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VASCULAR STATUS DURING DIETARY INTERVENTION IN PERIPHERAL ARTERIAL DISEASE

by

© Kathleen Oberle

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF NURSING

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Abstract

In a one-year study to examine the effects of dietary manipulation on blood lipids and vascular status, 45 patients with confirmed peripheral arterial disease (PAD) were randomly assigned to either the American Heart Association hyperlipidemia diet C (AHA, n = 20) or a low fat, high fiber, complex carbohydrate diet (HF, n = 25). Both groups were encouraged to increase their weekly exercise and to decrease smoking.

A pretest-posttest two-treatment groups design was used for the study. Baseline values for vascular and lipid variables were established at entry. Following intensive diet instruction, patients were maintained on the therapeutic diets for a period of one year. Monthly diet assessments and interviews with the dietitian were used to determine diet intake and to increase compliance. Vascular status and blood lipids were monitored at 2, 4, 6 and 12 months.

Within-group differences in vascular and lipid variables were examined using paired t-tests. Between-group differences were analyzed using analysis of variance for all variables except treadmill walking distance (WD), for which analysis of covariance was used.

Walking distance increased significantly ($p < .05$) in both diet groups, with no significant difference between groups. No other vascular parameters changed significantly and there were no statistically significant between-group

differences. It was concluded that the most probable explanation for the increased WD was increased patient motivation and the effects of training on muscle metabolism.

A trend to lower mean values of cholesterol, triglyceride and LDL-cholesterol, and to higher mean values of HDL-cholesterol was observed in both groups, again with no statistically significant between-group differences.

Associations between vascular and other variables were examined. No apparent pattern of correlations was seen between vascular status and per cent ideal weight. The small sample size precluded any meaningful statistical analysis of the associations between vascular variables and weekly exercise or smoking habits. However, most patients were seen to increase their weekly exercise, and many decreased their smoking.

Poor correlations were observed between WD and other vascular variables, suggesting that WD was measuring something apart from peripheral vascular status.

It was concluded that patients with PAD could benefit from a conservative program of diet and exercise. Increased functional ability and improved psychological outlook were experienced by most patients in the study. It would appear that the AHA and HF diets, both coupled with regular exercise, are equally effective therapeutic regimens.

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I. Introduction

A. Nature of the Problem

Peripheral arterial disease (PAD), or atherosclerosis obliterans, is an important cause of disability in Western societies. The pathological process of peripheral atherosclerosis involves the development of obstructive lesions, or atheroma, in the arterial wall of the large and medium-size arteries, most commonly in the lower extremities (Coffman, 1975). The lesion, which develops insidiously, consists of deposits or plaques of varying amounts of cholesterol and other lipids, smooth muscle cells, collagen, elastic fibers, calcium and blood pigments. Plaque development results in a narrowing or occlusion of the artery, with a consequent interruption of peripheral blood flow (Juergens & Bernatz, 1980; Strandness, 1969).

Signs and symptoms of PAD are a result of inadequate blood supply to the tissues distal to the lesion. One of the earliest symptoms to develop is intermittent claudication (IC), ischemic muscular pain brought on by exercise. The gradual nature of the plaque development fosters the opening and dilatation of collateral channels around the arterial obstruction, with the result that, except in severe disease, total blood flow to the muscles distal to the lesion is normal or near-normal at rest. However, during exercise, the collaterals are unable to keep pace with the increased flow demanded by the exercising muscle and IC develops, most

frequently in the muscles of the calf but sometimes in the thigh, buttock or lower back, depending on the site of the obstruction. The pain disappears quickly with rest, but is usually severe enough to force the patient to discontinue the activity, sometimes after only a few seconds. Thus, the patient may be drastically limited in his ability to perform exercise; some patients can walk only a few meters at most. As the disease increases in severity, other symptoms may develop, including cold sensitivity, leg pain at rest, numbness and tingling, and eventually ulceration and gangrene (Juergens & Bernatz, 1980).

Long-term prognosis in PAD is extremely variable; some patients may stabilize and even improve after the appearance of initial symptoms, but others become progressively worse, and amputation of one or both lower limbs is not an uncommon result (Coffman, 1975; Juergens & Bernatz, 1980; Strandness, 1969). In addition, patients with PAD often suffer from other clinical manifestations of atherosclerosis, including coronary artery disease (CAD) and cerebral artery disease (Mann & Hughson, 1979). In fact, mortality from myocardial infarction and stroke in patients with IC is known to be two or three times higher than in subjects of the same age without such symptoms (DeBacker, Kornitzer, Sobolski & Denolin, 1979).

Information on the prevalence of PAD is scarce, in part because the early stages of the disease are asymptomatic. However, studies such as that conducted by Schilling and

colleagues (Schilling, Christopher, Hempel & Orbach, 1974) have indicated that a large proportion of the population suffers from some degeneration of the arteries by middle age. These investigators found atherosclerotic changes in the aorta or iliac arteries in approximately 10% of 875 healthy 40 year old men who voluntarily underwent arteriography; in the 64 year old group (n = 364), the prevalance had climbed to 65%. Studies of symptomatic PAD have focused primarily on the occurrence of IC, the earliest and most recognizable symptom, in the population. In the Framingham study, a 24-year epidemiological project conducted in the United States, approximately 3% (79 males, 46 females) of the 4,030 patients who remained in the study after 14 years had developed IC (Dawber, 1980; Kannel, Skinner, Schwartz & Shurtleff, 1970). Other workers have observed a similar prevalence (Rose, McCartney & Reid, 1977).

Epidemiological and animal data have linked the development of atherosclerosis in man with certain underlying "risk" factors, including hypercholesterolemia, high plasma concentrations of low density lipoprotein cholesterol (LDL-cholesterol), low concentrations of high density lipoprotein cholesterol (HDL-cholesterol), smoking, lack of exercise and obesity (Chucker, 1977; Havel, 1979; Kannel, Castelli & Gordon, 1979; Kinlough-Rathbone & Mustard, 1981; Stamler, 1979; Winsor, Winsor & Maranga, 1978). Recent studies have indicated that regression of

atheroma can be effected if risk factors are minimized (Kinlough-Rathbone & Mustard, 1981; Mann & Hughson, 1979; Rifkind, Goor & Levy, 1979; Stamler, 1979), in particular through maintenance of blood values of cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol within accepted normal ranges (Castelli, 1979a, b). However, debate continues as to the most effective way to reach and maintain ideal blood lipid levels. There is some evidence to suggest that an increase in fiber in the human diet can result in a decrease in serum cholesterol (Burkitt, Walker & Painter, 1974), and several investigators have had success using high complex carbohydrate, low fat diets to lower blood lipid levels (Albrink, Davidson & Newman, 1976; Anderson, Chen & Sieling, 1980). Thus, although many factors may affect lipid components of the blood, manipulation of the diet may be a useful method for prevention and treatment of hyperlipidemia.

Among the many lipid-lowering diets that have been designed, one of the more recent is that originated by Pritikin and associates, who have made claims of dramatic amelioration of symptoms of PAD in patients following the Pritikin protocol (Pritikin & McGrady, 1979, pp. 79-97). Through a measurement of treadmill walking time, Pritikin recorded startling improvements in patients with PAD after 6 months on a program of strict adherence to a very high fiber, low fat, complex carbohydrate diet coupled with regular exercise (Pritikin, Kern, Pritikin & Kaye, 1975;

Pritikin & McGrady, 1979). Thus, it has been suggested that a conservative treatment such as the Pritikin program can provide an effective therapeutic regimen for the treatment of PAD.

B. Significance of the Problem

Currently, morbidity from PAD is high, placing considerable strain on both patients and health service resources (Mann & Hughson, 1979). An effective conservative treatment for PAD would be welcomed by patients, who must at present turn to palliative surgery for relief from disabling symptoms. The high concern among PAD sufferers with finding appropriate therapy is evidenced by the apparent success of the Longevity Research Institute in California. Founded and directed by Nathan Pritikin, it offers a month-long program of treatment (as described above), advertising relief of symptoms from a wide variety of diseases, including PAD, CAD and hypertension. However, to-date no long-term controlled studies examining the efficacy of the therapeutic regimen have been reported, nor has the Pritikin program been compared with other lipid-lowering regimens.

C. Purpose of the Study

The purpose of the present study was to examine the effectiveness of two conservative diet regimens in the treatment of PAD. The thrust was two-fold: (1) to determine if vascular status and blood lipids could be effectively

altered over 1 year in two groups of PAD patients managed on separate therapeutic diets, and (2) to determine if one conservative diet regimen was more effective than the other in lowering blood lipids and altering vascular status. One group followed the American Heart Association Hyperlipidemia Diet C (Subcommittee on Diet, 1973), while the other group followed a more rigorous low fat, high fiber, complex carbohydrate diet similar to the Pritikin maintenance diet (Pritikin & McGrady, 1979). Extensive details of the actual dietary manipulation have been reported elsewhere by Whyte (1982).

The present study focuses on vascular assessment and the relationships between certain vascular variables and risk factors. Vascular status was determined by non-invasive means, and the associations between vascular variables and diet group, serum lipids, smoking, exercise and obesity were examined.

Specifically, the questions that were asked were:

1. Were there within-group differences from baseline at 2, 4, 6 and 12 months after commencement of dietary manipulation in mean values of certain blood lipid variables, i.e. TG, cholesterol, HDL-cholesterol and LDL-cholesterol?
2. Were there within-group differences from baseline in either group at 2, 4, 6 and 12 months after commencement of dietary manipulation in certain non-invasive vascular variables, i.e. ankle/brachial systolic pressure ratio

(ABR), pulsatility index (PI), transit time (TT), per cent pressure drop after exercise (% PD), treadmill walking time (WT) and treadmill walking distance (WD)?

3. Was there a between-group difference in mean values of blood lipids at baseline and at 2, 4, 6 and 12 months after entry into the study?
4. Was there a between-group difference in vascular variables at 0, 2, 4, 6 and 12 months?
5. Was there any association at 0, 2, 4, 6 or 12 months between the vascular variables and any or all of four blood lipid variables, i.e. cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol?
6. Was there any association between WT and WD and other vascular variables at 0, 2, 4, 6 and 12 months?
7. Was there any association between vascular variables and % ideal weight at 0, 2, 4, 6 and 12 months?
8. Was there any association between vascular variables and smoking habits?
9. Was there any association between vascular variables and amount of exercise done?

II. Review of the Literature

The etiology of the atherosclerotic lesion of PAD is similar to, if not the same as, that of CAD (Mann & Hughson, 1979), but it is the latter that has received the greatest attention in the literature. Although limited empirical work has been done on PAD directly, considerable information about the disease can be gained from studies of other atherosclerotic diseases, particularly CAD. Therefore, although much of the work reviewed below was directly related to CAD, the results should be applicable to the very similar process of PAD.

This review will focus on several different but related areas in the literature: the natural history and etiology of the atherosclerotic lesion, the associations between the various risk factors and the development of atherosclerosis, the relationships between diet and atherosclerosis and the effects of dietary manipulation on blood cholesterol levels, non-invasive methods for following the course of PAD, the effects of exercise training in PAD, and the difficulties in monitoring compliance with therapeutic regimens.

A. Pathogenesis and Natural History of Atheroma

The arterial wall consists of three distinct layers, the intima, the media and the adventitia. The intima, or innermost layer, consists of endothelium, basement membrane,

a gel-like ground substance and an elastic lamina. The media is composed of smooth muscle cells together with collagen and elastic fibers and some mucopolysaccharides. The adventitial layer contains fibroblasts, smooth muscle cells and bundles of collagen. Separating the media from the adventia is another elastic sheet, the external elastic lamina (Ross & Glomset, 1976).

Atherosclerotic lesions most commonly involve the intima, although secondary changes may occur in the media. Three different types of lesions have been described: the fatty streak, the fibrous plaque and the complicated lesion. Fatty streaks, flat yellowish intimal lesions commonly found in most arteries, cause no narrowing of the arterial lumen. It is not clear if fatty streaks are necessarily precursors of the more serious lesions. The fibrous plaque is raised and whitish in appearance and consists principally of cholesterol-laden smooth muscle cells, lipid, collagen and elastic fibers. These components form a fibrous cap that covers a deeper layer of free lipids and cell debris. The arterial lumen is compromised by the elevated plaque. The complicated lesion is similar to the fibrous plaque, with the additional features of ulceration, calcification, thrombosis or hemorrhage (Ross & Glomset, 1976; Strandness, 1969).

Atherogenesis is poorly understood despite intensive research. It is extremely difficult to trace the precise history of the development of atheroma in man because

arterial lesions cannot be sampled at various time intervals. Consequently, it has been necessary to extrapolate in certain areas from animal experimentation, although the inherent limitations of such an approach are recognized (Haust, 1981). Numerous hypotheses regarding the cause and sequence of plaque development have been advanced. The major events appear to be (1) hemodynamic stress, endothelial injury and arterial wall-platelet interaction, (2) smooth muscle cell proliferation, (3) lipid and lipoprotein entry and accumulation, (4) altered mechanisms of lipid removal, (5) fibrosis and development of thrombi, and (6) ulceration, calcification and formation of aneurysms (Fuster, Kottke & Juergens, 1980).

Currently, clinicopathologic and experimental evidence indicates that damage to the endothelium is the primary event in the development of atheroma. Factors injurious to the endothelium can be chemical, physical, metabolic and/or biological. Theory suggests that minor damage to the vessel walls leads to alterations in the permeability characteristics of the endothelial cells, allowing plasma constituents such as lipoproteins to move into the intima, resulting in focal serous edema. If the damage is prolonged and severe, there is endothelial cell death and desquamation. The resultant exposure of the underlying connective tissue to circulating platelets results in platelet adherence (at the site). In some way, the platelets appear to stimulate the migration of smooth muscle cells

from the media to the intima, and smooth muscle cell proliferation, possibly also stimulated by platelets, occurs within the plaque. Lipids and lipoproteins infiltrate the site, perhaps causing further smooth muscle cell proliferation. It appears that cholesterol cannot be degraded within the arterial wall, resulting in a progressive accumulation of lipids. Collagen and elastin formation are stimulated, possibly by smooth muscle cells, and fibrosis occurs, with eventual calcification. Hemorrhage into the lesion and weakening of the vessel wall, with resultant aneurysm, are further complications. The developing plaques are generally widely dispersed throughout the arterial tree, although certain arterial segments appear to be preferred sites. Branch points, bifurcations and areas where the artery leads a tortuous course are most commonly involved (Fuster et al., 1980; Kinlough-Rathbone & Mustard, 1981; Minick, 1981; Ross, 1981; Ross & Glomset, 1976; Steinberg, 1979).

Research evidence suggests that not all early lesions progress to the advanced forms (Haust, 1981). It would appear that if the injury is a single event, the lesions may be reversible, whereas if the injury is continuous and chronic, the lesions become progressive. How extensive the endothelial injury must be to induce proliferative atheroma is not clear. However, it appears that even early lesions may reach a point at which they are no longer easily reversible (Ross, 1981).

B. Risk Factors and Arterial Disease

Although the etiology of atherosclerosis is unclear, research has identified several factors that may increase the individual's risk of developing the disease, and may accelerate its course. These "risk factors" include abnormal plasma lipids, lack of exercise, smoking, and obesity.

Plasma Lipids

A strong association between blood lipid levels and development of atherosclerosis has been demonstrated in both animals and man (Dawber, 1980; Report of the Committee on Diet and Cardiovascular Disease, 1976; Minick, 1981; Wissler & Vesselinovitch, 1974). Early epidemiologic studies focused primarily on the level of blood total cholesterol and its role as a precursor to atherosclerotic disease. In the past two decades, however, much work has been done on lipid metabolism and transport, with the result that attention has turned to the partition of blood total cholesterol into various lipid fractions, which have been variously implicated in atherogenesis (Kannel et al., 1979; Steinberg, 1979).

Only about 7% of the body's cholesterol circulates in the blood; the remainder is found in the cells, where it performs vital structural and metabolic functions (Brown & Goldstein, 1981). Blood cholesterol is carried in conjunction with protein (as lipoprotein), and several specific types of lipoproteins have been identified, each having a certain average composition of lipid and protein

and a particular average density. Five major kinds of lipoprotein particle systems are recognized: the chylomicrons, the very low density (VLDL), the low density (LDL), the intermediate density (IDL) and the high density lipoproteins (HDL) (Kannel et al., 1979). Currently, there is little epidemiologic data on the atherogenic risk associated with chylomicrons and IDL; in the general population, the three most important cholesterol-bearing lipoprotein fractions appear to be VLDL, LDL and HDL (Kannel et al., 1979). About two-thirds of the circulating cholesterol is carried in the LDL fraction and about one-quarter in the HDL fraction. Most of the plasma triglyceride in the fasting state is carried in the VLDL (Rifkind & Levy, 1975).

The precise role of cholesterol in atherogenesis is not understood. It is thought that circulating cholesterol may in some way damage the arterial endothelium, favoring platelet aggregation and altering permeability characteristics of the wall, thus promoting plaque development. In addition, it is possible that plasma lipoproteins may penetrate into the arterial wall through an intact endothelium (Ross & Glomset, 1976). Why this occurs in some individuals but not in others remains a mystery. Furthermore, it is not at all clear what level of cholesterol in the blood predisposes to arterial disease (Steinberg, 1979). Although development of atherosclerosis is strongly associated with total blood cholesterol level,

it has been noted that at any cholesterol level risk may vary widely, in part depending on the presence of other risk factors such as smoking (Kannel et al., 1979). Thus, values within the commonly accepted normal range for total cholesterol (200 to 250 mg/dl) might be associated with a high risk, making it very difficult to establish optimal or ideal values and prompting some researchers to suggest that the so-called normal values are, in fact, too high for the maintenance of healthy arteries (Nash, Gensini, Simon, Arno & Nash, 1977). Certainly, patients with familial hyperlipidemia have been shown to be at great risk of early development of atherosclerosis (Zelis, Mason, Braunwald & Levy, 1970); however, many persons who would not be considered hyperlipidemic by normal standards develop atherosclerosis (Dawber, 1980).

Recently, it has become evident that a clue to the mystery may be provided by an examination of the properties of the various lipid fractions. Epidemiologic and biochemical data suggest an atherogenic role for LDL-cholesterol and a "protective" role for HDL-cholesterol (Havel, 1979; Miller & Miller, 1975). The Framingham study revealed a striking inverse correlation between HDL-cholesterol and the incidence of CAD, and although the relationship appeared somewhat weaker between HDL-cholesterol and PAD, the direction of association was, nevertheless, the same. Plasma LDL-cholesterol concentration was correlated positively but somewhat less strongly with

the incidence of CAD (Gordon, Castelli, Hjortland, Kannel & Dawber, 1977). Goldstein and Brown (1977) maintain that elevated levels of LDL-cholesterol in the blood produce atherosclerosis, whereas high levels of HDL-cholesterol are actually associated with a reduction in symptomatic atherosclerosis. Furthermore, results from prospective studies have indicated that a low blood HDL-cholesterol level precedes clinical atherosclerosis (Miller, 1980). Zilcher, Kaliman and Muller (1979), studying 96 patients with PAD and 80 patients with CAD, discovered significantly lower levels of HDL-cholesterol in both PAD and CAD patients compared with controls, who were free of symptomatic atherosclerotic disease. There was no significant difference between patients with CAD and PAD. Thus, the observation that patients without hyperlipidemia may develop atherosclerosis could be explained by the relative blood levels of HDL-cholesterol and LDL-cholesterol.

The role of TG in atherogenesis is even more controversial than that of HDL-cholesterol or LDL-cholesterol. In the Framingham study, levels of TG were found to have little predictive value in determining who was at risk of developing atherosclerosis (Dawber, 1980, p. 137). Similarly, Brown and colleagues (Brown, Kovanen & Goldstein, 1981) believe VLDL (the lipoprotein fraction carrying most of the TG) to have a "neutral" role in atherogenesis. However, other workers have observed significantly elevated levels of blood TG in PAD patients

compared with symptom-free control subjects, most patients in the study having normal total cholesterol levels (Greenhalgh, Rosengarten, Mervart, Lewis, Calnan & Martin, 1971). Davignon and others (Davignon, Lussier-Cacan, Ortin-George, Lelièvre, Bertagna, Gattereau & Fontaine, 1977) studied 114 patients with PAD and found the severity of atherosclerosis to be positively and significantly correlated with plasma TG concentration. Of the 50 patients classified as hyperlipidemic (cholesterol >250 mg/dl, TG >150 mg/dl), 45 had elevated TG levels, while only 13 had elevated total cholesterol.

