

THE EFFECT OF MODERATE EXERCISE ON  
STORED BODY IRON  
IN POST-MENOPAUSAL WOMEN

By

Sylvia Oosterveen

A Thesis submitted to  
the Faculty of Graduate Studies  
in Partial Fulfillment of the Requirements  
for the Degree of Master of Nursing

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## ABSTRACT

The relationship between serum ferritin and exercise in post-menopausal women in Manitoba was studied. Exercise has been identified in epidemiological studies as having an independent role in the primary prevention of coronary artery disease. One mechanism to explain the association is exercise-induced reductions in iron either through iron loss or enhanced iron storage. The purpose of this study was to determine the effect of a moderate intensity 24 week walking program on serum ferritin values in sedentary, healthy post-menopausal females. Subjects (mean age 62 years) were randomly selected into non-walkers (control n=25) three day walkers (n=27) and five day walkers (n=27). There was no significant difference in pre-exercise mean serum ferritin values between the three groups. Statistically significant differences were noted in serum ferritin levels for post-menopausal women who exercised regularly (60 minutes five times per week) compared to their sedentary counterparts. No significant differences were noted in the group walking three times per week. This study demonstrates that moderate regular exercise five times per week is associated with a decrease in serum ferritin levels, suggestive of a further basis for the prevention of cardiovascular disease in a vulnerable segment of the population.

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DEDICATION

This thesis is dedicated to the memory of my mother and  
to the future research of women and heart disease.

To my father who has always given me  
love and support in all that I do

and finally, this thesis is dedicated to  
my loving daughter, Julia  
who gives me endless joy and emotional support.

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## LIST OF ABBREVIATIONS

BMI:	Body mass index
WT:	Weight
WHR:	Waist to hip ratio
SE FERRITIN:	Serum ferritin
LOG OF FERRITIN:	Log transformation of serum ferritin
VO2 max:	Maximum oxygen uptake expressed in weight relative units (ml/Kg/min) or in absolute values (L/min)
ml/Kg/min:	Milliliters per kilogram per minute
L/min:	liters per minute
HGB:	Hemoglobin measured in grams per liter
HCT:	Hematocrit measured in international Units per liter
CVD:	Cardiovascular disease
IHD:	Ischemic heart disease
LDL:	Low density lipid cholesterol

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## CHAPTER ONE: INTRODUCTION

### 1.1 Background to the Problem

In Canada, rates of cardiovascular disease (CVD) and its major component ischemic heart disease (IHD), are higher than in other industrialized countries, such as France and Japan (Minister of Supply and Services Canada, 1992; Statistics Canada, 1991; Sullivan, 1989). Figures released by Statistics Canada in November, 1993 show that CVD is the leading cause of death, accounting for 39% of all deaths in Canada in 1991 (see Figure 1). This translates into over 75,000 annual CVD deaths for both sexes (Nair, Colburn, McLean and Petrasovites, 1991; Heart and Stroke Foundation of Canada, 1994). Although there is a yearly decline in CVD mortality rates, IHD remains the main cause of premature death in Canadians and one of the major causes of disability prior to age 65. After age 65, IHD is the major cause of death (Minister of Supply and Services Canada, 1992; Canadian Press, November 1993).

For the past three decades IHD has been considered a disease afflicting only the male population, when in fact the incidence of IHD rises steadily in both men and women as they age (Fields and Toffler, 1993). Heart disease and stroke accounted for 41% of all female deaths in Canada in 1991. A woman's risk for CVD increases progressively during her lifetime and rises dramatically in her post-menopausal

