COMPARISON OF THE CARDIOVASCULAR HEMODYNAMIC ADAPTATIONS OF ANGINA PECTORIS TO "SECOND WIND"

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Motto, Rosemary E. Comparison of the cardiovascular hemodynamic adaptations of angina pectoris to "second wind". M.S. in Adult Fitness-Cardiac Rehabilitation, 1979. 81 pages. (Dr. Glen H. Porter).

Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), rate-pressure product (RPP), the mean maximal MET level and the mean maximal painfree MET capacity were studied in 38 patients with exertional angina pectoris (AP) due to coronary occlusive disease. The investigative conditions were at rest and during two maximal graded exercise tests, separated by a 10 minute walk at a workload of 1.5 mph with a 0% grade. The data that were collected from each S were analyzed by student's t-test for paired means. Mean maximal MET level increased from 3.64 on first effort to 4.38 on second effort. Mean painfree MET capacity increased from 2.97 to 3.85 on second effort. Maximum HR increased from 131 bpm, maximum SBP decreased from 166 mmHg to 163 mmHg, maximum RPP increased from 220 to 228 and maximum DBP decreased from 84.4 to 82.1. At the MET level provoking AP on first effort, HR on second effort was unchanged, RPP was decreased from 227 to 220, SBP was decreased from 168.6 to 163, and the DBP was decreased from 84.6 to 81.9. The observed increase in musculoskeletal performance and cardiac work capacities may be explained by enhanced arteriolar dilation or by augmentation of the peripheral circulation as seen by dilatation of the conductance vessels.

CHAPTER I

INTRODUCTION

Exercise testing is frequently used as an evaluation technique for patients with angina pectoris (AP) in order to determine their functional exercise capacity. It also has a role in the various therapeutic interventions in the treatment of AP.

Some patients with exertional angina, due to coronary artery disease (CAD), show a great variability in exercise tolerance. It has been found that these individuals may develop a "second wind" following an episode of exercise-induced AP. This "second wind" allows them an increase in exercise capacity after the passing of the anginal pain.

This individual increase in exercise tolerance, first documented by Heberden in 1785 and referred to as "second wind" by Wenckebach (1924; 1928), continued to be mentioned though only briefly, throughout medical literature through the following decades (Wenckebach, 1924; 1928; Wayne and LaPlace, 1933; Wayne and Graybiel, 1934; Patterson and Clark, 1942; Price, 1951; Leftwich, 1953; MacAlpin and Kattus, 1968; Obma, 1978).

While most investigators have found relatively few individuals who elicit "second wind", Obma (1978) in a study of patients with documented CAD and exertional AP, found these

individuals to significantly increase their exercise tolerance after an initial bout of exercise which was followed by a ten-minute "cool-down" walk. An increase in heart rate (HR) and rate-pressure product (RPP) was observed along with an increase in the musculoskeletal performance (increased MET capacity).

The exact cardiovascular mechanism which mediated the increase in performance is not known. Those who have studied the phenomenon have held that the adaptation which makes the "second wind" possible must be dilatation of the coronary vessels in response to the stimulus of myocardial ischemia (Gallavardin, 1925; Price, 1951; MacAlpin and Kattus, 1966). However, another possible hypothesis alluded to is an increase in the peripheral circulation, i.e., an enhancement of peripheral conductance (Wenckebach, 1924; Clausen, 1976). Except for the observations of Wayne and Graybiel, Patterson, et al., MacAlpin and Kattus, and Obma, subjective studies (i.e., documentation of heart rate and blood pressure response, electrocardiographic changes, etc.) have been minimal.

Statement of the Problem

The purpose of this study was to compare the cardiovascular hemodynamic adaptations of exertional AP to "second wind" in an attempt to possibly help define the mechanism and/or mechanisms resulting in the "second wind" phenomenon.

Need for the Study

The need for the present study stems from the fact that few investigations have been conducted in determining the cardiovascular hemodynamics of "second wind." The study may enable us to fill this gap and further increase our understanding of the cardiovascular dynamics during the occurrences of this phenomenon. This study may also aid in documentation of the mechanism(s) and the eventual treatment and management of exertional AP.

Hypothesis

For this investigation the null hypothesis was chosen. It was hypothesized that there would be no significant difference in the cardiovascular hemodynamic adaptations of exertional AP to "second wind" when comparing first effort to second effort.

Assumptions

This is an ex post facto study, therefore, the author assumed the following:

1. All values were correctly recorded by the instrumentation and technicians in charge.

2. All subjects exercised to the point of onset (+1) of AP during the first effort of the treadmill test and exercised to this same level of pain during the second effort of the treadmill test.

Delimitations

1. All subjects experienced angina during their first effort on the treadmill test.

2. All subjects recovered from the exertional AP during the cool-down walk.

3. Subjects were patients of the physician's private practice and were tested in the St. Francis Hospital Human Performance Laboratory.

Limitations

1. The author was not present during all the exercise testing sessions.

2. There was no control over the subject's motivation to perform the test.

3. There was no control over the subject's daily activity, dietary or personal health habits.

4. Individual physiologic responses to exercise testing may have produced some variability (i.e., location of myocardial infarction, labile hypertension, congestive heart failure, etc.).

Definition of Terms

Alpha adrenergic receptor--one of the two types of receptors of the sympathetic autonomic nervous system which are present in coronary arteries.

Angina pectoris (AP)--a paroxysmal affection characterized by severe chest discomfort which is the result of an imbalance between myocardial oxygen demand and supply that is typically related to a restricted coronary circulation due to coronary atherosclerosis.

Beta adrenergic receptor--one of two types of receptors of the sympathetic autonomic nervous system. Stimulation of beta adrenergic receptors produces dilatation of the blood vessels, relaxation of bronchial muscle and increases in heart rate and the force of ventricular contraction.

Blood pressure--the pressure exerted by the blood on the wall of any vessel; (1) systolic blood pressure (SBP)--the greatest force caused by the contraction of the left ventricle of the heart; (2) diastolic blood pressure (DBP)--that existing during relaxation phase between heart contractions. It is primarily dependent upon the elasticity of the arteries and peripheral resistance which in turn is dependent upon the caliber of arterioles and capillaries.

Capacitance vessels--mainly voluminous venous section; containing some 80 percent of regional blood volume. Changes of smooth muscle tone in these vessels can produce hemodynamically important shifts in regional blood content and thus influence venous return and cardiac output.

Cardiac output ($\dot{Q}$)--the amount of blood discharged from the left or right ventricle per minute; the product of heart rate and stroke volume.

Contractile state--the velocity of fiber shortening of the heart muscle.

Coronary artery disease (CAD)--also called coronary atherosclerosis; an irregular thickening of the inner layer of the walls of the arteries which conduct blood to the heart muscle. The internal channel of these arteries becomes narrowed and the blood supply to the heart is diminished.

Coronary blood flow (CBF)--a measure of the circulation of the heart muscle, determined by coronary driving pressure and coronary vascular resistance.

Double product--also referred to as rate-pressure product (RPP); an index of myocardial oxygen consumption. It has been demonstrated that there is a close correlation between myocardial oxygen consumption at the point of AP and the product of heart rate times the systolic blood pressure.

Heart rate (HR)--the number of times the heart contracts per minute.

Ischemia--a local, usually temporary, deficiency of blood in some part of the body, often that part caused by a constriction or an obstruction in the blood vessel supplying that part of the body or heart.

MET--metabolic equivalent; the name for the resting metabolic unit equal to approximately 3.5 ml O_2/kg/minute.

Myocardial infarction--the damaging or death of an area of the heart muscle resulting from a reduction in the blood supply reaching that area.

Myocardial oxygen consumption ($M\dot{V}O_2$)--the oxygen consumed by muscular tissue of the heart determined primarily by: (1) intramyocardial tension; (2) the contractile state of the heart; (3) HR; and (4) the myocardial systolic wall stress.

Rate-pressure product (RPP)--also known as double product; an index of $M\dot{V}O_2$. It has been demonstrated that there is a close correlation between $M\dot{V}O_2$ and the product of HR times the SBP.

Resistance vessels--determining the overall resistance function, and hence, regional blood flow. There are two adjustable resistance sections:

a. Precapillary resistance vessels--mainly small arteries and arterioles; responsible for by far the largest fraction of regional resistance.

b. Postcapillary resistance vessels--venules and veins; the ratio of precapillary to postcapillary resistance determines capillary hydrostatic pressure and, therefore, the fluid filtration exchange.

Second wind--ability of certain patients, susceptible to AP at the beginning of a particular effort, to undertake further and even greater exertion without pain following the alleviation of the anginal pain.

Stroke volume (SV)--the amount of blood ejected by the left ventricle at each beat.

Vasoconstriction--the contraction of the muscles of the

arterioles, thus narrowing the arterial passage, increasing the resistance to blood flow and raising the blood pressure.

Vasodilatation--the relaxation of the muscles of the arterioles, thus enlarging the arteriole passage, reducing resistance to the flow of blood and lowering blood pressure.

Ventricular volume--a component of intramyocardial tension; the volume of the left ventricle.

CHAPTER II

REVIEW OF LITERATURE

Introduction

The purpose of this study was to determine the adaptation of cardiovascular hemodynamics in patients, with documented CAD and exertional angina, to "second wind." Exertional AP is generally observed at a similar level of RRP which is the most accurate noninvasive index of myocardial oxygen consumption ($M\dot{V}O_2$) (Amsterdam, Hughes, DeMaria, Zelis and Mason, 1974). $M\dot{V}O_2$ has been recognized as the limiting factor in the functional capacity of patients with exertional AP. However, some patients with exertional angina have been found to increase their exercise capacity after a first treadmill test followed by a period of rest (Burkhart and Sowton, 1967; MacAlpin and Kattus, 1966 ; Wayne and Graybiel, 1934; Obma, 1978). Little research has been published, however, on the mechanisms of this phenomenon. Any increase in exercise capacity of these individuals would allow them a higher level of exertion prior to the onset of pain.

Second Wind

Heberden in 1785 quoted a patient:

> ". . . I have frequently, when in company, borne the pain, and continued my pace without indulging it: at which time it has lasted for five to perhaps ten minutes and then gone off, as well as I can recollect, rather suddenly as it came on, then lessening gradually" (in Price, 1951; p. 197).

General information. Patients with AP due to coronary disease may have great variability in exercise tolerance. In some cases there is a specific pattern wherein the increase in exercise tolerance is dependent upon a preceding episode of exercise-induced AP (MacAlpin and Kattus, 1966). A common manifestation of this phenomenon is when the patient, after experiencing exertional angina, and therefore, discontinuing his exercise, is subsequently able to resume the same effort and continue indefinitely with further discomfort (Adams, Effler, Kattus, Russert, Sheldon and Taylor, 1970).

Prior investigations. Gallavardin in 1925, wrote that his subjects were better able to continue their outings after being halted several times by their angina. It was his contention that these subjects have a mechanism which is slow to adapt itself. He felt this mechanism fitted coronary spasms (in Price, p. 197).

In 1924, Wenckebach first touched on the phenomenon. He felt the mechanism involved changes in the peripheral circulation, particularly in its regulation. He surmised:

> ". . . It may be, in such cases, that the heart and aorta, owing to some initial difficulty in discharging the greater amount of blood returned to them by the great veins. Indeed, the course of angina may depend not only on aortic conditions but also on circumstances which affect the peripheral circulation." (p. 815).

Wenckebach is 1928 again wrote of the strange oppression noticed at the onset of major physical exertion. This pain lasted for a short while and if the activity was continued, sometimes consciously at a slower pace, the pain disappeared allowing the individual to continue further. He felt the beginning of exertion brought about an increased blood flow to the heart originating in the venous splanchnic bed. He then hypothesized, that the blood flow from the central arteries to the periphery and into the veins was at first blocked.

Lewis (1932) in his description of pain in muscular ischemia, felt while the phenomenon of "second wind" was difficult to explain on a simple basis of pressure and rates, it was easy to understand if it was believed that the coronary circulation accommodates itself gradually to the condition of exercise. Wayne and LaPlace (1933) felt they had not yet met a patient with a similar history suitable for observation. They did document five patients who were able to exercise further after the disappearance of the pain. However, these individuals showed a tendency to work at a lesser work load during the second effort. These investigators documented the blood pressure as being raised after the first attack of angina; the blood pressure was higher during the second effort while the heart rate remained the same. They felt the heart rate was a chief factor in determining the onset of the attack.