The precise way in which the various lipid fractions exert their effects is unclear. Studies of lipid transport and metabolism indicate a very complex interrelationship between the lipoprotein particles (Brown et al., 1981). The importance of VLDL-triglyceride probably rests in the fact that it is the major source of LDL-cholesterol (Miller, 1980). It appears that the concentration of LDL-cholesterol in the plasma is a determinant of the rate at which cholesterol enters the arterial wall. In addition, LDL-cholesterol has been seen to cause arterial smooth muscle cell proliferation in vitro (Lewis, 1980). An inverse relationship between HDL-cholesterol and both TG and LDL-cholesterol has been demonstrated in some populations (Miller & Miller, 1975), but not in all (Miller, 1980). It appears, however, that a high level of LDL-cholesterol associated with a low level of HDL-cholesterol is

atherogenic (Coffman, 1979). Mechanisms whereby HDL slows atherogenesis have been postulated. HDL may compete with LDL for cell binding sites, thus reducing the cellular uptake of LDL-cholesterol in the arterial wall (Steinberg, 1978) and may facilitate removal of cholesterol from the tissues and a subsequent excretion of cholesterol from the body (Coffman, 1979). The chemical structure of HDL is such that it does not bind readily with certain substances in the arterial wall, with the result that it makes little, if any, contribution to the lipid of the atheromatous lesions (Miller, 1980).

In summary, blood total cholesterol levels have been strongly associated with risk of atherosclerosis. The particular lipid fractions that appear to be atherogenic include LDL-cholesterol and VLDL-cholesterol, whereas HDL-cholesterol appears to have a protective effect. Therefore, based on current theories, methods for reducing LDL-cholesterol and TG and increasing HDL-cholesterol are sought (Gotto, 1981).

Exercise

Physical inactivity has been implicated as a major risk factor in the development of atherosclerosis. In the Framingham study, sedentary individuals had two to three times the incidence of CAD compared with the most active individuals (Dawber, 1980). No association was seen between amount of exercise done and development of IC, but the

author states that the evidence was "confounded by the obvious fact that people developing any manifestations of leg discomfort would tend to remain inactive" (Dawber, 1980, p. 162). This problem arises in any attempt to relate physical inactivity to development of PAD, and could explain the paucity of epidemiological studies on the subject.

An association between lack of exercise and development of CAD appears to have been well established (Simko, 1978), and several mechanisms by which physical exercise could influence atherogenesis have been postulated. These include an alteration in lipid metabolism (Simko, 1978) and the release of enzymes, hormones or steroids which could in some way prevent cholesterol uptake by the arterial wall (Lopez-S, Vial, Balart & Arroyave, 1974). Most recent work has focused on the effects of exercise on blood lipid levels. In a randomized controlled trial, Huttunen and co-workers (Huttunen, Lansimies, Voutilainen, Ehnholm, Hietanen, Penttila, Siitonen & Rauramaa, 1979) studied the effects of a mild to moderate exercise program on serum lipoproteins in middle-aged men (n = 100) and observed a significant decrease in serum TG and a significant increase in HDL-cholesterol in the exercise group compared with the control group. Similarly, 13 medical students engaged in an exercise program were seen to have decreased TG and LDL-cholesterol and increased HDL-cholesterol after 7 weeks (Lopez-S et al., 1974), and Schamberger (1981) noted significant increases in HDL-cholesterol and significant

decreases in TG in subjects participating in a 16-week running program. These observations are supported by some epidemiological data; from the Framingham study, Castelli (1979b) concluded that blood HDL-cholesterol levels rise even with mild to moderate exercise. Thus, although Keys (1975) criticized available epidemiological evidence relating inactivity to increased risk of developing atherosclerosis, an accumulating body of evidence would appear to support the association.

Smoking

A strong association between smoking and atherosclerosis has been demonstrated (Kinlough-Rathbone & Mustard, 1981). In Framingham, the incidence of all forms of atherosclerotic disease was higher in smokers than in non-smokers. This relationship was particularly pronounced in PAD, the incidence being two to three times higher in smokers (Dawber, 1980, p. 180). In a study of 34,440 British male doctors, Doll and Peto (1976) observed a significantly higher mortality from CAD and PAD in smokers than in non-smokers, with the risk increasing with the number of cigarettes smoked. Furthermore, the recent decline in cardiovascular mortality in North America has been linked to the decreased use of cigarettes in the population (Feinleib, Garrison, Stallones, Kannel, Castelli & McNamara, 1979; Mustard, Packham & Kinlough-Rathbone, 1981).

Empirical studies, too, have provided evidence of an association between smoking and atherosclerosis. Strong and Richards (1976) autopsied 1,320 men 25 to 64 years of age and observed atherosclerotic lesions of the aorta and coronary arteries to be greatest in heavy smokers and least in non-smokers (smoking habits determined by interview with families of the deceased). Brooks and associates (Brooks, Blankenhorn, Chin, San Marco, Hanashiro, Selzer & Sylvester, 1980) studied atherosclerosis by femoral angiography in 54 men and found that smoking history was the strongest variable associated with the degree of atherosclerosis.

Again, the mechanism whereby smoking affects atherogenesis is not understood (Dawber, 1980), but several hypotheses have been investigated, including the possibility of damage to the endothelium by carbon monoxide (Mustard et al., 1981), a smoking-induced release of toxic vasoactive substances from platelets and leukocytes (Minick, 1981), and increased platelet adhesiveness predisposing to plaque formation (Strong & Richards, 1976). Recently, epidemiological evidence has indicated that blood lipid levels might be affected by smoking. Increased LDL-cholesterol and decreased HDL-cholesterol levels were observed in smokers in a study of 10,000 Israeli men (Goldbourt & Medalie, 1977). Similarly, significantly lower HDL-cholesterol levels were seen in non-smokers compared with smokers (total n = 477) in one Canadian study (Dedonder-Decoopman, Fievet-Desremaux, Campos, Moulin,

Dewailly, Sezille & Jaillard, 1980), although others (Heyden, Heiss, Manegold, Tyroler, Hames, Bartel & Cooper, 1979) found that this relationship was evident only if the subjects, in addition to being smokers, consumed five or more cups of coffee per day.

Although the nature of the association between the atherosclerotic process and smoking is not perfectly understood, what is clear is that patients with PAD benefit from a cessation of smoking (Coffman, 1979). On the basis of observation of 401 patients with PAD, Juergens and colleagues (Juergens, Barker & Hines, 1960; Juergens & Bernatz, 1980) concluded that cigarette smoking increased vasoconstriction and decreased blood flow to the already compromised limb, thus aggravating the condition and increasing the possibility that severe complications such as amputation would develop. Coffman (1975) observed that smoking even two cigarettes a day resulted in a highly significant decrease in the blood flow to the foot, both at rest and during exercise. Thus, medical management of PAD must include the recommendation that the patient stop smoking (Chucker, 1977).

Obesity

The relationship between obesity and PAD is somewhat less clear. Certainly, it is recommended that obese PAD patients lose weight; the extra weight carried increses metabolic demands on the exercising muscle, which can

perform only a limited amount of work when the blood supply is compromised (Chucker, 1977; Coffman, 1975). However, whether obesity contributes directly to atherogenesis is questionable (Chucker, 1977). The Committee on Diet and Cardiovascular Disease established by the Canadian Federal Government (Report of the Committee, 1976) reported that, although an association between obesity and atherosclerosis was seen, it was difficult to separate the effects of obesity from the effects of other coincidental risk factors. Some workers (Dedonder-Decoopman et al., 1980; Rifkind et al., 1979; Taylor, Carter, Valente, Wright, Smith & Matthews, 1981) observed a positive correlation between relative body weight and both LDL-cholesterol and TG, whereas a negative association between HDL-cholesterol and body weight existed. These relationships were particularly evident in men. The group at Framingham (Kannel et al., 1979) looked at the association between lipids and obesity, and found HDL-cholesterol to be most strongly (negatively) obesity-related, with TG almost as strongly (positively) correlated. These authors felt that, whereas "lipid abnormalities, particularly elevations of triglycerides, are an acknowledged concomitant of obesity" (p. 1243), it was also true that "weight gain does not explain more than a small fraction of the variation ... in atherogenic traits, and some persons are able to gain weight without much change in their cardiovascular risk attributes" (p. 1242). Thus, the question of obesity and atherogenesis remains

unanswered, and patients with PAD are cautioned to lose weight for palliative rather than curative reasons (Juergens & Bernatz, 1980).

C. Diet and Atherosclerosis

There is considerable epidemiologic evidence that the incidence of atherosclerotic disease is associated with the intake of certain dietary components, notably cholesterol and saturated fat (Keys, 1975; Mancini, Farinaro, Postiglione, Rubba & Strazzullo, 1980). An examination of vital statistics from 30 countries revealed a strong positive correlation between death from CAD and intake of total calories, total fat, animal fat, meat, cholesterol, eggs, animal protein and sugar in men aged 55 to 59 years (Mahley, 1976). In the Seven Country study, a prospective 5-year study of 40 to 59 year old men, saturated fat intake was strongly correlated (r = .84) with serum cholesterol and the incidence of CAD (Keys, 1970). In addition, despite multiple methodological difficulties, several trials of primary prevention of CAD appear to indicate that dietary changes, particularly a reduction of total fat calories and/or substituting unsaturated for saturated fat, may lower the incidence of CAD in middle-aged men (Shaper, 1976). However, these studies are far from conclusive, and Mann (1977) has criticized the deductions drawn from such "soft" data. He maintains that there is no sound scientific evidence linking specific dietary components with

atherosclerosis, as the evidence cited above has failed to differentiate between the effects of diet and other lifestyle factors.

Animal studies have provided more direct evidence. Non-human primates are frequently used for such studies because of their apparent similarity to man, and it has been shown that atherosclerosis can be induced in various primate species fed a cholesterol-rich diet (Gresham, 1980). Mahley (1976) fed a semisynthetic diet containing 25% lard and .5% cholesterol to 20 patas monkeys for 1 to 2 years. Control groups were fed commercial monkey chow or the semisynthetic diet containing 25% lard and no cholesterol. Control monkeys on the chow diet had a mean serum cholesterol of 130 mg/dl; those on the lard-only diet had a mean serum cholesterol of 150 mg/dl. However, the monkeys on the lard plus cholesterol diet had significantly elevated serum cholesterol levels (550 ± 200 mg/dl) and considerably more extensive atherosclerosis than control monkeys after 2 years. There was little difference in the development of atheroma between the two control groups. Rhesus monkeys fed high or moderately high cholesterol diets develop marked hypercholesterolemia and atherosclerosis (Armstrong, Megan & Wainer, 1974), but it is not clear if the diet-induced atherosclerosis must necessarily be associated with elevated blood cholesterol levels. Armstrong et al. (1974) fed Rhesus monkeys low supplements of dietary cholesterol for 18 months and found that, although the blood levels of cholesterol

were not significantly different from those of control monkeys fed on standard monkey chow, there was increased intimal thickening and a greater incidence of aortic lesions in the monkeys who had received cholesterol. Thus, they concluded that dietary cholesterol could affect the delivery of cholesterol to the arterial wall, even in the absence of hypercholesterolemia.

Further support for the role of diet comes from an accumulating body of evidence that suggests that actual regression of atheroma can occur if the dietary stimulus is removed. Armstrong (1976a) studied 40 adult male Rhesus monkeys, sacrificing 10 at the outset to establish a baseline and feeding the remaining 30 a cholesterol-rich atherogenic diet for 17 months. At the end of this period, 10 monkeys were sacrificed for autopsy and the remaining 20 were placed on a low cholesterol "regression" diet for 40 months. At baseline, minimal atheromatous lesions were seen; after 17 months on the atherogenic diet, an average of almost 60% luminal narrowing was observed in selected peripheral arterial sites. After the regression diet, arterial narrowing was reduced to 20%. Thus, the authors concluded that the cholesterol-rich diet had induced the development of atheroma, and that the lesions had regressed when the cholesterol was removed from the diet. Vesselinovitch and colleagues (Vesselinovitch, Wissler, Schoffner & Borenstzajn, 1980) fed male Rhesus monkeys diets high in fat and cholesterol using various regimens in which

amounts of saturated and unsaturated fats were manipulated. All diets, but particularly those high in saturated fat, produced serum hyperlipidemia. Abundant atherogenic plaques were seen in the monkeys fed saturated fat and in those fed (unsaturated) peanut oil with added cholesterol. In the latter group, only moderate hypercholesterolemia was noted. Weber and others fed monkeys an atherogenic diet for 1 year, then placed half the animals on a low fat, low cholesterol regression diet. Reversal of advanced aortic lesions was almost completely accomplished after 12 months of the regression diet (Weber, Fabrini, Resi, Jones, Vesselinovitch & Wissler, 1977).

From the studies cited above, it appears that cholesterol is the causative factor in diet-induced atheroma. Unfortunately, there is an inherent danger in extrapolating experimental results from animals to humans. Such important variables as mechanisms of fat metabolism may be very different across species (Malinow, 1980). In addition, human studies are more complex than simple controlled animal studies, as the factors underlying the development of atheroma in man are often multiple, rather than single (Kuller, 1980). Nevertheless, there is a limited amount of evidence that regression of atheroma can occur in humans if serum lipids are lowered significantly (Armstrong, 1976b; Kent, 1979; Wissler & Vesselinovitch, 1974). In one frequently cited study, Knight and co-workers (Knight, Schiebel, Amplatz, Varco & Buchwald, 1972) conducted pre-

and post-operative arteriograms on patients who had undergone partial ileal bypass for the treatment of hyperlipidemia. Twenty-two patients were submitted to coronary arteriograms from 2.5 to 8 years post-surgery; of these, 13.6% demonstrated a reduction in the size of atherosclerotic plaques in the coronary arteries. No change, however, was seen in the atherosclerotic lesions in the peripheral arteries of 14 patients who underwent pelvic arteriograms.

Perhaps the most convincing evidence of regression in humans comes from Barndt and colleagues (Barndt, Blankenhorn, Crawford & Brooks, 1977; Blankenhorn, Brooks, Selzer & Barndt, 1978), who used femoral angiograms to evaluate change in early atherosclerosis in 25 hyperlipoproteinemic patients 22 to 65 years of age. Patients were treated with diet and drugs to reduce blood lipids; after an average of 13 months, repeat angiograms showed plaque regression in 9 patients, no change in 3 patients and progression of the disease in 13 patients. Those with plaque regression had significantly lower serum cholesterol levels ($p < .01$) than those with progression.

From this work, Blankenhorn (1981) concluded that regression was most likely to occur if serum cholesterol was lowered by more than 20%. Less directly, in a study of nine hyperlipidemic patients whose cholesterol and triglycerides were lowered to within normal limits and held there for 3 to 6 months, a 55% improvement in post-exercise blood flow to

the legs (as measured by venous plethysmography) was observed. The researchers concluded that the increase in flow was most likely to have occurred as a result of "resorption of cholesterol-rich atheromata" (Zelis, Mason, Braunwald & Levy, 1970, p. 1014). Thus, a lowering of blood cholesterol would appear to result in a regression in plaque size.

What, then, is the most effective way to reduce blood cholesterol in humans? Various drug regimens have been used, and some have been shown to lower blood cholesterol by as much as 20%, but none of these drugs is without a degree of risk (Hunninghake & Probstfield, 1977). As certain dietary components have been shown to have decisive effects on plasma lipid and lipoprotein concentrations, Ricci and colleagues have stated that "the prescription of a diet low in saturated fats and cholesterol and rich in polyunsaturated fats (PUF) is the first step in the treatment of hypercholesterolemia. Persisting high cholesterol levels after prolonged dietary treatment suggest the advisability of a pharmacological approach" (Ricci, Angelico, Amodeo, Borgogelli, Cantafora, Montali & Vergari, 1980, p. 23). The question, then, remains as to which dietary protocol is most effective in lowering serum lipids (Connor & Connor, 1977). Numerous dietary prescriptions have been tested, most emphasizing a reduction in total calories obtained from fat, a decrease in cholesterol intake (<400 mg/day) and an increase in the unsaturated/saturated

fat ratio. Reductions in blood cholesterol have ranged from 3 to 22%, with a mean of about 8% (Gotto, Foreyt & Scott, 1980). In one lipid clinic, almost 40% of hyperlipidemic patients have been reported to reach normal blood cholesterol levels after 2 months of treatment on a diet consisting of 26 to 31% fat (mostly unsaturated) and ≤300 mg cholesterol per day (Mancini et al., 1980).

Based on epidemiological evidence in developing countries, which showed a lower incidence of atherosclerosis to be associated with a high intake of dietary fiber, it has been suggested that the addition of fiber to the diet can assist in lowering blood lipid levels (Burkitt et al., 1974; Trowell, 1976). Knowledge of the normal pathway of cholesterol excretion provides a logical basis for such a conclusion. Normally, the liver takes up dietary cholesterol and disposes of it in the bile, either as unesterified cholesterol or as bile acids; the bile is then excreted into the intestine. In the colon, much of the cholesterol and bile acid is reabsorbed and delivered again to the liver, thus forming an enterohepatic circulation (Brown et al., 1981). It is thought that dietary fiber may interfere with the enterohepatic circulation in two ways: (1) by increasing colonic motility and causing rapid fecal excretion of bile acids, or (2) by adsorbing bile acid in the bowel and thus interfering with reabsorption. Either mechanism would result in increased excretion of cholesterol from the body (Dietary Fibre and Plasma Lipids, 1975; Eastwood, 1977).

Nevertheless, Hegsted (1977), having done considerable experimental work with animals, considers "the likelihood that dietary fiber is a primary factor in regulating serum lipids to be remote" (p. 48).

In consideration of the research linking diet and atherosclerosis, the American Heart Association has endorsed a lipid-lowering diet to be used in the therapy of hyperlipidemia. Termed a modified fat diet, it is low in polyunsaturated/saturated fat and low in cholesterol (Subcommittee on Diet, 1973). However, Pritikin and co-workers (Pritikin et al., 1975; Pritikin & McGrady, 1979) feel that a more vigorous approach is necessary to effectively reduce serum lipids. Their diet, which is primarily vegetarian, includes severe restrictions on total fat calories (5 to 10% of total calories) and is high in complex carbohydrates and fiber (about 80% of total calories). The low fat content necessitates that most meat be eliminated from the diet. Both diets are claimed to lower serum lipids; however, to-date, no controlled trial comparing the relative efficacy of the two diets has been conducted.

D. Non-Invasive Diagnosis of PAD

In the diagnosis of PAD, a well-taken history is most important in establishing a basis for the patient's complaints. Leg pain that: occurs during exercise and is evoked by a fairly consistent amount of exercise, is worse

going up stairs or up a hill, and is relieved by rest, is almost certainly IC. However, a few neurospinal disorders can mimic IC, and it is important to establish a differential diagnosis (Strandness, 1977). Physical findings in the patient with obstructed peripheral arteries generally include diminished or absent peripheral pulses. Systolic bruits heard over pulsating arteries are a frequent result of turbulent flow caused by a stenosis. Color changes in the skin of the feet may occur; in severe cases, the skin of the feet may be red, bluish, pale or mottled. During and following exercise, pronounced foot pallor may occur. The foot of the affected limb often feels cold to the touch; a temperature difference between the feet is a significant indication of arterial insufficiency to one limb. Often, there is a loss of hair on the limb below the lesion. When the disease is very severe, ulceration and gangrene can occur (Juergens & Bernatz, 1980).