years (Campaigne, 1994; Statistics Canada, 1991). The results of the Framingham Study, a famous and large epidemiological prospective study of heart disease, indicated that post-menopausal women 45-54 years of age had 2.7 times the incidence of IHD compared to pre-menopausal women of the same age (Gordon, Kannel, Hjortland and McNamara, 1978). Scientific knowledge gained in the last 30 years has shown that traditional risk factors for IHD i.e. smoking, hypertension, elevated blood cholesterol and inactivity, apply equally to both men and women (Health and Welfare Canada, 1992; Powell, 1987; American Heart Association, 1993). Recently, it has been suggested that there is a link between stored body iron and coronary heart disease. It is hypothesized that iron may increase the risk of IHD by promoting the formation of free radicals and the modification of low density lipid cholesterol (LDL) contributing to the pathogenesis of atherosclerosis. The relationship between high iron stores and heart disease was first suggested by Sullivan in 1981 to explain the sex difference in heart disease risk. High levels of stored iron measured as serum ferritin apparently increase the risk of heart disease in males (Salonen, 1992). In contrast to the previous theory that endogenous estrogens protect women from myocardial infarction, it has been suggested that the increased incidence of IHD in post-menopausal women may be

due to increased stored iron associated with the cessation of menses (Lauffer, 1990; Sullivan, 1991).

A recent prospective three year study of 1,931 Eastern Finnish men supports the "Iron Hypothesis". In this study, men with serum ferritin levels greater than 200 ug/L had a 2.2 fold greater risk of acute myocardial infarction than men with lower serum ferritin levels. A one percent increase in the level of serum ferritin was associated with a 4% increase in the risk of myocardial infarction (Salonen, Nyssonen, Korpela, Tuomilehto, Seppanen and Salonen, 1992).

Physical exercise is a crucial element of health promotion and there is increasing evidence of its effectiveness in enhancing well-being, physical abilities, bone density and in reducing IHD risk factors (Ebrahim and Williams, 1992). There is also evidence in the literature to suggest that regular physical exercise promotes iron excretion (Lauffer, 1991, Salonen et al., 1990). It is thought that regular exercise may be protective in part because of increased iron loss through the gastrointestinal tract and in sweat (Lauffer, 1991; Salonen et al., 1992). There is evidence that there are higher levels of serum ferritin in post-menopausal women who do not exercise compared to post-menopausal women who do exercise (Bartfay, 1993). The amount of exercise necessary to decrease serum ferritin levels is unclear at this time. Most of the research to date has been done on males and it has been

suggested that further research should be done involving post-menopausal women to determine the validity of the iron hypothesis and the role of exercise as it pertains to iron levels (Sullivan, 1991; Lauffer, 1993). If it is confirmed that iron is a risk factor for IHD, there may be new implications for health promotion strategies.

## **1.2 Research Question**

The purpose of this study was to determine the effect of a moderate intensity six month walking program on stored body iron, measured as serum ferritin values in sedentary but otherwise healthy (no cardiovascular, pulmonary, or metabolic diseases) post-menopausal women. Specifically the study was designed to provide basic information to determine if a six month walking program would lower the level of stored body iron in post-menopausal women and, to compare the effect of walking 60 minutes per day, three times per week vs five times per week at an equivalent intensity of 60%max VO<sub>2</sub>.

## **1.3 Hypotheses**

1. Walking for 60 minutes at 60-70 % VO<sub>2</sub> max three days per week for 24 weeks will significantly lower levels of stored body iron (as measured by serum ferritin levels) compared to the control group.

2. Walking for 60 minutes at 60-70 % five days a week for 24 weeks will significantly decrease stored body iron more so than walking three days per week.

#### 1.4 Definition of Major Terms

(1) **Post-menopausal women**: For the purposes of this study, post-menopausal will include all women who had their last menstrual period 12 or more months ago. This includes naturally occurring menopause as well as surgically induced menopause and is characterized by the end of ovarian activity (Harper, 1991).

(2) **Ferritin**: The majority of body iron is present in hemoglobin, myoglobin and tissue enzymes. Approximately 30% of body iron is stored as the protein ferritin in various organs and body tissues. When the quantity of iron in the plasma falls, iron is removed from ferritin and transported to portions of the body where it is needed. The level of stored body iron is estimated by serum ferritin measurements.

(3) **Non-heme iron**: is sometimes called vegetal iron and comes from cereals, fruits, vegetables, eggs and iron supplements (Bource, 1981). It is an inorganic form of dietary iron and is not readily absorbed in the small intestine.