Wayne and Graybiel (1934) documented the effect upon exercise tolerance by food, distension of the stomach, external temperature and repeated exercise in people with angina. They determined by use of a two-step exercise, the number of efforts required to induce pain under the various conditions. Two of their subjects showed an increase in exercise capacity on repeated exercise. They also found minimal change or a decrease in exercise if the second effort was made within two minutes of the first exertion or delayed for more than 30 minutes.

A study by Patterson, Clark and Levy (1942) documented electrocardiographic changes in certain patients with coronary atherosclerosis.

> "In many cases of coronary sclerosis the total RS-T deviation increased in linear fashion as the test progressed. In some, the degree of deviation rose to a peak and then decreased. The latter sequence of events suggested that compensatory mechanisms in the circulation had brought about a favourable adjustment in coronary blood flow. One of the methods of adaptations appeared to be an increase in pulmonary ventilation." (p. 840).

Leftwich (1953) theorized while the concept of coronary spasm explained exertional angina, it did not account for the "second wind" phenomenon. Burns (1961) felt the clinician should investigate if their anginal patients were hampered by "first effort angina." He described this individual as one who is aware of the discomfort when he first sets out in the morning. In this paper he described a "second

wind" phenomenon in golfers. He stated that they experience AP during the early stages of the game and are ultimately able to complete the round. The author, however, failed to offer any possible mechanism.

Price (1950) in his monologue assumed there is some delay in coronary dilatation at the beginning of exercise. He felt that the mean aortic pressure on coronary flow overbalances the active vasomotor changes. If a general vasoconstriction occurs, especially in the coronary arteries, and the blood pressure is increased, the flow through the heart will increase. Price further stated that the narrowing of the larger coronary arteries not only predispose the spasm of the arterioles, but might prevent a sufficient "head of pressure" to be developed in order to overcome the spasm or constriction. The "second wind" he concluded might occur when the arterioles dilate independently.

Kattus (1966) described the walk-through phenomenon in a 45 year old oil field worker. Walking at a constant rate of 2.0 mph up a 10 percent grade, he began to have angina in the third minute. The pain rose to 2+ level in the eighth and ninth minutes, and then declined until it disappeared during the 27th minute. The ST segments which first became depressed in the sixth minute, reached a maximum of 3mm in the ninth minute, and finally became normal in the 28th minute, several minutes after the pain had disappeared. Later, when the speed was advanced to 2.5 mph, the pain returned,

but the ST segment depression did not reappear. Pulse and blood pressures declined and reached a steady state as the walk-through was completed. These observations suggested the adaptations in this case were due to a decreasing work load on the heart; as dilation of the arterioles in the skeletal muscles decreased the resistance to blood flow. Kattus felt both extracardiac and intracardiac factors may be playing a role in the adaptive mechanisms that permit the phenomenon to occur.

In 1970, Kattus further quantified the concept of "second wind." He described these persons as having one of two patterns of disease in their coronary arteries. The coronary arteries at angiography display either one or more local stenotic areas in major arterial branches or one or more total obstructions with collateral filling of the vessel distal to the obstruction. He felt these findings have led to the theory that exercise, the stress that leads to myocardial hypoxia, also aids somewhat to the increase in exercise capacity through dilation of the collateral channels.

MacAlpin and Kattus (1966) described twelve patients with angina pectoris who manifested an ability to adapt to exercise during treadmill stress testing with electrocardiographic monitoring. Three patterns of adaptation were seen. Nine subjects had the ability to continue walking after the onset of angina with eventual disappearance or lessening of the pain and the associated ischemic changes. Four subjects

were able to continue walking for long periods of time during a state of angina and ischemic ST depression. Three subjects demonstrated an increase in exercise capacity after being warmed up by a preceding bout of exercise-induced angina. The blood pressures and heart rates during the initial "warming up" effort tended to be higher than those during the early stages of the second effort.

Redwood, Rosing, Goldstein, Beiser and Epstein (1971) while evaluating exercise protocols found a slight, but not significant, increase in exercise capacity after successive exercise trials. They found no significant increase in RPP at the onset of angina.

Obma (1978) in his work with exertional angina, found adaptation to this phenomenon occurring in approximately 70 percent of the patients. The author felt the higher incidence of adaptation, as compared to previous studies, may have been due to a difference in exercise protocols; a modification of Balke's protocol with fine MET increments and a ten minute cool down walk between efforts may have allowed for better documentation of the phenomenon. A protocol with large MET increments may prevent the phenomenon as a certain stage may exceed the individual's critical angina threshold. Obma felt that there may be an enhancement of the peripheral circulation allowing an improvement in myocardial work capacity without an increase in $\dot{M}VO_2$ on second effort.

Angina Pectoris

Epstein, Redwood, Goldstein, Beiser, Rosing, Glancy, Reis and Stinson (1971) described the anginal syndrome as caused by a temporary inability of the coronary arteries to supply sufficient oxygenated blood to the heart muscle (the pain is thought to be due to stimulation of afferent nerve endings in the myocardium by the accumulation of unoxidized metabolic products resulting from myocardial hypoxia). Conditions tending to precipitate ischemic pain, i.e., meals, cold, exercise, are usually associated with changes in the circulatory system that may increase heart rate and blood pressure. The increases in turn, are related to heightened levels of adrenergic activity. Interventions causing symptomatic improvements, including nitroglycerine, beta-blocking drugs and physical training, produce the opposite effect; that is, diminished levels of adrenergic activity (Epstein, et al; Blackburn, Taylor and Keys, 1970; Mueller and Rorvik, 1957; Reynolds, Turtinen, Kerr and Swan, 1975; Nordenfeld, 1974).

Elevations of the pulmonary capillary wedge pressure, left atrial pressure and left ventricular end diastolic pressure have been reported to occur during angina. It appears angina may be associated with left ventricular failure. Elevation of the pulmonary artery pressure with exertion in normal subjects, and with both pain and non-pain provoking

exertion in patients with coronary artery disease has been reported (Aranow, Lurie, Turbow, Whittaker, Van Camp, and Hughes, 1979; Clausen, Klausen and Trap-Jensen, 1969; Grimby, Haggendahl and Saltin, 1967; Holmberg, Serzysko and Varnauskas, 1971). Roughgarden (1966) stated that Malmborg's study revealed normal subjects had higher flow rates for the same increase in pulmonary artery pressure as in patients with angina. Increases in the mean pulmonary artery pressure implied that the left atrial pressure was elevated, but changes in pulmonary artery pressure did not follow changes in left atrial pressure in a linear fashion, until left ventricular failure occurred. Pulmonary capillary pressure did not necessarily rise in parallel with pulmonary artery pressure.

Amsterdam, Gorlin and Wolfson (1974) and Sonnenblick, Ross and Braunwald (1968) implied that angina pectoris can be treated either by increasing the myocardial oxygen supply or by decreasing the myocardial oxygen requirement. Drug therapy acts primarily through reduction of myocardial oxygen requirements. The use of beta adrenergic blockade causes attenuation of adrenergic stimuli to the myocardium, thereby reducing myocardial mechanical effort and decreasing myocardial oxygen need.

Myocardial Oxygen Consumption

The major determinants of $M\dot{V}O_2$: (1) heart rate (HR),

(2) the contractile state of the myocardium, (3) intramyocardial tension, and (4) the myocardial systolic wall stress. Alteration of any of these components has the capacity to influence myocardial oxygen consumption.

Heart rate. Epstein, Robinson, Kahler and Braunwald (1971) found that "other things being equal, a faster heart rate. . would predispose one to ischemic pain because of greater oxygen need" (p. 262).

Contractile state of the myocardium. Amsterdam, et al., and Sonnenblick, et al., concluded that $M\dot{V}O_2$ has been shown to be directly proportional to the contractile state of the myocardium.

Intramyocardial tension. Intramyocardial tension is determined by ventricular pressure and ventricular volume. An increase in either component would augment intramyocardial tension and thereby $M\dot{V}O_2$ (Epstein, et al.; Monroe, 1964).

Myocardial systolic wall stress. The systolic wall stress is directly proportional to the ventricular systolic pressure and the ventricular radius and inversely proportional to the wall thickness (Hurst, p. 1136).

According to Amsterdam, et al., angina may be defined as an imbalance in the myocardial oxygen demand and supply. This imbalance is a result of a decrease in coronary circulation due to coronary atherosclerosis. Coronary circulatory reserve is compromised and, in response to increases in $M\dot{V}O_2$ as seen in exercise, coronary blood flow and thereby oxygen

delivery cannot be augmented beyond a limit fixed by the degree of arterial obstruction. The level of $M\dot{V}O_2$ is an index of maximal tolerated stress which is directly related to the cardiac functional capacity in angina pectoris. In the absence of alterations in delivering capacity of the coronary circulation, as one may see in the progression of coronary artery disease, $M\dot{V}O_2$ at the onset of pain is constant for a given patient. Clinically, the simple product of HR and systolic blood pressure is a useful index of changes in myocardial oxygen requirements. Although this index obviously does not take into account all the determinants of $M\dot{V}O_2$, it is readily measured under clinical conditions.

Peak $M\dot{V}O_2$ also provides a relative measure of maximal attainable coronary blood flow. This relation is a result of the exclusively aerobic pattern of the cardiac metabolism, requiring near maximal oxygen extraction by the myocardium even under basal conditions, thereby precluding use of this mechanism for increasing oxygen supply. Alterations in $M\dot{V}O_2$ therefore, may be affected by changes in coronary blood flow (Amsterdam, et al., 1974; Sonnenblick, et al).

Rate Pressure Product

$M\dot{V}O_2$ can be directly determined as the product of myocardial arteriovenous oxygen difference and coronary blood flow. Indirect approaches to assessing $M\dot{V}O_2$ have been determined to be consistent with their importance as major

determinants of myocardial oxygen utilization. The derived indices of BP and HR have provided a reasonable approximation of relative $M\dot{V}O_2$. These have included the product of mean aortic pressure and HR, the tension-time index (a product of the integral of left ventricular pressure during systole and HR), the triple product of HR, SBP and systolic ejection period and the double product of HR and SBP (Monroe, 1964).

The importance of HR in the precipitation of angina has been recognized for decades, yet, the relation of HR and BP was discounted as a significant factor in the production of angina in the early studies (Wayne and LaPlace, 1933). Re-evaluation of the relation of HR and BP to the occurrence of angina has confirmed the significance of both variables and upheld the applicability of indirect indices of $M\dot{V}O_2$ in the evaluation of angina. It has been demonstrated that for the individual patient, the onset of angina occurs at a constant value of RPP (Amsterdam, et al, Sonnenblick, et al; Roughgarden, 1966).

METS

One MET (metabolic equivalent) is equal to the resting or basal oxygen consumption of about 3.3 to 3.5 ml/kg/minute. Metabolic equivalents or units quantify the amount of energy spent in the various activities. The average middle-aged man who has had an uncomplicated myocardial infarction is capable of performing at a level of 8 to 9 METS in a supervised

exercise program. Exercise capacity of a post-coronary patient may be lowered to less than 4 METS if activities of daily living elicit symptoms (Naughton and Hellerstein, 1973).

Cardiovascular Circulatory Changes With Exercise

The increase in sympathetic vasoconstrictor activity during exercise, which results in a graded decrease in flow to the inactive muscle in proportion to the work load, helps to conserve part of the cardiac output for the active muscle and the skin circulation. Since increased sympathetic activity confined only to the inactive muscles in unlikely, such activity is presumably overcome in the active muscle, either by the more powerful local dilation mechanism or by the fact that sympathetic stimulation does not constrict vessels concerned with metabolic exchanges (Bevegard and Shepard, 1966; Clausen, 1976; Clausen and Trap-Jensen, 1970; Clausen and Trap-Jensen, 1976).

A reflex venoconstriction, also graded to the severity of the exercise, accompanies these reflex changes in caliber of the resistance vessels. This venoconstriction occurs in the active muscles in spite of the powerful local mechanisms causing dilatation of the resistance vessels. The role of the reflex regulation of the resistance vessels during exercise is to provide for efficient distribution of the left ventricular output according to the metabolic needs and temperature regulation. The reflex constriction of capacitance

vessels seems to be important for the attainment and maintenance of a high $\dot{Q}$ during exercise (Bevegard and Shepard; Grimby and Haggendal; Clausen, Klausen, Rasmussen and Trap-Jensen, 1970; Saltin and Stenberg, 1964; Mellander and Johansen, 1968).

