AEROBIC EXERCISE TRAINING FOR PATIENTS SUFFERING FROM INTERMITTENT CLAUDICATION

by

Allen M. Bostian

Thesis submitted to the Faculty of the Virginia Polytechnic Institute and State University in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE IN EDUCATION in Health and Physical Education

Approved:

William G. Herbert, Ph.D.
Committee Chairman

Don R. Sebolt P.E.D.
Committee Member

Janet L. Walberg Ph.D.
Committee Member

E. R. McDannald Jr., M.D.
Committee Member

April, 1986
Blacksburg, Virginia
Acknowledgements

I would like to take this time to thank the many people who helped me achieve this lifelong goal. I would like to extend individual gratitude, respect, and admiration to my committee members:

To Bill Herbert: Thanks for all your help and guidance through my education program at Tech, and with this study. If it had not been for your interest, dedication, trust, and hard work, I would not have been able to complete this investigation. Your patience and willingness to talk were greatly appreciated.

To Janet Walberg: Thank you for supporting my topic and research development. Although I did not have the opportunity to spend as much time with you as I would have liked, you listened intently to my ideas and provided good feedback. I hope we can work together again in the future.

To Don Sebolt: Thank you for the no nonsense approach you are so famous for. Your statistical knowledge and experience helped me make the right decisions for the study.

To Dr. McDannald: Thank you for everything. If not for you, I would not have had the opportunity to work with a research topic as this. Your knowledge, patience, and acceptance of the indications for this study made it all
possible. Your patience and willingness to put your trust in me and the program are greatly appreciated. Thanks again.

A special thanks is also extended to my diligent subjects: , , , , , , , and . Way to go gang!!!

I would like to thank , , , , and the staff of Community Hospital Laboratory for their prompt analysis and of my blood work and assistance with the exercise program.

A special thanks goes out to CHRV and . You gave me a free hand with this program, and I hope it does well for you. Thank you for the opportunity to work for, and with you.

And finally, thanks . You listened, suggested, followed up, and supported me throughout. Your love and belief in me got me through the tough times, and made the good ones even better. You opened doors, covered for me, and made me a better person. Thanks are not enough.
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIST OF FIGURES</td>
<td>vi</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>vii</td>
</tr>
<tr>
<td>I. INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>Statement of Problem</td>
<td>2</td>
</tr>
<tr>
<td>Statement of Justification</td>
<td>4</td>
</tr>
<tr>
<td>Research Objectives</td>
<td>7</td>
</tr>
<tr>
<td>Delimitations of the Study</td>
<td>7</td>
</tr>
<tr>
<td>Limitations of the Study</td>
<td>8</td>
</tr>
<tr>
<td>Definitions and Symbols</td>
<td>8</td>
</tr>
<tr>
<td>II. REVIEW OF THE LITERATURE</td>
<td>10</td>
</tr>
<tr>
<td>Skeletal Muscle Metabolism and Circulation</td>
<td>11</td>
</tr>
<tr>
<td>Healthy Individuals</td>
<td>11</td>
</tr>
<tr>
<td>Patients Suffering from Intermittent Claudication</td>
<td>14</td>
</tr>
<tr>
<td>Medical Aspects of Claudication</td>
<td>17</td>
</tr>
<tr>
<td>Pathophysiology</td>
<td>17</td>
</tr>
<tr>
<td>Medical Management Regimens</td>
<td>19</td>
</tr>
<tr>
<td>Exercise Therapy for Intermittent Claudication</td>
<td>22</td>
</tr>
<tr>
<td>Unique Instrumentation</td>
<td>27</td>
</tr>
<tr>
<td>Walking Tolerance Test</td>
<td>27</td>
</tr>
<tr>
<td>Doppler Ultrasonography</td>
<td>28</td>
</tr>
<tr>
<td>Determination of Serum HLa Accumulation</td>
<td>29</td>
</tr>
<tr>
<td>Section</td>
<td>Page</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Evaluation of Perceived Exertion</td>
<td>30</td>
</tr>
<tr>
<td>Summary</td>
<td>32</td>
</tr>
<tr>
<td>III: JOURNAL MANUSCRIPT</td>
<td>33</td>
</tr>
<tr>
<td>Abstract</td>
<td>34</td>
</tr>
<tr>
<td>Introduction</td>
<td>36</td>
</tr>
<tr>
<td>Methods</td>
<td>38</td>
</tr>
<tr>
<td>Results</td>
<td>41</td>
</tr>
<tr>
<td>Discussion</td>
<td>43</td>
</tr>
<tr>
<td>References</td>
<td>48</td>
</tr>
<tr>
<td>Tables</td>
<td>52</td>
</tr>
<tr>
<td>IV: SUMMARY</td>
<td>57</td>
</tr>
<tr>
<td>Implications for Practitioners</td>
<td>61</td>
</tr>
<tr>
<td>Recommendations for Further Study</td>
<td>62</td>
</tr>
<tr>
<td>BIBLIOGRAPHY</td>
<td>64</td>
</tr>
<tr>
<td>APPENDIX A:</td>
<td></td>
</tr>
<tr>
<td>Detailed Methodology</td>
<td>77</td>
</tr>
<tr>
<td>Medications</td>
<td>91</td>
</tr>
<tr>
<td>APPENDIX B:</td>
<td></td>
</tr>
<tr>
<td>Data Tables</td>
<td>93</td>
</tr>
<tr>
<td>APPENDIX C:</td>
<td></td>
</tr>
<tr>
<td>Informed Consent</td>
<td>105</td>
</tr>
<tr>
<td>VITA</td>
<td>109</td>
</tr>
</tbody>
</table>
List of Figures

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1</td>
<td>Effect of Physical Training on Weekly Mean Walking Distance</td>
<td>55</td>
</tr>
<tr>
<td>Figure 2</td>
<td>Effect of Physical Training on Exercise Systolic Blood Pressure</td>
<td>56</td>
</tr>
</tbody>
</table>
List of Tables

Table 1: Effect of Physical Training on Total Performance and Pain Threshold .......... 52
Table 2: Effect of Physical Training on Local Limb Blood Flow (API) ................. 53
Table 3: Effect of Physical Training on Serum Lactic Acid Accumulation ............. 54
CHAPTER I
INTRODUCTION
Introduction

Peripheral vascular disease includes disorders of peripheral arteries, cerebral vessels, veins, and lymphatics. Along with coronary artery disease, vascular disorders are the leading cause of death and disability of adults in the United States (Barnes and Hume, 1979).

Although angiography and surgical reconstruction for vascular disease have been available for several decades, the fact that most patients do not require operations has led to an appropriate reluctance of physicians to perform surgery (Barnes, et al, 1979). Compounding this dilemma are the risks associated with major surgical procedures. Hemorrhage, hematoma formation, infection, and failure of suture lines occur (Simeone, 1984). These complications are particularly risky in vascular procedures. A major artery may be occluded by thrombosis or by imperative ligation with an end result of limb loss, or occasionally loss of life (McDannald, unpublished data, 1985). It then clearly is the role of the primary physician to accurately estimate the risk-benefit ratio of surgery.

Statement Of Problem

A number of therapies have been incorporated in an attempt to lessen the severity of symptoms and increase an individual's physical capabilities. In the past, arterial reconstruction was widely accepted as routine treatment for arterial occlusive
disease (Andrews-Ekers, 1984). However, no clinical or hemo-
dynamic evidence has been presented to substantiate its
efficacy (Snow, et al, 1984). The surgical procedure is
complicated and associated with numerous risks and limitations
for the patient. For this reason, reconstructive surgery has
been limited to those patients who suffer from advanced disease
states which result in severe impairment of tolerance for
physical activity.

Pharmacological therapies, which have been used for the
treatment of peripheral vascular disease, include
vasodilators, anticoagulants, antilipidemic agents, and those
agents which affect the rheologic properties of blood (Dahn,
Ekman, Lassen, Nilsen, and Westling, 1969). The long term
use of oral anticoagulants in claudicators has failed to
demonstrate advantages in terms of improved prognosis
(VanVroonhove and Slot, 1976). A few vasodilators administered
orally can increase the blood flow to affected limbs at rest
in subjects with normal peripheral circulation. However,
clinical investigations with peripheral vascular disease
patients have failed to reproduce such effects (Verstrate,
1982).

Etiologically, the atherosclerotic processes which
account for the interruption of blood flow to an ischemic
limb have been directly linked to certain chronic patterns
of elevated blood lipids (Hutchison, Oberle, Crock, Ford,
Grace, Whyte, Gee, Williams, and Brown, 1983). Chronic hypercholesterolemia, low plasma values of high density lipoproteins (HDL), and high plasma values of low density lipoproteins (LDL) appear to have particularly strong influences on development of atherosclerotic disease in large populations (Brandt, Blankenhorn, and Crawford, 1977). Therefore, the importance of examining the effects of dietary manipulations in chronic hyperlipidemic patients with peripheral vascular disease manifestations is clear (White, 1983).

The fate of patients who suffer from intermittent claudication remains obscure. Surgeons are reluctant to bypass occluded arteries due to associated risks and limitations. Medication therapy has not been shown to be significantly efficacious within groups. Therefore, those patients who suffer from peripheral vascular disease are often left untreated until ischemic pain or gangrene develops, making life unbearable (Ekroth, Dahllof, Gundeyall, Holm, and Schersten, 1978).

Statement Of Justification

It is the purpose of this study to investigate whether aerobic physical training results in increased psychophysiological responses of a group of claudicants. The changes of limb blood flow, muscle oxidative capacity, and pain
tolerance following six weeks of supervised training were evaluated as to changes in exercise performance.

It has been reported that regular exercise can increase walking distances for those individuals who suffer from intermittent claudication (Verstrate, 1982). Such increased physical tolerance for these individuals would be expected to result in increases in employability, productivity, and also decreased anxiety and depression.

The mechanisms responsible for the expected increase are not clear. There is a lack of published data that lends strong support to any single factor (Snow, et al., 1984). Some possible mechanisms which have been investigated individually include psychomotor factors (pain tolerance and mechanical efficiency), metabolic adaptations of the affected limb (anaerobic and aerobic processes), and hemodynamic mechanisms (peripheral vascular resistance changes, perfusion pressures in metabolically active tissue and blood flow redistribution), (Snow, et al., 1984).

In 1984, Vecchiet, Marini, Colozzi, and Feroldi reported that submaximal exercise produced a hyperalgesic state in active muscle tissue of apparently health individuals. However, Snow, et al., (1984) presented evidence that contradicted this effect in diagnosed claudicators. Carlson, Dahllof, and Holm (1974) did report that improved muscle coordination and mechanical efficiency in the active muscle
could reduce the oxygen requirement and therefore enable the patients to walk further.

Various metabolic adaptations have been investigated which lend support to increased aerobic metabolism in ischemic muscle tissue. Ruell, Imperial, Bonar, Thursby, and Gass (1984) reported lower concentrations of venous lactate following training. Similarly, Kohler (1971) found that training led to a significant decrease in femoral venous lactate concentrations during and after dynamic exercise. In addition, Salmons and Henriksson (1981) reported increased glycolytic potential of active muscles.

The response of ischemic muscle tissue to endurance training might include changes in the microvasculature, but attempts to demonstrate such results have produced conflicting reports. Hall, Dixson, Barnard, and Pritikin (1982) reported a significant increase in blood flow due to dilation of deep femoral arteries and existing collateral vessels. While in 1978, Ekroth, Dahllof, Gundeval, Holm, and Schersten reported no evidence of increased collateral circulation was found in a group of training claudicators.

Physical training has been shown to provide symptomatic relief for patients suffering from intermittent claudication. However, no clear cut mechanism has been shown that accounts for this relief. Thus, it is the purpose of this investigation to study selected physiological adaptations of ischemic muscle
tissue to aerobic exercise. In addition, important psychological perceptions of pain tolerance and adaptability will be investigated.

**Research Objectives**

To quantify psychophysiological responses of ischemic muscle tissue to a supervised aerobic exercise program in non-surgical candidates with peripheral vascular disease.

1. To examine the effect of training on aerobic metabolism, as indicated by changes in venous lactate concentration in the ischemic limb.

2. To investigate changes in limb blood flow following training, as indicated by differences in ankle pressure index of the affected limb.

3. To examine the effect of training on patient tolerance, as indicated by changes in a subject's perception of pain and total treadmill time.

**Delimitations of the Study**

The following delimitations were imposed on the study:

1. The sample size was limited to 9 experimental group members.

2. Only individuals who were diagnosed as having intermittent claudication of at least 6 months duration, and who were not surgical candidates were selected for the study.

3. Responses to aerobic exercise were evaluated only after 6 weeks of supervised activity.
4. The study was limited to evaluation of limb blood flow only by lactic acid determination and ankle pressure index.