Once the presence of PAD is suspected, definitive diagnosis must be made. In addition, long-term follow-up requires an objective method of assessment of the patient's vascular status. For follow-up, the assessment should be reliable, relatively inexpensive and without risk to the patient. Currently, the most commonly accepted tool for measurement of arterial disease is arteriography, a painful, expensive procedure which requires highly skilled technology and is not without risk to the patient (Morris, Woodcock & Wells, 1975). Recognizing the need for non-invasive methods

of vascular assessment, researchers and clinicians have recently expended considerable effort toward the development of reliable and valid non-invasive techniques. The most promising and widely accepted innovation has been the introduction of Doppler ultrasonography. Combined with several other non-invasive tests, ultrasound is proving to be a most useful tool for long-term follow-up of PAD patients (Morris et al., 1975).

Understanding and interpretation of non-invasive methods of vascular assessment requires a knowledge of peripheral circulatory dynamics. Strandness (1977) has outlined the salient features. He states:

1. In the normal arterial circulation, the pressure pulse is amplified as it traverses the peripheral arteries. This means that the systolic pressure at the ankle will exceed that of the central aorta.

2. The normal arteries are a low-resistance system down to the level of the arterioles. This is reflected in the less than 10 mm Hg drop in mean pressure between the central aorta and small peripheral arteries.

3. There is a gradual reduction in peak velocity of flow toward the periphery.

4. Under resting conditions, flow in the peripheral arteries normally goes to zero, with a very transient reversal of flow in early to mid-diastole.

5. With exercise, flow (volume and velocity) goes up and systolic and mean pressures are maintained, but flow reversal disappears and the flow itself may become quasi-steady during the hyperemic phase. (p. 275)

Arterial disease has very definite effects on the above variables. When the artery becomes stenosed or occluded by an atherosclerotic plaque, effects on pressure and flow relationships within the artery can be anticipated. Pressure is not uniform throughout the vascular tree, and a comparison of a regional circulation with a simple electric circuit is useful in describing pressure changes that occur in the normal and abnormal systems (Hutchison, 1981). Pressure changes are dependent on two variables, flow and resistance, and the degree of pressure drop across a segment, for example across the arterioles, can be calculated using an analogy with Ohm's law as follows:

$$\underline{P}_1 - \underline{P}_2 = \underline{RQ}$$

where $\underline{P}_1 - \underline{P}_2$ is the pressure drop across a segment, $\underline{Q}$ is the volume flow and $\underline{R}$ is the resistance to flow.

It can be seen that as both flow and resistance increase, the pressure drop across the segment increases (Strandness & Summer, 1975).

Normally, the major site of resistance in the circulation is in the arterioles. When an arterial stenosis develops, the narrowing of the lumen is an added site of resistance. From the above formula, it can be seen that there will be a pressure drop across the stenosis directly proportional to the resistance created (Strandness, 1969). The effects of resistance in series are additive; therefore,

both the stenosis and the arterioles will contribute to the total resistance and to the total pressure drop. The proportion of the total pressure drop across each resistance depends on its relative contribution to the total resistance. If, for example, the pressure drop across the combined stenotic and arteriolar segment were 100 mm Hg and the stenosis comprised 60% of the total resistance, 60% of the total pressure drop would occur across the stenosis (Hutchison, 1981). If a stenosis is not severe and causes little resistance, there may be little pressure drop across it at rest (Strandness, 1977). However, during exercise, the arterioles dilate but the stenosis remains fixed in diameter, and as arteriolar resistance decreases, the relative contribution of the stenosis to the total resistance increases, with the result that there is a much greater pressure drop across the stenosis. In addition, as pressure drop is dependent on flow as well as resistance, the increase in flow during exercise contributes to the pressure drop across the stenotic segment. Thus, when there is an arterial lesion in the lower limbs, systolic pressures measured at the ankle may or may not be normal at rest (depending on the severity of the lesion), but will always be lower than normal following exercise (Strandness & Summer, 1975).

As the arterial obstruction progresses, collateral channels develop around the block. The degree of collateral development depends largely on time and the severity of the

disease (Sorlie, Straume, Grimsgaard & Johnsrud, 1978), but initial development appears to stabilize at about a year after claudication is first experienced (Strandness, 1969). Since the collaterals are of a smaller diameter than the normal artery, they offer a greater resistance to flow; there will therefore be a pressure drop across the collateral circuit. However, the presence of numerous large diameter collaterals will result in a lesser pressure drop than would occur if all flow were exclusively through the stenotic segment. As with a stenosis, there is a greater pressure drop across the collateral channels during exercise, the magnitude of the drop being dependent on flow rate and collateral diameter. Thus, if over time an individual experiences a lesser degree of pressure drop, it may be difficult to determine if the change is due to an improvement in collateral circulation or to an increase in the patency of the main artery (Skinner & Strandness, 1967a, b).

Another consideration in the hemodynamics of arterial obstruction is the effect of the obstruction on the total blood flow to the affected limb. Under normal conditions, a change in arteriolar resistance is primarily responsible for a change in blood flow; as arterioles dilate during exercise, resistance decreases and flow increases. When an arterial obstruction occurs, a resistance (either through the stenosis or the collaterals) is added in series and the arterioles partially dilate to keep total resistance and

blood flow constant. Thus, resting blood flow to the affected limb remains essentially normal until the disease becomes severe (Strandness, 1977). When the arterial lesions are very extensive and the collateral channels are narrow or absent, adding a high resistance, the arterioles may be unable to dilate sufficiently to compensate, and total segmental resistance goes up while total flow to the limb decreases. The result of this decreased flow is ischemic pain or "rest pain" (Strandness, 1977).

Although total flow may be sufficient at rest, the picture changes during exercise. The increased demand for blood flow during exercise is partially met by arteriolar dilatation. However, in the presence of the fixed proximal resistance provided by the stenosis or the collaterals, the arterioles are unable to decrease the resistance and increase the flow to meet metabolic demands, and IC develops (Hutchison, 1981). In addition, with the reduced pressure in the artery, the pressure exerted on the artery by the exercising muscle causes the artery to collapse partially, increasing resistance and decreasing flow even further (Lieberman, 1980).

With the changes in the flow and pressure relationships in the diseased artery, the mean pressure falls and the pulsatile nature of the blood flow disappears. Flow no longer returns to zero during diastole and there is no flow reversal; instead, flow becomes fairly steady throughout the cardiac cycle (Strandness, 1977).

The above principles are utilized in the non-invasive diagnosis and follow-up of PAD. Ankle/brachial blood pressure ratio is an important diagnostic measure. As was mentioned above, the pressure pulse is amplified toward the periphery, and the ankle/brachial ratio at rest should be greater than or equal to 1, that is, the ankle pressure should be the same as or higher than the arm pressure (Baron & Heisiger, 1979). Therefore, a drop in ankle pressure compared with arm pressure indicates an obstruction to flow in the lower limbs, and a below-normal ankle/brachial ratio is indicative of PAD (Strandness, 1970). Excellent correlations between resting ankle/brachial ratios and arteriographic findings have been demonstrated, substantiating the validity of the technique. Ratios of .95 to .97 have been seen to be the lower limits of normal (Carter, 1972; Johnson, 1975, Lewis & Yao, 1974; Marinelli, Beach, Glass, Primozich & Strandness, 1979).

Accurate measurement of systolic pressure has been made possible by the development of the Doppler ultrasound blood flow detector. The Doppler sound, in place of the familiar Korotkoff sounds which are very difficult to detect in the diseased lower extremities, can be used to determine ankle systolic blood pressure. Simultaneous recording of ankle and brachial pressures can be used to calculate the ankle/brachial ratio (Baron & Hiesiger, 1979).

A further use of the Doppler flowmeter provides a method for quantitative assessment of the dynamic conditions

of flow (Fitzgerald & Carr, 1975). Gosling (1976) has described a method whereby the Doppler-shifted sound is analyzed and used to indicate actual blood flow velocity through the diseased artery. Since the blood flow through the normal artery is pulsatile, returning to zero and actually reversing for a brief time in mid-diastole, the Doppler-shifted sound, which is a reflection from moving blood, will not be of the same frequency throughout the cardiac cycle. It will increase in frequency as blood flow velocity increases and decrease as velocity decreases. Gosling and associates (Fitzgerald, Gosling & Woodcock, 1971; Gosling, 1976; Gosling, King & Woodcock, 1972) presently record the audible Doppler signal and computer-analyze it using Fourier transforms, producing a waveform or sonogram, the upper frequency envelope of which represents maximum blood velocity/time throughout the cardiac cycle. The normal waveform has a distinct shape, with a peak flow and a reverse flow component. The waveform is then assigned a pulsatility index (PI) defined as the "sum of the maximum energy of the Fourier harmonics divided by the mean energy term" (Fitzgerald et al., 1971, p. 66). However, Hutchison and colleagues (Hutchison, Oberle, Scott & French, 1981) have shown that a much simpler calculation of PI, a ratio of the peak-to-peak amplitude to mean flow, correlates very highly (r = .99) with the more complex harmonic PI, and can be considered equivalent for diagnostic purposes.

Gosling (1976) has defined normal PI's for the various peripheral pulses (femoral, popliteal, posterior tibial and dorsalis pedis). PI increases distally as the pressure pulse is amplified. Blood flow through collateral channnels or through a stenosis causes damping of the waveform and a reduction in the PI because of loss of pulsatile flow and the gradual decline in mean flow. The flow distal to the stenosis no longer returns to zero, and the waveform is flattened and continuous throughout the cardiac cycle. Thus, the pulsatility index provides a single numerical index of the degree of damping, which is proportional to the degree of arterial obstruction (Gosling, 1976). PI is compared with the normal value, allowing a quantitative assessment of the blood flow to each peripheral pulse. This technique has been found to be a valid indicator of the degree of arterial insufficiency, correlating well with arteriographic findings, and as such is useful for long-term follow-up of the course of PAD (Harris, Taylor, Cove & Charlesworth, 1974; Hutchison et al., 1981; Johnston & Taraschuk, 1976; Ward & Martin, 1980).

It is evident from the above discussion that blood flow may reach the arterial pulse site through a stenosis and/or through collateral channels, producing similar waveforms. Gosling and co-workers (Gosling, Dunbar, King, Newman, Side, Woodcock, Fitzgerald, Keates & MacMillan, 1971) have recorded flow-velocity waveforms simultaneously from two points along the vessel to determine transit time (TT), or

the time taken for the pulse wave to travel between the two sites, and have defined normal TT's for each arterial segment. TT is dependent on the elasticity of the vessel wall and on the length of the vessel pathway between sites. Thus, TT will be shortened in a stiff, inelastic vessel, and lengthened if blood flow is through a collateral path around an arterial occlusion. The TT, therefore, would allow the investigator to determine if an improvement in flow to a pulse site were due to a widening of collateral channels or a regression in occlusive lesions.

Another method of calculating TT has been described by Hutchison et al. (1981). These researchers simultaneously recorded the Doppler sound and an ECG; the transit time was taken as the time from the R wave of the ECG to the foot of the pulse wave. This technique eliminates the need for simultaneous monitoring of two pulse sites and should provide essentially the same information.

There is some question about the usefulness of the TT in distinguishing between the degrees of severity of atherosclerotic disease. Hutchison et al. (1981) classified arterial segments according to the severity of arterial lesions as measured by arteriography, and found that while mean transit time increased with increasing disease, there was considerable overlap between grades. Similarly, Ward and Martin (1980) found the TT to have little correlation with arteriographic findings. Nevertheless, the TT is frequently used in vascular laboratories, and is felt by many to be a

useful variable (Gosling, 1976).

Another non-invasive test in frequent use is the measurement of treadmill walking distance (WD) or walking time (WT) to claudication and the recording of ankle systolic pressure drop after exercise. Strandness and Sumner (1975) have pointed out that "measurement of the quantity of work performed before the development of claudication provides a[n] ... accurate and objective means of assessing circulatory improvement" (p. 291). Ebel and Kuo (1967) have shown the test to be reproducible. In repeat tests on 49 PAD patients, a 2% error of the mean was observed. Thus, as Sumner and Strandness (1975) have pointed out, although there is considerable variation in exercise tolerance among individuals with the same amount of disease, each patient serves as a good control for himself. The capacity of the peripheral circulation to deliver blood to the exercising muscle is the major determinant of claudication distance. Thus, improvements in the circulation should be evidenced by increases in exercise tolerance. Similarly, a lessening of the pressure drop after exercise should be an indication of improvement or worsening in the vascular lesions (Lewis & Yao, 1974; Lieberman, 1980; Marinelli et al., 1979; Raines, Darling, Berth & Brewster, 1976; Strandness, 1969; Sumner & Strandness, 1969; Yao, 1973).

Although arteriography continues to be preferred when precise localization of the arterial obstruction is required (Gosling et al., 1971), non-invasive vascular assessment has

been shown to provide a sensitive and acceptable alternative to arteriography for diagnosis and follow-up of patients with PAD. As it involves little risk to the patient and can be conducted by paramedical personnel, it is a useful technique for long-term follow-up in clinical risk factor intervention trials.

E. Effects of Physical Training in PAD

The development of IC in patients with PAD is the primary functional limitation. Experience with treadmill testing has shown that, aside from the possible effects of exercise on the atherosclerotic process, physical training can cause an increase in walking distance (WD) to claudication in many PAD patients (Jonason, Jonzon, Ringqvist & Persson-Rydberg, 1979; Lorensten, 1973; Snow, 1980). The most common explanation for the improved walking ability with physical training has been an increase in collateral circulation around the arterial obstruction with a resultant increase in blood flow (Skinner & Strandness, 1967a, b). Alpert, Larsen and Lassen (1969) observed an improvement in the WD along with an increase in blood flow in all but 2 of 19 PAD patients engaged in a moderate exercise program for 6 months. These authors postulated that the improvements in walking ability were probably due to both increased collateral circulation and improved muscle coordination. Similarly, Ericsson, Haeger and Lindell (1970) observed an increase in WD and blood flow in seven male PAD

patients on an 11-month exercise program. No changes in walking ability or blood flow were seen in controls.

However, Zetterquist (1970) challenged the hypothesis that improvements were due to total blood flow increases. He observed 9 men with PAD who were actively trained for 3 to 4 months; all increased their WD. No increase in total blood flow was measured, but a more effective peripheral oxygen utilization was seen. Zetterquist maintained that a regional distribution of the available blood flow towards the active muscles was probably responsible for the observed results, although he did not discount improved muscle coordination, increased metabolic capacity of the muscles and psychological effects. Larsen and Lassen (1966) found no significant change in the calf blood flow in exercised or control patients. However, there was a significant increase in painless walking time in the experimental group, leading the authors to suggest that more efficient walking and better oxygen utilization were responsible. Blumchen, Landry, Keefer and Schlosser (1970) came to a similar conclusion. Although they saw an increase in maximal calf blood flow after 85 days, a decrease in blood flow in many patients was recorded by the end of the study, despite increases in WD. They felt that improved movement skills and possibly a higher pain threshold could explain these results.

Others have hypothesized that there are local changes in metabolism in the muscle. Following the observation by

Zetterquist (1970) of increased oxygen extraction by the exercising muscles in PAD patients, Sorlie and Myhre (1978) examined the effects of training on 10 subjects with PAD. Results showed a lowered lactate level, indicating an improved local aerobic working capacity and decreased anaerobic glycolysis in the calf muscles. Bylund and others (Bylund, Hammersten, Holm and Schersten, 1976) studied enzyme patterns in the gastrocnemius muscles of patients with PAD. They concluded that intermittent low oxygen tensions resulting from increased metabolic demands and decreased blood flow to the exercising muscle could trigger changes in muscle enzyme activity, thereby increasing its metabolic capacity. In another study (Dahllof, Bjorntorp, Holm & Schersten, 1974), improvements in WD were found to correlate with enzyme changes and improved metabolic capacity of the muscle. A similar result was observed by Ekroth and colleagues (Ekroth, Dahllof, Gundenvall, Holm & Schersten, 1978), who conducted a 4 to 6 month physical training program for 148 PAD patients. In the 129 subjects who completed the training period, mean walking ability more than doubled but calf blood flow remained unchanged, suggesting an increase in the metabolic capacity of the muscle, rather than an increase in collateral circulation and blood flow.

In most of the above studies, the exercise training consisted of walking to claudication, resting, and walking again, for up to 1 hour per day. Thus, exercise regimens may

lead to psychological improvement, increased collateral blood flow, improved muscle coordination, use of non-ischemic muscles, or improved metabolic capacity of the exercising muscle. Whatever the mechanism, even mild to moderate physical training can have positive effects on the exercise capacity in PAD patients. Therapeutic regimens designed to improve the vascular status in these patients must ultimately be concerned with the patient's functional ability and should include some form of exercise as part of the therapeutic mode (Coffman, 1979). In addition, an examination of exercise and its effects should be considered in risk factor intervention trials with PAD patients.

F. Compliance With Therapeutic Regimens

Attempts to assess the effectiveness of lipid-lowering diets and risk factor intervention trials may be confounded by the problem of patient compliance with the therapeutic regimen. Although considerable work has been done on the question of patient compliance with medical recommendations, particularly in drug studies, relatively little has been written about compliance to a therapeutic diet (Sackett & Snow, 1979). Glanz (1980), in reviewing the literature on dietary compliance, has stated that "there are unique and unresolved problems involved in measuring and quantifying dietary compliance, and difficulties with respect to practicality and feasibility of collecting valid information with which to make such assessments" (p. 788).

Gordis (1979) has indicated two general methods for evaluating compliance: (1) direct methods, using urine or blood assays for specific substances, and (2) indirect measures, including outcome measures, interview and staff assessment of compliance. Feinstein (1979) suggests that the interview technique, coupled with a more objective assessment, provides the greatest amount of reliable information (p. 312), but Glanz reports that, because of the many confounding factors such as variable absorption and utilization of nutrients, objective (direct) measures are probably poor indicators of dietary compliance. She points to several articles which indicate that interviews can be a valid method of obtaining information (p. 792). Given, Given and Simoni (1979) point out that "while inaccuracies exist in patient self-reports of compliance, it remains the most frequently used method available to clinicians for assessing patient compliance" (p. 90).

In the National Diet-Heart Study, three methods of compliance estimate were used: the 24 hour recall, the 7 day food record, and a subjective evaluation of compliance by the nutritionist (Majonnier & Hall, 1968). A similar approach was used in a study of the effects of a lipid-lowering diet on male survivors of myocardial infarction (Leren, 1966). Although the limitations of such methods are recognized, to-date there appears to be no completely reliable method for assessing dietary compliance; work in this area is just beginning (Sackett & Snow, 1979).

In several of the exercise trials cited earlier in this review, training was unsupervised and invariably involved walking, sometimes along with other exercises (Alpert et al., 1969; Larsen & Lassen, 1966; Sorlie & Myhre, 1978). Self-report measures of amount of exercise performed were used in these studies. Whereas it is recognized that there are limitations to such a technique (Snow, 1980), it appears that no more suitable method, beyond actual supervision of training, has been devised.

G. Summary

The etiology of atherosclerosis, and therefore atherosclerotic diseases such as PAD, is uncertain. However, a growing knowledge of the natural history of the atherosclerotic lesion has led to several hypotheses regarding its origin. Currently the prevailing belief is that the primary event in atherogenesis is endothelial damage. Injury to the endothelium may cause changes in its permeability characteristics, with the result that lipoprotein particles infiltrate the wall, initiating the sequence of smooth muscle cell proliferation and further lipoprotein infiltration. Another possibility is that endothelial damage may expose underlying collagen, causing platelet aggregation and the release of a substance that stimulates smooth muscle cell proliferation and endothelial permeability.

The critical question appears to be the cause of the damage to the arterial wall. Epidemiological studies have shown that an association exists between development of atherosclerosis and several so-called risk factors, which include hypercholesterolemia, smoking, lack of exercise and obesity. From the epidemiological evidence and observations of the large lipid components of the atherosclerotic lesion, researchers have investigated the possibility that a high level of cholesterol in the blood is the main causative factor in atherogenesis. It has been suggested that cholesterol either damages the arterial wall or, if the damage is caused by something else, rapidly infiltrates the site where damage occurs.

Recent understanding of lipid metabolism and transport has shown that more information may be gained from an examination of lipid fractions. Three of these fractions, LDL-cholesterol, HDL-cholesterol and TG, are thought to be of importance in atherogenesis, LDL-cholesterol and TG by contributing to plaque development and HDL-cholesterol by protecting against it. Thus, the relative values of each of these fractions are important; high levels of LDL-cholesterol and TG and low levels of HDL-cholesterol could be atherogenic.