(4) **Heme iron**: A form of dietary iron that comes from animal tissues (i.e. beef, pork, lamb, liver, kidney, heart,

fish and veal) and is readily absorbed in the small intestine. The proportion of heme iron absorbed from our diet is high in comparison with non-heme iron (Bjorn-Ramussen, Hallberg, Isaksson and Arvidsson, 1974; Ledoux, 1992). About 1/3 of the iron consumed by humans is from animal tissue and its absorption is higher than inorganic iron as a source (Bource, 1981).

**5) Sedentary lifestyle:** For the purposes of this study, sedentary lifestyle will refer to lack of regular exercise i.e. not walking for more than 15 minutes, 2 days a week at a brisk pace or aquacise, badminton, exercise bicycle more than once a week, during the past year.

**(6) Cardiovascular disease:** Includes all diseases of the heart and blood vessels, the most common being ischemic heart disease (IHD).

**(7) Ischemic heart disease:** Refers to cardiac disease of diverse etiology with the common factor being an imbalance between myocardial oxygen supply and demand. IHD is most often due to atherosclerotic obstruction of large coronary arteries (Petersdorf, Adams, Braunwald, Isselacher, Martin and Wilson, 1992).

**(8) VO2 max:** Refers to the maximal amount of oxygen the body can use and may be expressed in (ml per Kg of body weight per minute or L per min). There can be as much as 20% difference between active and sedentary people at any given age, causing an active 60 year old to be in better

condition than a sedentary 40 year old (Pate et al., 1991). The VO<sub>2</sub> max can decrease by 1% a year in the general population due to an aging process and a decrease in physical activity (Rohan, 1994). Increasing physical activity can affect changes in VO<sub>2</sub> max as well as increases or decreases in body composition, body mass index and percent fat composition. Most sedentary, healthy individuals can begin a moderate and progressive exercise program such as walking at an exercise intensity of 40 to 60% of maximal oxygen uptake (VO<sub>2</sub> max) (Pate et al., 1991).

(9) **Free radicals**: Highly reactive oxygen molecules produced by enzymatic oxidation. Free radicals have been implicated as important pathologic mediators in many clinical disorders including IHD by damaging compounds of all biochemical classes. Among some causes of proliferation of oxygenated free radicals are smoking and passive smoke, radiation from sunlight, toxic pesticides or herbicides, infection, stress, alcohol and possibly high levels of stored body iron.

(10) **Antioxidants**: Antioxidants, sometimes referred to as free radical scavengers, help the body get rid of free radicals by inhibiting cell mediated oxidation of LDL thereby reducing cellular damage in the heart.

### 1.5 Conceptual Framework

The theoretical perspective of this study was grounded in the role of pathophysiology of cardiovascular disease and the effects of stored body iron as a possible risk factor for heart disease.

### 1.6 Summary

Cardiovascular disease is the leading cause of death in women in Canada. It was long thought to be only a disease affecting men, but CVD accounts for 43% of female deaths in Canada (Heart and Stroke Foundation, 1994). It is obviously a condition that affects women, especially as they grow older. A review of the literature suggests that high levels of stored iron may be a risk factor for heart disease (Salonen et al., 1992; Monsen, 1992) and that heart disease may be lowered with iron depletion (Sullivan, 1989). It has also been suggested that exercise may lead to lower levels of serum ferritin in post-menopausal women. The studies relating the relationship between exercise and iron excretion have been carried out primarily in males or in young athletes and ballerinas (Blum, Sherman and Boileau, 1986; Lauffer, 1991; Taylor, Rogers, Goodman, Baynes, Bothwell, Benswoda, Kramer and Hattingh, 1987; Salonen et al., 1992; Fields and Toffler, 1993; Douglas, 1986). Little research has been directed towards the change in iron status resulting from an exercise program specifically in post-



menopausal women. In a recent study by Bartfay (1993), it was determined that post-menopausal women who reported that they exercised regularly had lower serum ferritin levels, however no attempt was made to quantify the amount of exercise. Considering that lack of exercise may be a potential health liability, and may be associated with elevated stored body iron levels, it is of considerable interest to determine the amount of exercise needed to reduce the serum iron level in post-menopausal women.