5. The study was limited to evaluation of the subject's pain perception by total treadmill time and time to pain threshold measurements.

**Limitations of the Study**

The limitations of the study were:

1. Subjects were selected in a non-random fashion.
2. Due to the clinical nature of the population, a complete age matched control group was not possible.
3. Results from this study cannot be applied to situations and environments other than those employed in the investigation.
4. Due to the selectivity of patients for the study, results can be applied only to those individuals who were selected for this investigation.

**Definitions And Symbols**

Ankle Pressure Index (API) - A numerical comparison of the systolic blood pressures in the arm and ankle. It is obtained by dividing the ankle pressure by the arm pressure. Values below 1.0 indicate varying degrees of ischemia.

Arterial Occlusive Disease (AOD) - Any disease process which closes (occludes) the arteries.
Intermittent Claudication (IC) — Repetitive pain and dysfunction of the extremity due to arterial insufficiency during exercise and relieved with a brief rest.

Collateral Circulation — The circulation established through anastomotic communicating channels, when the normal blood supply is compromised or abolished.

Doppler — A diagnostic instrument which emits an ultrasonic beam into the body. This ultrasound is reflected back from moving structures within the body at a frequency higher or lower than this transmitted frequency (Doppler Shift). This shift is amplified and presented as sound, or graphic, or graphic (chart) display.

Lactic Acid (HLa) — A metabolic end product of anaerobic glycolysis.

Paresthesia — Slight or partial paralysis.

Segmental Pressures — A series of blood pressure cuffs placed at regular intervals on an extremity to determine severity and level of arterial disease.
Review of Literature

The literature pertinent to this investigation is presented in two major sections. The first primarily address skeletal muscle metabolism and circulatory adaptations to training and deconditioning. Special emphasis is given therein to acute and chronic changes seen in healthy individuals, and those suffering from intermittent claudication. In addition, the initial section contains a review of the natural pathogenesis of peripheral vascular disease with special emphasis on medical treatment regimens. The second section presents a review of the effects of exercise training for claudicants, and background research pertinent to the methodological aspects of this study. The latter section also includes brief reviews of potential instrumentation, testing protocols, and the dependent measures selected for this investigation.

Skeletal Muscle Metabolism and Circulation

Healthy Individuals

When an individual begins to walk, run, swim, cycle, or perform other similar large-muscle dynamic exercises, the contraction of skeletal muscles requires an immediate expenditure of energy. To supply this energy, the working muscle increases its rate of metabolism through increased degradation of fats and carbohydrates (Gollnick, Pernow, Essen, Jansson, and Saltin, 1980). The muscle cells begin to increase their rate of metabolism through the use of
available substrates, including glycogen, fat, blood glucose, and free fatty acids that are transported in the blood from remote fat stores to the working muscles (Haskell, 1983).

During intense exercise, lactic acid is formed and accumulated within the muscle (Sahlin & Henriksson, 1984). The associated accumulation of subsequently hydrogen ions will ultimately decrease cellular pH and subsequently reduce the ability of a muscle to generate force (Sahlin, Edstrom, and Sjoholm, 1983).

Skeletal muscles undergo profound changes in morphology, physiology, and biochemistry when subjected to demanding physical training (Salmons and Henriksson, 1981). One adaptation to endurance training that has been examined thoroughly is the capacity for oxidative metabolism. Salmons, et al, (1981) reported that an increased oxidative capacity is accompanied by a corresponding increase in the capacity for regeneration of ATP via oxidative phosphorylation. Evidence also exists for increased utilization of free fatty acids as a substrate for muscle oxidation after training (Holloszy and Booth, 1976). An attendant increase in activity of the oxidative enzymes is also coupled with a parallel increase in the protein content of the mitochondrial fraction (Kiessling, Piehl, and Lundquist, 1971, and Morgan, Cobb, Short, Ross, and Gunn, 1971).
Endurance training has been shown to result in lower blood lactate levels during submaximal exercise in both young and middle age subjects (Seals, Hurley, Schultz, and Hagberg, 1984). In addition, the respiratory exchange ratio is lower at the same exercise intensity, reflecting a shift in substrate utilization toward an increased use of fat (Henriksson, 1979, and Hurley, Hagberg, Allen, Seals, Young, Cuddihee, and Holloszy, 1984).

In addition to adaptations in metabolism, marked in regional blood flow occur. Circulation to a working muscle is almost immediately enhanced by an instantaneous vasodilation of the resistance vessels (Haskell, 1983). Also, a drop in venous resistance occurs which results in increased venous return (Salonen, Puska, and Tuomilehto, 1982). These alterations in resistance can increase the blood flow to an exercising muscle as much as 600 ml. minute during submaximal exercise (Haskell, 1983).

Attempts to demonstrate enhanced microvasculature development in human skeletal muscle consequent to endurance training have yielded conflicting results. Early reports by Hermansen and Wachtlova (1971) failed to reveal a difference in capillary density, whereas more recent studies by Andersen (1975) and Broday, Ingjer, and Hermansen (1977) revealed higher capillary density in trained individuals. A report by Andersen and Henriksson (1977) revealed a 50% increase in
the number of capillaries per fiber following two months of training.

The oxidative potential and circulatory perfusion of human skeletal muscle responds rapidly to modifications in physical activity levels. However, rapid decreases toward initial levels is seen after termination of the training regimen (Henriksson and Reitman, 1977). In 1968, Saltin, Blomqvist, Mitchell, Johnson, Wildenthal, and Chapman reported dramatic decreases in maximal oxygen uptake, heart rate, hematocrit, red cell mass, and plasma volume, following five (5) days of bed rest. In addition, increases in lactic acid accumulation have been reported following submaximal exercise in a group of sedentary individuals (Stalin, Nazar, Costill, Stein, Jansson, Essen, and Gollnick, 1976). These responses clearly indicate that declines in the capacity for exercise are largely a reflection of reduced muscle metabolic capability.

Patients Suffering From Intermittent Claudication

Individuals who have intermittent claudication suffer from blood supply that is exacerbated by exertion. However, at rest, tissue perfusion appears to approximate that of normals, as evidenced by levels of lactate release and values for pH on cellular surfaces (Dahllof, Bjorntorp, and Schersten, 1973). This would appear to agree with clinical experience, since symptoms only arise when blood flow cannot match the
metabolic demands of the muscle, i.e. with a certain amount of physical exertion.

In 1984, Bylund-Felenius, Walker, Elander, and Schersten reported spontaneous adaptation in muscle tissue that is intermittently exposed to a reduced blood supply. Similar adaptations in oxidative enzyme capacity, mitochondrial density, and increased capillary density have been reported in the skeletal muscle of claudicants (Sjostrom, 1980, and Hammarston, Bylund-Felenius, Holm, Schersten, and Krotiewski, 1980).

The results of O'Donnell, Clowes, Browse, Ryan, and Blackburn (1977) support these impressions by demonstrating that a higher percentage of glucose and oxygen is extracted to maintain cellular processes in patients with pain at rest.

In 1977, O'Donnell, et al, did report that lactate release and glucose extraction were comparable with an age-matched group of controls at rest. This is supported by Perry, Shires, and Albert (1984), who reported similar tissue perfusion at rest for a group of claudicants and their age-matched controls.

Increased activity of oxidative enzymes in skeletal muscle tissue is one of the adaptive changes in patients with claudication (Bylund-Felenius, 1984). Other changes include increased capillary density (Sjostrom, 1980), and increased mitochondrial activity (Hammarston, et al, 1980). These adaptations help to demonstrate that one consequence of
advancement of the disease is spontaneous adaptation toward increased oxidative metabolism of muscle tissue.

As early as 1974, Dahllof, et al, speculated that physical training might induce an increased metabolic capacity in ischemic tissue with an increased ability of the muscle cell to utilize oxygen and substrates. This hypothesis was supported in 1977 by O'Donnell, et al, who reported that improved glucose extraction may be an adaptive mechanism in trained claudicants, the exercising muscles of whom are forced to produce a greater than normal amount of energy in a potentially hypoxic state.

In addition, Bylund-Felenius (1984) reported an increase in oxidative enzyme capacity and thus a lower lactate/pyruvate ratio at different oxygen tension levels. This indicates a higher oxidative rate, and lower lactate production at submaximal exercise levels with training.

Other adaptive responses of ischemic muscle tissue to training include an increase in muscle succinic oxidase activity (Bjorntorp, Fahlen, Holm, Schersten, and Seberg, 1971), and increased rate of glucose-carbon incorporation into glycogen, lipids, and CO2 (Dahllof, et al, 1974). Furthermore, Bylund-Felenius (1984) noted increases in Citrate syntase and cytochrome-C-oxidase, while phosphofructokinase remained unchanged in ischemic muscle tissue subjected to exercise.
Whether regular training has a beneficial effect on the circulation of ischemic tissue still remains unanswered (Snow et al, 1984). While early research reported an increased collateral blood flow (Skinner et al, 1967), later reports supported increased local aerobic working capacity, despite virtually unchanged peak exercise blood flow (Dahllof et al, 1978, Ruell et al, 1984, and Holm et al, 1973). Despite the lack of explanation regarding the mechanisms of improvement, there is clear evidence that regular physical activity can increase a claudicant's physical working capacity.

Medical Aspects of Claudication

Pathophysiology

The heart and blood vessels form an extremely complex system with branching vessels of varying dimensions (Carter, 1981). Under normal conditions, with a high level of arterial pressure, the flow to body tissues is adjusted to their particular needs at a particular time.

When an individual suffers from intermittent claudication, he is experiencing a reduction in blood flow to an extremity. Intermittent claudication is diagnosed as extremity pain on exertion, which is relieved by rest. The pain is consistent, reproductive, and is often described as a muscle cramp. Upon physical examination, the practitioner may detect some universal claudication signs. These include pallor on elevation, cyanosis, tight shiny and dry skin, thick
coarse nails, or hair loss on the affected extremity. Additional signs of claudication are blanching of nails or skin of foot, cool skin temperature, and a lack of discernible pulses (Andrews-Ekers, 1984).

The flow of blood to a body part is determined largely by the radius of a particular vessel and the concept of laminar flow (Carter, 1981). Since volume flow is proportional to the fourth power of a vessel radius (Poiseulles Law), even small changes in radius may result in large changes in flow (Kaufman, 1962). With intermittent claudication patients, the development of atherosclerotic lesions has resulted in a decrease of flow to the extremities.

The concept that intermittent claudication is a progressive disease has been derived from well documented medical and pathologic observations (Malinow, 1984, and McGill, 1968).

The first pathologic lesions found in arteries are the fatty streaks (McGill, 1968). These fatty streaks do not produce significant arterial narrowing. Second stage lesions are fibrous plaque. These consist of a fibrous connective cap covering a lipid-rich core (McGill, 1984). These fibrous plaques can narrow, and even occlude the artery lumen. The final stage consists of complicated lesions, in which the intimal plaques have become calcified, undergone hemorrhage, ulceration, or thrombosis (McGill, 1984).
The patient with intermittent claudication has most likely progressed into the second stage of pathophysiological development (Dahllof, Holm, and Schersten 1982). The generally do not suffer from pain at rest, but are restricted in their normal or professional life. Once the progression of disease has reached the third stage, some form of operative procedure is required to salvage existing tissue (Coffman 1979).

**Medical Management Regimens**

Patients who suffer from intermittent claudication without ischemic symptoms at rest, and who are not disabled from their occupation, should be treated conservatively (Coffman, 1979). In 1961, Schadt, Hines, and Jeurgens reported that 93% of the patients with intermittent claudication from femoral artery disease, and without diabetes, either had no change (69%), or improved (24%) when treated noninvasively. A similar report by Imparto, Kim, and Davidson (1975) found 79% of a group of intermittent claudication patients remained stable or improved over a mean period of 2.5 years, regardless of the initial severity of symptoms.

The decision to treat intermittent claudication conservatively is based on the unusually good prognosis, for symptoms, the success rate of surgery, and an estimate of life expectancy (Coffman, 1979). A report by Verstrate (1982) concluded that claudication is thus not uncommon, but may be a rather benign manifestation, since 40% of the patients
improve, 40% remain unchanged, and only 20% need vascular surgical repair. It is these considerations that must be reviewed prior to selected treatment for intermittent claudication.

The most popular management regimens for the treatment of intermittent claudication are lifestyle modification, medication therapy, reconstructive surgery, and ultimately limb amputation. The locality and severity of the disease will greatly influence a physician's decision for treatment.

When considering lifestyle modifications, one must evaluate certain underlying causes of atherosclerotic lesions. Loss of weight and an appropriate diet, physical exercise, and abstinence from cigarette smoking are therefore the initial treatment for intermittent claudication (Coffman, 1979).

