-1}$) and grade accuracy and once per month with a subject on the treadmill belt. Any differences noted in standard gas values pre-to-post test were utilized during metabolic calculation of the $\dot{V}O_2$; one-half of the recorded difference was added, or subtracted, as necessary to the recorded gas concentration values to correct for instrument drift during the second half of the exercise test. Treadmill speed and grade remained accurate throughout the experimental procedures (< 2% error).

Heart Rate and Blood Pressure

During each test, heart rate was recorded electrocardiographically (Hewlett-Packard 1500 B on the Q 24-72 treadmill; Quinton 2000 on the Q-55 treadmill). A

standard 12-lead clinical ECG system was employed and provided a basis for clinical monitoring by the physician, as well as calculation of resting heart rate measures and minute exercise and recovery heart rates. ECG signals were also monitored continuously on an oscilloscope.

Blood pressure recordings were taken at rest and once each stage of exercise beginning with the 2nd stage, and every 2 minutes during recovery. Rate of perceived exertion (RPE) using the Borg (1970) scale was also obtained once per stage until termination of the exercise tests. Finally, a blood lactate sample was obtained immediately post-exercise via fingertip lancet procedure. In addition to the physician, all tests were administered with the technical support of a registered nurse and an ACSM certified Exercise Specialist.

Perceived Exertion

Ratings of perceived exertion were recorded using the Borg (1970) 6-20 point scale (Appendix F). Subjects were instructed to relate the level of effort associated with the exercise stage by pointing to the number on the RPE scale which best described that effort. On the scale, a value of 6 denoted a feeling of very, very light (the lowest effort), while a value of 20 was considered a maximal effort.

Blood Lactate Determination

L-lactate assays of blood concentration were performed using a Yellow Springs Instruments Co., Inc. Model 23L automated fast-response Lactate Analyzer. A 25 ul of whole blood was obtained from the subject's fingertip, then injected by syringe pipet into a sensing chamber. The sensing chamber contained a site where both chemical and electrochemical reactions occurred. A silver-platinum electrode affixed to a 3-layer membrane containing polycarbonate, l-lactate oxidase and cellulose acetate received whole blood which then diffused through the membrane. A lactate-oxidase-lactate reaction occurred resulting in an electrical current proportional to the lactate concentration in the sample. Calibration of the lactate analyzer occurred immediately prior to, and following analysis of, each sample.

Reliability and Validity Estimates

Test-retest reliability coefficients and validity estimates were not conducted on this test protocol for practical reasons and due to the reproducibility data of the Balke protocol available from Froelicher et al. (1974). These researchers reported a coefficient of variation of 5.8 (mean $\dot{V}O_2$/sd x 100) with no significant difference in mean maximal $\dot{V}O_2$ ($p>.05$) reproduced in three test trials. Furthermore, the Balke test protocol has been recommended

for use in treadmill testing by the American Heart Association (AHA, 1979). In the present study, within stage $\dot{V}O_2$ values at minute 3 for the submaximal stage IV yielded a reliability coefficient of r=.89, SEE=1.58 $ml \cdot kg^{-1} \cdot min^{-1}$.

Statistical Procedures

Descriptive statistics, analyses of variance, multiple correlation, and step-wise linear regression under the Statistical Analysis System (SAS, 1986) computer program were utilized for statistical computations. A Spearman Rho correlation was used to estimate the reliability of VO_2 and ventilation measurements taken at submaximal stage IV (3/10%), minutes 2 and 3. Appendix G contains the reliability data obtained.

For the variables at max stage $\dot{V}O_2$ ($ml \cdot kg^{-1} \cdot min^{-1}$), $\dot{V}E$, % FEO_2, % $FECO_2$, and RER, a repeated measures two-way analysis of variance (ANOVA) procedure was utilized to determine whether any significant difference existed between the three groups of: apparently healthy (AH); cardiac/beta blocker (CBB); or cardiac/no beta-blocker (C-NBB), $p<.05$ across the 3 minutes of the stage. For submaximal stage IV (3/10) the aforementioned variables were again analyzed through the two-way repeated measures ANOVA and significant differences in mean values between the three groups across minutes of the stage ($p<.05$) were noted. Post-hoc comparison tests (Duncan multiple range) were utilized to

determine which group means were significantly different when a significant f-ratio resulted.

To determine if significant differences between the three groups in mean peak $\dot{V}O_2$, HR, RPE, RER, and lactate, a one-way analysis of variance was utilized. This same procedure also was used to analyze submaximal HR and RPE. Again, Duncan post-hoc comparison test were used to determine which group's means were significantly different, if significant ANOVAs were found. Appendix G contains the summary ANOVA tables.

Interpretation of Statistical Analyses

Review of Research Objectives

The purposes of this study were:

1) To determine differences in the peak oxygen uptake between the 3 subject groups of apparently healthy, cardiac/beta-blocker, and cardiac/no beta-blocker;

2) To determine the difference in mean minute O_2 uptake, $\dot{V}E$, RER, % FEO_2, and % $FECO_2$ values between the three groups for a maximal and submaximal exercise stage;

3) to determine whether ventilatory steady-state of cardiac groups could be attained by extending test stages to three minutes; and

4) to obtain from the administered test protocol a regression equation that accurately predicts maximal oxygen consumption for the populations studied.

Peak Exercise Variables

To accomplish the first objective of the study, maximal attained $\dot{V}O_2$ was recorded for each subject using the gas analysis procedures described earlier. Peak $\dot{V}O_2$ data were accepted as maximal if 3 of the following five criteria were met: 1) maximal attained HR not more than 5% lower than the last previous GXT; 2) a respiratory equivalent of 1.0 or greater; 3) lactate reading of 4.0 mMol or greater; 4) evidence of achieved ventilatory anaerobic threshold; 5) maximal RPE $\geq$ 15.

Of 26 subjects who participated in the study, 23 met 90% of the established criteria. Results of a one-way ANOVA indicated a significant difference between groups in mean VO_2max achieved ($F(2,25) = 12.80$, $p<.01$). A Duncan post-hoc test revealed that the apparently healthy subject group was significantly different from the two groups of cardiac patients for maximal O_2 consumption ($Qcv=6.86$, $df = 23$, $p<.05$). Similarly, maximal HR, RPE, R, and HLa were subjected to a one-way ANOVA and results indicated a significant difference between the three groups for HRmax ($F(2,25) = 12.93$, $p<.01$) and HLAmax ($F(2,25) = 11.84$, $p<.01$). No significant differences were noted between the three groups for maximal RER and RPE ($p>.05$). Duncan post-hoc comparison tests revealed that all of the groups were significantly different from each other in HRmax (Qcv =

13.90, df = 23, p<.05) with the AH group significantly greater than the C-NBB group and the C-NBB group significantly greater than the C-BB group. Only the apparently healthy group was significantly different from the two cardiac groups in HLa max (Qcv = 24.60, df = 23, p<.05). Appendix B contains the mean maximal values of $\dot{V}O_2$, HR, RPE, HLa and RER for all groups.