The importance of lipids in atherogenesis is evident from both human and animal studies in which blood cholesterol has been lowered and regression of atheroma demonstrated. Various methods have been utilized to lower

blood cholesterol, but one of the most effective appears to be dietary manipulation. Strong epidemiological and empirical evidence has linked certain dietary components, in particular saturated fat, total fat, cholesterol, and dietary fiber, with atherogenesis. It has been shown that a reduction in each or all of these components can be effective in lowering cholesterol levels.

Other risk factors are also important. The association between smoking and atherosclerosis is strong. Individuals who smoke have been shown to be at high risk of developing PAD, although the mechanism for this effect is not clear. Lack of exercise, too, has been implicated as a risk factor, although the association is somewhat tenuous, particularly in the case of PAD. The effect of obesity on atherogenesis is also unclear, but obese persons have been shown to have high blood TG levels. It is evident, however, that individual risk of atherosclerosis increases as risk factors increase; the obese, sedentary smoker has a far greater probability of developing atherosclerosis than does his lean, active, non-smoking counterpart. In addition, the effects of exercise on PAD are positive; PAD patients who undergo physical training generally appear to have an increase in walking ability.

Incorporating these ideas, various therapeutic regimens aimed at halting the progression and possibly effecting a regression of atherosclerosis have been designed. Most have involved dietary manipulation to alter blood lipid levels.

These regimens have met with varying degress of success.

To assess the progress of the atherosclerotic process in the limbs, and to facilitate long-term diagnosis and follow-up of PAD, a number of non-invasive techniques have been developed. Measurement of ankle/brachial systolic pressure ratio and ankle pressure drop after exercise, and calculation of PI and TT from a flow-velocity waveform, have been made feasible with the Doppler flowmeter. Together with a monitoring of treadmill walking time to claudication, these tests have been shown to be useful in the assessment of PAD.

III. Hypotheses and Definitions

The current investigation was a pilot study designed to examine associations between dietary manipulation and selected vascular and lipid variables in patients with PAD. Each subject participating in the clinical trial was maintained on one of two lipid-lowering diets, either the American Heart Association (AHA) diet or a high fibre, low fat (HF) diet, for a period of 1 year. To help the patient to obtain maximum benefit from the conservative treatment program, a prescription to increase exercise and decrease smoking was included in both therapeutic regimens.

A pretest-posttest two-treatment groups design was used for the study (Campbell & Stanley, 1963). Subjects were randomly assigned to either the American Heart Association (AHA) diet group or the high fibre (HF) diet group.

A. Research Hypotheses

Hypotheses formulated for investigation could be grouped under five general statements:

1. In both diet groups, there will be within-group changes from baseline in mean values of blood lipids and vascular variables at each of four follow-up periods.
2. There will be between-group differences in mean values of blood lipids and vascular variables at each of four follow-up periods.
3. In both diet groups, blood lipids and vascular variables will be correlated at baseline and at each of four

follow-up periods.

4. In both diet groups, WT and WD will be correlated with other vascular variables at baseline and at each of four follow-up periods.
5. In both diet groups, vascular variables will be correlated with smoking, % ID WT and weekly exercise at baseline and at the final follow-up period.

Details of individual hypotheses are summarized in Figures 1 to 5. Included in each figure are specific examples of hypotheses.

B. Operational Definitions

1. **Vascular variables**: ABR, PI, TT, % PD, WT and WD
2. **Blood lipids**: TG, cholesterol, HDL-cholesterol and LDL-cholesterol.
3. **Baseline**: Values of vascular variables and blood lipids measured for each patient on entry into the study and prior to dietary intervention.
4. **Follow-up Periods**: Two, 4, 6 and 12 months after commencement of dietary intervention.
5. **ABR**: Ankle/brachial ratio – the ratio of ankle to brachial systolic blood pressure, obtained using the Doppler flowmeter and standard blood pressure cuffs on

FIGURE 1. VARIABLES HYPOTHESIZED TO SHOW WITHIN-GROUP CHANGES IN THE AHA AND HF DIET GROUPS AT THE FOUR FOLLOW-UP PERIODS

VARIABLE (MEAN)	EXAMPLE
Blood Lipids: TG, cholesterol, HDL-cholesterol, LDL-cholesterol	There will be a change from baseline in the mean blood value of TG in both the AHA and HF diet groups at each of the four follow-up periods
Vascular Variables: ABR, PI, TT, % PD, WT, WD	There will be a change from baseline in the mean of ABR in the AHA and HF diet groups at each of the four follow-up periods

FIGURE 2. VARIABLES HYPOTHESIZED TO SHOW BETWEEN-GROUP DIFFERENCES AT THE FOUR FOLLOW-UP PERIODS

VARIABLE (MEAN)	EXAMPLE
Blood Lipids: TG, cholesterol, HDL-cholesterol, LDL-cholesterol	There will be a difference between the two diet groups in the mean blood values of TG at each of the four follow-up periods
Vascular Variables: ABR, PI, TT, % PD, WT, WD	There will be a difference between the two diet groups in the mean values of ABR at each of the four follow-up periods

FIGURE 3. VARIABLES HYPOTHESIZED TO BE CORRELATED IN BOTH DIET GROUPS AT BASELINE AND AT EACH OF THE FOUR FOLLOW-UP PERIODS

VARIABLE (MEAN)	EXAMPLE
TG, cholesterol, HDL-cholesterol, LDL-cholesterol with ABR, PI, TT, % PD, WT, WD	In both diet groups, TG will be correlated with ABR at baseline and at each of the four follow-up periods
WT and WD with ABR, PI, TT, % PD	In both diet groups, WD will be correlated with ABR at baseline and at each of the four follow-up periods
ABR, PI, TT, % PD, WT, WD with % ID WT	In both diet groups, ABR will be correlated with % ID WT at baseline and at each of the four follow-up periods

FIGURE 4. VARIABLES HYPOTHESIZED TO BE CORRELATED IN BOTH DIET GROUPS AT BASELINE AND AT 12 MONTHS

VARIABLE	EXAMPLE
ABR, PI, TT, % PD, WT, WD with current smoking habits	In both diet groups, ABR will be correlated with current smoking habits at baseline and at 12 months
ABR, PI, TT, % PD, WT, WD with weekly exercise	In both diet groups, ABR will be correlated with weekly exercise at baseline and at 12 months
ABR, PI, TT, % PD, WT, WD with smoking history	In both diet groups, ABR will be correlated with smoking history at baseline

on ankle and arm.

6. **PI**: Pulsatility index – a unitless number obtained using computer analysis of the Doppler waveform from the posterior tibial or dorsalis pedis pulse of the claudicating limb.
7. **TT**: Transit time – the time in milliseconds from the R wave of the ECG to the foot of the Doppler waveform from the posterior or dorsalis pedis pulse of the claudicating limb.
8. **% PD**: Per cent pressure drop – the drop in systolic blood pressure at the ankle of the claudicating limb after treadmill exercise, obtained using the Doppler flowmeter and a standard blood pressure cuff.
9. **WD**: Walking distance – the distance in meters which the patient could walk on a treadmill before complaining of severe claudication.
10. **Triglyceride**: The amount of triglyceride in milligrams per deciliter (mg/dl) in venous blood after the patient had fasted for at least 8 hours.
11. **Cholesterol**: The amount of total cholesterol in milligrams per deciliter in venous blood after the patient had fasted for at least 8 hours.
12. **LDL-cholesterol**: The amount of total cholesterol in milligrams per deciliter carried in the low density lipoprotein fraction in the venous blood after the patient had fasted for at least 8 hours.
13. **HDL-cholesterol**: The amount of total cholesterol in

milligrams per deciliter carried in the high density lipoprotein fraction in venous blood after the patient had fasted for at least 8 hours.

14. **% ID WT**: The subject's weight expressed as a per centage of the ideal weight as calculated from standard tables based on height and wrist circumference (Lindner & Lindner, 1973).
15. **Smoking History**: The patient's smoking history calculated as years (number of 25-cigarette packs smoked per day times the number of years smoking) as determined by personal interview.
16. **Current Smoking Habits**: The number of cigarettes smoked daily by the subject, as determined by personal interview.
17. **Exercise Habits**: The amount of exercise in the form of walking or cycling performed weekly by the subject, recorded by frequency and time, as determined by personal interview.

IV. Methodology

A. Setting and Design

The present study was part of a 3 year multidisciplinary pilot project involving the Faculties of Medicine, Surgery, Physiology and Home Economics at the University of Alberta, and funded by the Medical Services Research Foundation of Alberta. This study focuses on the vascular status of the subjects throughout the study period; details of the dietary aspects are reported elsewhere by -- Whyte (1982).

The project was carried out in two separate sites. All diet teaching and follow-up and the collection of blood samples took place at the Metabolic Center, University of Alberta Hospital. The Peripheral Vascular Laboratory, Clinical Sciences Building, University of Alberta, was the site for vascular assessment and follow-up. Teaching and data collection were conducted on an outpatient basis; at no time during the study were subjects retained as inpatients.

A pretest-posttest two-treatment groups design was used for the study. As was mentioned previously, the two treatment groups consisted of subjects randomly assigned to either the AHA or HF diet. Equal prescriptions for alteration of lifestyle factors, notably smoking and exercise, were included for both groups to help maximize benefits to the patient. Subjects were patients with PAD, and included all willing participants who met various

stringent criteria, as described below. Although random selection of patients was impossible, random assignment of subjects to the treatment groups was used to control some threats to internal validity, including those of maturation, statistical regression and selection, as described by Campbell and Stanley (1963, pp. 8-16). In addition, any differences between groups in baseline data were controlled through the use of analysis of covariance for certain statistical analyses. Attempts were made to give all individuals in both groups equivalent teaching, attention and feedback, thus ensuring that each person had equal opportunity to benefit from the program.

B. Sample

The search for and selection of possible study candidates extended from September 1978 to December 1979. Most subjects were identified through a search of patient files of four major Edmonton hospitals. Initially it had been hoped that physician referrals would be the main source of candidates. Vascular specialists at the University and General Hospitals, together with a number of general practitioners, were contacted and agreed to cooperate. However, only two suitable candidates were referred over several months, and permission was sought from the various hospitals to conduct a chart search.

All charts for the previous 5 years in which a diagnosis of PAD appeared on the discharge summary either as

the primary diagnosis or as one of multiple diagnoses were examined. Approximately 1200 files were reviewed, and from these close to 300 possible candidates identified. Patients considered suitable for the study met the following criteria:

1. **PAD of greater than 1 year's duration prior to entry into the study**: A year's time period was chosen as collateral development has probably stabilized at about 1 year after the appearance of symptoms (Strandness, 1969); observed improvements after this time are therefore less likely to be due to collateral development. The diagnosis of PAD was to have been confirmed by a vascular specialist, preferably with the use of arteriography. Only two patients in the study had never had an arteriogram, and their symptoms were clearly consistent with PAD.
2. **Between the ages of 45 to 75 years of age at the time of entry into the study**: Since vascular disease is known to be positively associated with age, an age limit was established to reduce the age spread and to eliminate those patients in the extremes of the distribution whose disease is more likely to be influenced by alternate pathology (Brown & Goldstein, 1981).
3. **Absent or stable CAD**: Stable CAD was defined as the bsence of anginal pain or cardiac arrhythmias on exertion. This requirement was primarily for patient safety during exercise testing.

4. **No requirement for insulin**: As insulin-dependent patients require strict dietary control, this criterion was introduced to eliminate possible conflicts between the requirements of the study and the diabetic diet. In addition, as arterial disease in insulin-dependent diabetes is possibly of a somewhat different pathology than that in other PAD patients (Juergens & Bernatz, 1980), inclusion of these patients could have introduced a confounding variable.
5. **Absence of other diet-related or diet-controlled diseases**: Again, this criterion was introduced to eliminate possible conflicts between the study diet and any therapeutic diet. In addition, it was felt that the requirements of the study diets, in particular the HF diet, might exacerbate symptoms in patients with certain gastrointestinal problems. Therefore, patients with such diseases as active peptic ulcers, Crohn's disease, ulcerative colitis and sprue were not considered suitable candidates.
6. **No arterial reconstructive surgery within 1 year prior to entry into the study**: In light of the frequent recurrence of symptoms following vascular surgery, post-surgical patients were considered if they were experiencing claudication. One year was selected as sufficient time for the effects of surgery to be minimized and new disease to have stabilized (Strandness, 1969).

After the 300 possible candidates had been identified, personal physicians, including both the admitting doctor and the family physician, were contacted for permission to approach the patient(s). In only one case was permission refused. Each patient was then contacted by telephone and questioned regarding his present symptoms. If he was found to have a current history consistent with IC, the study was explained and the subject invited to participate. Those requesting further information were asked to attend a small group session at the Metabolic Center, University of Alberta Hospital, where the study was explained in greater detail. All patients were informed that two therapeutic regimens were being compared, and that they would be randomly assigned to one of the two.

In total, 53 patients, including the two referred by physicians, agreed to participate. Reasons for refusal included unwillingness to maintain the therapeutic regimen for the required time, unavailability for teaching or follow-up, lack of transportation, residence too far from project center, personal problems, and complicating medical reasons.

After the patient expressed a willingness to participate, he was interviewed by the dietitian to determine any social and/or lifestyle factors that might prevent his maintaining the therapeutic regimen for the study period. Two individuals who were found to have a lifestyle which included considerable travel and which would

make it impossible for them to follow a strict diet, were eliminated as possible candidates.

Each remaining patient was then given a complete physical examination by one of the two project physicians to substantiate the diagnosis of PAD and to screen for any complicating factors that might prevent his participation in the study. Of two patients with questionable unstable heart disease who were referred to a cardiologist to ensure that exercise testing was not contraindicated, one patient was judged unfit to participate.

The 50 patients considered to be suitable subjects were then asked to sign consent forms(Appendix A).

After physician's approval was obtained, each patient was subjected to two non-invasive vascular assessments (see below) to confirm the presence of IC and to establish a baseline. Only patients who had an ankle/brachial systolic pressure ratio of .90 or less at rest or following exercise, and who developed IC in less than 30 minutes on the treadmill, were considered to have disease that was sufficiently severe to be followed by non-invasive means. By these criteria, five patients were found to be unsuitable candidates for vascular follow-up and were excluded from the study, leaving a total of 45 participants (33 males and 12 females).

As individuals entered the study, they were assigned from a random numbers table to either the AHA diet group ($\underline{n}$ = 20) or the HF diet group ($\underline{n}$ = 25).

C. Procedure

Diet Teaching and Follow-Up

Precise details of the dietary management of study subjects is reported elsewhere (Whyte, 1982). In brief, patients underwent the following schedule:

1. Attendance at a 4 day teaching session which included diet lectures, food preparation, daily meal planning, and two consultations with a physician. It was requested that a spouse or other person who might be involved in meal preparation accompany the patient.
2. Monthly visits with the dietitian for diet counselling and feedback, including a 48 hour recall in which the patient was asked to list all foods and beverages consumed in the preceding 48 hours. This was used to monitor the patient's actual intake and to measure compliance with the dietary regimen.
3. Patient completion of a 3 day food record to be submitted to the dietitian 2 weeks before the next counselling session. This was used to reveal problems in meal planning and as a measurement of compliance.

Instruction was given in small groups of two to five patients and their accompanying relatives or friends. Patients in the two diet groups were kept strictly separate through initial teaching and subsequent follow-up. Although each person was aware of the diet he was on, he was unaware of the nature of the comparison diet.

The energy distribution in the normal North American diet is approximately 40% carbohydrate (CHO), 15 to 20% protein (PRO) and 40 to 45% fat (Pritikin & McGrady, 1979). Thus, both study diets differed from the norm. The two dietary regimens were as follows:

1. **American Heart Association (AHA) Diet**: a moderate fiber, moderate fat diet (Subcommittee on Diet, 1973). The energy distribution was 50 to 55% carbohydrate (CHO), 15 to 20% protein (PRO) and 25 to 30% fat, with a polyunsaturated/saturated (P/S) fat ratio of 1:7. Dietary fiber intake was 25 to 30 g/1000 Kcal.
2. **High Fiber (HF) Diet**: a modified Pritikin diet, high in fiber, low in fat, and high in complex CHO (Longevity Research Institute, 1978). The energy distribution was 70 to 75% CHO, 15 to 20% PRO and 5 to 10% fat. P/S ratio was not calculated. Dietary fiber intake was 40 to 45 g/1000 Kcal.

Both diets were designed to be nutritionally adequate and to meet the Canadian Dietary Standard recommendation for adults 45 to 75 years of age. Diets were individually designed for each patient following interview with the dietitian. Where necessary, calorie restrictions were imposed to assist the patient to reach or maintain ideal weight. Each patient was requested to weigh and measure all food portions to ensure that the energy distribution and nutrient composition were as delineated. At each follow-up visit, the patient's weight was taken and calculated as

per cent ideal weight (% ID WT) to provide feedback for the patient and to act as a compliance measure. As reported by Whyte (1982) and as discussed later in this report, it was felt that the compliance measures used were reasonably accurate. By these measures, compliance in both groups was judged to be excellent, thus permitting the examination of the effects of the conservative treatment programs.

Lifestyle Changes

In addition to the dietary regimen, all patients were instructed to restrict cigarettes (and/or any other form of tobacco consumption) as much as possible and to walk or cycle at least 45 minutes per day. The daily exercise period(s) could be divided according to the patient's ability and/or convenience, but exercise was to continue for a minimum of 15 minutes each time, with the patient instructed to persist until IC became severe, then to rest and resume exercise, if possible, when the IC had abated.

Baseline and follow-up values of exercise and smoking variables were collected through personal interview using a questionnaire (see Appendix B) which was completed separately by the dietitian and research nurse at the first visit and at each follow-up visit. Information was collected about the type and duration of exercise and the amount smoked. Smoking habits were categorized by average number of cigarettes smoked per day as 0, less than 20, or greater than or equal to 20, and overall smoking history was

recorded in pack years. Amount of exercise was similarly categorized by frequency (0 to 2, 3 to 4, 5 to 7, >7 times per week) and time (0 to 15, 16 to 30, 31 to 45 and >45 minutes per time). A final comparison by the dietitian and the nurse of the results thus obtained was used to assess the accuracy of the patient's self-report. When there was a discrepancy between the two reports regarding the amount of weekly exercise, the information obtained by the nurse was used. It was felt that, as the nurse was involved with exercise testing, the patient would be more likely to present an accurate report to her. Discrepancies were, in fact, infrequent, occurring in only two cases. Following a similar rationale, the information collected by the dietitian regarding smoking habits was used if the reports did not coincide. Here again, discrepancies were infrequent.

At the time of each follow-up visit, the patient was asked for a personal evaluation of his feelings and progress. In particular, he was questioned about his ability to exercise and his general feeling of well-being. This information was recorded on the lifestyle questionnaire and used to provide a subjective evaluation of the patient's response to the therapeutic regimen.

Biochemical Assessment

Fasting blood samples were drawn by venipuncture from each subject on entry into the study (month 0) and at months 1, 2, 4, 6 and 12. The 1 month value was collected

primarily to provide the patient with feedback and was not used in the statistical analysis. Due to cost considerations, no samples were collected at 8 and 10 months. All samples were drawn by the same technician and were analyzed by the Department of Laboratory Medicine at the University of Alberta Hospital using standardized techniques. Normal blood lipid values were considered to be the normals accepted by that laboratory. Serum cholesterol, TG and HDL-cholesterol were directly measured. Due to the difficulty and expense of direct analysis, LDL-cholesterol was estimated from the following formula:

LDL-cholesterol = Total cholesterol - HDL-cholesterol - 1/5 TG

This formula has been used by others and is recommended as an accurate estimate of actual LDL-cholesterol levels (Kannel et al., 1979; Stone, 1977).

Vascular Assessment

Assessment of vascular status was made without the investigator's knowledge of the patient's diet group. The patient was cautioned to avoid mentioning diet and any diet-related problems to the investigator, thus ensuring that the investigator remained "blind".