Medication therapy is based on the philosophy that certain drugs can increase blood flow by direct or indirect actions on the peripheral blood vessels (Coffman, 1979, and Verstrate, 1982).

Fibrinolytic therapy is generally reserved for the most severe stages of atherosclerosis. The indications for this type of therapy must be considered heavily due to a large incidence of minor and major bleeding (Coffman, 1979) These agents are therefore not the drug of choice for intermittent claudication therapy (Verstrate, 1982).
The use of vasodilator drugs for intermittent claudication therapy has resulted in little uniformity. In 1979, Coffman reported that vasodilators could act to dilate blood vessels or stimulate collateral growth, thus resulting in blood flow increases. For a vasodilator drug to be effective, it must act to increase the pressure of the circulation distal to a stenosed or obstructed artery (Verstrate, 1982). Vasodilators have a tendency to lower the peripheral systemic arterial pressure through blockage of alpha receptors (Coffman, 1979). There exists little substantive evidence that vasodilator agents are routinely effective in the treatment of intermittent claudication.

The decision for reconstructive surgery must be made when the disease has progressed to a stage where the limb itself is in jeopardy. Before submitting to surgery, the risk-benefit ratio must be explored thoroughly (Simeone, 1984). In arterial surgery, there exists the risk of wound complications or a major artery may become occluded by thrombosis. In addition, hemorrhage, hematoma formation, infection, and failure may arise (Simeone 1984).

A report by Glickman, Hurwitz, Kimmins, and Evans (1983) stated that of 41 patients who underwent femoro-popliteal bypass procedures, only 26% were not able to return to work. In the same study, it was reported further that 81% of 17 patients who underwent femoral distal bypass surgery were not
able to return to work. Reasons cited included age, degree
of occlusion, and location of obliterans.

Before this irrevocable step is taken, every effort
should be made to retard tissue damage and gain time for limb
salvage (Dahn, Ekman, Lassen, Nilsen, and Westling, 1974).

**Exercise Therapy For Intermittent Claudication**

Wilhelm Erb suggested as early as 1898 that physical
training may possibly be used as therapy for intermittent
claudication. In what has become a classic study, Skinner
and Strandness (1967) reported that three (3) to eight (8)
months of training increased maximal walking time by an average
of 692% for a group of patients with intermittent claudication.
Other reports have concluded that physical training can provide
symptomatic relief from intermittent claudication (Sorlie and
1984).

While increased performance levels following physical
training for claudicants is well documented, contradictory
reports exist as to the mechanisms responsible. Skinner, et
al, (1967) appears to be the first to suggest that collateral
circulation improves with exercise training in intermittent
claudication. This was apparently validated by an improvement
in the resting and post exercise ankle pressure index (API) of
a group of claudicants who trained on a walking treadmill. In
a similar case report, Hall, Dixson, Barnard, and Pritikin
(1982) saw a significant increase in blood flow due to dilation of deep femoral arteries, and existing collaterals. In this report, a 46 year old male presented with symptoms of peripheral vascular disease. Subsequent arteriography revealed 100% occlusion of both femoral arteries at mid-thigh, and some reconstitution of flow via collaterals into the popliteal region. Following an intense 26 day exercise program, he was able to complete three (3) miles of walking in just over one (1) hour. Segmental Doppler tests showed only a 30% drop in pressure of the left leg, and 40% in the right, indicating significant increases in blood flow. A transvenous digital arteriogram was performed, and demonstrated complete obstruction of the superficial femorals. However, the profunda femorals were patent, and showed significant dilation of run of vessels indicating increased collateral utilization. Verstrate (1982) hypothesized a number of factors that may influence increased blood flow for trained claudicants. These include development of collateral circulation, increased capillarization of the vascular bed of skeletal muscles, and redistribution of blood flow to more ischemic tissue. Snow, et al, (1984) also suggested that changes in resistance (Collateral circulation, muscular contraction, and viscosity), driving pressure (arterial and venous pressure), and blood flow redistribution (shunting and capillary density) may be responsible for increases in performance.
There are numerous reports that support increases in circulation following training of claudicants. However, a number of investigators have presented evidence that consider other factors as well. Holm Dahllof, Bjorntorp, and Schersten (1973) reported that change in blood flow are probably not the only reason for improvement of claudication symptoms following physical training. In 1970, an investigation by Zetterquist indicated that regular training induced a reduction in venous oxygen saturation level during exercise in a group of nine (9) trained claudicants. The total amount of work performed during one legged cycling exercise was, in each patient, higher after training. The average amount of leg work tolerated increased from 1950 ± 185, to 2783 ± 259 kpm, representing mean improvement of 43% (p<0.001). These increases in work performance were coupled with no changes in total oxygen uptake at rest and exercise (Zetterquist, 1970). In addition, arterial oxygen saturation was normal in all nine (9) patients (>95 percent) before, as well as after training. However, during exercise, the oxygen saturation of femoral venous blood was significantly lower than before training, at identical loads (p<0.01). This would indicate that regular training brings about a more effective utilization of the available leg blood flow. Holm, et al, (1973) hypothesized that physical training might induce an increased metabolic capacity of the muscle tissue. More
recent studies by Sorlie, et al, (1978) and Jonason (1979), stated lower anaerobic glycolysis (as evidenced by lactate release) is associated with an increased local aerobic working capacity, despite virtually unchanged blood flow. In a group of ten (10) claudicants, Sorlie, et al, (1978) showed a considerable improvement of claudication distance, despite an 8 percent lower leg blood flow following training (p<.05). The venous concentration of lactate was reported 1365 micro mol + or - 78 SEM before training, and 1044 micro mol + or - 44 SEM after 3-4 months of training on an exercise bicycle. In 1984, Ruell, Imperial, Bonas, Thursby, and Gass presented evidence that lends support to a decrease in lactic acid release following training of claudicants. A group of seven (7) patients with diagnosed intermittent claudication (IC) underwent a physical training program lasting eight (8) weeks. While resting venous lactate concentrations were not significantly different before and after training (p<0.01), values were significantly lower after two and four minutes of walking, and exhaustion. Maximum lactate levels of 4.56 micro mol .l (+ or - .51) were reported before training, while values fell to 2.12 micro mol .l (+ or - .31) following training (Ruell, et al, 1984). This investigation reported changes between lactate concentration and walking tolerance demonstrated that improvements were likely to result from metabolic, rather than blood flow increases. An explanation
of this and similar lactate responses to training is provided by Dahllof, et al, (1982). In an overview of a 15 year longitudinal study in Sweden, Dahllof, et al, (1982) has indicated that no appreciable effect in calf blood flow has been found following training. Furthermore, blood flow resistance did decrease. This may be interpreted as an increased ability to dilate blood vessels during work.

The concept that an increase in metabolic function of an ischemic limb is responsible for increases in physical performance of claudicants is well documented in the literature (Sorlie, et al, 1973). Metabolic adaptations of leg muscle have been shown to occur after physical training in healthy persons and patients with intermittent claudication (Dahllof, et al, 1982). In a study of 148 patients with IC, exercise training resulted in a mean increase in walking distance of 234%, while calf blood flow remained unchanged. In addition, prior to training, only 16% of the subjects could walk more than 1000 meters on the treadmill after training, 88% of the patients increased their walking ability. There is little doubt that walking exercise can improve considerable the quality of life of patients with intermittent claudication. Further research is needed to elucidate the mechanisms of these observed responses, and to accurately assess training regimens.
Unique Instrumentation

The disease intermittent claudication (IC) is based upon a careful evaluation of signs and symptoms (Rutherford, 1977). With a thorough evaluation of a patient's history, physical limitations, and simple noninvasive procedures were utilized for Rutherford's study (1977). A walking tolerance test and Doppler ultrasonography were simultaneously conducted attempt determination of blood lactic acid accumulation to attempt to validate adaptations to exercise therapy. To confirm the diagnosis of IC, it is sufficient to rely on these simple noninvasive procedures to diagnose the disease and evaluate therapy (Kallero, Ericsson, and Bergentz, 1983).

Walking Tolerance Test

The utilization of a standardized tolerance test is commonly relied on as basis for management and assessment of therapy (Clyne, Tripolitis, Jamieson, Gustave, and Stuart, 1979). Since a patient suffering from IC has apparently no symptoms at rest, a walking tolerance test serves to effectively elicit an ischemic response. Most walking tests utilize a pre-set speed and percent grade. These are based on an individual's pre-existing physical tolerance levels (Rutherford, 1977). There are no uniform protocols to follow, but most researchers utilize total walking time and onset of pain as limiting factors (Kallero, et al, 1983). This investigation reported that in 349 patients with diagnosed
intermittent claudication (IC), a physical walking tolerance test using walking time and onset of pain as limiting factors confirmed 87-95% of the cases. Investigations of numerous reports has shown total treadmill walking time to be limited to 5 minutes (Kallero, et al, 1982, Ekroth, et al, 1978, Ruell, et al, 1984, Dahllof, et al, 1982).

In 1979, Clyne, et al, reported that the utilization of a standard walking tolerance test was successful in evaluating IC in 117 patients. In a similar study, Kallero, et al, (1983) validated the presence of IC in a group of 289 men and 60 women who underwent a standard walking test, and determination of ankle pressure index (API). In this report, the utilization of these tests confirmed the disease severity and location in 87% of the population (p<0.05).

**Doppler Ultrasonography**

The use of Doppler ultrasonography has been an effective means of evaluating the presence and location of atherosclerotic obliterans (Mannick, 1983). Laboratory data to quantitate the degree of vascular insufficiency can accurately be obtained via Doppler segmental pressures. The diagnostic accuracy of this technique has been documented by many investigators (Le Gerfo and Mason, 1974, Prichard, Martin, and Sherriff, 1979, and Yao, Flinn, and Bergan, 1984). In 1967, Skinner et al, reported using Doppler ultrasonography for the diagnosis of IC in 5 men with arteriosclerosis
obliterans who were being considered for an exercise program. These individuals consistently showed pressure ratios of below .80. A similar report by Qvardfort, Ekroth, Ohlin, Plate, and Saltin, 1984, reported using the Doppler ultrasonography procedure for the evaluation of blood flow changes associated with exercise therapy in a group of a 9 diagnosed claudicants. The major advantages of the procedure have been simplicity of performance, exact positioning capabilities of the Doppler, and economical (Yao, et al, 1984).

The Doppler procedure itself is used for evaluating the characteristics of blood flow in arteries and veins. The sound source (ultrasonic transducer) is placed in direct contact with external skin surface, and the ultrasound beam is directed toward the vessel of interest. The source of the beam being the red blood cells flowing in the vessel (Zagzebski, 1981). The Doppler ultrasonography technique is essential for the determination of ankle pressure index (API) which is defined as the ratio of ankle systolic blood pressure to the highest brachial artery pressure at rest and immediately following exercise. Values of below .90 and above .50 are frequently associated with IC (Kallero, et al, 1983).

Determination of Serum Lactate Accumulation

The determination of serum lactate accumulation in exercising claudicants is not a diagnostic procedure. The accumulation of lactate is widely recognized as a biochemical
30

hallmark of incomplete oxidation (Hermansen and Stensvold, 1972). Several studies have documented the onset of serum lactate accumulation after exercise therapy in normal subjects (Salmons, et al, 1981, and Jacobs, Kaiser, and Karlsson, 1981), and those suffering from IC (Ruell, et al, 1984, and Sorlie, et al, 1978). Ruell, et al, (1984) reported a significant drop (p<0.01) in venous lactate concentration following a physical training program for IC lasting 8 weeks. This lends support to investigations made by Hermansen, et al, (1972), and Jacobs, et al, (1981) who show a decline in lactate responses to regular training programs in apparently healthy individuals. The highest removal rate of lactate was 8 mg/100ml reported by Hermansen, et al, (1972). Therefore, the usefulness of serum lactate determination lies in its evaluative importance of metabolic reactions to training.

A detailed description of the Dupont Automatic Clinical Analyzer (ACA) procedure is provided in Appendix B. This method is a modification of the Marbach and Weil method which employs the oxidation of lactate to pyruvate (Herold, Savory, and Bruns, 1980).

Evaluation of Perceived Exertion

The role of perceived exertion in training and exercise prescriptions has been approached may times in the literature (Heft, Gracely, Dubnar, and McGrath, 1980, Hage, 1981, Noble, 1982, and Vecchiet, Marini, Colozzi, and Feroldi, 1984). In
1984, Vecchiet, Marini, Colozzi, and Feroldi reported a hyperalgesic response in active muscle tissue of 10 healthy individuals. The intensity of pain was recorded by visual analog scale. Pandolf (1984) reported the relationships between perceived exertion and heart rate, oxygen uptake (VO₂), and blood lactate, for continuous and intermittent exercise at identical mean power outputs. A high degree of correlation was found to exist. The r values were as follows:

- Heart rate 0.88
- Oxygen uptake 0.97
- Blood lactate 0.77

For the patient suffering from IC, the usefulness is widespread. As the nature of IC is highly related to symptoms, the perception of pain is extremely useful for indication of initial treatment (Coffman, 1979). The pain felt is a secondary response to an imbalance between the metabolic demands of skeletal muscle and its blood supply (Boyd, Bird, Teates, Wellons, McDougall, and Wolfe, 1984).