$\dot{V}O_2$ Dynamics within Maximal Exercise Stage

When the $\dot{V}O_2$ values within the final stage (last full stage of 3 min), were analyzed at 30 sec intervals a two-way repeated measures ANOVA revealed a significant difference between the three groups ($F(2,24) = 74.82$, $p<.01$) and a significant difference across time ($F(5,131) = 2.20$, $p<.05$). There was no significant interaction noted for group x time for mean $\dot{V}O_2$ ($F(10,126) = .21$, $p>.05$). The Duncan post-hoc test revealed that the significant difference in mean $\dot{V}O_2$ across groups was attributable to the apparently healthy group, (df = 23, p<.05). Similarly, a Duncan test across 30 sec intervals revealed that mean $\dot{V}O_2$ differed significantly between intervals 5 and 6 (minute three) vs 1 and 2 (minute one) p<.05. Figure 3 (Appendix B) contains the mean $\dot{V}O_2$ values during the max stage for each of the three groups and indicates an increase in $\dot{V}O_2$ for each interval as the stage progresses; however, this increase is significant only between minutes 1 and 3.

Ventilation Dynamics within Maximal Exercise Stage

Results of a two-way repeated measures ANOVA on mean ventilation for the max stage indicated a significant difference between the three groups ($F(2,24) = 71.93$, $p<.01$) and a significant difference across time intervals ($F(5,131) = 4.83$, $p<.01$). No significant interaction was noted for group x time, ($f(10,26) = .43$, $p>.05$). Duncan post-hoc tests demonstrated that the significant difference in mean ventilation across groups existed between the AH group and the two cardiac groups, $p<.01$. The two cardiac groups were not significantly different from each other ($p>.05$); and the difference ($p<.01$) in mean ventilation across time was between minute three (intervals 5 and 6) and minute 1 (intervals 1 and 2). None of the other intervals were significantly different from each other. Figure 4 (Appendix B) contains the mean $\dot{V}$ values for the max stage for each of the three groups.

No significant differences ($p>.05$) were noted between groups for the variables % FEO_2, % $FECO_2$ and RER during the final 3 minute exercise stage.

$\dot{V}O_2$ Dynamics at Submaximal Exercise Stage IV

To determine whether a significant difference existed in mean $\dot{V}O_2$ between the three groups for the six time intervals of submaximal stage IV, a two-way repeated measures ANOVA was conducted. An examination of the

statistical procedure yielded results similar to the max stage and indicated a significant difference between groups ($F(2,23) = 65.72$, $p<.01$) and a significant difference across the six 30 sec time intervals ($F(5,120) = 4.53$, $p<.01$). No significant interaction was noted for group x time ($F(10,120) = .28$, $p>.05$).

A Duncan post-hoc test revealed that the significant difference in $\dot{V}O_2$ between groups was again attributable to differences between the AH vs the two cardiac groups ($p<.05$). Duncan test across the 30 second intervals revealed the significant difference in $\dot{V}O_2$ was related to minute 3 (intervals 5 and 6) vs minute 1 (intervals 1 and 2) only. Figure 5 (Appendix B) contains the mean $\dot{V}O_2$ values for submaximal Stage IV for each of the three groups.

Ventilation Dynamics at Submaximal Stage IV

A two-way repeated measures ANOVA revealed a significant difference between groups in mean $\dot{V}$ ($F(2,21) = 7.32$, $p<.01$) and a significant difference across stage time ($F(5,120) = 3.37$, $p<.01$). No significant interaction was noted ($F(10,120) = .40$, $p>.05$).

Duncan post-hoc tests again revealed that the significant difference between groups existed only between the AH group vs the two cardiac groups ($p<.05$), and that significance across time occurred between intervals 4, 5, and 6 vs intervals 1 and 2 ($p<.05$). Figure 6 (Appendix B)

contains the mean $\dot{V}$ scores for submaximal stage IV for each of the three groups ($p>.05$).

Other Submaximal Exercise Variables

Again, no significant differences were noted for % FEO_2, % $FECO_2$ and RER for this stage ($p>.05$). A one-way analysis of variance indicated a significant difference between groups in mean HR ($F(2,25) = 10.90$, $p<.01$) and a two-way repeated measures ANOVA indicated a significant difference between groups in mean RER ($F(2,18) = 5.45$, $p<.05$). Duncan post hoc comparisons revealed that the AH group was significantly greater than the C-NBB group who was significantly greater than the C-BB group on HR ($Qcv = 12.70$, $df = 23$, $p<.05$) as in peak exercise. The Duncan post-hoc test revealed that the C-NBB group was significantly greater than the AH group only on RER ($Qcv = 10.21$, $df = 18$, $p<.05$); the C-BB group was not significantly different from either the C-NBB group or the AH group.

Regression Data Analyses

Results of a step-wise regression analysis within and across groups indicated several significant ($p<.075$) predictor variables for $\dot{V}O_2max$. Multiple correlation of predicted vs measured $\dot{V}O_2$ was highest in the AH group under 3 variables: body fat, maximal grade and body weight ($r=.92$, SEE=± 1.23 $ml \cdot kg^{-1} \cdot min^{-1}$). The C-NBB group was next with three significant variables: age, grade, and body

weight (r=.81, SEE=± .363). The C-BB group held only one significant variable (r=.72, SEE=± .245). The individual group regression equations of the form y=bx+c (where b = slope, x = predictor variable and c = constant) were as follows:

C-BB: $\dot{V}O_2max$ = .5606 (grade) + 14.95

C-NBB: $\dot{V}O_2max$ = -.2045 (grade) - .3059 (age) - .0272 (BWT) + 47.11

AH: $\dot{V}O_2max$ = 1.0223 (grade) - 1.0859 (bfat) - .232 (BWT) + 61.01

Analysis of predictor variables across groups produced a correlation of r=.77, SEE± 18.14 $ml \cdot kg^{-1} \cdot min^{-1}$ using grade, speed, age, and body weight. The resulting equation was:

$\dot{V}O_2max$ = 1.047 (gr) - .2747 (age) - .132 (BWT) + 24.587 (sp) - 36.69.

The variable of speed produced the extremely high standard error and should likely be eliminated as a predictor as it remained constant for all but the most fit subjects. Grade alone was the best overall predictor with a multiple correlation of r = .70, SEE = ± .291 $ml \cdot kg^{-1} \cdot min^{-1}$.

APPENDIX B

TABLE I

PHYSICAL CHARACTERISTICS OF SUBJECTS*

	Experimental Group			
Variable	AH	C-NBB	C-BB	Total
N	8	8	10	26
Age (yr)	47.8 ± 9.9	60.4 ±6.3	55.6 ± 8.2	55.7 ± 9.0
Wt (kg)	88.8 ±13.5	80.6 ±8.4	93.3 ±20.3	87.0 ±14.9
B Fat (%)	21.4 ± 4.9	19.9 ±5.6	22.2 ± 4.3	21.1 ± 4.9

* Values are means ± standard deviations.
N = number of subjects; WT = weight; BFat = predicted body fat (based on Skinfold equations).

TABLE II

CARDIOPULMONARY AND METABOLIC CHARACTERISTICS OF SUBJECTS AT MAXIMAL EXERCISE

	Experimental Group			
Variable	AH	C-NBB	C-BB	Total
N	8	10	8	26
$\dot{V}O_2max$* ($ml \cdot kg^{-1} \cdot min^{-1}$)	37.9 ± 9.4	23.3 ± 2.0	24.5 ± 6.9	28.2 ± 9.1
HRmax* ($b \cdot min^{-1}$)	165.6 ±10.9	137.3 ±20.8	116.5 ±23.7	139.6 ±27.1
RPEmax*	16.6 ± 2.0	16.5 ± 1.7	15.4 ± 4.4	16.2 ± 2.7
HLamax* (mMol)	8.3 ± 1.9	5.0 ± 1.3	5.0 ± 1.2	6.0 ± 2.1
RERmax*	1.1 ± .1	1.1 ± .1	1.1 ± .1	1.1 ± .1

*Mean±SD

$\dot{V}O_2max$ = maximal oxygen consumption; HRmax = maximal heart rate; RPEmax = maximal rate of perceived exertion; HLamax = peak blood lactic acid; RERmax = peak respiratory exchange ratio.