This study proposes to extend the existing areas of research related to iron by examining the relationship between serum ferritin and exercise in post-menopausal women.

## CHAPTER TWO: REVIEW OF THE LITERATURE

### 2.1 Introduction

Life expectancy of Canadians has increased by 25 years during the last two decades (Nachtigall, 1990). It is projected that by the year 2000, there will be 3,866,200 people in Canada over 65 years of age and 2,264,800 of them will be women (Statistics Canada, 1989). Despite the increasing life expectancy, there has been very little research done to investigate the health, lifestyle and longevity of post-menopausal women. Most of the literature describes a predominantly male population, and the findings are very often generalized to include women. Women generally live approximately 7 years longer than men, and as a result of this increased longevity, women can expect to live nearly one third of their lives after menopause (Fishbein, 1992).

There is a stereotypical image attached to post-menopausal women who are often seen as high users of health care, visiting physicians with complaints of a broad range of vague symptoms. Although menopause itself does not cause an increase in medical utilization, nor does it cause poorer health status, post-menopausal women are prone to major age-related diseases such as IHD (McKinlay, J., McKinlay, S., and Branbilla, 1987). Post-menopausal women have a high incidence of angina. Although men have a high incidence of

myocardial infarction, women experiencing myocardial infarctions have a higher rate of mortality than men.

## **2.2 Cardiovascular Disease**

Some risk factors for IHD are categorized as modifiable and include smoking, high cholesterol, hypertension, inactivity and a sedentary lifestyle, obesity, psychosocial factors and diabetes. Non-modifiable risk factors include gender, age, menopause, family history and race. Since IHD is the primary cause of mortality in older women, knowledge of risk factors is an essential part of health promotion.

A report produced by the Manitoba Heart Health Survey (MHHS) (Gelskey, Macdonald and Young, 1991) indicates that sixty-three percent of all Manitobans have at least one of the three major modifiable risk factors for IHD (high blood pressure, smoking and high blood cholesterol). In the case of Manitoba females, MHHS indicated that three-quarters of cardiovascular deaths can be "attributed" to smoking, high blood pressure, high blood cholesterol and diabetes (Gelskey et al., 1991).

### 2.2.0 Risk Factors

Common risk factors that have been identified in the literature are briefly described below:

#### **Modifiable Risk Factors**

**Smoking:** is a major cause of heart disease. It is also a preventable cause of IHD and has a synergistic effect in conjunction with other risk factors (Cunningham, 1992; Willett, Stampfer, Bain, Lipnick, Spelzer, Rosner, Cramer and Hennekens, 1983). Smoking and passive smoke trigger the chain reaction of free radicals eventually destroying cell membranes and creating mutant cells. Smoking increases the susceptibility of lipids to peroxidative modification and enhanced metabolism by macrophages thereby contributing to coronary heart disease (Harats, Ben-Naim, Dabach, Hollander, and Stein, 1989). Women who smoke tend to go through menopause earlier than non-smoking women (Matthews, Meilahn, Kuller, Kelsey, Caggiula and Wing, 1989).

**Cholesterol:** Blood cholesterol levels below 5.2 mmol/L are considered desirable whereas levels above 6.2 mmol/L are considered to be in the "high risk" range. In Manitoba, 50% of women between the ages of 35 and 64 have moderate to high levels of cholesterol (Gelskey, Macdonald and Young, 1991). Cholesterol levels should be measured in conjunction with triglycerides, low density lipoproteins and high density lipoproteins. Low-density lipoprotein (LDL) is made

primarily of cholesterol and has the greatest atherogenic potential. High-density lipoproteins (HDL) help to remove excess cholesterol, hence may protect against IHD (Gelskey, Macdonald and Young, 1991; Horlick, 1991). Studies have found that plasma levels of total cholesterol, low-density lipoprotein cholesterol and triglyceride are all positively associated with the incidence of IHD, whereas there is an inverse relationship between disease incidence and HDL (Cunningham, 1992). Studies of risk factors for coronary artery disease suggest that post-menopausal women have a higher risk of IHD than pre-menopausal women and that they also have a higher level of total cholesterol and triglycerides (Matthews, 1989; Hjortland et al., 1976). The Framingham study published data which indicated that lowering serum cholesterol levels in individuals would greatly reduce the risk of heart disease (Castelli, 1986; Heiss et al., 1980).