In 1982, Nobel developed a category-ratio perceived exertion scale which was an adaptation of the angina scale developed during the 1950's by Borg, Holmgren, and Lindblad. This scale was developed for evaluation of curvilinear responses (lactate and pulmonary ventilation). This scale is particularly applicable for claudicants, since it is an indirect measurement of the anaerobic stress associated with incomplete oxidation.
(Noble, 1982). Much of the literature cited uses lactate accumulation as an indicator of increased physical tolerance, so the applicability of Borg's Category-ratio scale would appear to be high (Ruell, et al, 1984, and Boyd, et al, 1984).

**Summary**

The indications for exercise therapy as treatment for intermittent claudication are based on the almost universal acceptance by practitioners (Ruell, et al, 1984). Although it is almost certain to result in increased metabolic efficiency of ischemic muscle tissue, the circulatory response of the exercising claudicant is vague. Simple noninvasive techniques (Doppler ultrasonography and walking tolerance tests) can effectively diagnose the disease and be used for treatment verifications. However, the use of serum lactate accumulation is necessary to validate any metabolic adaptations to training.

The disease known as intermittent claudication is rather a benign manifestation that if left untreated may or may not progress. However, the usefulness of simple, conservative treatment regimens are indicated to ensure a high quality of life for the individual.
CHAPTER III
JOURNAL MANUSCRIPT
AEROBIC EXERCISE TRAINING FOR PATIENTS
SUFFERING FROM INTERMITTENT CLAUDICATION

Allen M. Bostian, M.S., E. R. McDalland, Jr., M.D., William G. Herbert, Ph.D., Janet L. Walberg, Ph.D., Don R. Sebolt, P.E.D., and Melody S. Rakes, R.N.
Abstract

Nine patients with intermittent claudication diagnosed at least 6 months before this investigation were evaluated to determine the effects of walking exercise on serum lactate accumulation (HLa, mmol-l⁻¹), ankle pressure index (API), total treadmill time (sec), and onset of leg pain (sec) in the most severely diseased limb. Subjects were evaluated via a functional walking tolerance test before participation in a thrice weekly exercise program lasting 6 weeks. Post-treatment, the participants were re-evaluated on an identical walking test. Measurements of HLa accumulation and API were taken at rest and immediately following termination of the treadmill test. In the training sessions, body weight (kg), exercise heart rate (HR), systolic blood pressure (SBP), and distance traveled (m) were recorded daily. There were no significant changes (p<.05) after training in total time (mean increase = 23.7%) or time for onset of pain in the treadmill test (mean increase = 30.1%). Neither were there significant changes (p<.05) in API or HLa levels taken immediately after exercise, when pre- and post-training treadmill test data were compared. The weekly responses for exercise HR, and SBP, as well as body weight remained stable throughout. Mean distance walked by the subjects increased 203% (+ or - 45%) across the 6 weeks. These data suggest that increases in total distance walked in an exercise program were apparently
not related to HLa accumulation or API measurements in the working muscles, and that other mechanisms must be investigated in future studies to explain enhanced performance of such subjects.

Index Terms:

intermittent claudication, exercise training, walking tolerance test, ankle pressure index, serum lactate accumulation, distance walked.
Introduction

Wilhelm Erb\textsuperscript{22} suggested as early as 1898 that physical training could possibly be used as effective therapy for persons suffering from intermittent claudication (IC). In what has become a classic study, Skinner and Strandness (1967)\textsuperscript{21} reported that 3 to 8 months of walking exercise increased maximal treadmill walking time by an average of 692\% for a group of nine claudication patients. Since then, many investigations have been published which uniformly indicate that patients with intermittent claudication can improve substantially pain free walking distance and maximal walking distance through exercise.\textsuperscript{2,6,8,9,13,18,22}

While increased performance following physical training is well documented in patients with intermittent claudication, the mechanism(s) explicating the improvement remain unclear. Skinner, et al,\textsuperscript{21} suggested that perhaps collateral circulation in the trained musculature might occur with physical training. Their explanation was based on the finding that ankle pressure index (API) increased in both resting and post-exercise claudicants trained on a treadmill. Another investigation by Hall and Barnard (1982) corroborated the findings of Skinner, et al,\textsuperscript{21} for a single 46 year old male with intermittent claudication. In this report baseline arteriography revealed 100\% occlusion of both femoral arteries at mid-thigh with minimal reconstitution of flow via collaterals
into the popliteal region. Following an intense 26 day program of exercise and low cholesterol diet (Pritikin's diet), the subject was able to complete 3 miles of walking in just over 1 hour. Follow-up Doppler examination revealed only a 40% drop in API, resulting from increased collateral blood flow. These findings indicate that for this case, a program of exercise combined with a low cholesterol diet resulted in 60% more blood flow to occluded regions via collateral reconstitution. Further reports have hypothesized a number of factors that may contribute to increased blood flow in claudicants after training. These include development of collateral circulation, increased capillarization of the vascular bed in skeletal muscles, and redistribution of flow to more ischemic regions in exercising muscle.

A number of published investigations have demonstrated that exercise training in claudicants is associated with increases in metabolic capacity of ischemic tissue. Sorlie, et al, and Jonason, et al, stated that a decreased level of anaerobic glycolysis (evidenced by lactate release), is associated with increased local muscle working capacity despite virtually unchanged blood flow in active tissue. Favorable metabolic adaptations of leg muscle have also been shown to occur after physical training in both healthy persons and patients suffering from intermittent claudication (IC).
There exists little published research concerning the possible local circulatory and metabolic mechanisms responsible for increases in walking tolerance seen in claudication patients following training. The aim of this study was to evaluate the effect of physical training on physical endurance performance, as well as the blood flow and venous lactate concentration of the most occluded limb in a relatively select population suffering from intermittent claudication.

**Methods**

**Subjects**

Nine adult volunteers with diagnosed intermittent claudication (IC) participated in the study. Criteria for inclusion in the population included: a history of diagnosed IC of at least 6 months duration, and a prognosis by their attending physician that vascular reconstructive procedures were not indicated, and/or previous reconstruction techniques had not remained successful in maintaining circulation. All subjects were informed of the nature of the study before giving their written consent to participate.

**Functional Walking Tolerance Test**

Each subject underwent two identical treadmill walking tolerance tests, one at the outset of the study and another immediately following 6 weeks of thrice weekly exercise training. A standardized treadmill protocol was employed for each subject using a constant speed and grade; if the
participant had a resting ankle pressure index (API) below .60 the treadmill speed was set at 26.8 (=1 mph) m.min⁻¹ and 5% grade; and for subjects with a resting API greater than .60 treadmill speed was increased to 53.6 (=2 mph) m.min⁻¹.

The time (sec) at onset of pain and time (sec) of maximal tolerance were recorded. All tests were terminated when the subject reported unbearable leg pain, or following 5 minutes of treadmill exercise. Blood samples for determination of serum blood lactic acid (HLa) and pressure recordings for calculating API were also taken both before and immediately following exercise. All subjects were monitored during the test with a standard 12 lead EKG.

**Determination of Serum Lactic Acid**

Approximately 5 ml of blood were drawn from a 16 gauge 2 inch Deseret Angiocath (Cat. # 2814) secured in the deep femoral vein of the most diseased leg of each subject. Samples were collected at rest, immediately following treadmill exercise, and at 6 minutes post-exercise. Samples were assayed for serum HLa using the DuPont ACA Procedure. In the event the angiocath could not be properly inserted, individual samples were collected using 10cc disposable syringes with 20 gauge needles. In three out of 9 patients, the angiocath could not be secured and blood collection was therefore prevented.
Calculation of API Via Doppler Technique

The calculations for API were conducted using a Medasonics Vasculab noninvasive Vascular Diagnostic Bi-directional Doppler system, and a hand held Medasonics Ultrasound Doppler Blood flow detector (Model #BF4A). Each examination consisted of determination of segmental pressures over the brachial artery at the antecubital fossa of the left arm and the posterior tibialis artery of the most diseased leg. Pressures were determined at rest and immediately following exercise. Doppler evaluations included recording of analog wave tracings and calculation of API. All resting measurements were made in duplicate so that procedural reliability could be estimated.

Exercise Training Program

The training program involved a 60 minute supervised exercise program three times a week for 6 weeks. A 75% attendance level was set as a criteria for a subject to be in the study. Each subject was measured for body weight (kg), heart rate (bts./min.\(^{-1}\)), and sitting blood pressures (mmHg) prior to exercising at each training session.

Warm-up activities included dynamic and static leg exercises done in both the sitting and standing postures. After warm-up, subjects began walking on a 48.8 m circular track. Each was asked to walk until ischemic limb pain forced them to stop. While recovering, the subjects were asked to perform alternate modes of arm or leg ergometry. Immediately
upon completion of the exercise session each subject underwent measurement of exercise heart rate, blood pressure, rate of perceived exertion (Borg, 1982), and total exercise time. A required group cool-down was then conducted with special emphasis on static stretches.

Statistical Procedures

Data for all dependent measures were analyzed using dependent t-test procedures. An alpha level equal to or less than 0.05. was considered significant. Means (X), standard errors (SE), and correlation coefficients were calculated using standard statistical procedures.

Reliability of all dependent measures was assessed using the Spearman correlation coefficient procedure.

Results

Values for total treadmill time (sec) and the onset of pain (sec) are presented in Table 1. The mean increase for total treadmill time was 69.7 sec or 23.7%. A mean increase of 37.8 sec (30.1%) was noted for time of treadmill exercise of which claudication threshold was noticed. Neither of these variables showed statistically significant changes over time. It should be noted that the protocol design did not allow 4 out of 9 patients to improve in total treadmill time.

(Insert table 1 about here)
Tables 2 and 3 present the calculated ankle pressure index and serum lactate accumulation pre- and post-training, at rest and immediately post-exercise. For API, a mean decrease over the treatment period of .08 (9%) was reported in the resting measurements while IPE showed no change. These changes were not statistically significant. A mean increase in serum lactate accumulation of .13 m mol.l\(^{-1}\) (15.0%) was reported at rest and .92 m mol.l\(^{-1}\) (27.0%) IPE. Neither of these changes were statistically significant across the treatment period.

(Insert Tables 2 and 3 about here)

The mean weekly changes across the training period for exercise heart rate (bt. min.\(^{-1}\)), systolic blood pressure (mm Hg), and distance traveled (m) are depicted graphically in Figures 1-3. For the group, exercise heart rate and peak systolic blood pressure remained stable throughout the training period. The subjects' body weights also remained stable throughout the training period. However, mean distances covered each week showed an increase from 556.4 m (SE=+/−268.7) from week one of training to 1128.4 m (SE =+/-509.4) at week six of the study. This represents an increase of 203% for 6 weeks, with the greatest individual improvement being 498%, and the lowest being 115%.
Discussion

The results of this investigation are in agreement with several studies which show that patients who suffer from intermittent claudication (IC) have an increased walking ability following training.\textsuperscript{6,10,18}

In the present study, the group demonstrated an average increase in walking distance during the training session over 200\% with the majority of the improvement seen in the first 3 weeks. Patients varied considerably in individual improvements. The greatest changes were seen in those who suffered from disease of the inflow portion (proximal) of leg circulation versus those who suffered from distal runoff occlusions. This claim is supported by the data that show the proximal patients tended to have more of a training effect as evidenced by distance covered, total treadmill time improvements, and greater times to onset of claudication threshold.

The specific mechanism for the improvement in walking distance following physical training is unclear, but Ruell, et al,\textsuperscript{18} have suggested that peripheral rather than central factors are largely responsible. The results of this study do, however, suggest small central training adaptations. Increased exercise times and walking distances were covered
during training with little changes in exercise heart rates and systolic blood pressures. This low level central cardiovascular training effect appears to occur despite ambulatory restrictions and low metabolic intensity of training caused by atherosclerotic disease.

It has been suggested that physical training leads to increased blood flow due to growth of arterial collaterals.\textsuperscript{21,17,18} In the present investigation, no significant changes in local blood flow occurred after training as indicated by unaltered Doppler indices of blood flow following exercise.