It is felt, when evaluating changes in the exercise capacity of individuals with exertional angina, it is important to distinguish between an improvement in the circulatory response to exercise and the improvement in myocardial oxygen delivery (Redwood, Rosing, Goldstein, Beiser and Epstein, 1971). The attained SBP and HR are important factors in the determination of this improvement.

It is known from prior investigation that patients with CAD, previous myocardial infarction or an enlarged heart may show the usual signs of left ventricular failure with increased pulmonary vascular pressure and a tendency to reduced cardiac output during exercise (Muller and Rorvik, 1957). In the early fifties it was theorized that administration of nitrates led to the dilatation of coronary vessels. An increase in CBF subsequent to nitrates has been demonstrated in animals and its effect on anginal pain attributed to its influence in CBF in man (Wayne and LaPlace; Mueller and Rorvik; Mason and Braunwald, 1965).

The possibility has been considered that the therapeutic action of the drug may in part be due to their action on the peripheral circulation. Mason and Braumwald found after

administration of nitroglycerin, a mild decline in systemic arterial pressure and a concomitant elevation in forearm blood flow and, therefore, a decrease in the calculated forearm vascular resistance was apparent. It was felt that if similar increases, as in forearm flow, occurred in other skeletal muscle groups it would then appear that substantial redistribution of regional blood flow must occur following nitroglycerin. Therefore, the induced venous and arteriolar dilatation may account for the minution of ventricular size. This mechanism may reduce myocardial oxygen requirements and thereby relieve the pain of AP.

Summary

Most of those who have studied the phenomenon of "second wind" have held that the adaptation which makes it possible must be a dilatation of coronary vessels in response to the stimulus of myocardial ischemia, but there is little direct evidence to support this theory. Except for the observations of Wayne and Graybiel and MacAlpin and Kattus, objective studies are absent from the literature. Electrocardiographic and blood pressure monitoring during actual occurrence of the phenomenon have not been recorded.

The fact that a post-anginal adaptation occurs in possibly 70 percent of patients with exertional AP makes it important to attempt to clarify the cardiovascular mechanisms involved. Documentation of the hemodynamic adaptations of

the cardiovascular system to the phenomenon of "second wind" may possibly aid in the medical management and physical training of those individuals with exertional AP.

CHAPTER III

METHODS

Introduction

The purpose of this investigation was to describe and compare the cardiovascular hemodynamic adaptations of exertional angina pectoris to "second wind."

The subjects were given a graded exercise test (GXT) utilizing a modified Balke multistage protocol (Appendix A). During each stage of the GXT various cardiovascular hemodynamic measurements were made.

Subject Selection

A total of 38 subjects, all private patients of the Skemp-Grandview Clinic, were included in this investigation. Each subject was classified as having exertional angina due to coronary occlusive disease documented by either: (1) prior myocardial infarction; (2) at least 75 percent obstruction of one or more epicardial coronary arteries as established by previous coronary angiography; or (3) a positive GXT which elicited ST-segment depression of at least 1 mm, .08 mv-second duration. All the patients experienced exertional angina during their first run of the treadmill test. Patients with clinical pulmonary and/or valvular disease were

excluded. Witnessed, informed consent was obtained prior to the exercise test in the manner described by the American College of Sports Medicine Guidelines (Appendix B).

GXT Procedures

The patients were exercised at ambient laboratory temperatures. The testing was done in the morning between the time of 8:00 a.m. and 12:00 p.m. A conventional 12-lead electrocardiogram (ECG) was recorded before the test.

ECG. The patients were prepared by first thoroughly cleaning the skin sites with alcohol and rubbed dry with the use of "Kem-wipes." At this time five self-adherent NDM silver/silver chloride electrodes (Dayton, Ohio) were applied to: (1) the right arm at the right subclavian fossa; (2) left arm at the left subclavian fossa; (3) right leg at the right midclavicular line between the naval and the nipple; (4) left leg at the left midclavicular line between the naval and the nipple; (5) V5 at the fifth intercostal space at the anterior left axillary line. The lead wires were connected to the Physiocontrol one channel recorder (part. 09-00143). The electrocardiographic complexes of the V5 lead were monitored continually with an oscilloscope. Leads II, AVF and V5 were recorded during the third minute of each work load.

Blood pressure (BP). The BP was measured by the ascultatory method by the use of a Tycos sphygmomanometer placed on the left upper arm and the diaphragm of the

stethoscope placed over the antecubital brachial artery. All BP readings were made by the Cardiologist conducting the GXT.

The determination of the systolic blood pressure was at the onset of the first Korotkow sound. The diastolic value was determined at the point of disappearance of the fifth Korotkow sound.

The blood pressure was taken prior to the onset of exercise with the patient standing on the treadmill and during the third minute of each stage of the treadmill protocol.

Heart rate. Determination of the HR was made by multiplying the number of cardiac cycles (one R-R interval being one cycle) within the second marking of the rhythm strip by ten. For irregular rhythms, the rate was averaged over a one minute interval.

Baseline HR was taken prior to the onset of exercise with the patient standing on the treadmill and during the third minute of each stage.

GXT Protocol

The protocol utilized was a modification of the standard Balke protocol. The modified protocol started at a workload of 1½ METS with an increase of ½ MET increments in workload every three minutes. The patients were exercised until AP was elicited (1+), whereupon the treadmill speed and grade were decreased to 1.5 mph-0% grade for ten minutes. During this

time period a "cool-down" walk was performed by the patient. In this time interval of ten minutes the chest pain subsided and the initial protocol was repeated until symptoms were again elicited or limiting fatigue occurred. If the AP did not subside the test was discontinued after the first effort. The exercise capacity of each patient during each test was defined as the highest angina free MET level attained.

Cardiovascular Measurements

The following variables were measured during the third minute of each stage of both efforts of the GXT: (1) HR, (2) RPP, (3) SBP, and (4) DEP.

These variables were measured at maximal effort, at the mean maximal painfree level of each individual and at the level of AP on first effort and then compared to the same workload on the second effort.

A comparison was also made between the mean maximal MET level attained and the painfree MET capacity of each effort of the GXT protocol.

Statistical Treatment

Analyses of the obtained data were carried out utilizing the paired t-test to determine if there were significant differences in the measured cardiovascular hemodynamic variables between the first and second effort of the exercise test.

CHAPTER IV

ANALYSIS OF DATA

Introduction

This chapter is intended to present the statistical analyses and interpretation of all the raw data collected in the present study.

All the subjects were given a GXT utilizing a modified Balke multistage exercise test protocol (Appendix A). The subjects were exercised to the onset of AP (+1). At this time a ten minute cool-down walk at 1.5 mph-0% grade was completed by each subject. After the disappearance of the AP, the initial protocol was repeated until symptoms were again elicited or limiting fatigue occurred. Each individual was requested to exercise to the same level of AP during the second effort. If the pain had not passed during the ten minute cool-down the test was discontinued. At the end of each three minute stage of the exercise test, HR, SBP, DBP, and RPP were measured. Peak and painfree MET levels were also measured during each run of the GXT. Differences between the first effort and the second effort cardiovascular hemodynamic values of the subjects were statistically analyzed.

The statistical tool used to test for significant differences between the various mean hemodynamic variables

during the first and second effort of the GXT was a student's t-test for paired means. The .05 level of significance was used for rejection of the null hypotheses. Table A presents a summary of the characteristics of the 38 subjects and their resting cardiovascular data.

Table A

A Summary of the Subject Characteristics and Resting Cardiovascular Data

Sample	N	Prior MI	Prior Test	Positive GXT
Male	33	17	5	16
Female	5	1		4
(Mean age 56.1)				

Resting Data	Mean Value	Standard Error of Mean
Heart Rate	81.6	± 1.93
RPP	109.0	± 4.70
SBP	138.2	± 3.60
DBP	86.2	± 1.60

Mean Maximal Attained Values

Heart rate. Table 1 and Figure 1 contain the mean maximal HR values for each run of the treadmill test as expressed in beats per minute. The mean maximal HR attained during the first effort of the GXT was 131 beats per minute (BPM). The mean maximally attained HR at the completion of the second run was 138.5 BPM. The data demonstrate a significant increase in maximally attained HR during the second effort of the GXT as compared to the first effort of the test.

METS. The data in Table 2 and Figure 2 indicate that the mean maximal MET level attained during the first effort was 3.64 as compared to 4.38 METS at maximal second effort. The data demonstrate a significant increase in the maximally attained MET level during the second effort.

Of the 38 subjects tested in this investigation, it was found that 31 (81%) experienced exertional angina on the second effort of the GXT. Seven subjects (18%) did not experience AP on second effort and were limited by either dyspnea or leg fatigue.

RPP. The obtained data (Table 3 and Figure 3) indicate a slight increase in the attained mean maximal RPP during second effort (228×10^2) as compared to that attained during the initial run of the GXT (220×10^2). However, the increase was found not to be statistically significant ($p > .05$).

SBP. As the data in Table 4 and Figure 4 indicate, the mean maximally attained SBP during the second run of the exercise test was somewhat decreased as compared to the value attained at maximal effort during the first effort. This small difference was not statistically significant ($p > .05$).

DBP. The data in Table 5 and Figure 5 indicate that there was no significant difference ($p > .05$) between the mean maximally attained DBP at the completion of the second effort as compared to the value attained at the completion of the first effort.

Mean Maximal Painfree Hemodynamic Values

The maximal painfree hemodynamic values were determined for each of the subjects during each run of the GXT. Comparison of the differences between each mean hemodynamic value for the first and second effort were statically analyzed.

Heart rate. The data presently in Table 6 and Figure 6 reveal there was a significant increase in the mean maximally attained painfree HR during the second effort of the GXT.

METS. There was a significant increase in the mean maximal painfree MET level attained during the second effort (Table 7 and Figure 7). It was found that 22 of the 38 subjects were able to exercise to a higher MET level during the second effort.

RPP. The data in Table 8 and Figure 8 indicate that during second effort there was an increase in the mean

maximally attained RPP. This increase was found not to be statistically significant ($p > .05$).

SBP. The data presented in Table 9 and Figure 9, represent the comparison of the difference between the attained mean maximally painfree SBP during first effort to that attained during the second effort. There was a significant decrease in the SBP during the second effort run.

DBP. The data in Table 10 and Figure 10 show the significant decrease in the mean maximal painfree DBP attained during second effort as compared to the mean maximal painfree value on first effort.

Level of AP First Effort and Same Workload Second Effort

Heart rate. Table 11 and Figure 11 present data showing no significant difference ($p > .05$) when comparing the mean HR at the level of AP on first effort and the mean HR at the same workload on second effort.

RPP. Table 12 and Figure 12 present data that indicate there was no significant difference ($p > .05$) between the RPP attained at AP during the first effort and the RPP at the same MET level on second effort.

SBP. A comparison of the SBP at the level of angina during the first effort and at the same workload during second effort is given in Table 13 and Figure 13. There was a significant decrease in SBP on second effort.

DBP. The data presented in Table 14 and Figure 14 shows that there was no significant difference ($p > .05$) between the DBP attained at AP during the first effort and the DBP at the same MET level on second effort.