All testing was done in the Vascular Laboratory, Clinical Sciences Building, University of Alberta, by the

research nurse (this investigator) and an assistant. Baseline values were established through the average of two complete assessments taken at least 1 day apart prior to the patient's commencing the diet (Williams, Fenna & Macbeth, 1971). Follow-up continued every 2 months for 1 year. The results of the 8 and 10 month tests were used to provide the patient with feedback, but were not used in the statistical analysis, as no blood work was collected during this interval. Parameters included in the assessment were: resting ankle/brachial systolic pressure ratio (ABR), PI and TT from the ankle pulse, treadmill WD, and ankle systolic pressure drop (% PD) after exercise.

Pressure measures and PI and TT were obtained using a Parks 806 continuous-wave 10 MHz Doppler flowmeter. This instrument utilizes the familiar Doppler effect, in which the frequency of sound is changed when the sound waves are reflected off a moving surface. The shift in frequency is proportional to the velocity of the object. The Doppler device emits sound waves at a known ultrasonic frequency (10 MHz); the sound is beamed through the skin to an artery and reflected back at a slightly different frequency to a receiving crystal. The incoming frequency is compared with the outgoing frequency, the difference producing an audible signal. Since the frequency of the sound through tissue is constant, the shift in frequency must be accomplished by a reflection off the moving blood cells. If there is no flow, there will be no frequency shift and no audible sound

(Lieberman, 1980).

For testing, each patient was asked to arrive at least 15 minutes early for his appointment and to sit quietly during that time. He was then taken into the Vascular Laboratory and instructed to remove all clothing except light underwear, don a hospital gown, and lie on the examination table. The patient remained on the table for a second rest period of about 15 minutes. Thus, a total rest period of about 30 minutes was attained, during which time blood flow and pressure could return, if necessary, to resting values.

A standard blood pressure cuff (10 x 4.5 cm, bladder) attached to a mercury manometer was placed around the patient's upper arm and the ankle of the limiting leg, that is, the leg in which claudication was experienced. If both legs claudicated, the limb with the lowest ABR and highest % PD was used for analysis. Doppler probes were positioned over the radial and posterior tibial pulse, or the dorsalis pedis if the posterior tibial was unobtainable. Whichever ankle pulse was selected was used for all subsequent testing. A water soluble gel was placed on the end of the probe to improve the transmission of sound and to "connect" the probe to the skin. The pressures cuffs were then simultaneously inflated by an automated device to a point above systolic pressure, then gradually deflated. The point at which the arterial pressure exceeded the cuff pressure (the systolic pressure) was indicated by the return of the

Doppler sound at each pulse site, and read from the manometer. The ABR was calculated from the two simultaneous readings.

To determine PI and TT, the Doppler-shifted sound from the posterior tibial (or dorsalis pedis) artery of the limiting leg was recorded on an FM tape recorder together with the recording of an ECG (Lead II). The recordings were later analyzed on a PDP 11-03 minicomputer using two separate programs. The first program took samples of the sound which were digitized and stored for analysis by the second program. Sampling was triggered by the R wave of the ECG and continued at 100 microsecond intervals until the succeeding R wave was encountered. One hundred sets of 256 samples each were stored. The starting sample of each set was equally spaced so there was some overlap between sets except at very slow pulse rates. The second program analyzed the sampled sound using multiple fast Fourier transforms, which divide the sound into its component frequencies. The frequency spectrum of the 100 sample sets, each set representing a point in time in the R-R interval, was displayed as a vertical series of dots along the X axis, with frequency on the Y axis. For each spectrum, the upper frequency that was significantly above background noise was stored and used to define the peak velocity waveform. The TT was taken as the time in milliseconds from the R wave to the foot of the waveform. The PI was calculated as the ratio of the peak-to-peak amplitude of the waveform divided by the

mean flow. Mean flow was calculated by integration of the waveform. Hard copy, consisting of a plot of the waveform and a printout of calculated PI and TT, was obtained for each examination.

Determination of treadmill WT, WD and % PD was the last part of the examination. The protocol was a modification of that used by Pritiken and associates (Pritikin et al., 1975). Walking speed was set at 2.4 Kph for the first 10 minutes, 3.6 Kph for the next 10 minutes, and 4.8 Kph for the final 10 minutes, with maximum time set at 30 minutes. A 2% treadmill elevation was maintained throughout the test. Walking time (WT) was monitored by stopwatch and WD calculated from WT by the following formulae:

If time > 0 but ≤ 10 minutes, distance in meters =
40.23 x time in minutes

If time > 10 minutes but ≤ 20 minutes, distance in meters =
402.34 + (time in minutes - 10) x 60.35.

If time > 20 minutes but ≤ 30 minutes, distance in meters =
1005.8 + (time in minutes - 20) x 80.47.

Due to an excessive amount of data and the non-linear nature of WT, this variable was later eliminated from statistical analysis, and only WD used. Prior to testing, the ankle pressure cuff was taped in place to facilitate rapid pressure measurement post-exercise. The ECG leads were left on the patient's chest and connected via a preamplifier

to a dynagraph. As many of the patients were elderly and had coexisting (stable) CAD, a recording of the ECG was continued throughout the exercise, and the patient instructed to stop if submaximal heart rate ((220 - age) x .8) (Cutler, Wheeler, Paraskos & Cardullo, 1979) was reached, or if he felt weak or dizzy; otherwise he was to continue walking until severe IC developed. In two instances, the patient was asked to stop because of heart rate, and in one instance because of chest pain. Several patients became somewhat dizzy, but only in two cases were they forced to stop before claudication became very severe. As soon as the patient reported IC, the time was noted and the patient returned to the examination table as quickly as possible. The cuff pressure was monitored using a transducer connected to a pen recorder, providing simultaneous tracings of the pressure and the Doppler signal. The first ankle systolic pressure obtained after exercise was documented and % PD calculated as the pre- to post-exercise pressure difference divided by the pre-exercise pressure.

Data Analysis

All data were computer-coded and processed on the University of Alberta computer system using SPSS programs (Nie, Hull, Jenkins, Steinbrenner & Bent, 1975).

Frequencies, means and standard deviations were calculated for all continuous variables by group. For all inferential statistics, a significance level of .05 was

chosen.

To determine if there were any significant within-group changes from baseline in vascular and lipid variables, correlated one-sample (paired) t-tests were calculated at 2, 4, 6 and 12 months.

Independent two-sample (unpaired) t-tests, using the separate variance estimate, were used to compare between-group means of all baseline lipid and vascular variables. Analysis of variance (ANOVA) was used to compare between-group differences in mean values of vascular and lipid variables except when differences between means on entry were significant or were deemed clinically important. It should be noted that when only two groups are being compared, the F statistic is equal to t^2 and ANOVA will give the same results as the unpaired t-test. In this instance, ANOVA was chosen for convenience in data handling. When between-group differences on entry were noted, analysis of covariance, with the value on entry as the covariate, was used. In this way, the two groups were effectively equalized for any differences that might have existed on entry, providing a more exact comparison (Glass & Stanley, 1970).

The associations between vascular and lipid variables were examined using Pearson's product-moment correlation coefficient. However, smoking and exercise data were ordinal and discrete, and the expected cell frequencies were too small to allow further statistical analysis. Thus, associations between these variables and the vascular and

lipid variables could not be examined statistically.

For the above analyses, all patients who remained in the study at each time period were included in the calculations, thus preserving the maximum amount of data. In addition, the rationale was that elimination of those patients who did not complete the entire study would result in a bias toward those patients with "perseverence". Thus, because of patient withdrawals, the constituents of each group varied slightly at each time interval.

Summary

In a one-year study to examine the effects of dietary manipulation on vascular status and blood lipids, 45 patients with confirmed PAD were randomly assigned to either the AHA (n = 20) or HF (n = 25) diet groups. Both groups were given extensive dietary instruction, and were encouraged to increase their weekly exercise and decrease smoking. Monthly 3-day diet records and 48-hour diet recalls were used to provide patient feedback, increase compliance and monitor diet intake. Vascular status and blood lipids were monitored at entry and at 2, 4, 6 and 12 months.

Within-group changes in vascular and lipid variables were examined using paired t-tests. Between-group differences in means were assessed at baseline using unpaired t-tests, and comparisons between groups were made at 2, 4, 6 and 12 months using analysis of variance. Where differences between entry means were significant or

clinically important, analysis of covariance was used for between-group comparisons. Associations between vascular and lipid variables, between WD and other vascular variables, and between vascular variables and smoking, weekly exercise and % ID WT were determined using Pearson's product-moment correlation coefficient.

V. Results

A. Sample Characteristics

Of the 45 patients who agreed to participate in the study, 20 (13 males and 7 females) were randomly assigned to the AHA diet group and 25 (20 males and 5 females) to the HF diet group. Mean age of the AHA diet group was 60.1 years and of the HF diet group 62.4 years.

Thirty-seven candidates completed the study (AHA = 15, HF = 22), an attrition rate of 25% in the AHA diet group and 12% in the HF diet group (Table 1). Reasons for withdrawal from the study varied (Table 2), but there was no indication that any of the withdrawals were as a result of the diet programs.

B. Dietary Intake

Dietary intake was monitored through computer analysis of the diet components recorded in the 48 hour recall completed at the monthly interview with the dietitian. The 3 day food record was used only to assist the patient in meal planning and to verify compliance.

Tables 3 and 4 show the mean dietary intakes of CHO, protein, fat, cholesterol and fibre throughout the study period. From Table 3, it can be seen that intakes of the AHA diet group came very close to target values by the second month of the study and remained there throughout the study period. Similarly, in the HF diet group, all values except

TABLE 1. SAMPLE CHARACTERISTICS - NUMBER OF PARTICIPANTS AND SEX DISTRIBUTION IN THE TWO DIET GROUPS AT EACH TIME INTERVAL

Time Interval	Diet Group					
	AHA			HF		
	Total n	Males	Females	Total n	Males	Females
Baseline	20	13	7	25	20	5
Month 2	20	13	7	25	20	5
Month 4	18	12	6	25	20	5
Month 6	17	11	6	23	18	5
Month 12	15	10	5	22	18	4

TABLE 2. REASONS FOR SUBJECT WITHDRAWALS AND NUMBERS OF MALE AND FEMALE SUBJECTS WITHDRAWING FROM EACH DIET GROUP

Diet Group	Reasons for Withdrawal	n	
		M	F
AHA	Vascular surgery	2	1
	Deceased	0	1
	Relocated	1	0
HF	Abdominal surgery	0	1
	Stroke	1	0
	Insulin required	1	0

TABLE 3. MEAN PATIENT INTAKE OF SELECTED DIETARY COMPONENTS AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS COMPARED WITH DESIRED (TARGET) VALUES - AHA DIET GROUP

Dietary Component	Month					
	Base-line	2	4	6	12	Target Value
CHO (% total Kcal)	44	52	50	51	49	50-55%
Protein (% total Kcal)	16	20	20	20	19	15-20%
Fat (% total Kcal)	39	28*	30*	29*	32	25-30%
Cholesterol (mg/day)	286	199*	200*	167*	282	< 300 mg/day
Fiber (g/1000 Kcal)	18	21	24	24	24	25-30 g

* Significantly different from entry value (t-test, $p<.05$)

TABLE 4. MEAN PATIENT INTAKE OF SELECTED DIETARY COMPONENTS AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS COMPARED WITH DESIRED (TARGET) VALUES - HF DIET GROUP

Dietary Component	Month					
	Base-line	2	4	6	12	Target Value
CHO (% total Kcal)	43	66*	68*	66*	63*	70-75%
Protein (% total Kcal)	16	21	20	20	21	15-20%
Fat (% total Kcal)	41	13*	12*	14*	16*	10-15%
Cholesterol (mg/day)	309	98*	95*	102*	134*	< 100 mg/day
Fiber (g/1000 Kcal)	18	42*	46*	45*	39*	40-45 g

* Significantly different from entry value (t-test, $p<.05$)

dietary CHO were close to target by the second month and at 4, 6, and 12 months (Table 4). For this group, intakes of CHO, fat, cholesterol and fibre were significantly different from entry at each follow-up period (Table 4), whereas in the AHA diet group intakes of fat and cholesterol were significantly different from entry at 2, 4 and 6 months, but not at 12 months. (Table 3). Thus, subjects in the AHA diet group appeared to be gradually increasing their intakes of fat and cholesterol, although the mean values of these components remained close to or within target ranges at 12 months. There were no significant differences between the two groups of subjects in diet intake at baseline (Table 5). However, as expected, during the 12 months of dietary intervention, the intakes of the two groups differed in several components, as shown in Table 6. Significant between-group differences in dietary intake of fat, fiber and cholesterol were noted at each follow-up period. Mean intakes of CHO differed significantly at 2, 4 and 6 months, but not at 12 months. From these results, it appears that dietary intakes in both groups were very close to target at 2, 4 and 6 months, but that by 12 months both groups were exhibiting a slight drift back toward previous diet habits. Nonetheless, both groups remained close to target values throughout the study, up to and including the 12 month follow-up.

TABLE 5. COMPARISON OF MEAN INTAKES OF SELECTED DIETARY COMPONENTS IN THE AHA AND HF DIET GROUPS AT BASELINE

Dietary Component	AHA (Mean±SD)[1]	HF (Mean±SD)
CHO (g)	192±72	207±50
Protein (g)	71±23	79±25
Fat (g)	75±48	88±33
Cholesterol (g)	286±195	309±163
Fiber (g)	18±13	18±9

[1] To obtain the 95% confidence interval of the sampling distribution of mean values use mean ± $2SD/\sqrt{n}$, where n = sample size

TABLE 6. T-TEST COMPARISON OF MEAN INTAKES OF SELECTED DIETARY COMPONENTS IN THE AHA AND HF DIET GROUPS AT EACH FOLLOW-UP PERIOD (2, 4, 6 AND 12 MONTHS)

	Month							
	2		4		6		12	
Dietary Component	AHA (Mean±SD)	HF (Mean±SD)	AHA (Mean±SD)	HF (Mean±SD)	AHA (Mean±SD)	HF (Mean±SD)	AHA (Mean±SD)	HF (Mean±SD)
CHO (g)	174±46	248±66*	176±60	278±102*	186±78	268±93*	210±66	250±51
Protein (g)	70±18	80±20	73±25	83±18	74±26	83±23	80±33	86±19
Fat (g)	46±14	21±11*	47±19	24±12*	48±29	25±11*	61±36	28±12*
Cholesterol (g)	199±87	98±52*	200±124	95±36*	167±98	102±67*	272±248	134±66*
Fiber (g)	21±8	25±15*	24±12	46±15*	24±13	45±16*	24±10	39±12*

* Significant difference between groups ($p<.05$)

C. Lipids

Lipid values are summarized in Tables 7-13 and Figure 5.

Triglycerides

From Tables 7 and 8, it can be seen that on entry into the study, 6 patients (31%) in the AHA diet group and 10 (40%) in the HF diet group had triglyceride values above the upper limit of normal; by 12 months, this had dropped to four (27%) in the AHA diet group and six (23%) the HF diet group. At the final visit, 4 patients (64%) in the AHA diet group had triglyceride values that were higher than baseline, while 11 (71%) had lowered values. In the HF diet group, eight patients (36%) had increased TG values by 12 months, and 14 (64%) had decreased values. The mean value of triglyceride, as shown in Tables 9 and 10 and Figure 5, had dropped 7% in the AHA diet group and 16% in the HF diet group after 12 months.

Paired t-tests comparing within-group means at each time period with means on entry are shown in Tables 11 and 12. Note that the entry mean for comparison changed at each time interval because of patient withdrawals. In the AHA diet group, mean TG values were significantly lower than baseline at 4 and 6 months but were no longer significantly lower at 12 months. Mean TG values in the HF diet group were significantly lower than baseline at 2 and 4 months but not at 6 and 12 months, suggesting a trend back to baseline, perhaps associated with reduced dietary

TABLE 7. RANGES IN BLOOD LIPID VALUES AND PER CENT OF PATIENTS EXCEEDING NORMAL RANGE AT BASELINE AND AT 12 MONTHS - AHA DIET GROUP

Blood Lipid	Normal Values (mg/dl)	Observed Range		% of Patients Exceeding Normal	
		Baseline	12 Months	Baseline	12 Months
TG	80-177	91-<340	78-800	31	27
Cholesterol	116-271	132-473	170-375	20	20
HDL-chol	35-89	32-59	37-69	0	0
LDL-chol	77-193	57-1559	92-216	5	13

TABLE 8. RANGES IN BLOOD LIPID VALUES AND PER CENT OF PATIENTS EXCEEDING NORMAL RANGE AT BASELINE AND AT 12 MONTHS - HF DIET GROUP

Blood Lipid	Normal Values (mg/dl)	Observed Range		% of Patients Exceeding Normal	
		Baseline	12 Months	Baseline	12 Months
TG	80-177	83-302	53-321	40	23
Cholesterol	116-271	150-296	142-300	28	9
HDL-chol	35-89	30-70	30-67	0	0
LDL-chol	77-193	86-219	79-192	12	0

TABLE 9. MEAN[1] BLOOD LIPID VALUES AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - AHA DIET GROUP

Blood Lipid	Month				
	Baseline	2	4	6	12
TG	173±65	161±57	149±56	133±51	161±81
Cholesterol	245±72	216±56	225±57	206±50	218±47
HDL-chol	57±5	49±9	50±12	49±11	52±9
LDL-chol	143±53	120±50	145±52	130±42	133±36
n	20	20	18	17	17

[1] Mean in mg/dl ± standard deviation. To obtain the 95% confidence interval of the sampling distribution of mean values use Mean ± SD/$\sqrt{n}$, where n = sample size

TABLE 10. MEAN[1] BLOOD LIPID VALUES AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - HF DIET GROUP

Blood Lipid	Month				
	Baseline	2	4	6	12
TG	182±60	146±36	152±51	162±70	157±65
Cholesterol	242±35	204±26	207±31	221±39	224±39
HDL-chol	48±11	47±10	47±11	50±12	50±11
LDL-chol	158±31	129±23	131±25	138±33	145±33
n	25	25	25	23	22

[1] Mean in mg/dl ± standard deviation. To obtain the 95% confidence interval of the sampling distribution of mean values use Mean ± SD/$\sqrt{n}$, where n = sample size

TABLE 11. T-TESTS COMPARING WITHIN-GROUP MEANS OF BLOOD LIPIDS AT EACH FOLLOW-UP PERIOD (2, 4, 6 AND 12 MONTHS) WITH BASELINE MEANS - AHA DIET GROUP

Blood Lipid	Month	Means (± SD)[1]		n	Two-tail Probability
		Baseline	Follow-Up		
TG	2	173±65	161±64	20	.31
	4	172±67	149±56	18	.01*
	6	169±70	133±51	17	.01*
	12	174±70	161±81	15	.54
Cholesterol	2	245±72	216±56	20	.01*
	4	235±50	225±57	18	.31
	6	227±43	206±50	17	.054
	12	228±43	218±47	15	.31
HDL-chol	2	47±7	49±9	20	.42
	4	48±6	50±12	18	.36
	6	48±6	49±11	17	.84
	12	47±7	52±9	15	.08
LDL-chol	2	143±53	123±50	20	.00*
	4	153±44	145±53	18	.45
	6	145±36	130±42	17	.09
	12	146±37	133±36	15	.17

[1] in mg/dl
* $p<.05$

TABLE 12. T-TESTS COMPARING WITHIN-GROUP MEANS OF BLOOD LIPIDS AT EACH FOLLOW-UP PERIOD (2, 4, 6 AND 12 MONTHS) WITH BASELINE MEANS - HF DIET GROUP

Blood Lipid	Month	Means (± SD)[1]		n	Two-tailed Probability Level
		Baseline	Follow-Up		
TG	2	182±60	146±36	25	.00*
	4	179±60	152±51	24	.02*
	6	182±59	162±70	23	.24
	12	188±61	157±65	22	.07
Cholesterol	2	242±35	204±26	25	.00*
	4	242±35	207±31	25	.00*
	6	245±36	221±39	23	.00*
	12	243±37	224±34	22	.01*
HDL-chol	2	48±11	47±10	25	.31
	4	48±11	47±11	25	.34
	6	49±11	50±12	23	.64
	12	47±10	50±11	22	.06
LDL-chol	2	158±31	129±23	25	.00*
	4	158±31	131±25	25	.00*
	6	160±30	138±33	23	.00*
	12	158±32	145±33	22	.02*