These results are in accordance with much of the research which has been conducted to evaluate vascular research and exercise adaptation. Such investigations have demonstrated that aorto-iliac disease (proximal) with its limited potential for collateral growth responds as well to exercise training as femo-popliteal disease.\textsuperscript{10}

Other investigators have postulated that improvements in walking distances are related to increased aerobic working capacity of an exercising limb.\textsuperscript{12,23,18}

In this study, physical training of subjects resulted in no significant differences in femoral venous lactate concentrations at rest and immediately following exercise. Similarly, Ruell, et al,\textsuperscript{18} found that resting venous lactate samples were not significantly lower ($p<.05$) before or after
training, at rest, or after 4 minutes of exercise, but were significantly lower following 8, 15, and 30 minutes exercise. It is interesting to note that for their investigation, Ruell, et al, used the antecubital vein for blood collection, and the patient population exercised 8 weeks. In the present study, blood samples were drawn from the femoral vein of the most diseased leg, and exercise sessions lasted only 6 weeks. Also, three subjects were not able to be sampled due to catheter failure. These differences may account in part for the variations seen.

In addition, training induced reductions in venous lactate accumulation may not occur if training is of only moderate intensity. Also, there is a definite age related diminution of aerobic exercise capacity and ability to diffuse lactate. Other possible explanations include improvements in gait technique and alternate sample site for blood collection to maximize lactate accumulation measurement.

The distribution of lactate might be delayed as a result of age-related changes in vasomotor control which mediates redistribution of blood flow. In this investigation, subjects were limited by their age and severity of claudication. These limitations were maximized in the older subjects who had more deconditioning and subsequently had more difficulty walking.
Increased pain tolerance is difficult to estimate, but the fact that onset of pain and total treadmill time change to the same extent as a result of training may indicate that increased walking distances were not greatly influenced by pain tolerance changes. There does exist the potential for development of psychological adaptations to pain tolerance in IC. With the study population, several factors may have influenced a subject's perception of pain. These include conversational distractions, varying perceptual focus (e.g. not as apt to let leg pain bother them as much), and age related reductions in deep muscle lactic acid distribution.

The controlled training of patients with claudication pain appears to be an effective treatment mode. Apart from the beneficial effect on walking tolerance, it appears to have other benefits. It provides the patient with a feeling of well-being by working toward well trained muscles and becoming physically fit. The patients may perhaps be no longer afraid of their disease.

It should be noted that in 4 of the subjects, the time on the pre-training treadmill test was maximized. This may account for our apparent lack of increases in this dependent variable. Also, with the obvious defect in design from a lack of a control group, the data analyzed could provide little statistical verification. It must be concluded that from the tendencies seen that a combination of physiological mechanisms
with a positive psychological atmosphere is a major precursor for success.
References


<table>
<thead>
<tr>
<th>SS</th>
<th>PRE</th>
<th>POST</th>
<th>DIFF</th>
<th>t-RATIO</th>
<th>PRE</th>
<th>POST</th>
<th>DIFF</th>
<th>t-RATIO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>158</td>
<td>300</td>
<td>142</td>
<td></td>
<td>48</td>
<td>190</td>
<td>158</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>255</td>
<td>300</td>
<td>45</td>
<td></td>
<td>48</td>
<td>120</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>300</td>
<td>300</td>
<td>0</td>
<td></td>
<td>90</td>
<td>160</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>300</td>
<td>300</td>
<td>0</td>
<td></td>
<td>118</td>
<td>212</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>300</td>
<td>246</td>
<td>-54</td>
<td></td>
<td>145</td>
<td>129</td>
<td>-16</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>246</td>
<td>300</td>
<td>54</td>
<td></td>
<td>148</td>
<td>70</td>
<td>-78</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>120</td>
<td>300</td>
<td>180</td>
<td></td>
<td>50</td>
<td>100</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>300</td>
<td>300</td>
<td>0</td>
<td></td>
<td>120</td>
<td>46</td>
<td>-74</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>40</td>
<td>300</td>
<td>260</td>
<td></td>
<td>20</td>
<td>100</td>
<td>80</td>
<td></td>
</tr>
</tbody>
</table>

x= 224.3 294.0 *2.12 87.4 125.2 *1.92
SEM 83.46 17.60 44.70 51.18

*t-RATIO at p<.05=2.31, df=8
Table 2

Effect of Physical Training on Local Limb Blood Flow (API)

<table>
<thead>
<tr>
<th>Rest</th>
<th>SS</th>
<th>PRE</th>
<th>POST</th>
<th>DIFF</th>
<th>t-RATIO</th>
<th>PRE</th>
<th>POST</th>
<th>DIFF</th>
<th>t-RATIO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>.80</td>
<td>.87</td>
<td>-.07</td>
<td></td>
<td></td>
<td>.80</td>
<td>.87</td>
<td>-.07</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>.40</td>
<td>.79</td>
<td>.39</td>
<td></td>
<td></td>
<td>.40</td>
<td>.79</td>
<td>.39</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>.43</td>
<td>.51</td>
<td>.08</td>
<td></td>
<td></td>
<td>.43</td>
<td>.51</td>
<td>.08</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.43</td>
<td>1.71</td>
<td>.28</td>
<td></td>
<td></td>
<td>1.43</td>
<td>1.71</td>
<td>.28</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>.73</td>
<td>.68</td>
<td>-.05</td>
<td></td>
<td></td>
<td>.73</td>
<td>.68</td>
<td>-.05</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>.43</td>
<td>.18</td>
<td>.19</td>
<td></td>
<td></td>
<td>.43</td>
<td>.18</td>
<td>.19</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td></td>
<td></td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>.22</td>
<td>0.00</td>
<td>-.22</td>
<td></td>
<td></td>
<td>.22</td>
<td>0.00</td>
<td>-.22</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>1.05</td>
<td>.66</td>
<td>-.51</td>
<td></td>
<td></td>
<td>1.05</td>
<td>.66</td>
<td>-.51</td>
<td></td>
</tr>
</tbody>
</table>

x= .90  .82  *1.81  .68  .67  *.12
SE  .34  .28  .40  .51

*t-RATIO at p<.05=2.31, df=7
Table 3

Effect of Physical Training on Serum Lactic Acid Accumulation

<table>
<thead>
<tr>
<th></th>
<th>Serum Lactic Acid (mmol.1⁻¹)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>IPE</td>
</tr>
<tr>
<td></td>
<td>SS</td>
<td>PRE</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>.70</td>
</tr>
<tr>
<td>2</td>
<td>.30</td>
<td>.30</td>
</tr>
<tr>
<td>3</td>
<td>1.20</td>
<td>.80</td>
</tr>
<tr>
<td>4</td>
<td>xxxx</td>
<td>xxxx</td>
</tr>
<tr>
<td>5</td>
<td>.45</td>
<td>.70</td>
</tr>
<tr>
<td>6</td>
<td>xxxx</td>
<td>xxxx</td>
</tr>
<tr>
<td>7</td>
<td>xxxx</td>
<td>xxxx</td>
</tr>
<tr>
<td>8</td>
<td>1.25</td>
<td>.70</td>
</tr>
<tr>
<td>9</td>
<td>.45</td>
<td>2.10</td>
</tr>
<tr>
<td>x=</td>
<td>.72</td>
<td>.85</td>
</tr>
<tr>
<td>SE</td>
<td>.41</td>
<td>.63</td>
</tr>
</tbody>
</table>

*t-RATIO at p<.05=2.60, DF=5
Figure 1
Effect of physical training on weekly mean walking distance (m)
Figure 2

Effect of Physical Training on Exercise Heart Rate and Exercise Systolic Blood Pressure
CHAPTER IV

SUMMARY
Summary

Many investigations have been conducted that lend support to physical training as an alternative to surgery for patients suffering from intermittent claudication (IC). Exercise programs have resulted in improvements of walking ability, pain tolerance, and ultimately the quality of life for these patients. While the positive results of exercise programs for IC patients are widespread, the mechanisms responsible are vague. The possible contributions which have been explored include metabolic adaptations, hemodynamic, and psychomotor mechanisms.

Increased collateral circulation has been cited in previous published studies as a major factor in explaining improvements in exercise performance. However, more recent investigations either have not demonstrated significant changes, or showed only small variations indicating operation of other mechanisms.

Several reports had previously indicated that physical training leads to an increase in the oxidative capacity of the leg, resulting in an increase in the aerobic activity exercising muscles and a decreased blood lactate accumulation which may be responsible for increased walking tolerance. Also, improved muscle coordination and mechanical efficiency in the leg muscles could reduce the oxygen requirement, and
therefore enable the patient to walk further. Improved walking ability could result from an increase in pain tolerance as well.

The research for this study does not indicate that a single mechanism is responsible for improvements in walking capacity for intermittent claudication. Calculations show that small changes in a number of factors could lead to considerable increases in work performance. This study was conducted to determine the efficacy of physical training on walking distance, pain threshold and tolerance, venous lactate accumulation, and ankle pressure index (API) in a group of patients with diagnosed intermittent claudication.

Nine patients with diagnosed intermittent claudication (IC) of at least 6 months duration underwent a supervised exercise program lasting 6 weeks. Initially, each individual performed a maximal walking tolerance test on motorized treadmill. Pre-training measurements were taken for ankle pressure index (API), and serum HLa accumulation (micro mol/l) at rest, and immediately following exercise. The subjects then attended a thrice weekly training program lasting 6 weeks. During each session the individual was monitored for resting heart rate (bpm⁻¹), blood pressure (mmHg), and body weight (kg). Additional weekly measurements included distances covered, and perception of pain. The training sessions included group warm-ups and low level walking intermixed with supplemental upper body activities. Following the treatment period, each
subject underwent an identical walking tolerance test to ascertain the effectiveness of training. It was found that values for pre- and post-test total treadmill time and onset of pain were not altered significantly. In addition, no statistically significant difference was found after training for either serum HLa or API. There did exist an increase of 200% in the weekly mean distance traveled for the group. This was coupled with stable weekly means for heart rate, body weight, and pain perception, indicating that the exercise was not of a truly aerobic nature.

While psychosocial factors may have played a part in the large distance increases seen, the circulatory and metabolic adaptations of each individual appeared, at best, limited. Exercise may have played a role in the retardation of the atherosclerotic process as evidenced by the lack of any significant changes seen in API or serum HLa. The results from the API and serum HLa are in accordance with much of the research. The mechanisms of exercise adaptation appear to be more psychological than physiological.

Based on these results, it was concluded that a supervised submaximal exercise program was beneficial in increasing weekly walking distances attained for nine subjects with diagnosed IC. While the physiologic adaptations of API and serum HLa did not change significantly, the lack of subsequent increases may indicate that exercise helped retard the disease
process. The benefits of group interaction and cohesion were great. Group exercise played a major role in motivation and good attendance levels.

**Implications For Practitioners**

The investigations of exercise therapy for intermittent claudication are of prime importance in the allied health profession, since vascular disorders are one of the leading causes of disability in the United States. Attempts to provide therapy for intermittent claudication (IC) patients has met with variable success. If an efficient therapy can be proven universally successful, there may conceivably be a decrease in the disability and mortality associated with vascular disorders.

The prospect of exercise therapy for IC is especially appealing since it is relatively inexpensive, easy to maintain, and appears to be at least psychologically effective. The observation that the metabolic and circulatory adaptations of the subjects in this study appeared to be minimal could have important implications. A substantial reduction in blood flow and metabolic adaptations of obliterated tissue could result in earlier, and more severe levels of ischemia, pain, and ultimately amputation.

The negative psychological implications of untreated IC is severe. However, if distance walked until pain tolerance and fatigue can be ultimately increased, surely the quality of
a patient's life could greatly be enhanced. Increases in their ability to return to physical activities such as work, gardening, shopping, etc., would likely result in an enhanced psychological benefit. Since a reduction in walking ability and pain tolerance are the ultimate limiting factors in claudication, the benefits of influencing these with effective exercise therapy is almost unquestionable.

Recommendations For Further Study

This study leaves many unresolved questions about exercise and its effect on individuals with intermittent claudication (IC). Although increases in total distance covered and perception of pain are almost universally the result of regular physical activity, the mechanisms of metabolic and circulatory adaptations are still unclear. There is also a lack of consolidated research which lends support to a universal protocol for the effective prescription for exercise therapy in IC. This information is necessary for accurate management of exercise treatment for individuals suffering from IC. The following recommendations for further study are made to supplement the results of this investigation.

1. The inclusion of a variable treadmill testing protocol which would allow total treadmill time to be more representative of adaptations to training.
2. Validation of circulatory adaptation to submaximal walking programs via angiography and the inclusion of a spectral analysis imaging procedure.

3. Further investigation should be carried out on treatment with higher exercise intensities to accurately assess true aerobic training responses. The present study was limited to very low level conditioning intensities which may have influenced the lack of metabolic adaptation. In addition, study the combined effects of a low cholesterol diet, antiplatelet therapy, and smoking cessation on the physiological improvements after exercise training.