Table 1

A Comparison of the Differences Between
First Effort and Second Effort
Mean Maximal Heart Rates

Sample	N	Mean	Standard Error of the Mean
1st Effort	38	131.0	3.7
2nd Effort	38	138.5	3.9

t (37) 4.70, $p < .05$

Table 2

A Comparison of the Differences Between
First Effort and Second Effort
Mean Maximal MET Levels

Sample	N	Mean	Standard Error of the Mean
1st Effort	38	3.64	$\pm$ .24
2nd Effort	38	4.40	$\pm$ .28

t (37) 5.14, $p < .05$

Table 3

A Comparison of the Differences Between
First Effort and Second Effort
Mean Maximal Rate-Pressure Product

Sample	N	Mean	Standard Error of the Mean
1st Effort	38	220	$\pm$ 9.5
2nd Effort	38	228	$\pm$ 10.2

t (37) 1.92 $p > .05$

Table 4

A Comparison of the Differences Between
First Effort and Second Effort
Mean Maximal Systolic Blood Pressures

Sample	N	Mean	Standard Error of the Mean
1st Effort	38	166.7	± 4.3
2nd Effort	38	163.9	± 4.5

t (37) 1.42 $p > .05$

Table 5

A Comparison of the Differences Between
First Effort and Second Effort
Mean Maximal Diastolic Blood Pressures

Sample	N	Mean	Standard Error of the Mean
1st Effort	38	84.4	± 2.0
2nd Effort	38	82.1	± 2.1

t (37) 1.72, $p > .05$

Table 6

A Comparison of the Differences Between
First Effort and Second Effort
Mean Maximal Painfree Heart Rates

Sample	N	Mean	Standard Error of the Mean
1st Effort	38	123.8	± 3.3
2nd Effort	38	131.6	± 3.9

t (37) 4.30, $p < .05$

Table 7

A Comparison of the Differences Between
First Effort and Second Effort
Mean Maximal Painfree MET Levels

Sample	N	Mean	Standard Error of the Mean
1st Effort	38	2.97	± .22
2nd Effort	38	3.85	± .26

t (37) 5.91, $p < .05$

Table 8

A Comparison of the Differences Between
First Effort and Second Effort
Mean Maximal Painfree Rate-Pressure Products

Sample	N	Mean	Standard Error of the Mean
1st Effort	38	205	± 7.8
2nd Effort	38	212	± 9.3

t (37) 1.7, $p > .05$

Table 9

A Comparison of the Differences Between
First Effort and Second Effort
Mean Maximal Painfree Systolic Blood Pressures

Sample	N	Mean	Standard Error of the Mean
1st Effort	38	165.0	± 3.6
2nd Effort	38	160.9	± 3.9

t (37) 2.09, $p < .05$

Table 10

A Comparison of the Differences Between
First Effort and Second Effort
Mean Maximal Painfree Diastolic Blood Pressures

Sample	N	Mean	Standard Error of the Mean
1st Effort	38	86.0	± 2.0
2nd Effort	38	82.4	± 1.9

t (37) 2.33, $p < .05$

Table 11

A Comparison of the Mean Heart Rate at the Level
of Angina During First Effort and the Mean Heart Rate
at the Same Workload During Second Effort

Sample	N	Mean	Standard Error of the Mean
Angina on 1st Effort	33	134.4	± 3.5
Same Workload 2nd Effort	33	134.0	± 4.1

t (37) .25, $p > .05$

Table 12

A Comparison of the Mean Rate-Pressure Product at the Level of Angina During First Effort and the Mean Rate-Pressure Product at the Same Workload During Second Effort

Sample	N	Mean	Standard Error of the Mean
Angina on 1st Effort	33	227	± 9.1
Same Workload 2nd Effort	33	220	± 10.5

t (32) 1.82, $p > .05$

Table 13

A Comparison of the Mean Systolic Blood Pressure at the Level of Angina During First Effort and the Mean Systolic Blood Pressure at the Same Workload During Second Effort.

Sample	N	Mean	Standard Error of the Mean
Angina on 1st Effort	33	168.6	± 4.0
Same Workload 2nd Effort	33	163.3	± 4.5

t (32) 2.67, $p < .05$

Table 14

A Comparison of the Mean Diastolic Blood Pressure at the Level of Angina During First Effort and the Mean Diastolic Blood Pressure at the Same Workload During Second Effort

Sample	N	Mean	Standard Error of the Mean
Angina on 1st Effort	33	84.6	± 1.9
Same Workload 2nd Effort	33	81.9	± 2.0

$t(32)$ 1.89, $p > .05$

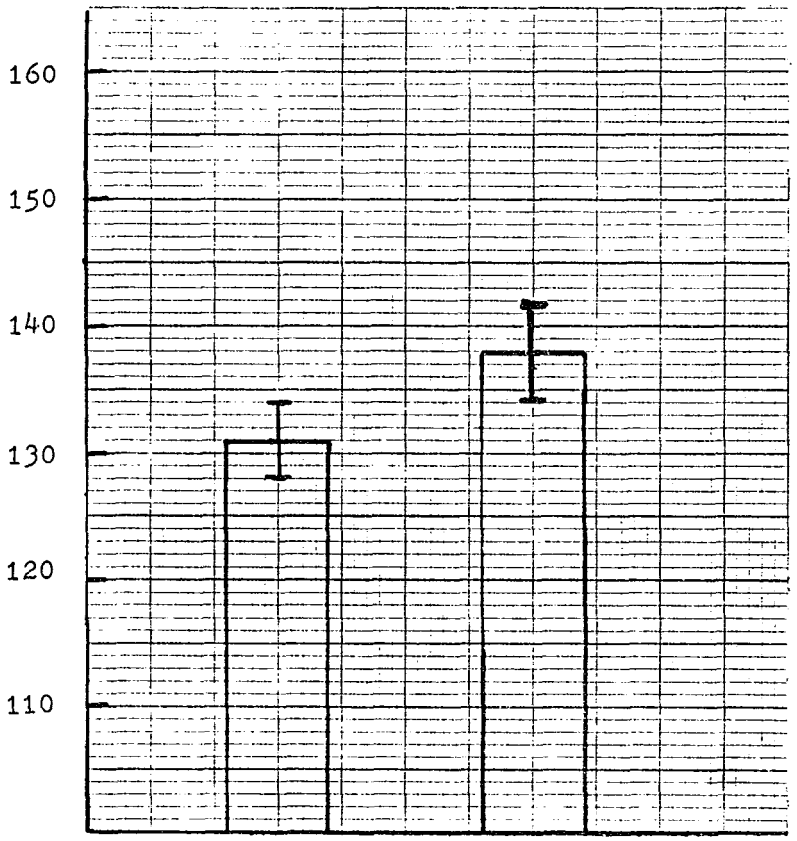

Figure 1. A Comparison of the Differences between First Effort and Second Effort Mean Maximal Heart Rates (± SEM)
Level of Significance=$p < .05$)

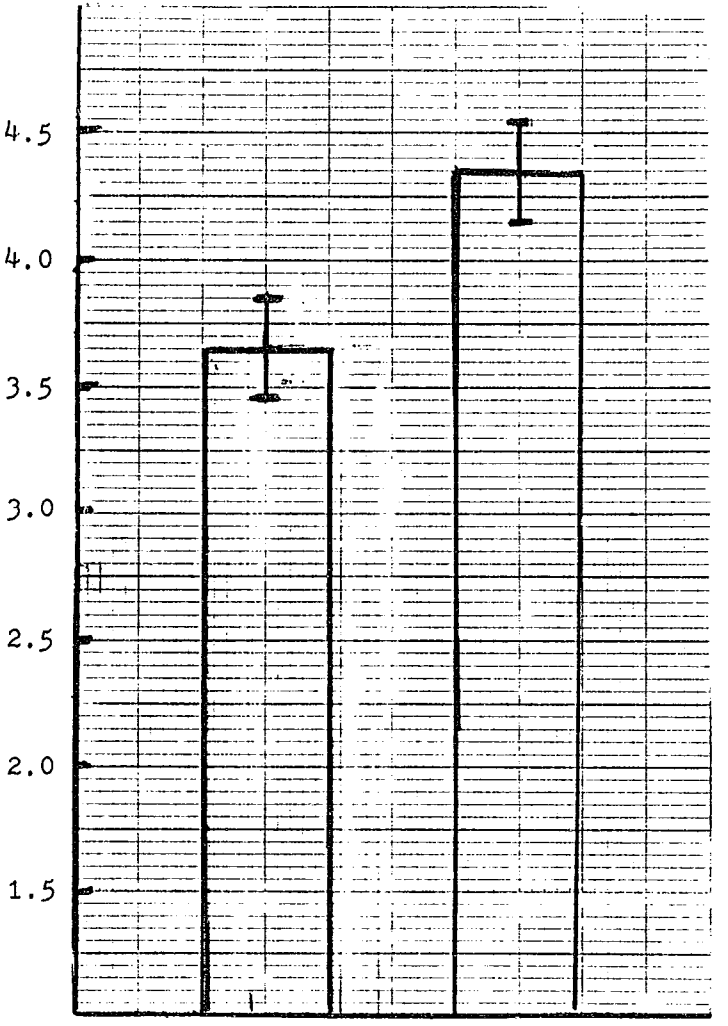

Figure 2. A Comparison of the Differences between First Effort and Second Effort Mean Maximal MET Levels (± SEM)
Level of Significance=$p < .05$

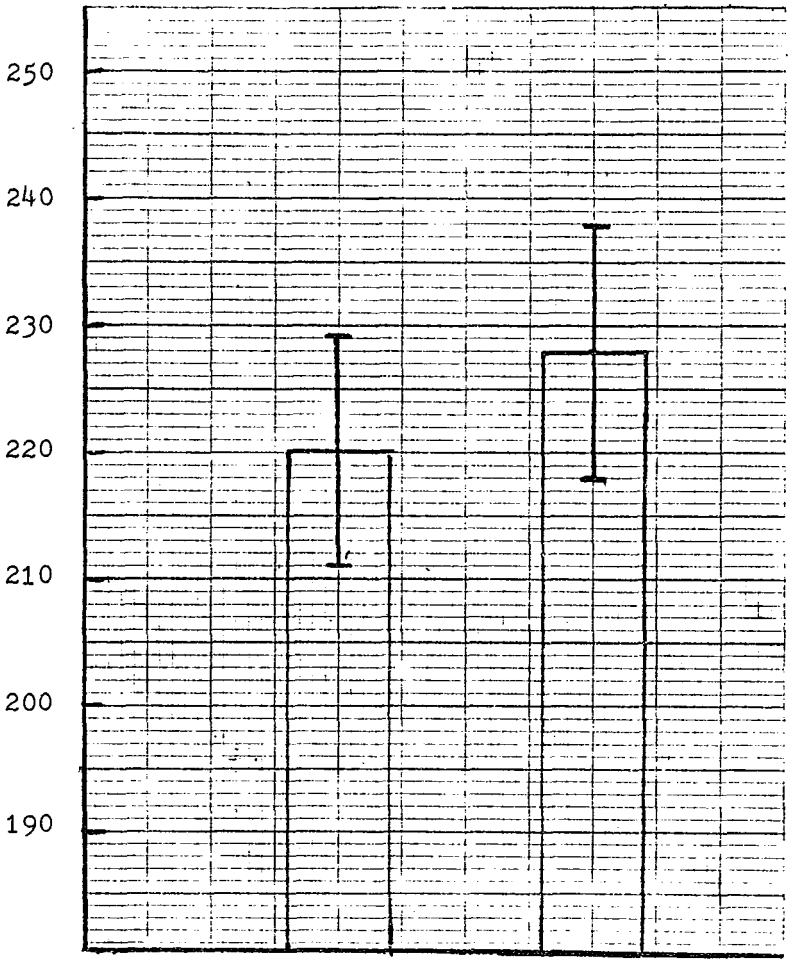

Figure 3. A Comparison of the Differences between First Effort and Second Effort Mean Maximal Rate-Pressure Products (± SEM)
Level of Significance=$p > .05$

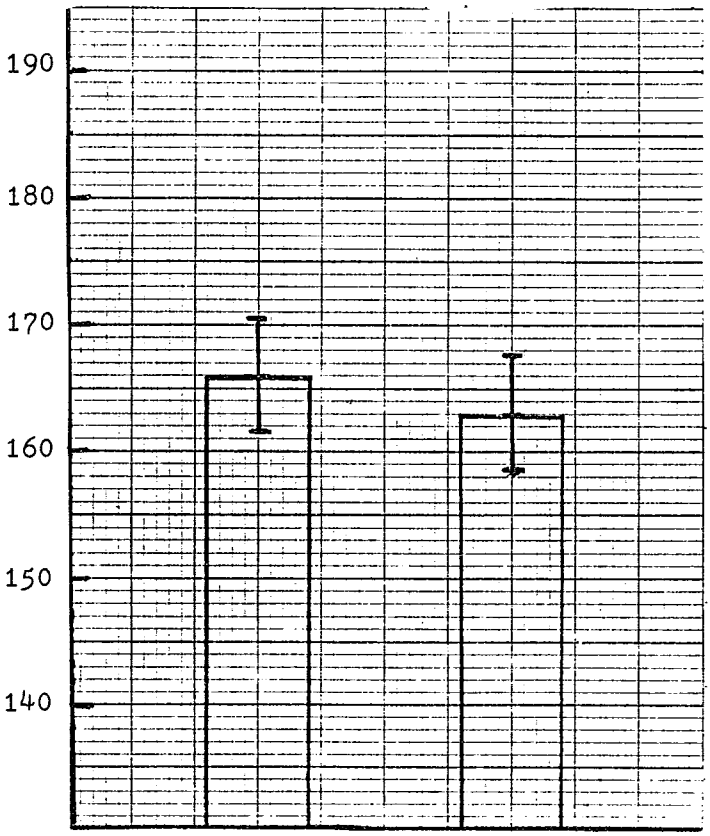

Figure 4. A Comparison of the Differences between First Effort and Second Effort Mean Maximal Systolic Blood Pressures (± SEM)
Level of Significance=$p > .05$