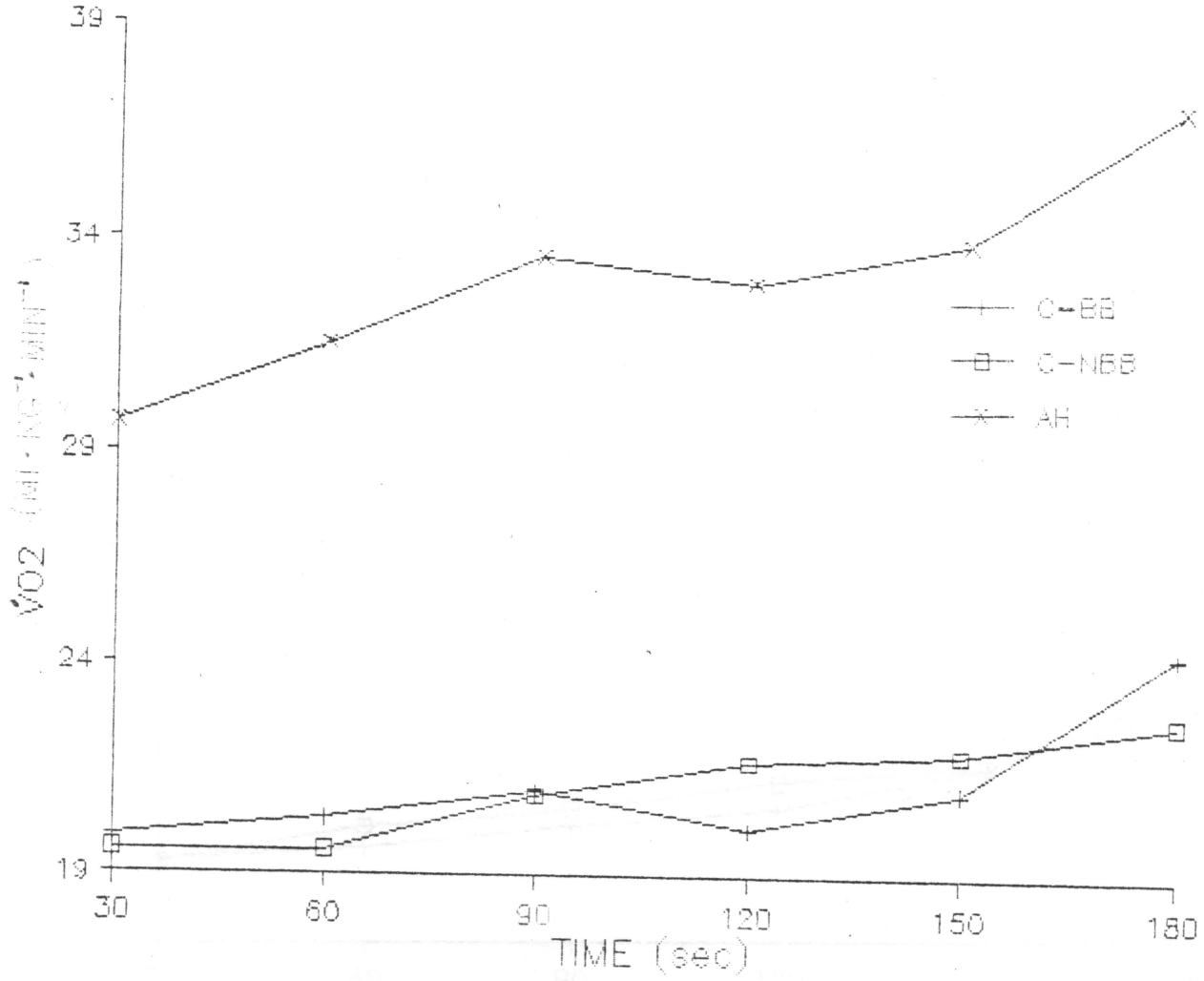

FIGURE 3

MEAN $\dot{V}O_2$ PLOTTED AGAINST TIME FOR MAXIMAL EXERCISE STAGE

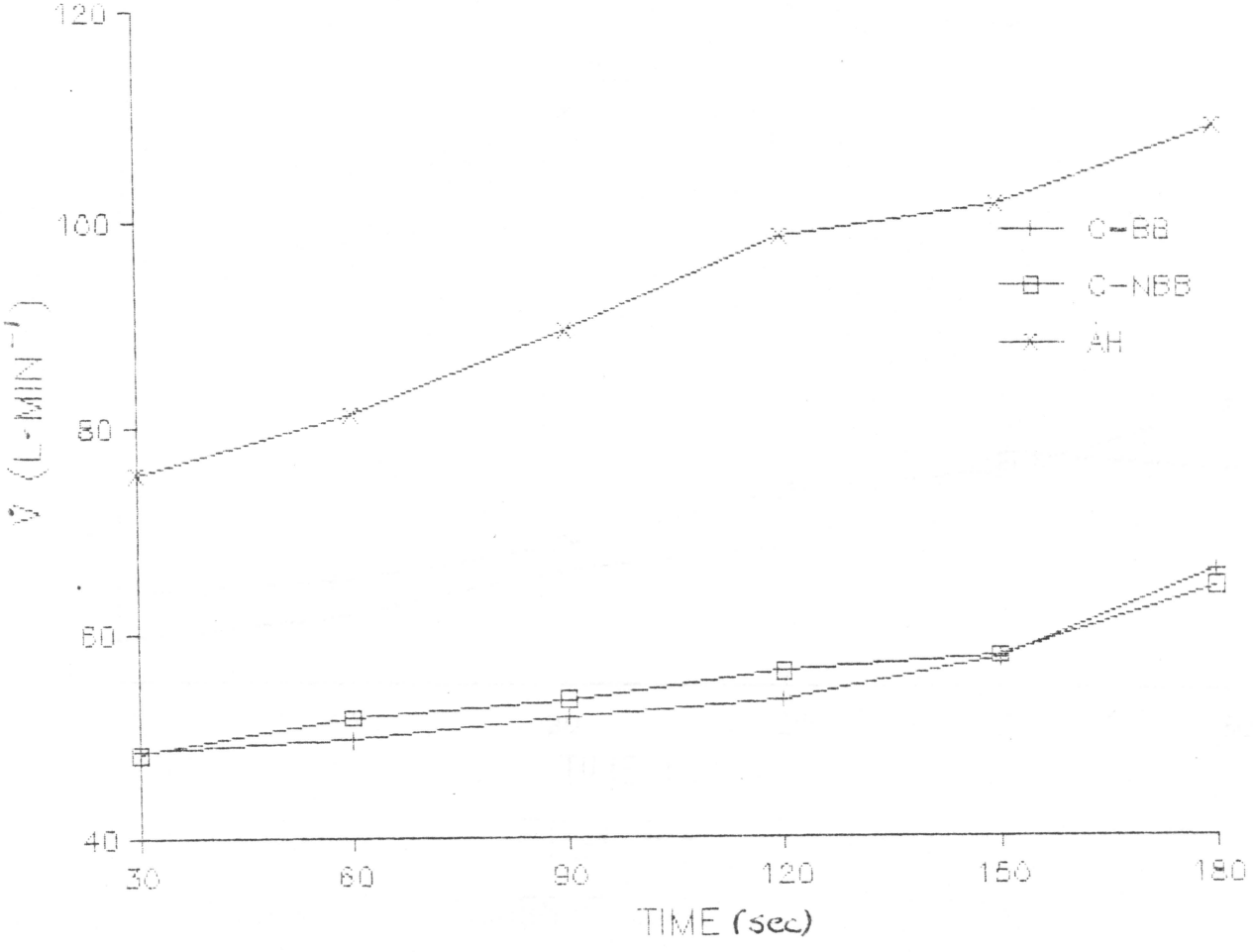

FIGURE 1

MEAN VENTILATION VALUES (V̇) PLOTTED AGAINST TIME FOR MAXIMAL EXE

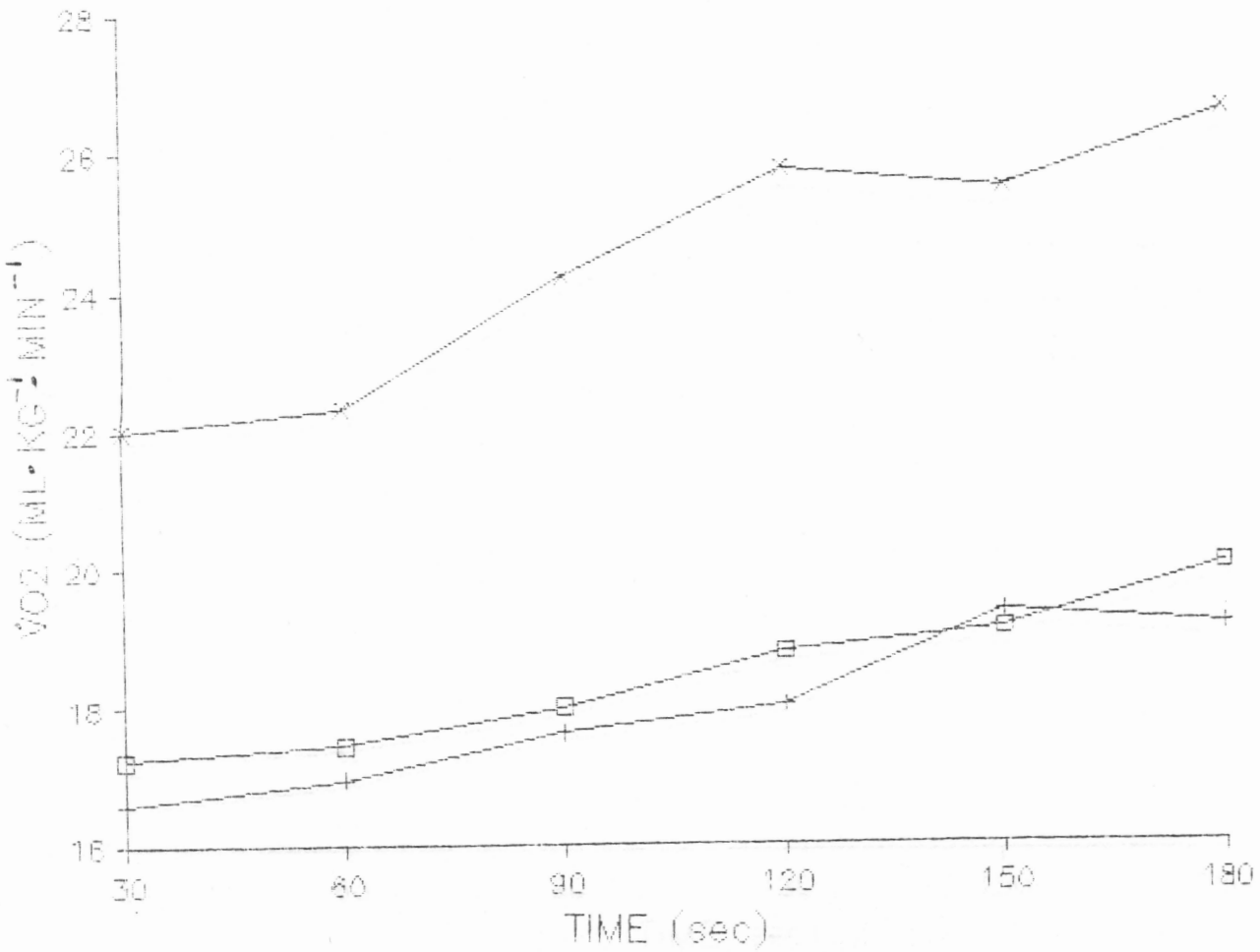

FIGURE 5

MEAN VO2 VALUES PLOTTED AGAINST TIME
FOR SUBMAXIMAL STAGE IV

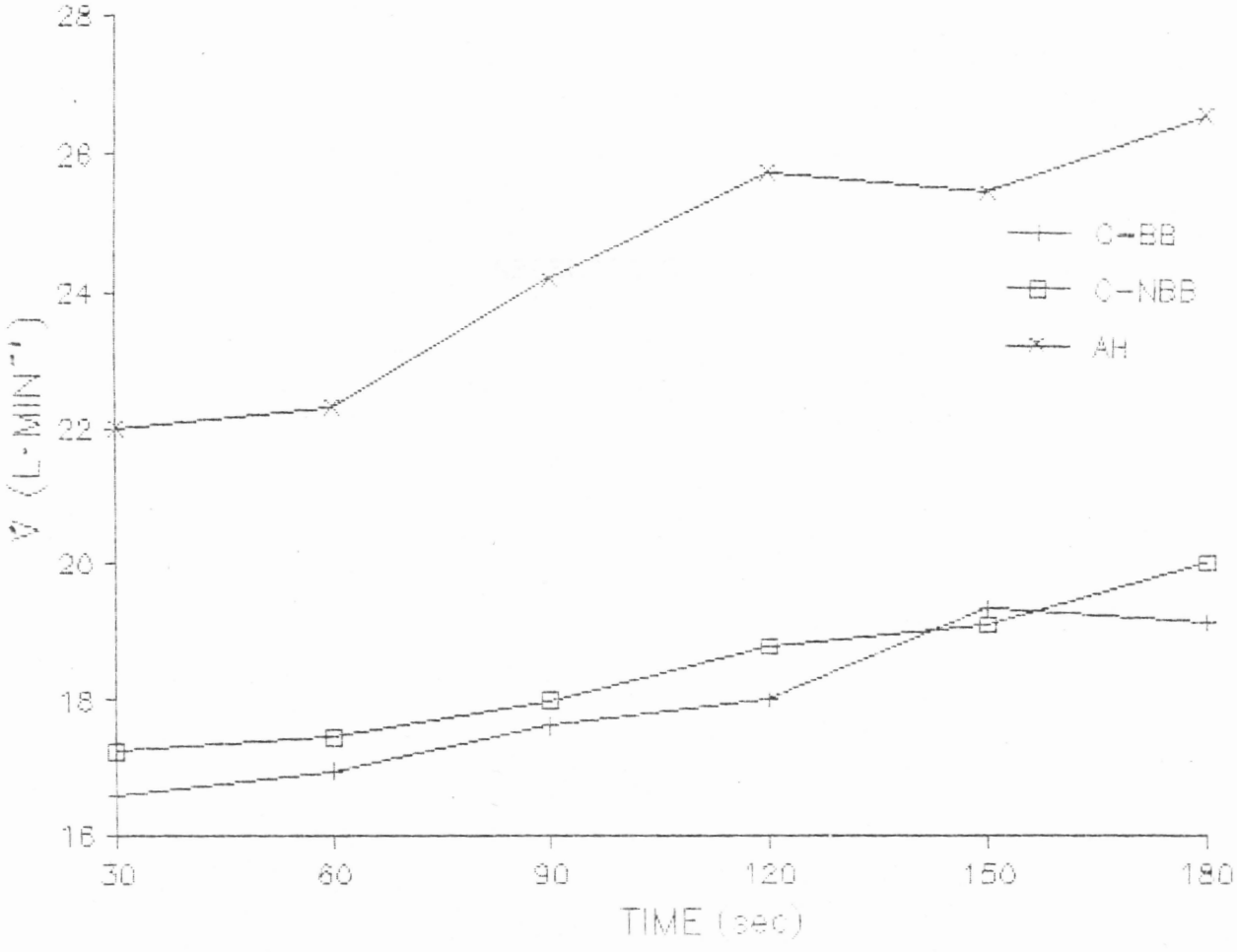

FIGURE 6

MEAN VENTILATION PLOTTED AGAINST TIME FOR SUBMAXIMAL STAGE IV

APPENDIX C

INFORMED CONSENT FOR PATIENTS WITH KNOWN HEART DISEASE

CARDIAC & INTERVENTION CENTER AT VIRGINIA TECH

1. Explanation of test and benefits to be expected

In order to determine an appropriate plan of treatment to assist in my recovery from my recent heart attack, I hereby consent to voluntarily engage in an exercise test to determine the state of my heart and circulation. I also consent to have a blood sample taken for blood chemistry analysis, to perform a lung function test and a body fat analysis, and to complete a series of stress management tests. The information thus obtained will help the program physician and staff in advising me as to the activities in which I may engage.

Before I undergo the test, I will have an interview with the physician who will review my records and determine if any condition exists that would contra-indicate the performance of the test. The test which I will undergo will be performed on a Quniton treadmill with the amount of effort increasing gradually. This increase in effort will continue until symptoms such as fatigue, shortness of breath, or chest discomfort may appear. At that point the treadmill will be slowed or stopped.

During the performance of the test, the physician or his trained observer will observe my pulse, blood pressure, and electrocardiogram. A sample of my exhaled air may be collected in order to measure oxygen consumption.

2. Risks

There exists the possibility of adverse changes occurring during the test. These could include abnormal blood pressure, fainting, disorders of heart rhythm, and very rare instances of heart attack. Every effort will be made to minimize these risks by preliminary examination and by observations during the test. Emergency equipment and trained personnel are available to deal with the unusual situations which may arise.