4. Further verification of metabolic adaptations to training through analysis of aerobic enzymes in muscles of exercising limbs, perhaps via a muscle biopsy procedure.

5. Longitudinal follow-up studies on participant's disability may provide insight on the extended benefits of a continuation of exercise therapy.

6. Investigation of alternate sites for catheter insertion for the collection of blood samples for serum lactate analysis with reduced subject anxiety.

7. Inclusion of a larger number of experimental subjects with age-matched controls could provide insight into true metabolic and circulatory adaptations to training by minimizing changes due to individual variability.
BIBLIOGRAPHY
Bibliography


Denis, C., Dormois, D., and Lacouit, J. "Endurance Training, VO2 Max, and OBLA: A Longitudinal Study of Two Different


Tzankoff, S., and Norris, A. "Age-related Differences in Lactate Distribution Kinetics Following Maximal


APPENDIX A

METHODOLOGY
Methods

The initial portion of this section describes subject selection and screening procedures for inclusion in the experimental group. A detailed description of all technical procedures and research methods is outlined in the next section. All preliminary testing procedures are covered in the ensuing portion. The experimental condition and testing protocol are covered next, followed by measurement procedures for all dependent variables. The final section discusses statistical analysis and reports data on reliability of important dependent measures.

Subject Selection

Nine adult volunteers were obtained from two program physicians' surgical practices. Criteria for inclusion in the participant sample was:

1. A history of diagnosed intermittent claudication of at least six months duration (diagnostic procedures include muscle cramping with exertion, pallor on elevation, diminished or absent segmental pulse, paresthesia, limb paralysis, and skin temperature).

2. A prognosis by their physician that vascular reconstruction surgical procedures are not indicated and/or previous reconstruction has proven ineffective. These entrance requirements were structured according to the clinical significance of each patient's disease.
A detailed chart of important physical characteristics is provided in Appendix B. Included in this chart will be: age (yrs), weight (kg), height (cm), disease location (dl), and medications (meds). Initially, each subject was interviewed as to their likelihood of participating in the study. All participants reviewed and signed an informed consent outlining the nature of the experiment with inherent risks and physical demands required (Appendix C). Next, a separate interview was conducted to further explain the use of a Borg-category ratio scale for pain determination (Appendix C). Chronic physical activity patterns were determined by a brief pre- and post-test interview.

Determinator Ankle Pressure Index (API)

All subjects were allowed to rest in the supine position at least 15 minutes prior to the measurement of any pressures. First, the brachial artery pressure was measured on the side where claudication and disease of the leg was most severe. A blood pressure cuff of appropriate size (2 X 10 cm) was placed on the arm approximately 2 cm above the elbow. The brachial artery was palpated in the antecubital fossa, and a small amount of acoustic gel was applied to the skin over the artery. The arterial signal was then located using a Medasonics Ultrasound Stethoscope, Doppler Blood Flow Detector (Model BF4A). The cuff was inflated until the audible signal
disappeared, then slowly deflated until a signal was again audible, at which time the pressure was noted and recorded.

During measurement of the appropriate brachial pressures, another pneumatic cuff (2 X 40 cm) was applied to the leg where claudication and disease were most severe. The cuff was placed approximately 3 cm proximal to the malleoli at the ankle. The posterior tibial artery was then palpated just posterior to the medial malleolus and marked for future reference. A small amount of acoustic gel was applied to the skin over the artery. The arterial signal was then located using a medasonics Vasculab (R) Noninvasive Vascular Diagnostic System Bi-directional Doppler. The cuff was automatically inflated to 200 mm Hg, then allowed to deflate slowly. A two channel analog chart recorder (Model R12B) was used to measure the return of flow. Following the test, all analog charts were analyzed and appropriate pressures recorded.

**Determination of Serum Lactic Acid (HLa)**

For the determination of serum HLa, the Dupont Automatic Clinical Analyzer (ACA) procedure was used. The ACA HLa method is a modification of the Marbach and Weil method which employs the oxidation of lactate to pyruvate. A split sample conversion between the ACA method and a manual enzymatic method gave a correlation coefficient of 0.977 (Herold, et al, 1980).
All subjects were allowed to rest in the supine position at least 15 minutes prior to the collection on any blood samples. First, the surgeon palpated the deep common femoral vein of the most severely diseased limb. Once located, the area was shaved, cleansed, then numbed with 3-5 cc of 1% sterile aqueous xylocaigne. The surgeon then attempted to insert a 16 gage, 2" (1.7 mm 5.1 cm) Deseret Angiocath (Cat #2814) into the prepared site.

A solution of 500 cc .9% sodium chloride with 5000 usp units/uL heparin (1000 usp units per 100 cc normal saline) was connected to a sterile Advit IV Adult Primary IV set (Cat. #VL445) via a Medex MX411 3-way stopcock to an IV extension set (McGraw, Cat #V5404). Approximately 10 cc of the heparinized saline solution was injected into the system to maintain the patency of the catheter. Once the catheter was in place and flushed, approximately 5 cc of blood was collected and placed into a test tube containing 10 mg sodium fluoride and 10 mg potassium oxalate. Prepared Vacutainer (Cat #3206-PS, gay stopper) were used. The samples were immediately taken to the chemistry lab at Community Hospital where the analysis was performed.
## Test Materials

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Item</th>
<th>DuPont Cat. #</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ACA LA Test Pack</td>
<td>705105-901</td>
</tr>
<tr>
<td>1</td>
<td>Sample System Packet</td>
<td>701989901</td>
</tr>
<tr>
<td></td>
<td>or</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Micro Sample System</td>
<td>702785000</td>
</tr>
<tr>
<td></td>
<td>Packet and Micro Sample System Holder</td>
<td>702785000</td>
</tr>
<tr>
<td></td>
<td>Dylux Photosensitive Primer Paper</td>
<td>7000360000</td>
</tr>
<tr>
<td>1</td>
<td>Tris Buffer</td>
<td>704212901</td>
</tr>
<tr>
<td>1</td>
<td>Cell Wash Solution</td>
<td>701864901</td>
</tr>
</tbody>
</table>
Test Steps for the ACA Procedure

When performing analytical test packs the operator need be concerned only with loading the sample and appropriate test packs into a properly prepared instrument. The ACA automatically advances the packs through the test steps and prints the results.

Pre-set LA Test Conditions

- Sample size: 40 ml
- Diluent: Tris Buffer
- Test temperature: 37.0 ± 0.1
- Reaction period: 261.5 seconds (initiation to measurement)
- Wave lengths: 340 and 383 nm
- Type of measurement: Two filter, endpoint
- Decimal point location: 000.0 m mol/l

Calibration

- Range of linearity: 0-15 m mol/l
- Reference materials: primary standards, or secondary calibrators, containing L-lactate
- Suggested calibration levels: 15, 5.1 m m mol/l
· Starting point (offset Co adjustment) For ACA replace zero offset (Zo) on the photometer method switching board

· Scale factor (linear term C) adjustment May be required for different pack locks

· Count by ACA 1

· Readout The ACA prints out in 0.1 m mol/l increments

Reference Intervals (Normal Range)

· 0.5 - 1.6 m mol/l arterial plasma (elevations in plasma lactic acid have been as high as .6 m mol/l and correspond to O2 debt after mild exercise).

· 0.6 - 2.2 m mol/l spinal fluid
Preliminary Testing Procedures

The pre-test procedures were identical for all trials. Subjects were requested to abstain from vigorous physical activity within 48 hours prior to each trial.

Upon arriving at the test site, each subject was asked to change into a surgical gown, and weighed. Each was then prepped for a standard 12 lead supine electrocardiogram. Heart rate signals were received on a Quinton Q2000 EKG monitor.

All subjects were allowed to lie supine while the surgeon attempted to insert a 2" 16 gage angiocath into the deep common femoral vein of the most severely diseased leg. Once the angiocath was secured, all IV extension tubing was flushed using a 10 cc sterile disposable syringe and a solution of heparinized saline (1000 usp units per 100 cc saline). When the system was cleared, a small sample of venous blood (5 cc) was drawn and immediately inserted directly into a B-D Vacutainer (Cat. #3206-PS) tube containing sodium fluoride and potassium oxalate (10 mg sodium fluoride and 10 mg potassium oxalate per 5 cc blood). In the event the femoral vein was not penetrable, a 10 cc disposable syringe fitted with a 20 gage needle was used to draw the appropriate samples.

Once the resting blood sample was secured, the API of the most diseased leg was calculated. A registered nurse and technician determined simultaneous segmental pressures in the brachial artery of the antecubital fossa and the posterior
tibial artery of the most severely diseased leg. All resting measurements (including blood samples) were repeated for the calculation of reliability coefficients.

Experimental Exercise Protocol

This section provides an overview of the supervised aerobic exercise protocol used for training. All sessions were held at a local fitness facility, and met 3 times per week for approximately 1 hour per session for 6 weeks.

Subjects were asked not to modify their physical activity patterns during the experimental period, and to exercise only during allotted times. The subjects exercised in one of two groups, the first meeting at 7:00 AM, and the second at 11:00 AM. These time slots were selected to accommodate working hours and visual deficiencies of some of the subjects. There were four enrolled at 7:00 AM and five who attended at 11:00 AM.

Each exercise session began with subjects being measured for body weight (clothed), resting blood pressures (mmHg), and resting heart rates (bpm). These values were recorded in a daily log kept for each participant (Appendix C). Once these parameters were measured and recorded, the subjects then participated in a brief warm-up routine led by an exercise specialist. Warm-up activities included dynamic and static leg contractions and stretches done in both the sitting and standing positions. These exercises were designed to increase blood flow to the active muscles prior to exercise.
Once the warm-up exercises were completed, each of the subjects began to walk on a circular 88 yard indoor synthetic track. The subjects were asked to walk until ischemic limb pain forced them to stop. While resting the affected limb, each subject was asked to perform some alternate form of arm or leg ergometry. Options included a Monark 88l arm ergometer, a Schwynn (R) variable resistance stationary cycle or upper body resistance exercises with 3 ½ pound bowling pins. All alternate exercises were done in the sitting position at zero tension and were continued until leg pain had dissipated. This active rest phase of the exercise session was done every time ischemic leg pain became extreme and the subject was forced to rest.

Immediately upon completion of the allotted exercise time and prior to supervised cool-down activities, each subject underwent measurement for exercise heart rates (bpm-l), blood pressures (mmHg), number of rest periods, rate of perceived exertion (Borg Category-Ratio scale), and total exercise time. These parameters were measured and recorded in the daily log of each subject. Each subject then participated in a group cool-down led by an exercise specialist. Once more, dynamic and static limb exercises were conducted with a greater emphasis on stretches upon the completion of cool-down activities, blood pressures (mmHg), and heart rates (bpm-l),
were again measured. All subjects were required to maintain 75% attendance levels for duration of the exercise sessions.

**Alternate Training Protocol**

Include a functional stress test that would allow the patient to obtain a 60-85% training heart rate and keep records of target training level during the exercise sessions to maximize aerobic conditioning phase.

**Walking Tolerance Test Protocol**

This segment provides an overview of the walking tolerance treadmill evaluation. All tests were conducted at the Community Hospital of the Roanoke Valley, in the Cardiac Diagnostic and Rehabilitative services department. The testing protocol was identical for all subjects.

Each subject underwent two walking tolerance tests, one at the outset of the study, and another following 6 weeks of exercise training. All subjects were instructed to abstain from eating or smoking at least 2 hours prior to each test. In addition, participants were instructed to take all medications according to normal time schedules. A thorough explanation of the informed consent and test protocol was provided with special emphasis on the use of the Borg Category-Ratio 10 point pain tolerance scale.

The treadmill workload was predetermined prior to the start of the test. The following represents the criteria used:
1. If the participant had a resting ankle pressure index (API) below .60, the treadmill speed will be set at 26.8 m minute (-1) at a 5.0% grade.

2. For subjects with a resting API exceeding .60, the treadmill speed was set at 53.6 m minute (2.0 (-1) 2.0 mph) at a 5.0% grade (if the patient could not maintain the 53.6 m minute (-1) treadmill speed for at least 120 secs, the speed was reduced to 26.8 m minute -1).

The onset of pain (secs) according to Borg's scale and maximal treadmill time (secs) was recorded. All tests were terminated when a subject's leg pain became intolerable, or following 5 full minutes of treadmill time. A minimum of 120 secs treadmill time were required for inclusion in the study. A short post test interview was conducted to more accurately assess pain levels at the endpoint.

During the treadmill evaluations, blood samples (5 cc) were drawn at rest, following 30 secs of exercise and every minute thereafter until the test was terminated. Post exercise samples were drawn at 6 minutes post exercise. Ankle pressure index recordings were made at rest, immediately post-exercise, and at 2, 4, and 6 minutes post-exercise.