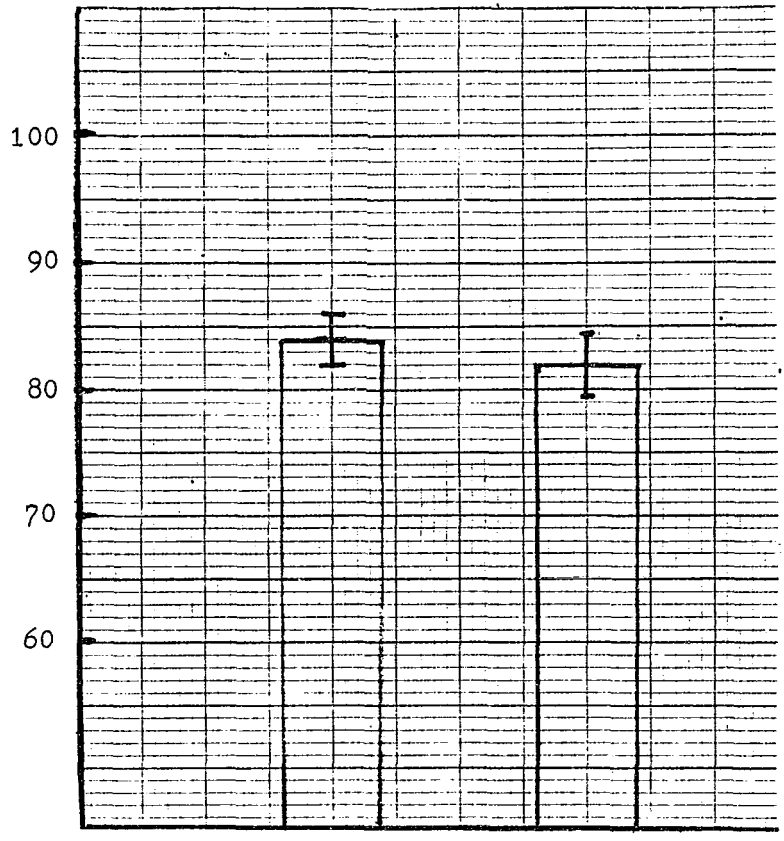

Figure 5. A Comparison of the Differences between First Effort and Second Effort Mean Maximal Diastolic Blood Pressures (± SEM)
Level of Significance=$p > .05$

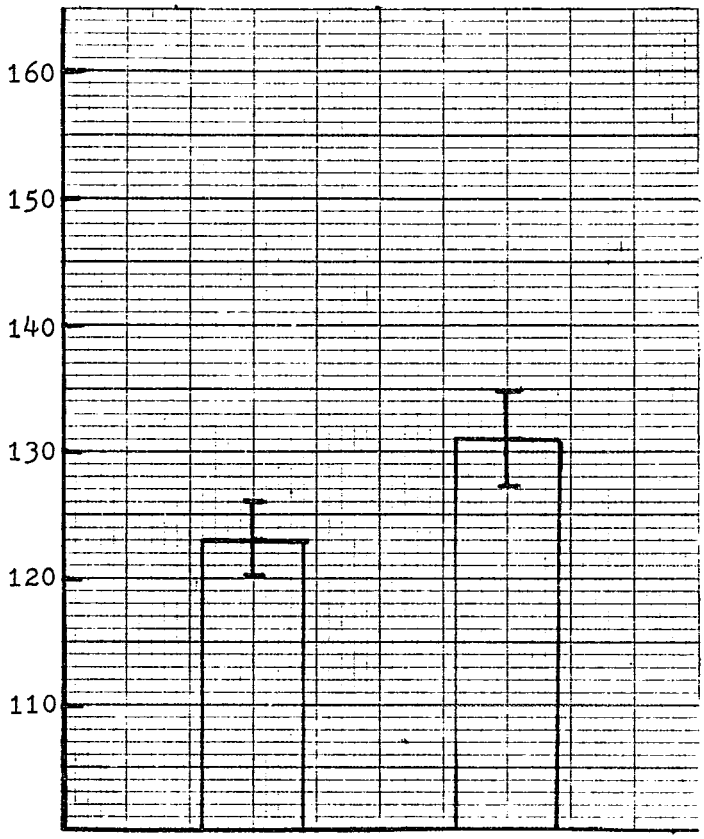

Figure 6. A Comparison of the Differences between First Effort and Second Effort Mean Maximal Painfree Heart Rates (± SEM)
Level of Significance=$p < .05$

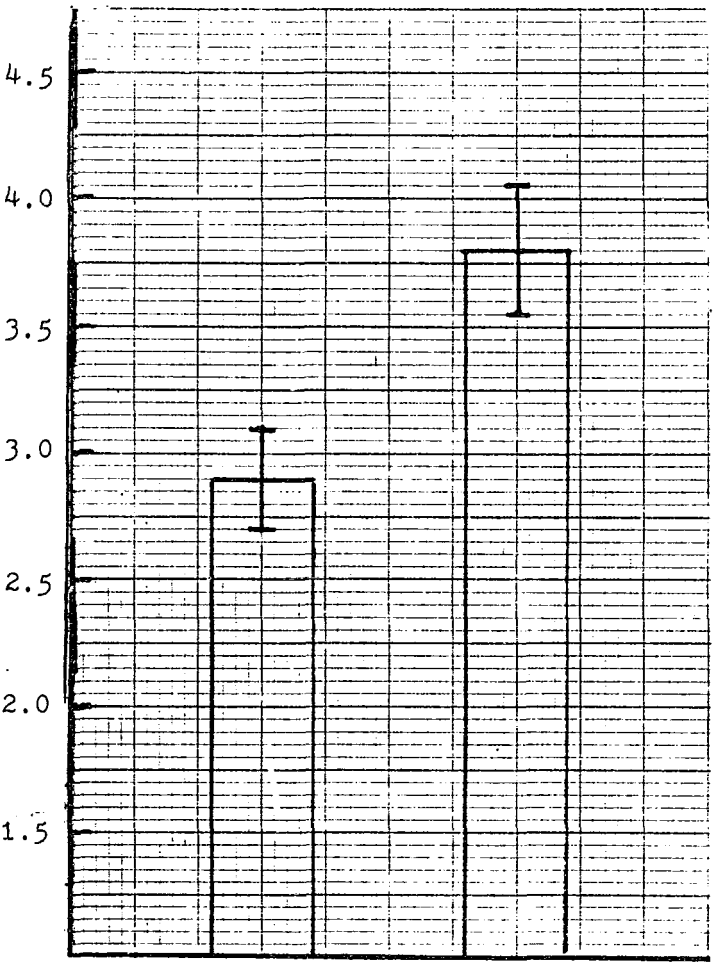

Figure 7. A Comparison of the Differences between First Effort and Second Effort Mean Maximal Painfree MET Levels (± SEM)
Level of Significance=$p < .05$

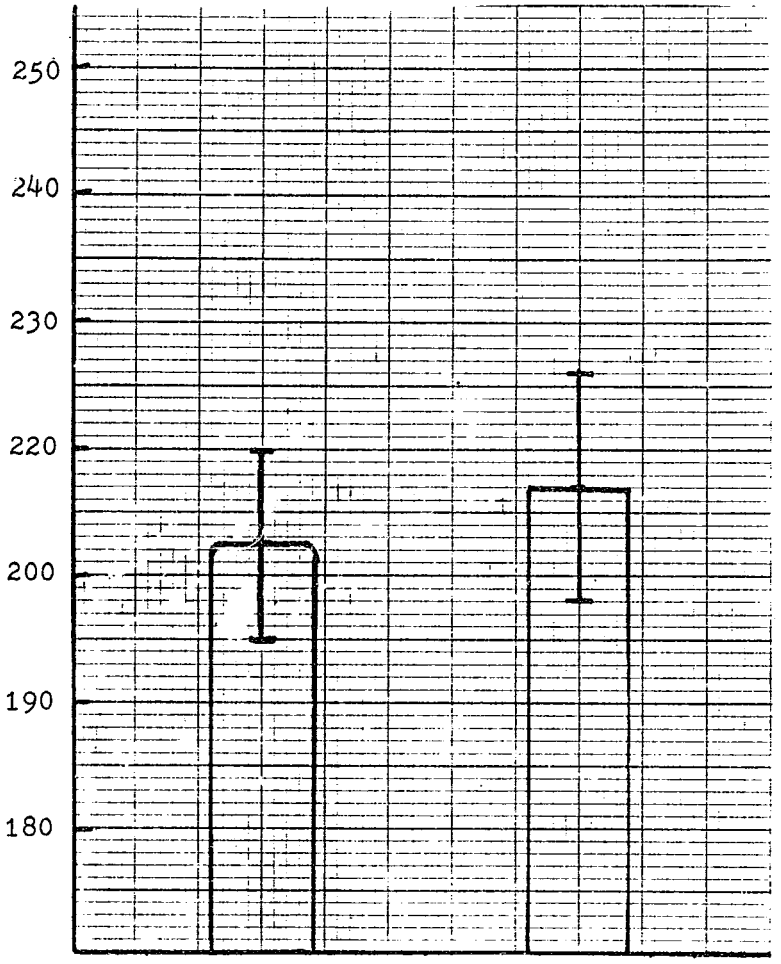

Figure 8. A Comparison of the Differences between First Effort and Second Effort Mean Maximal Painfree Rate-Pressure Products (± SEM)
Level of Significance=$p > .05$

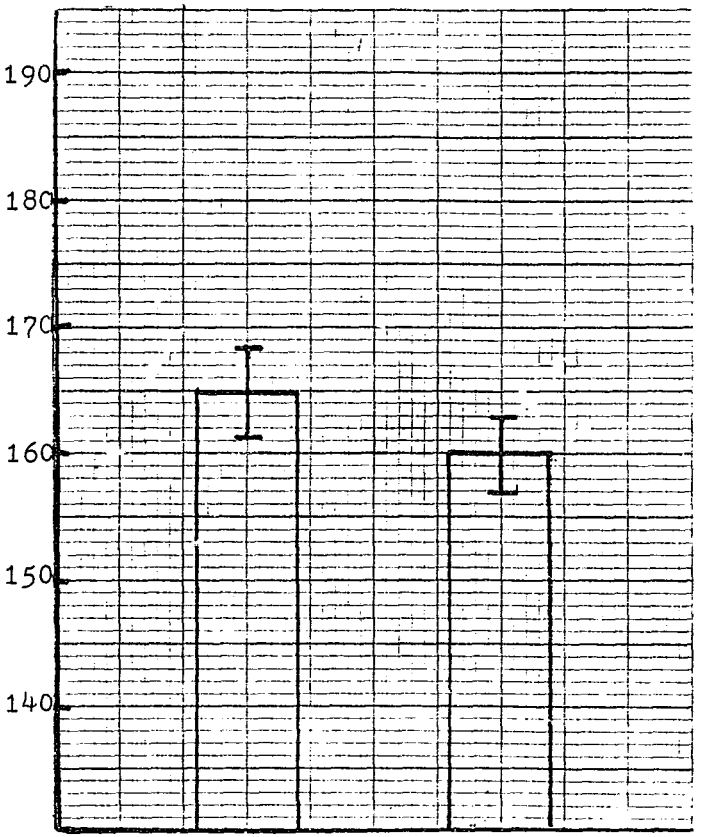

Figure 9. A Comparison of the Differences between First Effort and Second Effort Mean Maximal Painfree Systolic Blood Pressures (± SEM)
Level of Significance=$p < .05$