3. Confidentiality and Uses of Information

The information which is obtained will be treated as privileged and confidential and will not be released or revealed to any person without my express written consent. The information obtained, however, may be used for statistical or scientific purposes with my right of privacy retained.

4. Release

I hereby release Virginia Tech and all its officers, agents and employees from all liability and responsibility for any injury, illness or other similar occurrence, including heart attack or its resultant complications, which might arise out of or result from my participation in the cardiac therapy program.

5. Inquiries and freedom of consent

Any questions about the procedures used in these tests are welcome. If you have any doubts or questions, please ask for further explanation. I understand that the performance of these tests is voluntary and that I am free to withdraw from participation at any time. I have read this form and I understand the test procedures that I will perform and consent to participate in these tests.

_____ _____

Signature of participant Date

_____ _____

Witness (program staff) Physician supervising test

INFORMED CONSENT

Laboratory personnel, in an attempt to improve the quality of obtained data will be collecting additional information during your exercise test. This procedure will include the collection of a fingertip blood sample immediately following cessation of the exercise test to provide a better understanding of your reported exertion and test endpoints.

We sincerely appreciate your participation in this portion of the laboratory test procedures; please understand that any data used for research purposes will be of a confidential nature and not personally identifiable to you. Your signature below indicates your willingness to participate. Thank you again.

_____ Staff Witness

_____ Participant Signature

_____ Date

APPENDIX D

Client Pre-GXT Screening Form

Client _____ Age _____

Have you fasted for 12 hours? _____

Have you taken your medication(s) this morning? _____