An alternate protocol that would allow an individual to walk until pain forced them to stop may minimize individual variations by allowing patients to maximize their distance levels.
Measurement Procedures for All Dependent Variables

The dependent measures utilized in this study include: serum HLa, ankle pressure index (API), total treadmill time, and onset of pain. The following is an overview of measurement procedures for the respective variables.

For the determination of serum HLa, approximately 5 cc of blood was collected from a secured 2½" angiocath in the most diseased leg of the subject. In the event that an angiocath could not be secured, individual samples were collected using 10 cc disposable syringes with 20 gauge needles.

For the scope of the study, blood samples were collected at rest, immediately post exercise, and again at 6 minutes post exercise. All prepared samples were then taken to the chemistry lab of Community Hospital for analysis of serum HLa using the Dupont ACA procedures.

The calculation of API using the Doppler shift technique was done following 15 minutes of rest in the supine position, and again at the termination of the treadmill evaluation. Post exercise readings were analyzed after 6 minutes of recovery. Total treadmill time was calculated by recording the exact time in minutes and seconds that the individual requested the treadmill be stopped, or until 5 minutes of treadmill time had passed. The determination of onset of pain was recorded (minutes:seconds) by a technician noting
the exact time the subject reported any aberrant sensation according to Borgs Category-ratio scale.

All dependent measures were collected both pre- and post-training with repeat values being taken for serum HLa and API determination.

**Determination of Reliability Coefficients for the Dependent Measures and Statistical Methods Used**

The pre-test reliability for API determination and serum HLa levels were assessed by taking repeat resting measures for each subject. The Spearman rank difference correlational procedure was utilized. The resulting r values for both API and serum HLa were above .90 (Appendix C).

The research design utilized for this study include a student's t-test procedure for total treadmill time onset of pain measures, serum HLa, and ankle pressure index (API). A two-factor analysis of variance (ANOVA) procedure was used for analysis of HLa and API levels. The alpha level was set at .05. A Duncan multiple range test was employed to determine the degree of statistical significance between group means.

There was no significant difference found to exist for total treadmill time, onset of pain values, serum HLa levels, and ankle pressure index.

*Medications*

1. Trental (pentoxifylline) – its metabolites improve blood flow properties through decreasing its viscosaty. In
patients with chronic arterial peripheral disease, this increases blood flow to the affected microcirculation and enhances tissue oxygenation.

2. Coumadin (crystalline warfarin sodium). Coumadin anticoagulants act by depressing synthesis in the liver of several factors which are known to be active in the coagulation mechanisms.

3. Apresoline—(hydralazine) Apparently lowers blood pressure by exerting a peripheral vasodilating effect through a direct relaxation of vascular smooth muscle.

APPENDIX B

DATA TABLES
Table 1

Effect of Physical Training on Total Performance and Pain Threshold

<table>
<thead>
<tr>
<th>SS</th>
<th>Pre (sec)</th>
<th>Post (sec)</th>
<th>Diff (sec)</th>
<th>T-Ratio</th>
<th>Pre (sec)</th>
<th>Post (sec)</th>
<th>Diff (sec)</th>
<th>T-Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>158</td>
<td>300</td>
<td>142</td>
<td></td>
<td>48</td>
<td>190</td>
<td>158</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>255</td>
<td>300</td>
<td>45</td>
<td></td>
<td>48</td>
<td>120</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>300</td>
<td>300</td>
<td>0</td>
<td></td>
<td>90</td>
<td>160</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>300</td>
<td>300</td>
<td>0</td>
<td></td>
<td>118</td>
<td>212</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>300</td>
<td>246</td>
<td>-54</td>
<td></td>
<td>145</td>
<td>129</td>
<td>-16</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>246</td>
<td>300</td>
<td>54</td>
<td></td>
<td>148</td>
<td>70</td>
<td>-78</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>120</td>
<td>300</td>
<td>180</td>
<td></td>
<td>50</td>
<td>100</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>300</td>
<td>300</td>
<td>0</td>
<td></td>
<td>120</td>
<td>46</td>
<td>-74</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>40</td>
<td>300</td>
<td>260</td>
<td></td>
<td>20</td>
<td>100</td>
<td>80</td>
<td></td>
</tr>
</tbody>
</table>

x = 224.3 294.0 *2.12 87.4 125.2 *1.92
SEM 83.46 17.60 44.70 51.18

*t-RATIO at p<.05=2.31, df=8
Table 2

Effect of Physical Training on Local Limb Blood Flow (API)

<table>
<thead>
<tr>
<th>Rest</th>
<th>SS</th>
<th>PRE</th>
<th>POST</th>
<th>DIFF</th>
<th>t-RATIO</th>
<th>IPE</th>
<th>PRE</th>
<th>POST</th>
<th>DIFF</th>
<th>t-RATIO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>1.08</td>
<td>.89</td>
<td>-.19</td>
<td>.80</td>
<td>.87</td>
<td>-.07</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>.95</td>
<td>.80</td>
<td>-.15</td>
<td>.40</td>
<td>.79</td>
<td>.39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>.64</td>
<td>.77</td>
<td>.13</td>
<td>.43</td>
<td>.51</td>
<td>.08</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>1.48</td>
<td>1.33</td>
<td>-.15</td>
<td>1.43</td>
<td>1.71</td>
<td>.28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>1.01</td>
<td>.88</td>
<td>-.13</td>
<td>.73</td>
<td>.68</td>
<td>-.05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>.55</td>
<td>.42</td>
<td>-.13</td>
<td>.43</td>
<td>.18</td>
<td>.19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>.45</td>
<td>.51</td>
<td>.06</td>
<td>.22</td>
<td>0.00</td>
<td>-.22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>1.04</td>
<td>1.01</td>
<td>-.03</td>
<td>1.05</td>
<td>.66</td>
<td>-.51</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

x= .90 .82 *1.81 .68 .67 *.12
SE .34 .28 .40 .51

*t-RATIO at p<.05=2.31, dF=7
### Table 3

**Effect of Physical Training on Serum Lactic Acid Accumulation**

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>IPE</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SS</td>
<td>PRE</td>
<td>POST</td>
<td>DIFF</td>
<td>t-RATIO</td>
<td>PRE</td>
<td>POST</td>
<td>DIFF</td>
<td>t-RATIO</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>.70</td>
<td>.55</td>
<td>-.15</td>
<td>5.5</td>
<td>2.6</td>
<td>-2.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>.30</td>
<td>.30</td>
<td>.00</td>
<td>1.4</td>
<td>1.6</td>
<td>-0.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.20</td>
<td>.80</td>
<td>-.40</td>
<td>2.7</td>
<td>4.8</td>
<td>1.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>.45</td>
<td>.70</td>
<td>.25</td>
<td>1.10</td>
<td>3.00</td>
<td>1.90</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td>xxxx</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>1.25</td>
<td>.70</td>
<td>-.55</td>
<td>3.5</td>
<td>4.9</td>
<td>1.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>.45</td>
<td>2.10</td>
<td>1.65</td>
<td>0.1</td>
<td>3.0</td>
<td>2.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x=</td>
<td>.72</td>
<td>.85</td>
<td>*.41</td>
<td>2.38</td>
<td>3.80</td>
<td>*1.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SE</td>
<td>.41</td>
<td>.63</td>
<td></td>
<td>1.94</td>
<td>1.29</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* *t*-RATIO at $p<.05=2.60$, dF=5
Table 4

Physical and Clinical Characteristics of Experimental Patients

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Sex</th>
<th>Age (yrs.)</th>
<th>Wt. (kg.)</th>
<th>*Disease Location</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>W.M.</td>
<td>M</td>
<td>67</td>
<td>67.7</td>
<td>Proximal</td>
<td>Zantac; ASA PRN</td>
</tr>
<tr>
<td>A.B.</td>
<td>F</td>
<td>55</td>
<td>80.0</td>
<td>Proximal</td>
<td>Quinine Sulfate</td>
</tr>
<tr>
<td>R.P.</td>
<td>M</td>
<td>49</td>
<td>110.9</td>
<td>Distal</td>
<td>Trental; ASA</td>
</tr>
<tr>
<td>B.H.</td>
<td>M</td>
<td>75</td>
<td>61.8</td>
<td>Proximal</td>
<td>Coumadin</td>
</tr>
<tr>
<td>R.W.</td>
<td>M</td>
<td>71</td>
<td>75.4</td>
<td>Proximal</td>
<td>Apresoline; Hydergine</td>
</tr>
<tr>
<td>M.T.</td>
<td>F</td>
<td>79</td>
<td>59.1</td>
<td>Proximal</td>
<td>Trental</td>
</tr>
<tr>
<td>E.T.</td>
<td>F</td>
<td>81</td>
<td>67.2</td>
<td>Distal</td>
<td>Trental</td>
</tr>
<tr>
<td>H.W.</td>
<td>M</td>
<td>57</td>
<td>78.6</td>
<td>Distal</td>
<td>Trental</td>
</tr>
<tr>
<td>A.W.</td>
<td>F</td>
<td>63</td>
<td>57.2</td>
<td>Proximal</td>
<td>Trental</td>
</tr>
</tbody>
</table>

x
n(F)=4 66.3 73.1 Proximal n=6

SEM
n(M)=5 +/−6.4 12.7 Distal n=3

*Proximal - Atherosclerotic disease located above the distal run off position (outflow) of limb circulation. Includes the iliac, femoral, and profunda femoris arteries.

(table continues)
Table 4 (Cont.)

**Physical and clinical Characteristics of Experimental Patients**

**Distal - Atherosclerotic disease located below the inflow portion of limb circulation. Includes the popliteal, anterior tibial, posterior tibial, peroneal and dorsal pedal arch arteries.**
Table 5

**Weekly Mean Exercise Heart Rate (bpm⁻¹)**

<table>
<thead>
<tr>
<th>SS</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>93.3</td>
<td>95.0</td>
<td>93.3</td>
<td>92.0</td>
<td>92.0</td>
<td>82.0</td>
</tr>
<tr>
<td>2</td>
<td>94.5</td>
<td>94.0</td>
<td>96.6</td>
<td>83.3</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>3</td>
<td>111.6</td>
<td>107.0</td>
<td>100.0</td>
<td>85.0</td>
<td>100.0</td>
<td>87.5</td>
</tr>
<tr>
<td>4</td>
<td>80.0</td>
<td>90.0</td>
<td>82.6</td>
<td>80.0</td>
<td>90.0</td>
<td>82.0</td>
</tr>
<tr>
<td>5</td>
<td>80.0</td>
<td>66.0</td>
<td>66.0</td>
<td>70.0</td>
<td>70.0</td>
<td>71.5</td>
</tr>
<tr>
<td>6</td>
<td>91.3</td>
<td>90.0</td>
<td>82.3</td>
<td>93.3</td>
<td>85.0</td>
<td>83.3</td>
</tr>
<tr>
<td>7</td>
<td>86.0</td>
<td>100.0</td>
<td>100.0</td>
<td>83.3</td>
<td>80.0</td>
<td>90.0</td>
</tr>
<tr>
<td>8</td>
<td>117.3</td>
<td>104.3</td>
<td>119.5</td>
<td>110.3</td>
<td>102.3</td>
<td>103.0</td>
</tr>
<tr>
<td>9</td>
<td>96.6</td>
<td>86.6</td>
<td>86.6</td>
<td>90.0</td>
<td>80.0</td>
<td>81.3</td>
</tr>
<tr>
<td>x</td>
<td>94.5</td>
<td>92.6</td>
<td>91.8</td>
<td>87.5</td>
<td>88.9</td>
<td>86.7</td>
</tr>
<tr>
<td>SEM</td>
<td>9.3</td>
<td>8.2</td>
<td>10.2</td>
<td>7.9</td>
<td>10.3</td>
<td>9.2</td>
</tr>
</tbody>
</table>
Table 6

Weekly Mean Distance Covered (m)