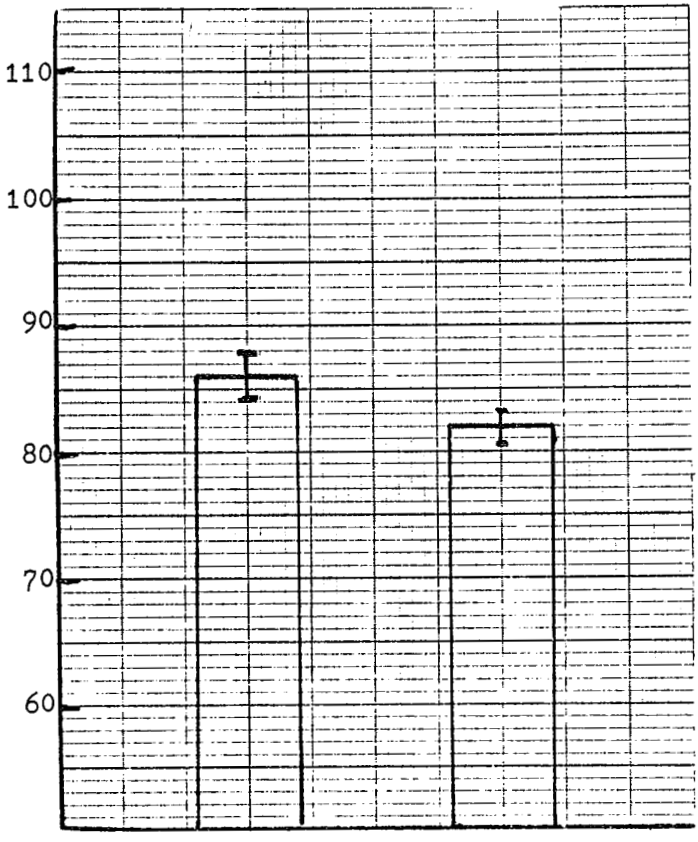

Figure 10. A Comparison of the Differences between First Effort and Second Effort Mean Maximal Painfree Diastolic Blood Pressure (± SEM)
Level of Significance=$p < .05$

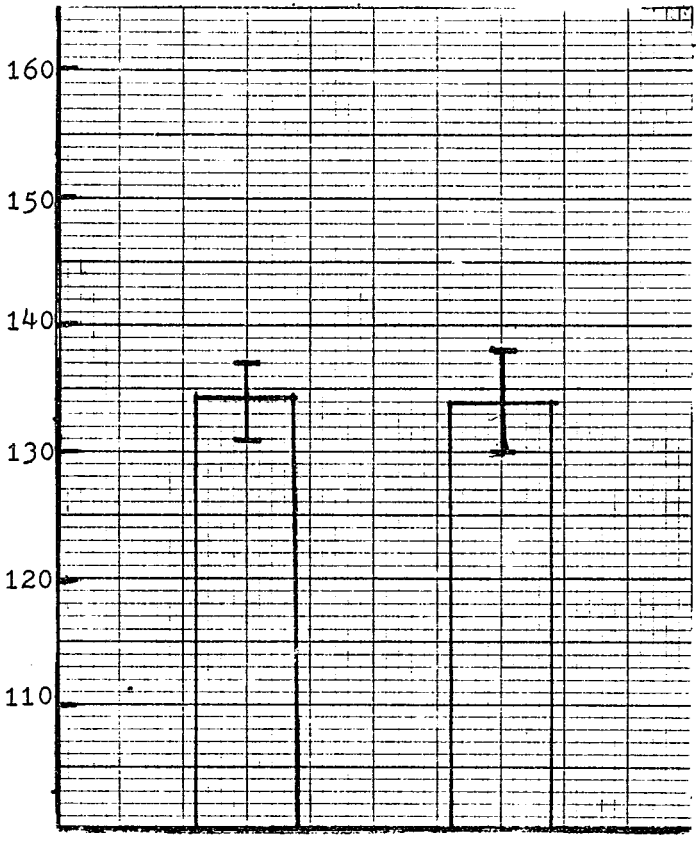

Figure 11. A Comparison of the Mean Heart Rate at the Level of Angina during First Effort and the Heart Rate at the Same Workload during Second Effort (± SEM) Level of Significance=$p > .05$

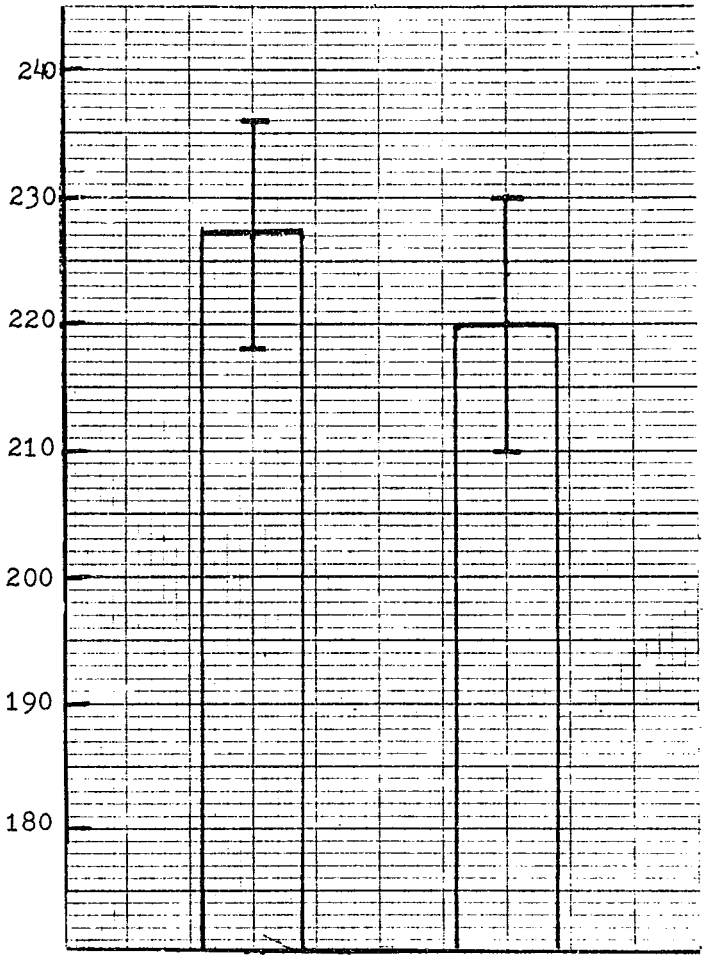

Figure 12. A Comparison of the Mean Rate-Pressure Product at the Level of Angina During First Effort and the Mean Rate-Pressure Product at the Same Work-load during Second Effort (± SEM)
Level of Significance=$p > .05$

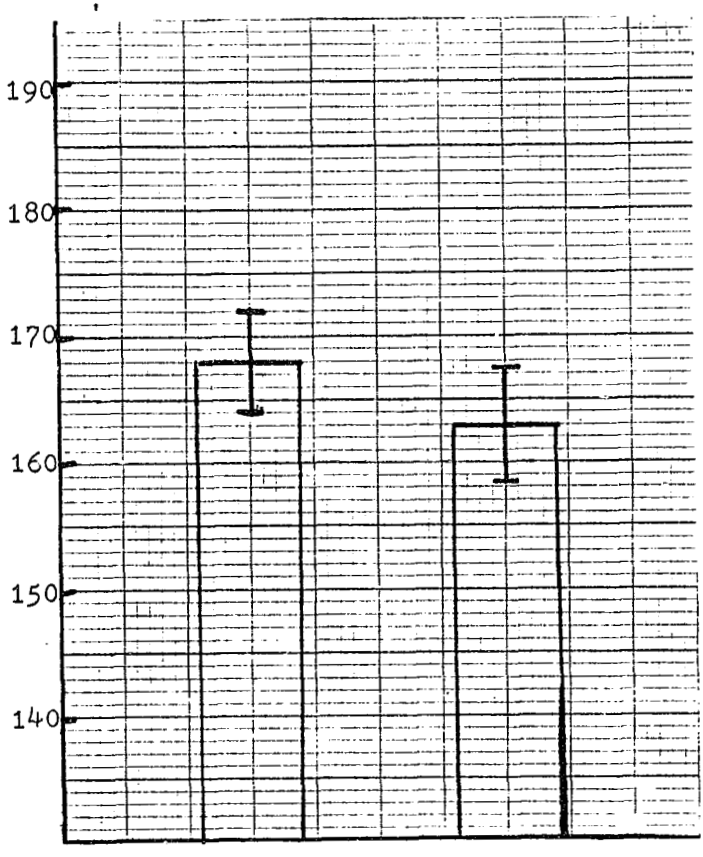

Figure 13. A Comparison of the Mean Systolic Blood Pressure at the Level of Angina during the First Effort and the Mean Systolic Blood Pressure at the Same Workload during Second Effort (± SEM)
Level of Significance=$p < .05$

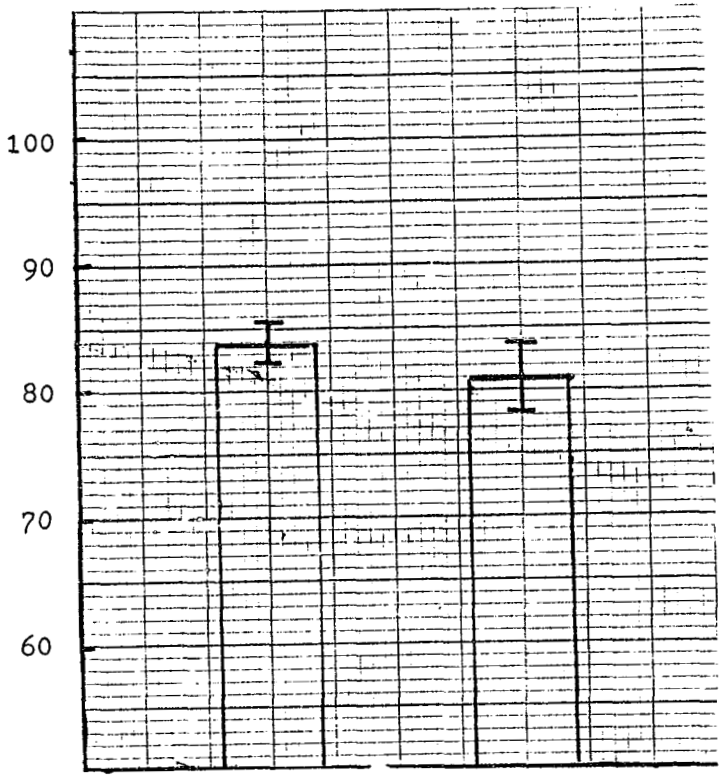

Figure 14. A Comparison of the Mean Diastolic Blood Pressure at the Level of Angina during First Effort and the Mean Diastolic Blood Pressure at the Same Workload during Second Effort (± SEM) Level of Significance=$p > .05$

CHAPTER V

DISCUSSION

The concept of exertional angina and its associated cardiovascular events was first described by Heberden in 1785. The relation of myocardial energy utilization in AP has also been the subject of special investigation.

Angina pectoris is the result of an imbalance between the myocardial oxygen demand and the supply. It is this imbalance that is related to restricted coronary circulation due to coronary atherosclerosis. Coronary circulatory reserve is compromised in response to increases in $\dot{M}VO_2$ as a result of exercise. The coronary blood flow and thereby oxygen delivery, cannot be augmented beyond a limit fixed by the degree of arterial obstruction. The level of $\dot{M}VO_2$ at which this disparity between myocardial oxygen supply and demand occurs represents the internal or cardiac threshold for angina (Amsterdam, et al; Braunwald). Physiologic studies in patients with exertional AP due to CAD have shown a remarkable reproducibility of musculoskeletal work capacity by indirect indices of coronary blood flow (RPP) and directly measured coronary blood flow at the onset of AP (Clausen).