What medication do you take? _____

_____

Have you been exercising regularly? (type, frequency, duration) _____

_____

Have you experienced any problems while exercising? (breathing, chest pain, dizziness, joints) _____

_____

Do you presently have orthopedic problems? _____

Have you had orthopedic problems in the past or orthopedic surgery performed? ___

_____

Have you been sick recently? (explain)_____

_____

Is there anything you wish to tell or ask the physician? _____

_____

Do you smoke or use tobacco products? _____

If yes, what type/brand? _____

If cigarette smoker, average number smoked/day _____

number cigarettes smoked today _____

time elapsed since you smoked last _____

Physician(s) to whom you wish medical records sent (other than referring physician):

M.D. name _____

Address _____

_____

APPENDIX E

Modified Balke Testing Protocol

Group	Stage	mph	% grade	min
AH	1	3	0	1
	2	3	5.0	1
	3	3	7.5	2-3
	4	3	10.0	2-3
	5	3	12.5	2-3
	6	3	15.0	2-3
	7	3	17.5	3
		.	.	.
		.	.	.
Cardiac	1	2	0	1
	2	3	0	1
	3	3	7.5	2-3
	4	3	10.0	2-3
	5	3	12.5	2-3
	6	3	15.0	3
		.	.	.
		.	.	.

APPENDIX F

15 Point RPE Scale*

6	
7	VERY, VERY LIGHT
8	
9	VERY LIGHT
10	
11	FAIRLY LIGHT
12	
13	SOMEWHAT HARD
14	
15	HARD
16	
17	VERY HARD
18	
19	VERY, VERY HARD
20	

*Borg Scale

APPENDIX G

TABLE III

SPEARMAN RHO RELIABILITY ESTIMATES FOR $\dot{V}O_2$ AND VENTILATION AT SUBMAXIMAL EXERCISE STAGE IV

	Minute 2 (Intervals 3 and 4)	Minute 3 (Intervals 5 and 6)
$\dot{V}O_2$	.75*	.89*
Ventilation	.96*	.97*

* $p < .01$

Table IV

One-Way Analysis of Variance Between Groups for Peak $\dot{V}O_2$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE
MODEL	2	1096.1275	548.063	12.80*
ERROR	23	985.146	42.832	
CORRECTED TOTAL	25	2081.274		

* $p<.01$

Table V

One-Way Analysis of Variance Between Groups for Peak Heart Rate

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE
MODEL	2	9740.178	4870.089	12.93 *
ERROR	23	8663.975	376.694	
CORRECTED TOTAL	25	18404.153		

* $p<.01$

Table VI

One-Way Analysis of Variance Between Groups for Peak Blood Lactic Acid

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE
MODEL	2	52.162	26.081	11.84 *
ERROR	19	41.845	2.202	
CORRECTED TOTAL	21	94.007		