<table>
<thead>
<tr>
<th>SS</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>789.5</td>
<td>1205.9</td>
<td>1368.9</td>
<td>1254.8</td>
<td>1173.3</td>
<td>1189.6</td>
</tr>
<tr>
<td>2</td>
<td>456.3</td>
<td>863.7</td>
<td>1336.3</td>
<td>1809.9</td>
<td>2200.0</td>
<td>2273.3</td>
</tr>
<tr>
<td>3</td>
<td>488.9</td>
<td>733.3</td>
<td>782.2</td>
<td>806.6</td>
<td>928.9</td>
<td>945.2</td>
</tr>
<tr>
<td>4</td>
<td>537.8</td>
<td>994.1</td>
<td>1352.6</td>
<td>1491.1</td>
<td>1320.0</td>
<td>1051.1</td>
</tr>
<tr>
<td>5</td>
<td>1059.2</td>
<td>1564.4</td>
<td>1890.4</td>
<td>1882.2</td>
<td>2004.4</td>
<td>2200.0</td>
</tr>
<tr>
<td>6</td>
<td>277.0</td>
<td>342.2</td>
<td>407.5</td>
<td>374.8</td>
<td>391.1</td>
<td>422.9</td>
</tr>
<tr>
<td>7</td>
<td>244.0</td>
<td>569.3</td>
<td>1024.8</td>
<td>1154.9</td>
<td>1512.8</td>
<td>1439.6</td>
</tr>
<tr>
<td>8</td>
<td>601.9</td>
<td>813.3</td>
<td>854.0</td>
<td>829.6</td>
<td>862.1</td>
<td>927.0</td>
</tr>
<tr>
<td>9</td>
<td>553.1</td>
<td>683.2</td>
<td>666.9</td>
<td>707.6</td>
<td>666.9</td>
<td>634.4</td>
</tr>
</tbody>
</table>

x  | 556.4 | 863.2 | 1079.5| 1145.6| 1228.8| 1128.4|
| SEM| 149.0 | 479.4 | 599.4 | 520.4 | 558.2 | 509.7 |
Table 7

Weekly Mean Exercise Systolic Blood Pressure (mm Hg)

<table>
<thead>
<tr>
<th>SS</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>122.3</td>
<td>120.6</td>
<td>125.3</td>
<td>115.5</td>
<td>120.0</td>
<td>116.0</td>
</tr>
<tr>
<td>2</td>
<td>118.0</td>
<td>116.6</td>
<td>125.3</td>
<td>124.0</td>
<td>122.6</td>
<td>122.0</td>
</tr>
<tr>
<td>3</td>
<td>132.6</td>
<td>150.0</td>
<td>137.0</td>
<td>132.0</td>
<td>131.3</td>
<td>128.0</td>
</tr>
<tr>
<td>4</td>
<td>135.3</td>
<td>129.3</td>
<td>132.0</td>
<td>133.0</td>
<td>132.0</td>
<td>141.0</td>
</tr>
<tr>
<td>5</td>
<td>127.3</td>
<td>125.0</td>
<td>128.0</td>
<td>122.0</td>
<td>122.7</td>
<td>123.0</td>
</tr>
<tr>
<td>6</td>
<td>122.0</td>
<td>120.0</td>
<td>125.0</td>
<td>115.3</td>
<td>131.0</td>
<td>127.3</td>
</tr>
<tr>
<td>7</td>
<td>138.0</td>
<td>139.3</td>
<td>158.6</td>
<td>148.0</td>
<td>158.6</td>
<td>157.0</td>
</tr>
<tr>
<td>8</td>
<td>137.3</td>
<td>137.3</td>
<td>126.0</td>
<td>124.0</td>
<td>127.3</td>
<td>136.6</td>
</tr>
<tr>
<td>9</td>
<td>145.3</td>
<td>144.0</td>
<td>141.3</td>
<td>142.0</td>
<td>140.0</td>
<td>142.0</td>
</tr>
<tr>
<td>x</td>
<td>130.9</td>
<td>131.3</td>
<td>133.1</td>
<td>128.4</td>
<td>131.5</td>
<td>132.5</td>
</tr>
<tr>
<td>SEM</td>
<td>8.5</td>
<td>11.9</td>
<td>10.5</td>
<td>11.2</td>
<td>11.1</td>
<td>12.1</td>
</tr>
</tbody>
</table>
Table 8

Weekly Mean Body Weight (kg)

<table>
<thead>
<tr>
<th>SS</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67.5</td>
<td>67.5</td>
<td>67.6</td>
<td>67.7</td>
<td>67.7</td>
<td>68.0</td>
</tr>
<tr>
<td>2</td>
<td>80.6</td>
<td>80.9</td>
<td>80.3</td>
<td>80.2</td>
<td>80.2</td>
<td>80.2</td>
</tr>
<tr>
<td>3</td>
<td>111.8</td>
<td>111.3</td>
<td>110.9</td>
<td>110.9</td>
<td>110.4</td>
<td>110.9</td>
</tr>
<tr>
<td>4</td>
<td>60.1</td>
<td>61.8</td>
<td>61.8</td>
<td>61.9</td>
<td>61.7</td>
<td>61.8</td>
</tr>
<tr>
<td>5</td>
<td>75.4</td>
<td>75.4</td>
<td>75.5</td>
<td>75.4</td>
<td>75.4</td>
<td>75.0</td>
</tr>
<tr>
<td>6</td>
<td>58.2</td>
<td>58.1</td>
<td>58.1</td>
<td>58.3</td>
<td>59.1</td>
<td>58.0</td>
</tr>
<tr>
<td>7</td>
<td>67.3</td>
<td>67.3</td>
<td>67.2</td>
<td>67.2</td>
<td>67.3</td>
<td>67.0</td>
</tr>
<tr>
<td>8</td>
<td>78.1</td>
<td>78.0</td>
<td>78.2</td>
<td>78.3</td>
<td>78.2</td>
<td>78.2</td>
</tr>
<tr>
<td>9</td>
<td>57.0</td>
<td>57.0</td>
<td>57.1</td>
<td>57.1</td>
<td>57.2</td>
<td>57.0</td>
</tr>
<tr>
<td>x</td>
<td>72.8</td>
<td>73.0</td>
<td>72.9</td>
<td>73.0</td>
<td>73.0</td>
<td>72.9</td>
</tr>
<tr>
<td>SEM</td>
<td>16.6</td>
<td>16.6</td>
<td>16.7</td>
<td>16.6</td>
<td>16.7</td>
<td>16.5</td>
</tr>
</tbody>
</table>
Table 9

Tests for Reliability, API – Resting

<table>
<thead>
<tr>
<th>OBS</th>
<th>Test</th>
<th>Retest</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.08</td>
<td>1.08</td>
</tr>
<tr>
<td>2</td>
<td>0.93</td>
<td>0.97</td>
</tr>
<tr>
<td>3</td>
<td>0.63</td>
<td>0.65</td>
</tr>
<tr>
<td>4</td>
<td>1.50</td>
<td>1.46</td>
</tr>
<tr>
<td>5</td>
<td>1.01</td>
<td>1.01</td>
</tr>
<tr>
<td>6</td>
<td>0.55</td>
<td>0.56</td>
</tr>
<tr>
<td>7</td>
<td>0.45</td>
<td>0.45</td>
</tr>
<tr>
<td>8</td>
<td>1.04</td>
<td>1.04</td>
</tr>
</tbody>
</table>

Spearman Correlation Coefficients

<table>
<thead>
<tr>
<th></th>
<th>Test</th>
<th>Retest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td>1.0</td>
<td>0.93</td>
</tr>
<tr>
<td>Retest</td>
<td>0.93</td>
<td>1.0</td>
</tr>
</tbody>
</table>
Table 10

Test for Reliability, Serum Lactic Acid - Pretest

<table>
<thead>
<tr>
<th>OBS</th>
<th>Test</th>
<th>Retest</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>2</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>3</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>4</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>5</td>
<td>1.3</td>
<td>1.2</td>
</tr>
<tr>
<td>6</td>
<td>0.4</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Spearman Correlation Coefficients

<table>
<thead>
<tr>
<th></th>
<th>Test</th>
<th>Retest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td>1.0</td>
<td>.98</td>
</tr>
<tr>
<td>Retest</td>
<td>.98</td>
<td>1.0</td>
</tr>
</tbody>
</table>
APPENDIX C

INFORMED CONSENT
**Exercise Training Protocol Alternative**

This section provides an alternate exercise training protocol for further research into the effect of varying exercise intensities on patients suffering from intermittent claudication.

In order to accurately assess training intensity, a normal maximal treadmill test would need to be added. This would enable a sufficient target heart rate (60-85% of maximum) to be established. Following the guideline set forth by the American College of Sports Medicine (ACSM), individuals would need to maintain this rate for a minimum of 20 minutes daily, 3 times weekly. Also, when the participant had to stop walking due to leg pain, the alternate upper body modes (Appendix A) could be initiated while maintaining accurate heart rates. With this or a similar protocol, an individual may actually train aerobically.
I, do hereby agree and consent to participate in a testing program conducted by personnel connected with Community Hospital of the Roanoke Valley and Downtown West Wellness and Fitness Center.

Title of the study: Aerobic Training For Intermittant Claudication Patients

The purpose of this study includes: to establish a comprehensive model of responses of intermittent claudication patients to a supervised aerobic exercise program in non-surgical candidates with peripheral vascular disease, and to establish whether aerobic exercise training is a viable alternative for the nonsurgical candidates suffering from intermittent claudication.

I voluntarily agree to participate in the testing program. It is my understanding that participation will include:

1. Medical referral to determine my suitability for participation in the study.

2. A pre-test interview concerning the pre and post test treadmill evaluations and the exercise protocol.

3. A maximum of two treadmill evaluations at a pre-determined speed and % grade. The treadmill tests will last for a maximum of 5 minutes. I understand that I am encouraged to walk on the treadmill until leg pain forces me to stop.
   A. All aforementioned trials will be held in the Cardiac Rehabilitation and Diagnostic Services Department at Community Hospital. The subsequent aerobic exercise session will be held at the Downtown West exercise facility and be under direct physician supervision.

4. During each of the treadmill evaluations the following measures will be taken at periodic intervals.
   A. Heart rate: this will involve a 12-lead standard electrocardiogram.
   B. Blood Pressure: Determined via the placement of a cuff on the upper arm.
   C. Ankle-Pressure Index: Determined by the placement of cuffs on the ankle of the affected limb only. An analogue Doppler ultrasound machine will be used to measure pressures.
   D. Blood Samples: Obtained from an angiocath placed in the vein by program physician.
   E. Perceived exertion: Subject reporting of the perception of leg pain based on Borg's 10 point category-Ratio scale.
   F. Spectral Analysis Procedure: Obtained from the non-invasive vascular laboratory personnel at CHRV. The procedure will use a doppler ultrasound stethoscope and monitor used to form visual wavelengths for analysis. This test will be completed prior to each pre and post training treadmill evaluation.
I understand that participation in this experiment may produce certain discomforts and risks. In addition, due to the severity and location of my disease, leg fatigue, and leg cramps may occur. During the treadmill tests, I understand that there is a remote chance of dizziness, nausea, and severe leg pain. It is also understood that the area of the angiocath insertion may be sore and develop slight swelling.

Certain personal benefits may be expected from my participation in this program. I may experience a relief of leg pain with exercise while increasing both my overall strength and pain tolerance levels on the treadmill evaluations.

I understand that at least 75% attendance is necessary for the duration of the 6 week exercise program. I may, however, abstain or dropout of the experiment should I feel the activities might be injurious to my health. The experimenter may also terminate my participation should he feel the activities might be injurious to my health.

Each treadmill evaluation and subsequent exercise programs will be approved and supervised by a physician, registered nurse and certified exercise specialist.

I have read the above statements and have had the opportunity to ask questions. I understand that the investigators will, at any time, answer my inquiries concerning the procedures used in this experiment.

Date: ___________________________ Time: :_________ A.M./P.M.

Participant Signature: ____________________________________________

Witness: ________________________________________________________

WITNESS

Project Director: Dr. E. R. McDannald, Jr.
Telephone: 982-1141
VITA
The vita has been removed from the scanned document.
Aerobic Exercise Training for Patients Suffering From Intermittent Claudication

By
Allen M. Bostian

Abstract

Nine patients with intermittent claudication diagnosed at least 6 months before this investigation were evaluated to determine the effects of walking exercise on serum lactate accumulation (HLa, mmol·l⁻¹), ankle pressure index (API), total treadmill time (sec), and onset of leg pain (sec) in the most severely diseased limb. Subjects were evaluated via a functional walking tolerance test before participation in a thrice weekly exercise program lasting 6 weeks. Post-treatment, the participants were re-evaluated on an identical walking test. Measurements of HLa accumulation and API were taken at rest and immediately following termination of the treadmill test. In the training sessions, body weight (kg), exercise heart rate (HR), systolic blood pressure (SBP), and distance traveled (m) were recorded daily. There were no significant changes (p<.05) in API or HLa levels taken immediately after exercise, when pre- and post-training treadmill test data were compared. The weekly responses for exercise HR, and SBP, as well as body weight, remained stable throughout. Mean distance walked by the subjects increased 203% (+or- 45%) across the 6 weeks. These data suggest that
increases in total distance walked in an exercise program were apparently not related to HLa accumulation or API measurements in the working muscles, and that other mechanisms must be investigated in future studies to explain enhanced performance of such subjects.

Index Terms:

intermittent claudication, exercise training, walking tolerance test, ankle pressure index, serum lactate accumulation, distance walked.