Certain patients with AP have the ability to increase their exercise capacity following an episode of exertional angina. This is the patient who is able to overcome the

attack of AP by persisting in the exercise until the pain subsides; he then is able to equal or increase his exertion without discomfort (MacAlpin and Kattus). This form of adaptation has been considered relatively uncommon, with documentation of very few cases, although the phenomenon has been alluded to throughout medical literature (Wayne and Graybiel; Wayne and LaPlace; and Lewis). MacAlpin and Kattus have documented the largest number of cases (12) accumulated over a two year study. The authors in that study state that the adaptation phenomenon occurs at a steady state in HR and blood pressure, yet the only documented variables in the report are electrocardiographic responses and increases in total exercise time.

A possible explanation for the larger number of subjects, 38, with the post-anginal adaptation in the present study may be due to the difference in exercise protocols. Redwood, et al, stated the beneficial effects of exercise and drug administration may not be seen in tests which use protocols with large increases in workloads. The large increases may surpass the critical threshold of angina in the individuals. In this present investigation a modification of the multi-stage Balke exercise protocol, with fine MET increments and a ten minute cool-down walk between exercise efforts, may have allowed for better documentation of the angina threshold in each individual. This protocol may also have allowed for a better hemodynamic adaptation during the second effort

and, therefore, permitted a significant increase in tolerated exercise capacity.

There may be an improvement in the biomechanical efficiency, or a learning effect, during the second exercise test effort. Burkart and associates postulated that repeated tests may allow for the subject to perform more efficiently with less energy expenditure and, therefore, a lower $\dot{V}O_2$ and $M\dot{V}O_2$. This is difficult to document as in the present study there was a significant increase in the mean maximal HR and a trend for an increase in RPP which possibly may signify an increase in oxygen utilization.

The observed significant difference in maximally attained HR and the trend for an increase in maximal RPP may be due to a "first test" phenomenon. In a "first test" phenomenon the individual undertaking his first exercise test may be nervous. This increase in stress with concomitant sympathetic stimulation may result in an abnormally increased hemodynamic response (i.e., elevated HR and blood pressure) to the exercise workload. Although this may be true, a study by Bartsokas, Obma, Wilson and Moss (1978), utilizing the same protocol as used in the present study, showed this adaptation to be present before and after the administration of beta-adrenergic blockade.

Lewis (1932) and Wayne and Graybiel (1934) felt the phenomenon of second effort was difficult to explain on a simple basis of rates and pressures, but was easy to

understand if one believed that the coronary circulation accommodated itself gradually to the condition of exercise. Price (1951) also wrote that "second wind" in AP was due to some form of adaptation of the coronary circulation during exercise. It was implied that coronary spasm, as suggested by Gallavardin (1925), occurred in AP and that narrowing of a main coronary branch might predispose this main branch's arterioles to spasm; it was this mechanism (dilatation of arterioles) that was overcome during second effort and allowed for an increase in exercise tolerance. The documented increase in musculoskeletal performance observed by the significant increase in the maximally attained MET level a significantly increased HR and a trend for an increase in RPP during the second effort, may indicate occurrence of coronary dilation. Further verification of this mechanism would be evidenced also by an increase in coronary driving pressure as seen by an increase in SBP and DBP. The present investigation noted a tendency for the maximally attained SBP and DBP to be decreased at maximal second effort. However, left ventricular and diastolic volume, ventricular wall thickness and tension, contractility due to sympathetic stimulation, myocardial arteriovenous oxygen extraction and regional distribution of the myocardial blood flow, may affect the relationship of ventricular perfusion and left ventricular work capacity (Amsterdam, et al.; Smith, Guyton, Manning and White, 1976). Alterations in one or more of these parameters

may well enhance myocardial work capacity without an increase in $\dot{M}VO_2$ during the second exercise effort. It may be possible that the cool-down walk performed between the two tests acted as a warm-up or stimulus for the second effort and resulted in a change in one or more of the parameters and aided in coronary circulatory adaptation (Burkart, et al).

Wenckebach (1928) felt the "second wind" phenomenon was due to a regulation in the peripheral circulation. He wrote:

> "It may be, in such cases, that the heart and aorta owing to some difficulty in discharging the greater amount of blood returned to them by the great veins. Indeed, the course of angina may depend not only on aortic conditions but also on circumstances which affect the peripheral circulation."

This regulation may refer to two mechanisms: (1) an increase in venous capacitance vessels and (2) changes in the peripheral conductance vessels.

A resulting increase in venous capacitance vessels may be applicable to the "second wind" phenomenon. When looking at this tenable mechanism, it is important to look at the MET level during second effort which elicited AP on the first effort of the exercise test. It was observed in this present investigation that there was a significant decrease in SBP and a downward trend in RPP and DBP. This may represent a decrease in cardiac output due to a shift of blood from the central to the peripheral circulation. This would then allow for an augmentation in the skeletal muscles ability to extract oxygen. This may be supported in a study by Burkart and associates, where in ten subjects with functional murmurs,

a decrease in cardiac output, SV and left ventricular work led to an increase in the AVO_2 difference and total exercise time during second effort.

The shift of blood from the central to the peripheral circulation would result in a decrease in venous return to the right side of the heart. This decrease would lower left ventricular end diastolic pressure and volume, as seen by the decrease in SBP in the present study. The decrease in volume would change the configuration of the left ventricle into a smaller possibly more efficient ventricle that is better able to attain higher workloads prior to the onset of angina, as observed by the decrease in RPP and the significant increase in MET capacity.

The other consideration is an alteration in peripheral vascular conductance (reciprocal of resistance). Enhanced conductance is a known feature of chronic exercise in individuals with CAD (Clausen). Supporting this supposition of increases in peripheral conductance is the apparent decrease in afterload as seen by the diminished RPP and SBP at the workload on second effort which originally elicited AP on the first exercise effort. To aid in this apparent decrease in peripheral vascular resistance, especially if the cardiac output is diminished, one would expect to see a concomitant increase in coronary perfusion or driving pressure reflected in a constant or increased HR or DBP at this workload. This was not observed in the present study.

Several studies (Burkart, et al; McDonough, Danielson, Wills and Vine, 1974) have shown the alterations of a decrease in cardiac output and SV with repeated and prolonged exercise. These changes may imply the affects of extracardiac alterations as seen by changes in local vasodilatation, peripheral vascular conductance or a combination of these mechanisms. If there is an increase in the diameter of the vessels in the working muscles with prolonged exercise, the individual who is working at a specified HR at the end of an exercise session, may not be receiving beneficial training effects. It may be necessary for the person to increase the HR at the completion of the exercise in order to provide an increase in driving pressure to the muscle to maintain stimulation or overload to provide a training effect.

There is a possibility that the adaptation mechanism may be similar to a nitroglycerin-like effect without the concomitant increase in HR. Administration of nitroglycerin has been found to reduce RPP at submaximal workloads and to increase the anginal threshold. The nitroglycerine affect is assumed to be mediated by dilatation of systemic resistance and capacitance vessels. Among the hemodynamic changes caused by the general vasodilation, a decrease in SBP and in ventricular size can be expected to lower $\dot{M}VO_2$, while the concomitant reflex increase in HR and inotropic state will tend to increase $\dot{M}VO_2$. It has also been documented that there is an increase in the total amount of musculoskeletal

work performed prior to the onset of AP after the administration of nitroglycerine (Clausen). This was observed in this present study as the RPP at the MET level on second effort which elicited pain on the first effort was found to be decreased and the mean maximal and painfree MET level on second effort was significantly increased. There was no change in the HR, as seen in this study, at this level on second effort. Possibly this stable HR may augment the length of cardiac diastole and thus the time for coronary collateral flow, whereas the decrease in diastolic pressure can be seen as a decrease in perfusion pressure. Possibly the net result in relation to a nitroglycerin-like effect is an improved relationship between oxygen requirements and supply to the coronary system.

A significant increase in the musculoskeletal performance along with a concomitant trend for an increase in RPP at the maximal and maximally attained painfree workloads occurs during the "second wind" phenomenon. It is important, however, to study more closely the MET level on second effort which elicited AP on the first exercise effort; it is here one sees the apparent adaptive mechanism(s) coming into play. This adaptation may prove to be important in the evaluation of the physical capacity of the subject with exertional AP. The possible significance of the hemodynamic alterations is seen in the apparent decrease in left ventricular work and $\dot{M}VO_2$, with a simultaneous increase in external work capacity

on second effort. It is felt this physiologic process may be present in all individuals with exertional AP due to CAD and may be augmented if sufficient cardiac and musculoskeletal "warm-up" is attained prior to the onset of physical exertion.

It is beyond the scope of this investigation to document one possible mechanism, as it is likely there is a combined effect on the cardiovascular system. There is a need to further study the cardiac output, contractility, left ventricular work patterns, and myocardial regional blood flow on first and second effort to better determine the possible mechanism of the "second wind" phenomenon.

CHAPTER VI

SUMMARY AND CONCLUSIONS

Summary

This investigation was designed to determine the cardiovascular hemodynamic adaptation to the phenomenon of "second wind". Specific objectives were to determine changes in the mean HR, RPP, SBP and DBP at maximal exercise and maximal painfree workload of the two phases of the treadmill protocol. These hemodynamic variables were also determined at the level of angina during the first exercise effort and then were compared to the same workload during the second effort of the exercise test. An analysis was made of the mean maximal MET level and the mean maximally attained painfree MET capacity on each run of the exercise test.

The subjects of this investigation consisted of 38 private patients of the Skemp-Grandview Clinic. Each individual received a graded exercise test utilizing a modified Balke multistage protocol. The subject was to exercise to the onset of AP. At this time the workload was decreased to 1.5 mph-0% grade (1.5 METS) for ten minutes. At the completion of this time period, and if the AP had been relieved, the same protocol was again given with instructions to exercise to the same level of AP. Heart rate, RPP, SBP and DBP were determined at the third minute of each stage.

All cardiovascular hemodynamic variables were treated by a paired student's t-test with the .05 level of significance selected for rejection of the null hypotheses.

FINDINGS

The subjects were observed to have significant ($p < .05$) second effort differences for the cardiovascular hemodynamic variables of HR, METS, RPP, SBP and DBP at the following levels of exercise:

Mean Maximally Attained Hemodynamic Values

1. An increase in maximal heart rate was observed.
2. An increase in the maximally attained MET capacity occurred.

Mean Maximal Painfree Hemodynamic Variables

1. An increase in heart rate.
2. A decrease in systolic blood pressure.
3. A decrease in diastolic blood pressure.
4. An increase in the painfree MET capacity.

Level of AP First Effort vs. Same Workload Second Effort

1. A decrease in the mean systolic blood pressure was observed.
2. It was noted that of the 38 individuals tested, 22 subjects exercised to a higher workload, while seven of those individuals did not experience AP on the second effort.

The subject group was found not to have a significant ($p > .05$) second effort exercise difference for the cardio-

vascular hemodynamic variables of HR, METS, RPP, SBP and DBP at the following levels of exercise:

Mean Maximally Attained Hemodynamic Variables

1. No significant increase in rate-pressure product.
2. A non-significant decrease in systolic blood pressure.
3. No significant change in diastolic blood pressure.

Mean Maximal Painfree Hemodynamic Values

A nonsignificant increase in the rate-pressure product was found.

Level of AP First Effort vs. Same Workload Second Effort

1. The heart rate was found to be the same for both exercise efforts.
2. There was a non-significant decrease in the rate-pressure product.
3. The decrease in the diastolic blood pressure was found not to be significant.

CONCLUSIONS

Within the limitations of the study, it was concluded that:

1. The maximally attained HR and MET level in subjects with documented CAD and exertional AP, were significantly increased during the second effort of the modified Balke multistage protocol.
2. There was a significant increase in the HR and attained value MET at the mean maximal painfree level of

exercise during the second effort as compared to the first exercise effort.

3. There was a significant decrease in the mean maximal SBP and DBP during the second exercise effort as compared to the first exercise effort.

4. There was a significant decrease in the SBP at the MET level during the second effort which resulted in AP on the first exercise effort.

5. There appeared to be no significant increase in the mean maximally attained or the mean maximal painfree RPP during second effort.

6. There was no significant decrease in SBP or DBP at the maximal workloads on second effort.

7. There was no significant decrease in RPP or DBP at the MET level on second effort that elicited AP on the first exercise effort.