* $p<.05$

Table VII

One-Way Analysis of Variance Between Groups for Peak Respiratory Exchange Ratio

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE
MODEL	2	0.011	0.005	0.45
ERROR	23	0.299	0.013	
CORRECTED TOTAL	25	0.310		

$p>.05$

Table VIII

One-Way Analysis of Variance Between Groups for Peak RPE

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE
MODEL	2	6.470	3.235	0.42
ERROR	22	170.089	7.731	
CORRECTED TOTAL	24	176.560		

$p>.05$

Table IX

Two-Way Repeated Measures ANOVA for $\dot{V}O_2$
Between Groups Across Maximal Exercise Stage

Source	DF	SS	F
Time	5	354.066	2.20**
Group	2	4785.57	74.82*
Group x Time	10	66.745	.21+
Error	126	415.055	
Corrected Total	131	5621.436	

* $p<.01$
** $p<.05$
\+ $p>.05$

Table X

Two-Way Repeated Measures ANOVA for $\dot{V}$
Between Groups Across Maximal Exercise Stage

Source	DF	SS	F
Time	5	1341.615	4.83*
Group	2	4318.041	71.93*
Time x Group	10	48.874	.43+
Error	126	2982.901	
Corrected Total	131	8691.431	

*p<.01
+p>.05

Table XI

Two-Way Repeated Measures ANOVA for $\dot{V}O_2$
Between Groups Across Submaximal Stage IV

Source	DF	SS	F
Time	5	195.448	4.53*
Group	2	1184.336	65.72*
Time x Group	10	24.866	.28+
Error	120	164.81	
Corrected Total	137	1569.46	

* $p<.01$
+ $p>.05$

Table XII

Two-Way Repeated Measures ANOVA for $\dot{V}$
Between Groups Across Submaximal Stage IV

SOURCE	DF	TYPE I SS	F VALUE
TIME	5	2135.90	3.37 *
GROUP	2	1855.671	7.32 *
TIME*GROUP	10	507.819	0.40 +
ERROR	120	15215.739	
CORRECTED TOTAL	137	19715.134	

* $p<.01$
+ $p>.05$

APPENDIX H

Descriptive and Peak Exercise Raw Data for All Subjects

OBS	GROUP	AGE	BWT	BFAT	HLA	VOMAX	RMAX	RPES	HRS	RPEF	HRF	RPEM	HRM	SP	GRADE
1	1	47	87.5	21.3	6.2	25.77	1.19	17	100	13	90	19	125	3.0	12.5
2	1	43	132.5	29.2	5.8	16.26	1.20	.	.	9	83	9	83	3.0	7.5
3	1	54	106.1	24.1	4.6	24.86	1.14	12	129	10	115	19	140	3.0	12.5
4	1	65	89.3	19.7	.	18.55	1.07	11	68	10	64	11	84	3.0	15.0
5	1	51	79.8	21.9	6.2	38.20	1.14	11	123	9	98	17	150	.	.
6	1	62	77.5	14.3	3.2	28.76	1.06	13	100	1	94	20	115	3.0	25.0
7	1	62	104.5	24.7	4.8	23.19	0.90	13	115	11	96	13	115	3.0	12.5
8	1	60	69.5	22.2	3.9	20.51	1.15	.	120	15	103	.	120	3.0	10.0
9	2	52	92.0	31.8	5.6	25.00	1.17	14	138	11	125	15	151	3.0	17.5
10	2	66	79.0	23.1	5.7	22.10	1.15	14	116	13	103	17	127	3.0	15.0
11	2	54	75.5	18.1	.	23.71	1.20	12	130	11	125	14	150	3.0	15.0
12	2	66	75.8	17.9	5.7	21.12	1.18	15	135	13	125	15	135	3.0	12.5
13	2	50	79.3	12.0	2.8	26.90	0.99	11	123	9	112	19	158	3.0	20.0
14	2	65	77.5	17.9	5.7	20.00	1.21	13	120	12	103	15	130	3.0	17.5
15	2	58	92.0	17.3	3.0	23.60	1.00	13	120	11	107	19	136	3.0	15.0
16	2	63	91.0	15.0	.	23.42	1.01	17	148	13	125	17	150	3.0	12.5
17	2	64	77.0	24.7	5.8	24.73	1.31	17	150	15	136	17	150	3.0	10.0
18	2	66	67.0	21.4	5.7	22.62	1.22	12	80	11	75	17	86	3.0	17.5
19	3	40	96.0	17.4	6.2	44.18	1.10	13	145	11	121	15	173	3.4	20.0
20	3	62	90.0	23.1	.	33.00	1.08	11	129	9	108	15	151	3.0	17.5
21	3	37	110.2	20.2	11.3	31.40	1.30	14	150	13	128	18	177	3.0	20.0
22	3	60	65.5	14.3	6.6	57.89	0.87	13	125	9	108	14	160	3.0	25.0
23	3	41	84.5	17.8	7.7	40.48	1.01	16	140	12	120	18	150	3.0	20.0
24	3	59	80.0	25.5	7.4	30.88	1.04	14	150	12	125	17	170	3.0	15.0
25	3	52	85.0	24.0	10.4	31.29	1.25	11	125	11	110	16	177	3.0	22.5
26	3	47	99.0	29.1	8.4	33.90	1.12	16	120	13	102	20	167	3.0	22.5

Bwt = body weight; Bfat = body fat percentage; Hla = post-exercise blood lactate; $\dot{V}O_2max$ = peak VO_2; Rmax = peak respiratory exchange ratio; RPES = RPE at Stage IV; HRS = heart rate at Stage IV; RPEF = RPE at Stage III; HRF = heart rate at Stage III; RPEM = peak RPE; HRM = peak heart rate; Sp = peak speed; GRADE = peak grade level.

Subject Attendance, Testing and Medication Characteristics

Subject	Attendance (%)	Number of Previous GXT's	Beta-Blockade Medication Type - Dose	Other Medications
1	73	19	Inderal 40 mg b.i.d.	Persantine Lanoxin Aspirin
2	76	3	Inderal 80 mg q.i.d.	Cardizem Nitrobid
3	100	5	Lopressor 50 mg b.i.d.	Nitroglycerine
4	92	7	Inderal 40 mg q.i.d.	Nitroglycerine
5	100	8	Lopressor 25 mg b.i.d.	Isordil
6	72	13	Inderal 20 mg t.i.d.	Quinidine Lanoxin Dyazide
7	77	4	Lopressor 10 mg b.i.d.	HCTZ Diltiazem Nitrobid
8	90	8	Lopressor 50 mg b.i.d.	Aldomet
9	73	2	-	Aspirin Indocin
10	89	4	-	-
11	73	7	-	Procaine
12	89	2	-	Lanoxin Aspirin Dyazide
13	100	9	-	Dipyridomole Aspirin
14	89	3	-	Quinaglute Lanoxin Verapanil Coumadin
15	92	9	-	-
16	100	10	-	HCTZ
17	100	4	-	Tocanide
18	95	4	-	Dypiridomole Glucatrol Aspirin
19	100	5	-	-
20	100	3	-	-
21	89	7	-	-
22	82	3	-	-
23	92	7	-	-
24	77	2	-	-
25	77	3	-	-
26	90	2	-	-

$\dot{V}O_2$max Raw Data Across Stage Time
(30-sec intervals)