[1] in mg/dl
* $p<.05$

TABLE 13. ANALYSIS OF VARIANCE COMPARING BETWEEN-GROUP MEANS OF BLOOD LIPIDS IN THE AHA DIET GROUP WITH MEANS OF BLOOD LIPIDS IN THE HF DIET GROUP AT 2, 4, 6 AND 12 MONTHS

Blood Lipid	Month	Means (±SD)[1]		Two-tailed Probability Level
		AHA	HF	
TG	2	161±57	146±36	.19
	4	149±56	152±51	.75
	6	133±51	162±70	.11
	12	161±81	157±65	.86
Cholesterol	2	216±56	204±26	.35
	4	225±57	207±31	.21
	6	206±50	221±39	.34
	12	218±47	224±34	.69
HDL-chol	2	49±9	47±10	.84
	4	50±12	47±11	.52
	6	49±11	50±12	.97
	12	52±9	50±11	.47
LDL-chol	2	123±50	129±23	.74
	4	145±53	131±25	.22
	6	130±42	138±33	.57
	12	133±36	145±33	.34

[1] in mg/dl

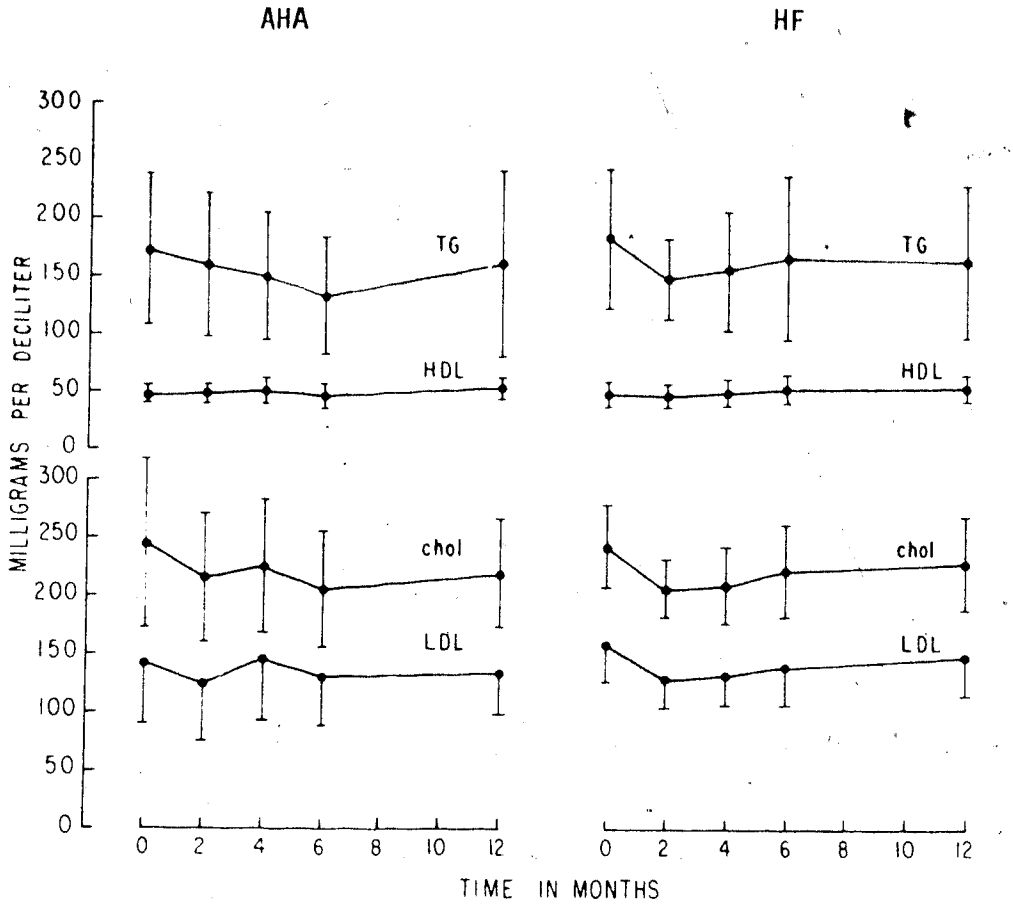

Figure 5. Means (± SD) of lipid parameters in the AHA and HF diet groups at baseline and at 2, 4, 6 and 12 months.

compliance.

There was no significant difference between the means of blood triglycerides of the two diet groups on entry (t-test). In the AHA diet group, the mean at baseline and 2 months was markedly distorted by the TG of one patient who was excluded from the study at 3 months due to vascular surgery. The inclusion or exclusion of this patient's values made no difference in the probabilities obtained by statistical analysis, and Tables 7, 9 and 11, and Figure 5 exclude this patient's values. Analysis of variance revealed no significant differences between the means of the two diet groups at 2, 4, 6 or 12 months (Table 13).

Cholesterol

Baseline values of blood cholesterol showed four AHA patients (20%) and seven HF patients (28%) to have cholesterol levels above the accepted normal limit. At the conclusion of the study, three AHA (20%) and four HF (9%) patients were above normal (Tables 7 and 8). Cholesterol values at 12 months had increased in five AHA (33%) and five HF (23%) patients, and had decreased in 10 AHA (67%) and 17 HF patients (77%), resulting in a drop in the mean of 4% in the AHA diet group and 8% in the HF diet group. Mean cholesterol values are presented in Figure 5 and in Tables 9 and 10, which show initial drops in both groups followed by a gradual return to baseline. These changes were statistically significant at 2 months in the AHA diet group

and at 2, 4, 6 and 12 months in the HF diet group (Tables 11 and 12).

There was no significant difference between the mean cholesterol levels of the two diet groups on entry into the study (t-test). Analysis of covariance revealed no significant differences between the means of the two diet groups at 2, 4, 6 or 12 months (Table 13).

HDL-Cholesterol

All but four subjects had HDL-cholesterol values within the normal range at the beginning of the study, three patients (15%) in the AHA diet group and one in the HF diet group (4%) having below-normal values at entry (Tables 7 and 8). At 12 months, two patients (9%) in the HF and none in the AHA diet group had below-normal values. Mean values of HDL-cholesterol had increased 11% in the AHA diet group and 6% in the HF diet group at 12 months, although 5 patients (33%) in the AHA group and 10 (45%) in the HF diet group had values lower than baseline at 12 months. In both groups, the means remained very stable (Tables 9 and 10, Figure 5), and at no time in either diet group were they significantly different from baseline (Tables 11 and 12).

There was no difference in mean HDL-cholesterol values between the two groups on entry into the study (t-test). Analysis of variance showed no difference between the two groups at any point during the study (Table 13).

LDL-Cholesterol

On entry, one subject in the AHA diet group (5%) and three in the HF diet group (12%) had above-normal LDL-cholesterol (Tables 7 and 8). At the conclusion of the study, two subjects in the AHA diet group (13%) and none in the HF diet group had above-normal values. The means dropped 8% in both groups. Four AHA patients (27%) and five HF patients (23%) showed an increase in LDL-cholesterol over baseline at 12 months; the remainder showed a decrease. Variations in the means are shown in Tables 9 and 10 and in Figure 5. The means were shown to be significantly lower at 2 months in the AHA diet group (Table 11) and at 2, 4, 6 and 12 months in the HF diet group (Table 12), although in both diet groups the lowest values were seen at 2 months.

T-tests revealed no significant differences between the means of the two groups on entry (t-test). Analysis of variance showed no significant differences between the two diet groups at any point in the study (Table 13).

D. Summary

There were significant changes in the mean values of blood cholesterol and LDL-cholesterol in the HF diet group at 2, 4, 6 and 12 months, whereas in the AHA group these means were significantly different at 2 months only. Blood triglyceride was significantly lower in the AHA diet group at 4 and 6 months, and at 2 months in the HF diet group. HDL-cholesterol remained essentially unchanged in both diet

groups throughout the 12 months. Analysis of variance revealed no differences between the two groups in any blood lipid variables at any point in the study.

E. Vascular Parameters

Results of vascular testing are summarized in Tables 14 to 20. Figure 6 shows the graphs of the means (± SD) of ABR, PI and WD. Note again that because of subject withdrawals and pairing of data, the n and entry mean used in the paired t-test changed at various study intervals.

Ankle/Brachial Ratio (ABR)

All patients on entry into the study had an ABR of .90 or less following exercise and all but two subjects, both in the AHA diet group (15%) had an ABR of less than .90 at rest. Resting ABR's in the remainder of the group ranged from .34 to .86. All patients in the HF diet group had a resting ABR of .90 or less, with a range of from .33 to .9. At the completion of the study, ABR's in the AHA diet group ranged from .37 to 1.00, three patients (20%) having a resting ABR of greater than .90. Values in the HF diet group ranged from 3.7 to 1.0 at 12 months, only one person (4%) exceeding an ABR of .9. Throughout the study period, the mean values of ABR remained very stable in both groups, as shown in Tables 14 and 15 and in Figure 6. Tables 16 and 17

TABLE 14. MEANS[1] OF VASCULAR PARAMETERS AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - AHA DIET GROUP

Vascular Parameter	Month				
	Baseline	2	4	6	12
ABR	.67±.18	.67±.18	.70±.22	.67±.23	.62±.22
PI	3.6±3.0	3.6±2.0	3.7±2.9	3.5±2.7	3.7±2.5
TT (msec)	265±58	262±63	276±68	271±71	272±72
% PD	46±26	44±31	44±32	40±25	41±26
WD (meters)	378±342	520±376	647±376	870±421	991±427
n	20	20	18	17	15

[1] ± standard deviation. To obtain the 95% confidence interval of the sampling distribution of mean values use mean ± SD/$\sqrt{n}$ where n = sample size.

TABLE 15. MEANS[1] OF VASCULAR PARAMETERS AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - HF DIET GROUP

Vascular Parameter	Month				
	Baseline	2	4	6	12
ABR	.62±.16	.64±.16	.65±.17	.64±.13	.62±.15
PI	3.1±1.9	3.3±1.9	2.9±1.8	3.3±2.1	3.2±1.5
TT (msec)	255±56	278±62	272±56	265±61	276±59
% PD	42±22	46±23	43±26	40±24	40±23
WD (meters)	555±409	783±383	1052±564	1215±531	1352±537
n	25	25	25	23	22

[1] ± standard deviation. To obtain the 95% confidence interval of the sampling distribution of mean values use mean ± SD/$\sqrt{n}$ where n = sample size

TABLE 16. T-TESTS COMPARING MEANS OF VASCULAR PARAMETERS AT EACH FOLLOW-UP PERIOD (2, 4, 6 AND 12 MONTHS) WITH BASELINE MEANS - AHA DIET GROUP

Vascular Parameter	Month	Means (±SD)		n	Two-tailed Probability Level
		Baseline	Follow-Up		
ABR	2	.67±.18	.67±.18	20	1.00
	4	.67±.19	.70±.22	18	.24
	6	.66±.19	.67±.23	17	.75
	12	.66±.21	.62±.22	15	.16
PI	2	3.6±3.0	3.6±2.0	20	.31
	4	3.6±3.0	3.7±2.9	18	.89
	6	3.7±3.1	3.5±2.7	17	.77
	12	3.7±3.2	3.7±2.5	15	.98
TT (msec)	2	265±58	262±63	20	.51
	4	271±58	276±68	18	.51
	6	270±59	271±71	17	.95
	12	270±63	272±72	15	.81
% PD	2	46±26	44±31	20	.31
	4	44±24	43±22	18	.89
	6	44±24	39±26	17	.09
	12	43±26	40±27	15	.55
WD (meters)	2	378±342	520±382	20	.001*
	4	379±362	648±376	18	.003*
	6	400±362	870±426	17	.000*
	12	438±372	991±443	15	.001*

* $p < .05$

TABLE 17. T-TESTS COMPARING MEANS OF VASCULAR PARAMETERS AT EACH FOLLOW-UP PERIOD (2, 4, 6 AND 12 MONTHS) WITH BASELINE MEANS - HF DIET GROUP

Vascular Parameter	Month	Means (± SD)		n	Two-tailed Probability Level
		Baseline	Follow-Up		
ABR	2	.62±.16	.64±.16	25	.31
	4	.62±.16	.65±.17	25	.18
	6	.63±.15	.64±.13	23	.82
	12	.64±.15	.62±.16	22	.41
PI	2	3.1±1.9	3.3±1.9	25	.41
	4	3.1±1.9	2.9±1.8	25	.63
	6	3.2±1.9	3.3±2.1	23	.87
	12	3.2±1.4	3.2±1.5	22	.98
TT (msec)	2	255±56	278±62	25	.46
	4	255±56	272±56	25	.64
	6	264±57	265±62	23	.93
	12	262±57	276±60	22	.29
% PD	2	42±22	46±23	25	.24
	4	42±22	43±26	25	.87
	6	43±22	40±24	23	.62
	12	40±23	40±24	23	.94
WD (meters)	2	555±409	783±383	25	.001*
	4	555±409	1052±564	25	.000*
	6	599±416	1215±531	23	.000*
	12	610±403	1352±537	22	.000*

* $p<.05$

TABLE 18. ANALYSIS OF VARIANCE COMPARING MEANS OF VASCULAR PARAMETERS IN THE AHA DIET GROUP WITH MEANS OF VASCULAR PARAMETERS IN THE HF DIET GROUP AT 2, 4, 6 AND 12 MONTHS

Vascular Parameter	Month	Means (±SD)[1]		Two-tailed Probability Level
		AHA	HF	
ABR	2	.67±.18	.64±.16	.57
	4	.70±.22	.65±.17	.40
	6	.67±.23	.64±.13	.57
	12	.62±.22	.62±.15	.88
PI	2	3.6±2.0	3.3±1.9	.61
	4	3.7±2.9	2.9±1.8	.28
	6	3.5±2.7	3.3±2.1	.72
	12	3.7±2.5	3.2±1.5	.50
TT (msec)	2	262±63	278±56	.39
	4	276±68	272±62	.85
	6	271±71	265±56	.81
	12	272±72	276±59	.84
% PD	2	44±31	46±23	.74
	4	44±32	43±26	.91
	6	40±25	41±24	.89
	12	41±26	40±23	.90

[1] in mg/dl

TABLE 19. ANALYSIS OF COVARIANCE COMPARING BETWEEN-GROUP MEANS OF WALKING DISTANCE (WD) IN THE AHA AND HF DIET GROUPS AT 2, 4, 6 AND 12 MONTHS

MONTH	MEAN[1] WD (± SD) AHA	MEAN WD (± SD) HF	TWO-TAILED PROBABILITY
2	520 ± 382	783 ± 383	.25
4	648 ± 376	1052 ± 564	.052
6	870 ± 426	1215 ± 531	.14
12	991 ± 443	1352 ± 537	.10

[1] in meters

TABLE 20. DEGREE AND DIRECTION OF CHANGE IN WALKING DISTANCE AND NUMBER OF SUBJECTS SHOWING A CHANGE IN THE AHA AND HF DIET GROUPS AT 12 MONTHS

Diet Group	Number of Subjects	Direction of Change	Change (Range in meters)	% Change (Range)
AHA	2	Decreased	195-332	12-39
	13	Increased	181-1735	15-2136
HF	2	Decreased	56-185	10-30
	20	Increased	76-1435	21-1527

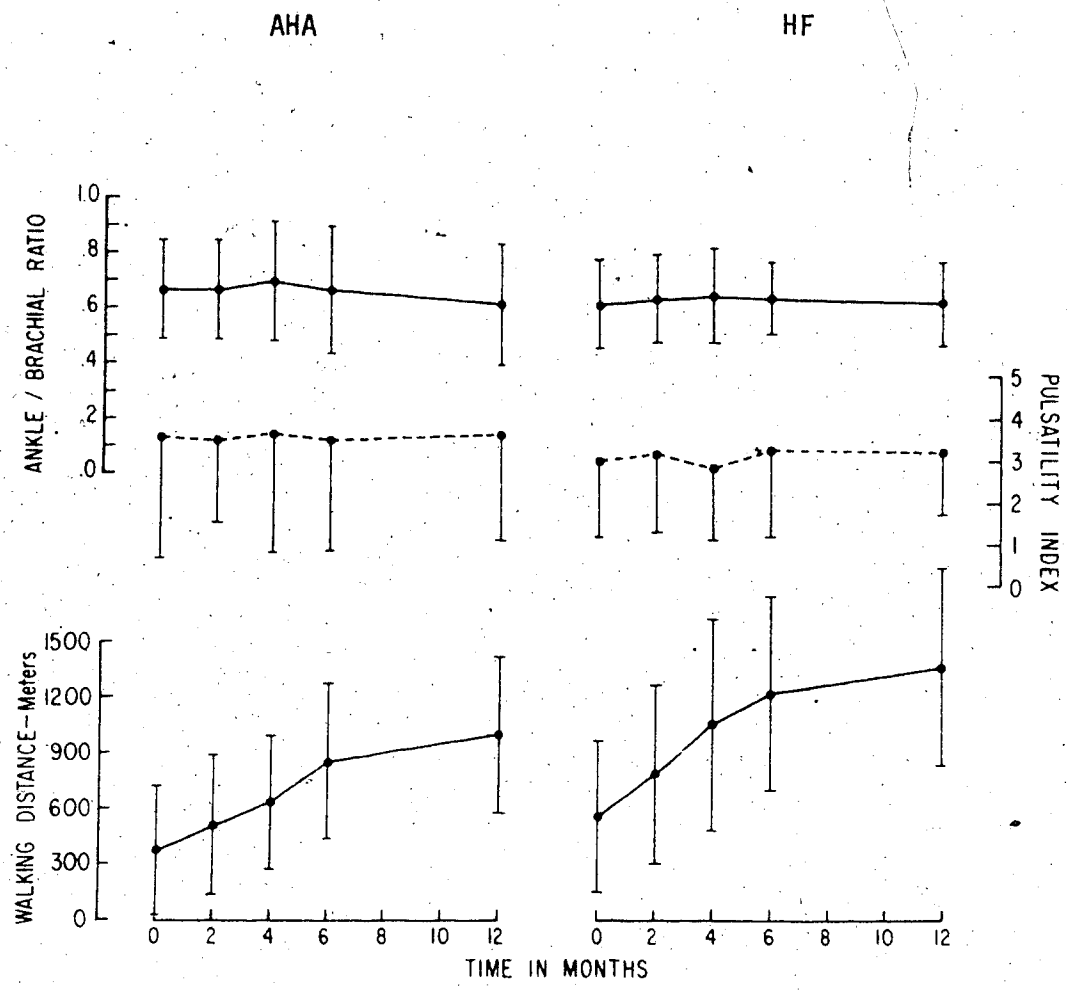

Figure 6. Means (± SD) of selected vascular variables in the AHA and HF diet groups at 0, 2, 4, 6 and 12 months.

show the results of paired t-tests comparing within-group means of vascular variables at each time period with means on entry. At no time were means of ABR in either diet group significantly different from entry means.

T-tests showed no significant differences in the mean ABR between the two groups on entry ($p>.05$). Analysis of variance showed no significant difference between the groups at any point in the study (Table 18).

Pulsatility Index (PI)

Gosling (1976) has defined normal PI for the posterior tibial and dorsalis pedis pulse as 8 to 16. On entry into the study, one patient (5%) in the AHA diet group had a PI within the normal range (PI = 12.3), while all others were below normal. In the HF diet group, no subject had an ankle pulse PI within normal limits. At 12 months, the ankle pulse was no longer detectable in two patients (13%) in the AHA diet group and in one patient (4%) in the HF diet group, and with the exception of one patient (7%) in the AHA diet group, all patients had below-normal PI's at 12 months. Again, within-group means and standard deviations remained very stable through the entire 12 months (Figure 6; Tables 14 and 15), and t-tests revealed no significant changes from entry in either diet group (Tables 16 and 17).

At baseline, there was no significant difference in mean PI between groups. Analysis of variance showed no significant differences in mean PI values between diet

groups at any point during the study (Table 18).