8. The mean HR was unchanged at the MET level on second effort that resulted in AP on the first effort.

RECOMMENDATIONS

1. A similar study could be conducted to observe the cardiovascular hemodynamic variations to the "second wind" phenomenon in the presence of beta and alpha adrenergic nervous system stimulation and blockade. Studying these effects, in addition to those without adrenergic blockade, may further aid in determining the mechanism(s) of the "second wind" phenomenon.

[leaf 68 is missing and not available for filming]

REFERENCES CITED

Adams, C. W., Effler, E. B., Kattus, A., Russek, H. E., Sheldon, W., & Taylor, W. J. Medical vs. surgical therapy for ischemic heart disease. Chest, 1970, 58, 293-314.

Amsterdam, E. A., Hughes, J. L., DeMaria, A. N., Zelis, R., & Mason, D. T. Indirect assessment of myocardial oxygen consumption in the evaluation of the mechanisms and therapy of angina pectoris. American Journal of Cardiology, 1974, 33, 737-743.

Aranow, W. S., Lurie, M., Turbow, M., Whittaker, K., Van Camp, S., & Hughes, D. Effect of prazosin vs. placebo on left ventricular heart failure. Circulation, 1979, 59, 344-350.

Bartsokas, T. W., Wilson, P. K., Moss, R. F., & Obma, R. T. Effect of beta adrenergic blockade on adaptation to angina. Medicine and Science in Sports, 1979, 11, 100 (Abstract).

Bevegard, B. S., & Shepherd, J. T. Reaction in man of resistance and capacity vessels in forearm and hand to leg exercise. Journal of Applied Physiology, 1966, 21, 123-132.

Blackburn, H., Taylor, H. L., & Keys, A. The electrocardiogram in prediction of 5 year coronary heart disease mortality among men aged 50 through 59. Circulation, 1970, 41, (Suppl. 1), 154-170.

Braunwald, E. Control of myocardial oxygen consumption. American Journal of Cardiology, 1971, 27, 416-432.

Burkhart, F., Barold, S., & Sowton, E. Hemodynamic effects of repeated exercise. American Journal of Cardiolocy, 1967, 29, 509-515.

Burns, C. R. Angina. New Zealand Medical Journal, 1961, 297-306.

Clausen, J. P., Klausen, K., Rasmussen, B., & Trap-Jensen, J. Central and Peripheral changes after training of the arms or legs. Journal of Applied Physiology, 1973, 225, 675-682.

Clausen, J. P., Larsen, O. A., & Trap-Jensen, J. Physical training in the management of coronary artery disease. Circulation, 1969, 40, 143-153.

Clausen, J. P., & Trap-Jensen, J. Effects of training on distribution of cardiac output in patients with coronary artery disease. Circulation, 1970, 42, 611-624.

Clausen, J. P., & Trap-Jensen, J. Heart rate and arterial blood pressure during exercise in patients with angina pectoris: Effects of tainiing and of nitroglycerin. Circulation, 1976, 53, 436-442.

Detry, J. M., Rousseau, M., Vandenbrouke, G., Kusumi, F., Brasseur, L. A., & Bruce, R. A. Increased arteriovenous oxygen difference after physical training in coronary heart disease. Circulation, 1971, 44, 109-118.

Dobbs, W., Prather, J. W., & Guyton, A. A. Relative importance of nervous control of cardiac output and arterial pressure. American Journal of Cardiology, 1971, 27, 507-512.

Elsner, R. W., & Carlson, L. D. Postexercise hypermia in trained and untrained subjects. Journal of Applied Physiology, 1962, 17, 436-440.

Epstein, S. E., Redwood, D. R., Goldstein, R. E., Beiser, G. S., Rosing, D. R., Glassey, D. L., Reis, R. L., & Stinson, E. B. Angina pectoris: Pathophysiology, evaluation, and treatment. Annals of Internal Medicine. 1971, 75, 263-270.

Epstein, S. E., Robinson, B. F., Kahler, R. L., & Braunwald, E. Effects of beta-adrenergic blockade on the cardiac response to maximal and submacimal exercise in man. Journal of Clinical Investigation, 1965, 44, 1745-1750.

Gobel, F. L., Nordstrom, L. A., Nelson, R. R., Jorgensen, C. R., & Wang, Y. The rate-pressure product as an index of myocardial oxygen consumption during exercise in patients with angina pectoris. Circulation, 1978, 57, 549-56.

Gorlin, R. Pathophysiology of cardiac pain. Circulation, 1965, 32, 138-148.

Grimby, G., Haggendal, E., & Saltin, B. Local Xen 133 clearance from the quadreceps muscle during exercise in man. Journal of Applied Physiology, 1976, 22, 305-310.

Holmberg, S., Serzysko, W., & Varnauskas, E. Coronary circulation during heavy exercise in control subjects and patients with coronary heart disease. Acta. Med. Scand., 1971, 190, 456-480.

Hurst, W. The Heart. New York: McGraw Hill Company, 1978. p. 339.

Kattus, A. A., Alvaro, A., & MacAlpin, R. N. Treadmill exercise tests for capacity and adaptation in angina pectoris. Journal of Occupational Medicine, 1968, 10, 627-635.

Leftwich, P. Angina pectoris with second wind. S. A. Medical Journal, 1953, 454-455.

Lewis, T. Pain in muscular ischemia. Archives of Internal Medicine, 1932, 29, 713-727.

MacAlpin, R. N., & Kattus, A. A. Adaptation to exercise in angina pectoris: The electrocardiogram during treadmill walking and coronary angiographic findings, Circulation, 1966, 33, 183-201.

Mason, D. T., & Braunwald, E. The effects of nitroglycerin and amyl nitrate on arteriolar and venous tone in the human forearm. Circulation, 1965, 32, 755-766.

Mellander, S., & Johanson, B. Control of resistance, exchange and capacitance functions in the peripheral circulation. Pharmacological Review, 1968, 20, 117-186.

Monroe, R. G. Myocardial oxygen consumption during ventricular contraction and relaxation. Circulation Research, 1964, 14, 294-300.

Muller, O., & Rorvik, K. Hemodynamic consequences of coronary heart disease: With observations during anginal pain and the effect of nitroglycerine. Respiratory Physiology, 1957, 302-309.

Naughton, J. P., & Hellerstein, H. K. Exercise Testing and Exercise Training in Coronary Artery Disease. New York: Academic Press, 1973.

Nordenfelt, I. Bloodflow of the working muscles during autonomic blockade of the heart. Cardiovascular Research, 1974, 8, 263-267.

Obma, R. T., Wilson, P. K., Campbell, S. V., Campbell, D. E., & Moss, R. F. Angina Pectoris of Second Effort, 1978 (Unpublished).

Patterson, J. E., Clark, T. W., & Levy, R. S. A comparison of electrocardiographic changes observed during the "anox emia test" on normal persons and on patients with coronary sclerosis, American Heart Journal, 1942, 23, 837-845.

Price, R. K. First effort angina: Second wind in angina pectoris. British Heart Journal, 1951, 13, 197-202.

Redwood, D. R., Rosing, D. R., Goldstein, R. E., Beiser, D. G., & Epstein, S. E. Importance of the design of an exercise protocol in the evaluation of patients with angina pectoris. Circulation, 1971, 43, 618-628.

Reynolds, D. G., Turtinen, L. W., Kerr, J. C., & Swan, K. G. Adrenergic theory: Application to clinical and experimental surgery. The American Surgeon, 1975, 185-188.

Roughgarden, J. W. Circulatory changes associated with spontaneous angina pectoris. American Journal of Medicine. 1966, 41, 947-961.

Saltin, B., & Stenberg, J. Circulatory response to prolonged severe exercise. Journal of Applied Physiology, 1964, 19, 833-838.

Smith, E. E., Guyton, A. C., Manning, R. D., & White, R. J. Integrated mechanisms of cardiovascular response and control during exercise in the normal human. Progress in Cardiovascular Disease, 1976, 18, 421-443.

Sonnenblick, E. H., Ross, J., & Braunwald, E. Oxygen consumption of the heart: Newer concepts of its multifactoral determination. The American Journal of Cardiology, 1968, 22, 328-336.

Wahren, J., & Byddeman, S. Onset of angina pectoris in relation to circulatory adaptation during arm and leg exercise. Circulation, 1971, 45, 432-441.

Wayne, E. J., & Braybiel, A. Observations on the effect of food, gastric distension, external temperature, and repeated exercise on angina of effort, with a note on angine sine dolore. Clinical Science, 1934, 1, 289-303.

Wayne, E. J., & LaPlace, L. B. Observations of angina of effort. Clinical Science, 1934, 1, 103-110.

Wenckebach, K. F. Angina Pectoris and the possibilities of its surgical relief. British Heart Journal, 1924, 4, 809-815.

Wenckebach, K. F. Toter punkt, "second wind," and angina pectoris. Wein, Klin, Wchnschr, 1928, 41, 1-5.

Wiggers, C. J., & Cotton, F. S. Studies on the coronary circulation. American Journal of Physiology, 1933, 106, 9-15.

APPENDIX A

APPENDIX A

MODIFIED BALKE PROTOCOL

Stage	Minutes	Speed	Grade	METS (estimated)
1	3	1.5	0%	1.5
2		2.0	0%	2.0
3		2.5	0%	2.5
4		3.0	0%	3.0
5		3.4	0%	3.5
6			2%	4.0
7			3%	4.5
8			4%	5.0
9			5%	5.5
10			6%	6.0
11			7%	6.5
12			8%	7.0
13			9%	7.5
14			10%	8.0
15			11%	8.5
16			12%	9.0
17			13%	9.5
18			14%	10.0

APPENDIX B

ST. FRANCIS HOSPITAL HUMAN PERFORMANCE LABORATORY

CONSENT FOR EXERCISE ECG TEST

I,_____, authorize Dr._____and such assistants as he may designate, to administer and conduct the exercise stress test. This test is designed to measure my fitness for work and/or sport; to determine the presence or absence of clinically significant heart disease; and/or to evaluate the effectiveness of my current therapy.

I understand that I will walk on a motor driven treadmill. During the performance of physical activity my electrocardiogram will be monitored and my blood pressure will be measured and recorded at periodic intervals. Exercise will be progressively increased until I attain a predetermined end point corresponding to moderate exercise stress, or become distressed in any way or develop any abnormal response the physician considers significant, whichever of the above occurs first.

Every effort will be made to conduct the test in such a way as to minimize discomfort and risk. However, I understand that just as with other types of diagnostic tests there are potential risks (approximately 2 to 3 per 10,000) associated with an exercise test. These include episodes of transient lightheadedness, fainting, chest discomfort, leg cramps and very rarely heart attacks or sudden death. I further understand that the laboratory is properly equipped for such situations and that its professional personnel are trained to administer any emergency care necessary I voluntarily accept the risks associated with the above procedure.

_____
(Signature of Patient)

WITNESS:_____

DATE: _____

APPENDIX C

Name _____ Age_____ Sex_____

Height: ___ft ___in ____cm Weight: _____lb _____kg

History:
Previous test_____
MI_____
Cath_____
GXT_____

Medications:
_____
_____
_____
_____

First Run	HR	SBP	DBP	RPP	Symptoms
1					
2					
3					
4					
5					
6					
7					
8					
9					
Second Run					
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					

Max MET Level	1st	2nd

Max Painfree MET

APPENDIX D

ST. FRANCIS HOSPITAL HUMAN PERFORMANCE LABORATORY

REPORT OF EXERCISE ECG TEST

NAME: AGE: PHYSICIAN:

DATE OF TEST: PREVIOUS EXERCISE TEST: DRUGS:

HISTORY:

PHYSICAL - HT: WT: BP: AUSCULTATION:

12 Lead ECG - RATE: PR: QRS: QT:

INTERPRETATION:

PROCEDURE: After warm-up and rest, progressive exercise was performed at the levels indicated; each stage 2 minutes unless stated otherwise.

Speed mph, grade %:

RESULTS: Highest sustained exercise: mph % METS (1 MET + resting energy expenditure

BP: Peak-exercise: End point:

Ausculation: Symptoms:

Maximum Heart Rate: ST changes:

Arrhythmias:

Systolic time intervals	Pre-exercise	Post-exercise
QS_2c		
LVETc		
PEP		

Functional Class: Physical Fitness:

Summary:

715-0773-8