SUBJ	GROUP	VO1	VO2	VO3	VO4	VO5	VO6
1	1	13.21	12.46	14.50	14.03	14.90	16.260
2	1	21.21	22.24	19.43	21.16	14.11	24.860
3	1	15.89	16.58	17.33	17.86	17.68	18.550
4	1	35.86	34.54	35.05	37.79	36.50	38.240
5	1	23.54	23.26	25.36	24.58	25.03	28.780
6	1	16.62	16.41	19.04	19.48	21.12	23.190
7	1	13.39	16.78	16.14	16.03	17.80	20.540
8	2	19.55	17.32	24.89	24.91	24.25	25.010
9	2	20.57	21.05	20.99	21.24	21.09	22.120
10	2	19.60	20.65	20.53	22.73	23.70	21.600
11	2	18.75	19.19	19.44	17.86	19.45	21.120
12	2	17.93	19.41	18.46	19.99	19.26	18.710
13	2	20.38	24.11	21.24	23.24	23.58	23.610
14	2	17.36	19.29	20.89	22.41	21.00	23.421
15	2	20.91	19.31	20.98	21.74	22.67	21.620
16	2	16.65	16.10	16.77	19.12	18.35	24.730
17	3	32.39	35.08	33.20	35.11	37.98	38.200
18	3	28.78	29.17	30.81	31.17	29.51	32.000
19	3	33.02	28.32	32.97	29.43	29.54	33.910
20	3	43.33	44.45	44.68	48.17	50.72	55.390
21	3	28.84	31.13	35.31	39.02	36.38	40.480
22	3	24.42	28.58	28.88	28.22	28.92	30.890
23	3	21.59	27.54	32.54	28.65	29.21	31.980
24	3	24.67	27.96	30.43	24.32	29.60	33.900

$\dot{V}O_2$ Raw Data for Submaximal Stage IV

SUBJ	GROUP	VO1	VO2	VO3	VO4	VO5	VO6
1	1	18.33	19.13	19.27	20.06	22.23	20.78
2	1	.	.	.	.	.	.
3	1	18.58	18.43	18.41	18.95	21.65	20.76
4	1	14.00	12.40	14.34	14.03	15.13	15.41
5	1	19.53	18.99	19.67	19.31	19.72	20.14
6	1	12.48	16.33	14.96	16.25	16.16	14.54
7	1	16.62	16.41	19.04	19.48	21.12	23.19
8	1	.	.	.	.	.	.
9	2	16.06	18.00	17.20	18.07	18.71	20.48
10	2	18.35	18.20	20.10	19.35	20.44	19.82
11	2	17.03	16.94	16.93	20.66	16.63	19.95
12	2	18.75	19.19	19.44	17.86	19.45	21.12
13	2	15.94	17.56	16.53	19.70	18.53	17.92
14	2	17.44	16.14	18.46	17.60	18.25	18.00
15	2	18.91	19.39	19.56	19.06	21.52	21.14
16	2	15.90	16.70	17.36	19.29	20.89	22.41
17	2	16.68	14.84	16.35	17.42	17.48	19.17
18	2	.	.	.	.	.	.
19	3	22.84	22.47	25.17	25.48	27.42	29.90
20	3	20.72	22.42	23.40	27.22	27.21	27.62
21	3	19.91	23.33	26.32	23.85	24.57	23.96
22	3	29.46	28.56	32.00	35.44	34.28	36.90
23	3	24.24	22.89	24.17	27.43	24.52	23.46
24	3	20.41	22.55	23.20	24.12	24.88	24.88
25	3	21.76	18.27	22.19	21.99	21.56	23.98
26	3	16.64	18.08	17.00	20.35	19.05	21.58

Ventilation ($\dot{V}_E$STPD) Raw Data for Maximal Exercise Stage

SUBJ	GROUP	VE1	VE2	VE3	VE4	VE5	VE6
1	1	24.0	23.0	31.2	31.1	39.4	43.5
2	1	67.2	66.4	61.6	71.0	58.6	87.8
3	1	40.4	39.8	43.4	44.0	44.4	48.4
4	1	92.6	94.6	93.0	90.0	106.0	116.0
5	1	54.2	57.8	59.6	61.0	64.2	68.8
6	1	37.0	35.0	41.0	42.4	48.0	42.2
7	1	24.2	31.0	33.0	34.8	40.4	53.6
8	2	48.6	50.2	71.4	68.8	72.4	74.8
9	2	51.4	50.2	53.4	54.6	53.4	59.6
10	2	45.0	49.2	51.6	50.4	55.0	59.6
11	2	49.0	47.2	47.0	47.2	51.4	61.0
12	2	41.6	.	42.8	44.0	47.2	79.2
13	2	54.4	59.6	56.0	65.6	64.0	66.4
14	2	47.2	55.6	50.0	52.4	54.4	48.4
15	2	55.0	58.6	59.4	66.2	62.4	69.8
16	2	57.2	56.2	59.4	62.8	68.2	67.6
17	2	33.0	39.6	44.0	49.6	47.6	56.0
18	3	83.4	93.6	98.6	108.0	125.4	131.2
19	3	59.2	64.6	68.2	71.2	70.6	78.4
20	3	116.4	106.4	118.6	121.8	123.0	134.4
21	3	95.0	95.6	103.2	113.4	120.4	126.4
22	3	85.6	88.6	94.0	103.0	113.6	118.6
23	3	51.6	66.8	69.6	76.4	74.4	81.0
24	3	53.2	76.0	85.6	92.8	93.6	104.4
25	3	57.8	57.6	76.8	100.0	89.8	95.0

Ventilation ($\dot{V}_E$STPD Raw Data for Submaximal Stage IV

SUBJ	GROUP	VE1	VE2	VE3	VE4	VE5	VE6
1	1	40.4	41.4	43.8	45.2	51.0	48.200
2	1	49.0	51.6	49.6	55.0	58.0	60.400
3	1	32.6	28.0	30.8	32.6	35.6	35.800
4	1	49.0	51.6	49.6	55.0	58.0	60.400
5	1	22.4	34.2	28.2	30.4	29.8	26.600
6	1	37.0	35.0	41.0	42.4	48.0	43.400
7	2	33.6	39.6	36.4	39.6	38.8	43.400
8	2	41.6	42.2	47.2	47.6	49.2	48.000
9	2	35.4	36.0	35.8	46.4	38.0	45.000
10	2	49.0	47.2	47.0	47.2	51.4	61.000
11	2	26.4	28.0	26.4	30.4	29.2	30.400
12	2	48.2	44.8	50.4	47.8	55.8	53.000
13	2	18.4	21.6	22.8	22.2	23.8	23.400
14	2	50.0	50.8	55.0	58.6	59.4	66.200
15	2	29.4	27.4	32.0	33.8	33.6	35.600
16	3	48.0	49.6	57.0	58.2	63.8	77.600
17	3	35.4	39.2	42.2	51.0	54.6	51.600
18	3	55.6	9.2	64.0	63.8	67.0	66.606
19	3	48.6	47.0	55.4	61.2	61.0	69.200
20	3	50.4	45.4	49.8	56.4	55.6	50.400
21	3	41.6	45.0	45.6	47.4	51.2	51.200
22	3	40.8	34.4	38.4	42.2	42.4	46.000
23	3	31.0	34.8	31.8	37.9	34.0	39.4