Transit Time (TT)

Mean TT's in both diet groups were slightly higher than that defined for young normals (250 ± 34) by Hutchison et al. (1981). Measured TT's at baseline ranged from 182 to 309 milliseconds (msec) in the AHA diet group, and from 204 to 352 msec in the HF diet group. On entry, two subjects in each diet group (10% AHA, 8% HF) had an almost flat (unpulsatile) waveform, from which no TT could be determined. As these flattened waveforms are indicative of severe arterial obstruction, which would necessarily lengthen the TT, a value of 400 msec, 50 msec higher than the highest value observed in either group, was designated for such cases. At the conclusion of the study, TT's ranged from 192 to 286 msec in the AHA group, and from 200 to 354 msec in the HF diet group. Three patients in each diet group (20% AHA, 14% HF) had a designated TT of 400 msec at 12 months.

In both groups, means and standard deviations remained very stable (Tables 14 and 15), and at no time were there significant differences from entry values (Tables 16 and 17). There were no significant differences in TT between groups on entry. Analysis of variance revealed no significant differences in mean TT between diet groups at 2, 4, 6 or 12 months (Table 18).

Per Cent Pressure Drop (% PD)

At baseline, two patients (10%) in the AHA diet group and one (4%) in the HF diet group had no pressure drop after exercise. In the remainder of the subjects, pressure drops ranged from 20 to 100% in the AHA diet group and from 6 to 100% in the HF diet group. A pressure drop of 100%, indicating that the pulse was not detectable immediately after exercise, was seen in one patient in each diet group on entry and in one patient (7%) in the AHA diet group at 12 months. Mean values of % PD were essentially unchanged throughout the study period (Tables 14 and 15) and were not significantly different from entry in either group at 2, 4, 6 or 12 months (Tables 16 and 17).

There was no significant difference in % PD between groups on entry. Analysis of variance showed no significant difference between groups at any point during the study period (Table 18).

Walking Distance (WD)

On entry into the study, all patients experienced IC before reaching the maximum WD of 1810 meters (30 minutes). As was mentioned previously, WT was eliminated from statistical analysis; only WD was used. Distances ranged from 30 to 1232 meters in the AHA diet group and from 30 to 1616 meters in the HF diet group. At 12 months, the range in WD was from 432 to 1810 meters in the AHA diet group and from 362 to 1810 meters in the HF diet group.

In both diet groups, mean WD increased throughout the study period, as shown in Figure 6 and Tables 14 and 15. The almost parallel rate of increase is indicated by the similar slopes of the two graphs. The differences between the means on entry and those at 2, 4, 6 and 12 months were statistically significant in both diet groups (Tables 16 and 17). Entry means of WD of the two diet groups were not significantly different from one another. However, the observed difference (378 meters in the AHA diet group vs 555 meters in the HF diet group) was felt by the investigators to have clinical significance. Therefore, analysis of covariance, with the value on entry as the covariate, was used for the between-group comparisons of WD.

After correcting for differences in the means on entry, covariate analysis showed no significant difference between the two groups at any point in the study period (Table 19).

Changes in WD are summarized in Table 20. Two persons in each group experienced a decrease in distance to claudication, while the remainder increased their WD. Increases ranged from 181 to 1735 meters (15 to 2136%) in the AHA diet group and from 76 to 1435 meters (21 to 1527%) in the HF diet group. In the AHA diet group, the median increase at 12 months was 371%, and the mean increase 404%. The median increase in the HF diet group was 155% and the mean 379%. At the final follow-up visit, 1 patient in the AHA diet group and 11 persons in the HF diet group were able to walk to the maximum of 1810 meters before experiencing

claudication.

F. Summary

There was a significant improvement in WD in both diet groups at 2, 4, 6 and 12 months. There were no significant changes in the remaining vascular variables at any of the four follow-up periods.

Between-group comparisons using analysis of variance for ABR, PI, TT and % PD, and analysis of covariance for WD, revealed no significant differences between diet groups at any point in the study.

G. Associations Between Vascular and Lipid Parameters

Pearson's product-moment correlation (r) was used to examine relationships between vascular and lipid variables. The results are shown in Tables 21 to 30.

The following correlations were statistically significant in the AHA diet group: ABR with LDL-cholesterol at 6 and 12 months (Table 21); PI with HDL-cholesterol and LDL-cholesterol at 2 months (Table 22); TT with TG at 6 months, cholesterol at 4 and 6 months, HDL-cholesterol at 2 months, LDL-cholesterol at 4, 6 and 12 months (Table 23); and % PD with HDL-cholesterol at 2 months (Table 24). WD was not correlated with blood variables at any point in the study (Table 25).

In the HF diet group, the following correlations were significant: ABR with cholesterol at 0, 4 and 12 months,

TABLE 21. CORRELATIONS BETWEEN BLOOD LIPIDS AND ANKLE/BRACHIAL RATIO AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - AHA DIET GROUP

	Month									
	Baseline		2		4		6		12	
Blood Lipid	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
TG	.02	.46	.30	.10	.09	.37	-.18	.25	.16	.29
Cholesterol	-.04	.44	.19	.21	-.12	.43	-.41	.06	.37	.09
HDL-chol	-.02	.46	.31	.09	.29	.13	-.11	.35	.22	.22
LDL-chol	-.05	.42	-.16	.25	-.22	.19	-.44	.05*	-.52	.02*

[1] r = Pearson's correlation coefficient
[2] prob = Two-tailed probability
* $p<.05$

TABLE 22. CORRELATIONS BETWEEN BLOOD LIPIDS AND ANKLE/BRACHIAL RATIO AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - HF DIET GROUP

	Month									
	Baseline		2		4		6		12	
Blood Lipid	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
TG	-.33	.08	-.37	.06	.37	.07	.51	.02*	.03	.46
Cholesterol	-.21	.18	-.14	.28	.45	.03*	.60	.01*	.42	.06
HDL-chol	-.16	.25	-.40	.04*	-.24	.18	-.10	.36	-.18	.26
LDL-chol	.28	.12	.32	.08	.49	.02*	.63	.01*	.58	.01*

[1] r = Pearson's correlation coefficient
[2] prob = Two-tailed probability
* $p<.05$

TABLE 23. CORRELATIONS BETWEEN BLOOD LIPIDS AND TRANSIT TIME AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - AHA DIET GROUP

	Month									
	Baseline		2		4		6		12	
Blood Lipid	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
TG	-.33	.08	-.37	.06	.37	.07	.51	.02*	.03	.46
Cholesterol	-.21	.18	-.14	.28	.45	.03*	.60	.01*	.42	.06
HDL-chol	-.16	.25	-.40	.04*	-.24	.18	-.10	.37	-.18	.26
LDL-chol	.28	.12	.32	.08	.49	.02*	.63	.01*	.58	.01*

[1] r = Pearson's correlation coefficient
[2] prob = Two-tailed probability
* $p<.05$

TABLE 24. CORRELATIONS BETWEEN BLOOD LIPIDS AND PER CENT PRESSURE DROP AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - AHA DIET GROUP

Blood Lipid	Month									
	Baseline		2		4		6		12	
	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
TG	-.17	.25	-.25	.15	.18	.24	.05	.42	.22	.22
Cholesterol	-.15	.27	-.03	.45	.31	.01	.06	.41	.37	.09
HDL-chol	-.20	.21	-.41	.04*	.36	.08	-.15	.29	-.13	.32
LDL-chol	.18	.32	.29	.10	.39	.06	.14	.30	.42	.06

[1] r = Pearson's correlation coefficient
[2] prob = Two-tailed probability
* $p<.05$

TABLE 25. CORRELATIONS BETWEEN BLOOD LIPIDS AND WALKING DISTANCE AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - AHA DIET GROUP

	Month									
	Baseline		2		4		6		12	
Blood Lipid	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
TG	-.02	.46	.21	.18	.03	.46	.04	.44	.13	.32
Cholesterol	.08	.37	.02	.47	-.29	.13	.13	.31	-.03	.45
HDL-chol	-.28	.12	-.14	.27	-.25	.16	-.18	.25	-.20	.24
LDL-chol	.02	.46	-.19	.21	-.27	.14	.16	.28	-.16	.28

[1] r = Pearson's correlation coefficient
[2] prob = Two-tailed probability

TABLE 26. CORRELATIONS BETWEEN BLOOD LIPIDS AND ANKLE/BRACHIAL RATIO AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - HF DIET GROUP

	Month									
	Baseline		2		4		6		12	
Blood Lipid	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
TG	.14	.25	-.18	.20	.21	.16	.10	.32	-.07	.38
Cholesterol	.34	.05*	.26	.10	.42	.02*	.33	.06	.37	.05*
HDL-chol	.04	.43	-.37	.04*	-.12	.29	.02	.47	.29	.09
LDL-chol	.30	.08	.52	.00*	.50	.01*	.34	.06	.38	.04

[1] r = Pearson's correlation coefficient
[2] prob = Two-tailed probability
* $p<.05$

TABLE 27. CORRELATIONS BETWEEN BLOOD LIPIDS AND PULSATILITY INDEX AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - HF DIET GROUP

Blood Lipid	Month									
	Baseline		2		4		6		12	
	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
TG	.23	.14	-.24	.13	.24	.12	.09	.35	-.19	.20
Cholesterol	.36	.04*	.20	.17	.22	.15	.38	.04*	.05	.42
HDL-chol	-.11	.30	-.20	.17	-.14	.26	.24	.14	.21	.18
LDL-chol	.35	.05*	.39	.03*	-.28	.10	.24	.13	.05	.41

[1] r = Pearson's correlation coefficient
[2] prob = Two-tailed probability
* $p < .05$

TABLE 28. CORRELATIONS BETWEEN BLOOD LIPIDS AND TRANSIT TIME AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - HF DIET GROUP

	Month									
	Baseline		2		4		6		12	
Blood Lipid	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
TG	-.11	.31	.02	.47	-.16	.23	.13	.29	.07	.38
Cholesterol	.02	.46	.20	.18	.05	.41	.15	.25	-.16	.24
HDL-chol	.00	.50	.09	.33	.35	.05*	.11	.31	-.15	.26
LDL-chol	.10	.32	.16	.22	-.03	.44	.07	.38	[illegible]	.20

[1] r = Pearson's correlation coefficient
[2] prob = Two-tailed probability
* $p<.05$

TABLE 29. CORRELATIONS BETWEEN BLOOD LIPIDS AND PER CENT PRESSURE DROP AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - HF DIET GROUP

	Month									
	Baseline		2		4		6		12	
Blood Lipid	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
TG	.04	.43	.10	.31	.03	.44	.03	.44	.07	.37
Cholesterol	-.26	.10	-.02	.45	.11	.30	.08	.37	-.19	.19
HDL-chol	-.20	.17	.23	.13	.11	.41	-.23	.16	-.15	.25
LDL-chol	-.23	.14	-.17	.20	.09	.33	.15	.26	-.13	.28

[1] r = Pearson's correlation coefficient
prob = Two-tailed probability

TABLE 30. CORRELATIONS BETWEEN BLOOD LIPIDS AND WALKING DISTANCE AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - HF DIET GROUP

Blood Lipid	Month									
	Baseline		2		4		6		12	
	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
TG	.25	.12	.18	.19	.09	.33	.05	.42	-.30	.09
Cholesterol	.22	.14	.22	.14	-.05	.41	.29	.10	.06	.40
HDL-chol	-.17	.21	-.28	.09	-.37	.04*	-.20	.18	.30	.09
LDL-chol	.19	.18	.32	.06	.07	.38	.47	.01*	.01	.49

[1] r = Pearson's correlation coefficient
[2] prob = Two-tailed probability
* $p<.05$

with HDL-cholesterol at 2 months, and with LDL-cholesterol at 2 and 4 months (Table 26); PI with cholesterol at 0 and 6 months, and with LDL-cholesterol at 0 and 2 months (Table 27); TT with HDL-cholesterol at 4 months (Table 28); and WD with HDL-cholesterol at 4 months and with LDL-cholesterol at 6 months (Table 30).

It can be seen that although a few correlations reached significant levels, the associations were neither high nor consistent in either group, and many were not in the direction anticipated. Logically, it may be argued that the few significant correlations observed were likely chance associations, for with independent tests and an alpha level of .05, five significant results out of 100 tests would be observed due to chance alone. Thus, these results demonstrated very little association between vascular and lipid variables.

H. Associations Between WD and Other Vascular Parameters

The associations between WD and the other vascular variables were examined using Pearson's r. The results are presented in Tables 31 and 32.

In the AHA diet group, no variable was significantly correlated with WD at any point during the study period (Table 31). In the HF diet group, significant correlations were seen between ABR and WD at 0, 2, 4 and 12 months, and between WD and PI, % PD and TT at 12 months (Table 32). All correlations were in the direction anticipated. No other

TABLE 31. CORRELATIONS BETWEEN WALKING DISTANCE AND OTHER VASCULAR PARAMETERS AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - AHA DIET GROUP

Vascular Parameter	Month									
	Baseline		2		4		6		12	
	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
ABR	-.14	.28	-.15	.26	-.06	.41	.30	.12	.09	.38
PI	.05	.42	.22	.18	.35	.08	-.03	.46	.33	.12
TT	-.15	.26	-.26	.14	-.18	.24	-.28	.14	-.23	.21
% PD	.08	.38	.02	.47	.01	.48	-.07	.40	-.14	.31

[1] r = Pearson's correlation coefficient
[2] prob = Two-tailed probability

TABLE 32. CORRELATIONS BETWEEN WALKING DISTANCE AND OTHER VASCULAR PARAMETERS AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - HF DIET GROUP

Vascular Parameter	Month									
	Baseline		2		4		6		12	
	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
ABR	.50	.01*	.70	.00*	.57	.00*	.32	.07	.52	.01*
PI	.10	.33	.32	.07	.24	.13	.09	.34	.42	.03*
TT	-.10	.32	-.05	.41	-.37	.04*	-.14	.27	-.52	.01*
% PD	-.18	.19	-.27	.10	-.15	.25	-.09	.34	-.48	.01*

1 r = Pearson's correlation coefficient
2 prob = Two-tailed probability
* $p < .05$

consistent patterns of association were seen. These results support the suggestion that WD measures something quite apart from or in addition to vascular status, as the significant correlations observed could well have been due to chance alone.

I. Associations Between Per Cent Ideal Weight and Vascular Parameters

To determine if % ID WT was associated with vascular variables, Pearson's *r* was computed for each variable. The results are shown in Tables 33 and 34.

The only correlation that reached significant levels in the AHA diet group was % ID WT with WD at 6 months (Table 33). In the HF diet group, ABR was significantly correlated with % ID WT at 0, 2, 4 and 12 months. The only other association that was significant was WD with % ID WT at 4 months (Table 34). Again, these results could well have been due to chance, considering the large number of tests that were run.

J. Vascular Status and Smoking Habits

On entry into the study, only four patients had never smoked; the remainder had a smoking history of from 3 to 99 pack years. Thirteen subjects in the AHA diet group and 11 in the HF diet group were non-smokers at baseline. Student's t-tests showed no difference between the two groups in smoking history (in pack years) at baseline.

TABLE 33. CORRELATIONS BETWEEN VASCULAR PARAMETERS AND PER CENT IDEAL WEIGHT AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - AHA DIET GROUP

Vascular Parameter	Month									
	Basline		2		4		6		12	
	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
ABR	-.03	.45	.09	.35	-.06	.40	.01	.49	-.18	.26
PI	.15	.26	-.26	.15	.03	.45	-.22	.19	-.08	.38
TT	-.04	.44	-.20	.20	.33	.09	.24	.17	.24	.20
% PD	.06	.40	.18	.22	.26	.15	.02	.46	.38	.08
WD	.14	.29	.14	.28	.12	.32	-.47	.03*	.26	.18

[1] r = Pearson's correlation coefficient
[2] prob = Two-tailed probability
* $p<.05$

TABLE 34. CORRELATIONS BETWEEN VASCULAR PARAMETERS AND PER CENT IDEAL WEIGHT AT BASELINE AND AT 2, 4, 6 AND 12 MONTHS - HF DIET GROUP

Vascular Parameter	Month									
	Baseline		2		4		6		12	
	r[1]	prob[2]	r	prob	r	prob	r	prob	r	prob
ABR	.40	.02*	.52	.00*	.44	.01*	.18	.21	.36	.05*
PI	.21	.15	.05	.40	.13	.26	.28	.10	.07	.38
TT	-.04	.42	-.29	.08	-.19	.18	-.11	.31	-.05	.41
% PD	-.27	.10	-.29	.08	-.18	.20	.01	.48	-.20	.18
WD	.12	.29	.33	.06	.47	.01*	.27	.11	.20	.19

1 r = Pearson's correlation coefficient
2 prob = Two-tailed probability
* $p<.05$

At 12 months, of the 37 patients completing the study, 11 had changed their smoking habits (3 AHA and 8 HF patients). In the AHA diet group, two individuals smoked less while one smoked more. Two subjects in the HF diet group had stopped smoking entirely, five had decreased the amount smoked and one had increased (Table 354).

Pearson's r was used to examine the associations between smoking history, as measured in pack years, and vascular variables on entry into the study. No significant associations were seen in either group (Table 36).

As the expected cell frequencies were too small in each category classifying smoking habits, no further statistical analysis was undertaken.

K. Vascular Status and Exercise Habits

As with smoking, exercise habits were classified into nominal groups. Due to the nature of the data, non-parametric statistics were required, and the expected cell frequencies for each category were again too small to permit further analysis. However, self-report measures of exercise indicated that most patients (9 in the AHA diet group and 14 in the HF diet group) had increased their weekly exercise by 12 months (Table 37).

TABLE 35. NUMBER OF SUBJECTS IN EACH DIET GROUP WHOSE SMOKING HABITS AT 12 MONTHS HAD INCREASED, STAYED THE SAME OR DECREASED COMPARED WITH BASELINE

Diet Group	Smoking Habits		
	Increased	Same	Decreased
AHA	1	12	2
HF	1	12	7

TABLE 36. CORRELATIONS BETWEEN SMOKING HISTORY (PACK YEARS) AND VASCULAR PARAMETERS IN EACH DIET GROUP AT BASELINE

Vascular Parameter	Diet Group			
	AHA		HF	
	r[1]	Two-tailed Probability	r	Two-tailed Probability
ABR	.14	.29	-.03	.44
PI	.01	.48	.17	.20
TT	.00	.50	.33	.06
% PD	.07	.38	-.04	.43
WD	-.25	.15	-.01	.48

r = Pearson's correlation coefficient

TABLE 37. NUMBER OF SUBJECTS IN EACH DIET GROUP WHOSE WEEKLY EXERCISE HABITS AT 12 MONTHS HAD INCREASED, STAYED THE SAME OR DECREASED IN FREQUENCY OR DURATION COMPARED WITH BASELINE

Diet Group	Weekly Exercise Habits		
	Increased	Same	Decreased
AHA	9	6	0
HF	14	5	1

VI. Discussion, Limitations and Conclusions

In the following discussion, an interpretation of the results regarding dietary intake, changes in blood lipids and vascular variables, and associations between vascular and other variables is presented. Some implications for nursing are outlined. Limitations of the study are discussed, and recommendations for future study are included.

A. Discussion of Results

Dietary Intake

An important problem in clinical trials involving dietary intervention is the assessment of patient adherence to the therapeutic regimen. As Marr (1971) has pointed out, "there is no generally accepted method of measuring the dietary intake of free-living individuals" (p. 106). She indicates two methods whereby individual data may be collected: (1) through the recording of present intakes, and (2) through a recall of past intake. Glanz (1980) has suggested that a combination of such methods with a subjective evaluation by a skilled interviewer leads to the most accurate results.