Respiratory Exchange Ratio Raw Data
for Maximal Exercise Stage

SUBJ	GROUP	R1	R2	R3	R4	R5	R6
1	1	.	.	.	.	.	.
2	1	0.79	0.86	0.99	1.09	1.19	1.20
3	1	1.06	0.98	1.06	1.13	1.30	1.14
4	1	1.04	0.99	1.02	1.02	1.04	1.07
5	1	1.06	1.09	1.02	1.29	1.14	1.10
6	1	1.07	1.11	1.06	1.08	1.11	1.06
7	1	1.16	1.11	0.97	0.99	1.07	0.90
8	1	0.82	0.87	0.93	0.99	1.05	1.15
9	2	1.09	1.13	1.11	1.04	1.15	1.17
10	2	1.15	1.11	1.15	1.16	1.15	1.16
11	2	1.04	1.09	1.14	1.00	0.99	1.20
12	2	1.14	1.09	1.15	1.12	1.14	1.18
13	2	1.86	.	0.91	0.93	0.96	0.97
14	2	1.17	1.18	1.19	1.21	1.22	1.29
15	2	0.99	0.97	0.99	0.98	0.97	1.00
16	2	1.11	1.03	0.97	1.03	1.01	1.01
17	2	1.18	1.14	1.21	1.21	1.21	1.24
18	2	1.10	1.12	0.94	1.23	1.26	1.31
19	3	1.04	1.11	1.12	1.16	1.23	1.28
20	3	0.93	0.97	0.97	1.01	1.01	1.03
21	3	1.07	1.12	1.03	1.16	1.20	1.09
22	3	1.03	0.94	0.99	0.93	0.97	0.94
23	3	1.09	1.01	0.95	0.90	1.03	1.01
24	3	0.92	0.96	0.99	1.05	0.91	1.02
25	3	1.10	1.17	1.04	1.26	1.20	1.25
26	3	1.01	0.91	1.09	1.66	1.17	1.04

Respiratory Exchange Ratio Raw Data
for Submaximal Stage IV

SUBJ	GROUP	R1	R2	R3	R4	R5	R6
1	1	0.99	1.01	1.02	1.06	1.08	1.07
2	1	0.94	0.99	0.98	0.99	0.93	1.02
3	1	0.93	0.94	0.90	0.95	0.95	0.96
4	1	0.80	0.84	0.91	0.81	0.87	0.85
5	1	0.86	0.95	0.88	0.89	0.92	0.82
6	1	1.16	1.11	0.97	0.99	1.07	0.90
7	2	0.90	0.91	0.88	0.93	0.90	0.88
8	2	1.09	1.13	1.15	1.19	1.12	1.14
9	2	0.98	1.00	1.00	1.02	1.08	1.09
10	2	1.14	1.09	1.15	1.12	1.14	1.18
11	2	0.86	0.84	0.86	0.85	0.88	0.89
12	2	1.17	1.14	1.15	1.17	1.21	1.20
13	2	0.90	1.02	1.03	1.03	0.97	0.98
14	2	1.07	1.04	1.11	1.03	0.97	1.03
15	2	0.94	1.04	1.07	1.03	1.02	0.94
16	2	0.94	1.23	1.26	1.31	.	.
17	3	0.88	.	1.00	0.99	1.04	.
18	3	0.97	0.89	0.87	0.84	0.96	0.94
19	3	0.84	0.84	0.83	0.85	0.89	0.92
20	3	0.88	0.85	0.83	0.84	0.89	0.82
21	3	0.84	0.84	0.88	0.88	0.90	0.90
22	3	0.88	0.90	0.83	0.90	0.93	0.90
23	3	0.94	0.96	0.94	0.93	0.95	0.88

FeO_2 Raw Data for Submaximal Exercise Stage IV

SUBJ	GROUP	O1	O2	O3	O4	O5	O6
1	1	16.28	.	16.34	16.41	16.46	.
2	1	16.34	16.56	16.40	16.71	16.42	16.70
3	1	16.58	16.44	16.24	16.55	16.60	16.54
4	1	16.34	16.56	16.40	16.71	16.42	16.70
5	1	16.15	16.75	16.35	16.30	16.21	16.20
6	1	18.10	18.00	18.00	10.00	18.10	18.20
7	1	.	.	.	.	.	.
8	2	16.11	16.20	16.04	16.16	15.92	16.04
9	2	16.91	16.97	17.00	17.15	17.12	17.13
10	2	16.75	16.82	16.80	17.01	17.05	16.99
11	2	17.44	17.25	17.58	17.49	17.43	17.75
12	2	15.40	15.20	15.20	15.00	15.10	15.50
13	2	17.55	17.58	17.52	17.49	17.85	17.74
14	2	15.50	16.10	16.30	16.30	16.10	16.10
15	2	17.50	17.40	17.50	17.40	17.20	17.30
16	2	16.57	16.68	16.90	16.90	16.87	16.80
17	2	.	.	.	.	.	.
18	3	16.00	16.20	6.30	16.30	16.40	16.80
19	3	15.40	15.50	15.60	15.80	16.10	15.80
20	3	16.30	15.90	15.70	16.20	16.20	16.30
21	3	16.40	16.40	16.60	16.50	16.70	16.90
22	3	16.20	16.00	16.20	16.30	16.60	16.40
23	3	16.40	16.30	16.20	16.40	16.40	16.40
24	3	15.70	15.60	15.30	15.80	15.90	15.80
25	3	15.10	15.27	15.12	15.07	14.84	15.06

$FeCO_2$ Raw Data for Submaximal Exercise Stage IV

SUBJ	GROUP	CO1	CO2	CO3	CO4	CO5	CO6
1	1	4.65	4.82	4.63	4.84	4.83	4.77
2	1	.	.	.	.	.	.
3	1	4.41	4.38	4.49	4.24	4.30	4.33
4	1	4.15	4.30	4.33	4.25	4.21	4.29
5	1	4.41	4.38	4.49	4.24	4.30	4.33
6	1	4.25	4.04	4.18	4.28	4.45	4.35
7	1	3.24	3.32	3.20	3.21	3.04	3.25
8	1	.	.	.	.	.	.
9	2	4.45	4.41	4.45	4.52	4.63	4.47
10	2	4.33	4.38	4.41	4.36	4.20	4.24
11	2	4.15	4.16	4.18	4.03	4.15	4.25
12	2	3.91	3.99	3.76	3.79	3.85	3.64
13	2	4.95	5.03	5.10	5.24	5.30	5.02
14	2	3.85	3.75	3.84	3.92	3.61	3.71
15	2	5.03	4.93	4.79	4.77	4.75	4.77
16	2	3.65	3.68	3.76	3.66	3.68	3.76
17	2	4.20	4.43	4.28	4.15	4.15	3.95
18	2	.	.	.	.	.	.
19	3	4.50	4.50	4.50	4.70	4.53	4.30
20	3	4.54	4.57	4.74	4.56	4.45	4.50
21	3	4.56	4.62	4.70	4.15	4.60	4.55
22	3	4.00	3.95	3.90	3.85	3.90	3.80
23	3	4.32	4.35	4.10	4.05	4.00	3.90
24	3	3.98	4.07	4.30	4.03	4.19	4.19
25	3	4.75	4.86	4.90	4.77	4.80	4.75
26	3	5.59	5.50	5.58	5.55	5.86	5.33

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