In the current investigation, both present intake (the 3 day food record) and past intake (the 48 hour recall) were used. The 48 hour recall indicated a high degree of patient compliance with the therapeutic diets, as revealed by the close approximation to the dietary target values seen in

both groups (Tables 3 and 4). In addition, body weight, expressed as per cent ideal weight (% ID WT) was maintained in both groups at near optimum (100% ID WT) throughout the study period, and in both groups at 12 months was significantly different from entry (Table 38). Other measures of dietary compliance included a subjective assessment by the dietitian at interview with the patient, and a record of the accuracy with which the 3 day food records were completed. By these measures, compliance with the therapeutic regimen was estimated to be very high in both groups. However, by subjective assessment by the dietitian, patients in the HF diet group were thought to be somewhat more highly motivated and enthusiastic than the AHA diet group, possibly because the HF diet was more "rigorous" than the AHA diet, and as such may have been interpreted by the subjects as being more "therapeutic". Nonetheless, both diet groups appeared to be highly compliant. Analysis of dietary compliance is treated extensively elsewhere (Whyte, 1982).

At baseline, both groups of subjects showed dietary intakes typical of current North American habits (Barndt et al., 1977). It can be seen from Tables 3 and 4 that intakes in both diet groups were near target values by 2 months and throughout the remainder of the study. However, in the AHA diet group, intakes of fat and cholesterol were significantly different from baseline at 2, 4 and 6 months, but not at 12 months. In the HF diet group, subjects at each

TABLE 38. MEAN BODY WEIGHT EXPRESSED AS PER CENT IDEAL WEIGHT FROM BASELINE TO 12 MONTHS

Diet Group	% Ideal Weight				
	Baseline	2	4	6	12
AHA	114	109	107	105	105*
HF	109	100	99	97	99*

* Significantly different from baseline ($p<.01$)

time interval were consuming significantly more carbohydrate and fiber and significantly less fat and cholesterol compared with baseline. Mean intakes of the two diet groups were significantly different for fat, cholesterol and fiber at 2, 4, 6 and 12 months, and for CHO at 2, 4 and 6 months, as shown in Table 6. Thus, it can be concluded that the two groups of patients were in fact consuming very different diets, and that the HF diet represented a fairly considerable departure from normal North American dietary habits. Nonetheless, results showed no significant differences between the two diet groups in any vascular or lipid variables over the 12 month period. Several possible reasons for the failure to find significant differences could be considered: 1) compliance measures and estimates of dietary intake were faulty; 2) the study period was too short to permit changes to occur; 3) the sample size and power of the study were inadequate; and 4) there is no difference between the two diets in their effects on vascular status and blood lipids. The evidence presented here is most suggestive that the latter point is correct. Further study, however, is required to examine these and other possibilities.

Changes in Blood Lipids

The observed changes in mean values of TG, cholesterol and LDL-cholesterol (Tables 7-10) compared favorably with changes reported by others employing lipid-lowering diets

(Gotto et al., 1980). However, in both groups, despite a trend to lower values in all three variables, in no instance was the 12 month mean the lowest (Tables 9 and 10). It appeared, in fact, that in each variable there was a gradual climb toward baseline after minimum values were reached, although no value had returned to baseline by 12 months (Figure 6). It is possible that the slight trend back to previous eating habits observed in both diet groups was reflected in blood lipid levels. However, a longer study period would be required before such an association could be properly determined.

The per cent change in mean blood cholesterol levels at 12 months was somewhat higher in the HF diet group than in the AHA diet group, but only the cholesterol value in the HF diet group was significantly different from entry. It should be noted, however, that in the AHA diet group, the entry mean of cholesterol used in the paired t-test (Table 11) dropped considerably over the 12 months due to patient withdrawals, indicating that those patients who withdrew had high cholesterol values on entry. It is tempting, but hazardous, to speculate as to the effects these patients would have had on mean values had they remained in the study. Fortunately, patient withdrawals appeared to have little effect on any other lipid variables in either group. Mean LDL-cholesterol dropped the same amount in both groups but, because of wider variation in the AHA diet group, only the HF diet group showed values significantly different from

entry.

The observed rise in HDL-cholesterol in both diet groups (Tables 12 and 13) was somewhat unexpected, as many investigators (Miettinen, Naukkarinen, Mattila & Ehnholm, 1980; Lewis, 1978) found a decrease in HDL-cholesterol to be associated with a drop in total cholesterol, TG and LDL-cholesterol. The increase in HDL-cholesterol in this study was not statistically significant in either group and may have been little more than chance variation. However, the direction of the change suggests the possibility of a redistribution of lipids occurring with the various lipoprotein fractions. Evidence suggests that, of the blood lipids, HDL-cholesterol is the most affected by exercise (Castelli, 1979b). Therefore, the fact that most patients increased their weekly exercise may have contributed to the observed increase in HDL-cholesterol. Unfortunately, due to the inadequate sample size, this association could not be examined statistically.

In summary, the failure to find a significant difference between the two groups on any of the lipid variables (Table 13) indicates that, whereas both diets may have had some success in altering blood lipid values, neither diet was superior to the other. Whether the two diets could be successful in maintaining lipids at nearer "optimum" values in the longer term has yet to be investigated.

Vascular Parameters

With the exception of WD, all vascular variables were very stable throughout the study period (Tables 14 and 15) in both diet groups. In addition, poor correlations between WD and other vascular variables at each time interval were observed (Tables 31 and 32). Although the relationship between WD and ABR was somewhat stronger in the HF diet group, the significant correlations were neither high nor consistent. Further, the association was higher at baseline, suggesting that any association evident later on was not attributable to treatment and was likely a chance finding. Thus, the changes in WD in both groups occurred without concomitant changes in the other vascular variables, indicating that the improvement in functional ability was due to something other than an improvement in the peripheral circulation.

Several alternative explanations for the increase in WD could be considered. It is possible that claudication distance, although useful as an indicator of functional ability, is too greatly influenced by subjective variables, such as placebo effect and patient motivation, to be a sensitive measure of circulatory conditions. Other workers (Blumchen et al., 1970; Ekroth et al., 1978; Larsen & Lassen, 1966; Zetterquist, 1970), using venous occlusion plethysmography or radioactive clearance techniques, have demonstrated increases in walking distances without apparent increases in blood flow to the affected limb. Thus,

functional changes can occur without actual circulatory improvement.

An interesting finding in this study was that, in the HF diet group, all vascular variables were significantly correlated with WD at 12 months (Table 32). This may indicate that patients in the HF diet group, who were assessed by the dietitian as being generally more motivated than the AHA diet group, pushed themselves closer to their real limits at 12 months, with the result that correlations between WD and other variables strengthened. The poor correlations observed earlier could, therefore, have been a result of the patient's failure to reach his real limit at each time, suggesting that the observed increase in WD was not a "real" improvement, but rather an increasing motivation. Certainly a limitation of WD as an indicator of vascular status is its subjective nature (Clement, 1979; Eklund, 1977). In this investigation, each patient was instructed to walk until he experienced severe claudication, and it is possible that his interpretation of "severe" varied at the different time periods. However, as Strandness (1969) has pointed out, if the improvement in WD were due merely to an increase in patient motivation, without an improvement in blood flow, there should have been a greater pressure drop after exercise as the patient pushed himself harder. Our failure to observe an increased pressure drop, despite a steadily increasing WD, therefore left some doubt that increased motivation was the primary reason for the

functional improvement.

Another possible explanation for the increased WD is the effect of training on muscle metabolism. A number of investigators working with PAD patients on an exercise program have observed improvements in WD and an increased oxygen uptake by the muscles distal to an arterial obstruction (Bylund et al., 1976; Dahllof et al., 1974; Jussila, Nunikoski & Inberg, 1979; Sorlie & Myhre, 1978). Although the investigator was unable, due to inadequate sample size, to use statistical analysis to test the associations between weekly exercise and WD, it was noted that most patients increased their exercise over the study period. Therefore, it is possible that the increase in WD was largely an effect of training.

Treadmill WD increased in both groups, covariate analysis showing no difference between groups (Table 19), although the mean and median increases were somewhat higher in the AHA diet group. However, it was noted that, while only 1 AHA patient reached the maximum of 1810 meters at 12 months, 11 HF patients reached this distance. The placing of an upper limit on the WD was felt to be necessary because of the patient's age and health, and indeed all patients who walked the full distance expressed a feeling of great fatigue. Nonetheless, there was a concern that the imposition of a maximum might have masked an even greater increase in WD in the HF diet group. If it were the case, however, that the patients who reached maximum could have

walked further, they should have experienced less of a pressure drop after being instructed to stop walking. Pressure drops at 0 and 12 months in the HF patients who walked the full distance are shown in Table 39. Six patients had a decrease in % PD, four had an increase and one stayed the same. A t-test showed no significant difference in % PD in these 11 patients between 0 and 12 months. Thus, there was no evidence to suggest that these patients could have walked further if given the chance.

In summary, functional ability, as measured by treadmill WD, increased significantly and steadily in both groups throughout the study period. There was no evidence to suggest that the improvements in WD were as a result of improved peripheral circulation. The most probable explanation of the observed increased was increased patient motivation and the effects of training on muscle coordination and metabolism.

Associations Between Vascular and Other Variables

The author failed to find any consistently significant correlations between vascular and lipid variables (Tables 20-31). The changes observed in blood lipids were small and over a relatively short period of time, particularly when compared with the time taken for the atherosclerotic plaque to develop. In addition, the sample size and sampling method limit conclusions. At least four possibilities exist: (1) there is no association between

TABLE 39. PER CENT PRESSURE DROP (% PD), IN SUBJECTS IN BOTH DIET GROUPS WHO REACHED MAXIMUM WALKING DISTANCE

Diet Group	% PD - Baseline	% PD - 12 Months
AHA	62	52
HF	16	00
	00	00
	62	47
	29	42
	47	53
	24	19
	40	53
	43	50
	42	1[illegible]
	17	00
	37	33

blood lipid levels and vascular status, (2) the fall in blood lipids was insufficient to effect a change in vascular status, (3) the study period was not long enough to allow regression of atheroma to occur, and (4) the vascular indicators were not sensitive enough to detect small changes in vascular status. Further study is required to determine which, if any, of these possibilities obtains. In consideration of research evidence presented by other investigators, it seems probable that all of the last three reasons contributed to the failure of this study to observe significant associations.

A somewhat surprising result in this investigation was the lack of association between WD and % ID WT (Tables 32 and 33). Chucker (1977) has pointed out that increased weight places extra metabolic demands on the exercising muscles, and should therefore further limit walking ability in patients with compromised circulation. However, despite the fact that mean WD increased and % ID WT decreased in both groups, the correlation was not statistically significant. This finding lends further support to the argument that WD was measuring something aside from true walking ability.

It was unfortunate that the small sample size and the use of discrete categories to record smoking information prevented an examination of the relationship between vascular variables and smoking habits throughout the study. On entry, only 4 of 45 patients had never smoked, a finding

in keeping with epidemiological evidence (Dawber, 1980) of a strong association between smoking and atherosclerosis. In this investigation, compliance with recommendations to stop or decrease smoking was relatively poor compared with the high compliance to the diet and exercise prescriptions. Only nine patients of the entire number had decreased their smoking by at the end of the 12 month period, a number too small to permit any meaningful analysis. Thus, a determination of the effects on vascular status of a decrease in smoking awaits future study.

Implications for Nursing

As has been noted above, the vast majority of patients in this study demonstrated an increased functional ability. In addition, most expressed a subjective improvement in their feeling of well-being. It seems quite possible that many of the observed benefits to the patients accrued, not from actual improvements in vascular status, but from their involvement *per se* in the research program.

Surprisingly, although most patients in the study had been submitted to frequent painful angiographic procedures and had undergone reconstructive surgery at least once, they expressed at best a limited understanding of their disease. For example, most patients believed that when they experienced claudication, they should immediately stop exercising or risk damaging the leg muscle. Research indicates, however, that, except in pre-gangrenous or

gangrenous conditions, the converse is true. Sustaining exercise for as long as possible after IC appears seems to be beneficial, either through promotion of collateral development (Strandness, 1969) or through an increase in the metabolic capacity of the muscle (Bylund et al., 1976).

Correction of these and other misconceptions required considerable patient teaching by the nurse. Almost without exception, subjects voiced great appreciation for their increased knowledge and understanding. Many expressed the sentiment that they had been given a "new lease on life" simply because someone cared enough to help them help themselves. Thus, although it is difficult to document, it appears that much of the observed patient improvement in the study was a kind of placebo effect. The care and feedback provided by the researchers appeared to restore some of the patients' confidence and enthusiasm for living. Many who appeared to have almost given up hope of improvement found new resources within themselves, with the result that, although their vascular status may have been unchanged, their overall condition improved.

This points to a definite role for the nurse in the conservative management of the PAD patient. Nursing's orientation is toward holistic care, the importance of which was evident in the response of subjects involved in this study. Thus, by providing information, support and encouragement, both in acute care and public health settings, the nurse can assist the patient with PAD to

remain an active and involved participant in his own health care, thereby helping him to maximize his potential for health.

B. Limitations

Conclusions drawn from this investigation are restricted by a number of important limitations, which include the following:

1. **Sampling method**: Although subjects were randomly assigned to diet groups, the lack of random sampling restricted generalization of results.
2. **Sample size**: It was felt that a minimum of 30 subjects in each group would be required to satisfy requirements for adequate statistical power. However, an extensive search failed to yield sufficient numbers of patients. Therefore, power was decreased and the probability of making a Type II error increased. Some statistical analysis could not be undertaken.
3. **Patient withdrawals**: The withdrawal of subjects may have left what Feinstein (1979) has described as a "compliance-confounded cohort" (p. 318), that is, a group of patients who can comply with treatment. Feinstein argues that this group "will be destined to have an outcome event rate that differs substantially from the corresponding rate in the people who do not maintain compliance" (p. 318).
4. **Study length**: The follow-up period may have been too

short to allow vascular changes to occur (Haeger, 1974) and to permit observation of long-term effects of the two diets on blood lipids.

5. **Effect of "reactive arrangements"** (Campbell & Stanley, 1963): The awareness of being involved in a study may have exerted an effect on patient performance, particularly on WD. This effect may have been unequal in the two groups. Although both groups were given equivalent treatment and attention, the HF diet was considerably more rigorous than the AHA diet, which may have affected patient motivation and enthusiasm.
6. **Inaccuracies in compliance measures**: It was not possible to determine the exact degree of dietary compliance in either group, which necessarily limits conclusions regarding the effectiveness of the diet regimen.
7. **Measurement of WD**: The imposition of a ceiling on WD may have masked a greater improvement in one group than the other. In addition, the patients' awareness that a maximum had been established may have effected patient performance.

C. Recommendations

The pilot study revealed a trend to lower lipid values and a definite increase in walking distance to claudication. Further study should therefore be undertaken to provide more definitive evidence regarding the efficacy of lipid-lowering diets and the effects of exercise. In recognition of the

above limitations, the following recommendations are made:

1. The study should be repeated with a much larger sample randomly selected from a pool of suitable participants. This would likely necessitate a multi-center approach, as it is improbable that a sufficient number of patients could be found in one city.
2. The follow-up period should be extended to at least 2 years. Most workers have observed vascular changes to occur within that period (Blankenhorn et al., 1978; Chilvers et al., 1975), and the extended period would permit observation of the trends in lipid values. In addition, as patients undergoing conservative treatment for PAD might anticipate having to follow a special diet for the rest of their lives, it would be instructive to observe the long-term compliance with a diet as rigorous as the HF diet.
3. The diet recall might be extended in time, that is, a 7 day recall might be used instead of a 48 hour recall. Glanz (1980) has indicated that the longer period might be more representative of actual intake and therefore more accurate.
4. In view of the patients' age and health status, it is recommended that the ceiling on WD be maintained. However, the patients should be unaware of the maximum, and the maximum should be increased to 40 minutes or 2810 meters.

D. Conclusion

From this pilot study, it appears that patients with PAD can benefit from a conservative program of diet and exercise. The large amount of epidemiological evidence pointing to the role of lipids in atherogenesis suggests that a diet that can effectively lower blood TG, cholesterol and LDL-cholesterol, and/or raise HDL-cholesterol, can be useful, if not in causing regression, at least in slowing the progression of the atherosclerotic process. As well, the improved functional ability and feeling of well-being, whether a result of true circulatory improvement, improved muscle capacity or increased patient motivation and enthusiasm, can be of enormous psychological benefit to PAD patients, many of whom experience the sense of hopelessness and frustration that commonly accompanies chronic progressive disease. Although in this study it was not possible for a number of reasons, including both study design and insufficient subjects, to differentiate between the effects of diet and other lifestyle factors, it is evident that an improved sense of well-being and an increased functional improvement can result from a conservative therapeutic regimen.

Therefore, it is concluded that the health professional has an obligation to ensure that the patient has an understanding of the disease and its contributing factors. The nurse is in an ideal position to encourage the patient to take an active role in combatting his disease through

risk factor intervention programs. In this study, as subjects in both groups experienced a small alteration in blood lipids and a definite functional improvement, it would appear that the AHA diet and the HF diet, both coupled with regular exercise, are equally effective therapeutic regimens. Definitive evidence awaits further research.

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APPENDIX A

CONSENT FORMS

UNIVERSITY OF ALBERTA HOSPITAL

CONSENT TO PARTICIPATE IN A STUDY

PATIENT _____ DATE _____ TIME _____

1. I agree to participate in an investigation and in relation to this hereby authorize Dr. _____ and/or such assistants as may be selected by him, to perform the following procedure(s):

_____

_____

_____

2. Dr. _____ has explained the purpose of this study and I understand this, the risks involved and the nature of the procedure(s) outlined in Paragraph 1. (Where pertinent a typed sheet detailing this should be prepared by the Investigator and attached to this form.)

3. I acknowledge that no guarantees have been made to me as to the results of the treatment.

_____ _____

Witness Signature of Patient

_____

If the patient is unable to sign or is under 18 years of age, complete the following:

The patient is a minor (_____ years of age).

or

The patient is unable to sign because _____

As the closest relative or legal guardian I hereby sign on his/her behalf:

_____ _____ _____

Witness Signature Relationship

UH-171 (Non-Surgical)

PERIPHERAL VASCULAR DISEASE STUDY

Assessment of arterial disease in this study requires a number of non-invasive physiological measurements. Blood pressure will be measured using an ultrasonic flowmeter before and after exercise on a treadmill. The exercise period will be limited by pain in the legs or by the achievement of submaximal heart rates. The risks of heart problems associated with this level of exercise are rare. However, if they should occur, treatment is immediately available.

Blood flow waveforms will be obtained using u[illegible]ound. Risks associated with this non-invasive measurement are negligible.

I consent voluntarily to these tests which have been fully explained to me.

Signed _____

Witness _____

Date _____

CONSENT FORM

PERIPHERAL VASCULAR DISEASE STUDY

I, the undersigned _____ hereby request Dr. Ken Hutchison and Dr. Gordon Brown and their associates to arrange a trial for me involving careful dietary treatment, which has been recommended in controlling blood vessel disease in the limbs.

I agree to participate in the study to determine the effect of one or other of two special diets, each of which has been designed, but not proven, to lessen the effects of blood vessel disease.

I understand that the diet selected for me may or may not be helpful. I understand that there is no conclusive evidence that either diet is harmful for a patient under careful observation during the trial period.

I understand that some laboratory tests will be required and I understand that not all of these will be necessary for the care of my condition.

The following blood tests will be determined initially, at one and then at 2, 4, 6 and 12 month intervals: cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol.

I understand that withdrawal from this study will be permitted at any time without malice or interference by the physicians and their assistants.

I understand that a reasonable amount of time will be required to assess whether or not, one or other of the diets, is effective.

Date_____ _____

(Patient's signature)

_____

(Witness)

APPENDIX B

EXERCISE AND SMOKING QUESTIONNAIRE

EXERCISE AND SMOKING ASSESSMENT

NAME -

DATE -

EXERCISE:

Do you exercise regularly?

How often?

Type of exercise, e.g. walking, cycling?

How far?

How long?

Have you noticed any changes in your ability to exercise since the study began?

SMOKING:

FIRST VISIT:

Do you smoke? - Never_____

Ex-smoker_____

Smoker - since when?_____

no. of cigarettes/day_____

other (cigars, pipe, etc.)_____

Does anyone in your residence smoke?

Do others smoke where you work?

SUBSEQUENT VISITS:

Do you smoke now?

If yes, how much (cigarettes or other/day)?

Does anyone in your residence smoke?

Do others smoke where you work?