**Hypertension:** Elevations in systolic and diastolic blood pressure ( $\geq 140$  mmHg systolic,  $\geq 90$  mmHg diastolic) are directly related to increased morbidity and mortality from heart disease and stroke (Stamler, 1989).

Lifestyle modifications to lower blood pressure include medications, diet and proper nutrition, sodium restriction, exercise and weight loss (Hopkins and Williams, 1981).

**Sedentary lifestyle:** A sedentary lifestyle has been shown to be positively correlated with increasing risk of

morbidity and mortality from IHD even after adjustment for other risk factors (Dawber, 1980; Paffenbarger et al., 1986; Salonen et al., 1988; Oberman, 1985). Other studies have shown that physical activity is universally related to blood pressure, weight, cholesterol and blood glucose (Hagberg, Montain and Martin, 1989; Hubert, Eaker and Garrison, 1987). Data from the Manitoba Heart Health Survey (1991), demonstrated that approximately 50 percent of Manitobans are sedentary. Reasons for not exercising include lack of incentives (40%), lack of time (34%) and lack of exercise partners (22%).

**Obesity:** Obesity increases the potential risk factor of coronary heart disease, however being thin does not necessarily serve as an automatic protective factor if high cholesterol, smoking and a sedentary lifestyle are major factors.

Body mass index (BMI), (weight in kilograms divided by height in meters squared) is used as a measure of overweightedness. Overweightedness is defined as a BMI of 25-27 and obesity as a BMI over 27 (Cunningham, 1992). Data from various studies show that as the BMI increases, the risk of IHD increases significantly (Manson, 1990; MHHS, 1991; Hubert, 1987; Rabkin, Mathewson and Hsu, 1977). Data from the Manitoba Heart Health survey (1991), indicated that two in five Manitobans are considered obese (BMI greater than to 27).

**Diabetes:** Diabetes has been shown to be associated with an increased incidence of heart disease, particularly in women (Abbott, 1987; Fuller et al., 1980; Wilson, 1990). Prior to menopause women are generally protected from coronary artery disease but this is not the case in women with diabetes. The Framingham study showed diabetic women have a five times greater risk of IHD than non-diabetic women (Garci, 1974). Modifiable lifestyle changes to control diabetes include proper nutrition and diet, weight control, compliance with medication regimen and regular exercise.

**Alcohol intake:** There is a relationship between excess alcohol consumption and IHD. There is a positive correlation between daily consumption of alcohol and the concentration of ferritin in serum among healthy men with no evidence of liver disease (Leggett, Brown, Bryant, Duplock, Powell, and Halliday, 1990). The Framingham study, showed that excess alcohol intake was positively associated with increase in blood pressure levels in both men and women (Hubert, 1987). However, other studies have suggested that moderate alcohol consumption on a regular basis, has a beneficial effect in reducing the risk of myocardial infarction (Heart and Stroke Foundation, 1994).

**Psychosocial and Socioeconomic Factors:** Stress and poor coping mechanisms have been associated with IHD and have been identified as a trigger for sudden death (Gomez,

1984). Type A personality has in the past been identified as a possible risk factor for heart disease, however recent evidence suggests that individuals with type A behavior may survive longer following a cardiovascular event because they have more adaptive coping mechanisms. Socioeconomic status, educational status, income, unemployment have all been associated with a higher cardiovascular risk profile (MHHS, 1991; Kraus, 1980; Lui, 1982; Pieper, 1989). Stress management and behavior change are a few of the many lifestyle modifications required to promote health and prevent IHD.

#### **Non-Modifiable Risk Factors**

**Sex and Age:** At younger ages, more men develop IHD than women (highest risk is 40-55 years). After about age 50, women are as likely to develop heart disease as men (Nurse Review, 1986; MacMahon, 1986) and the odds of developing IHD increases with the aging process. In both men and women aging is associated with higher levels of blood pressure, increasing levels of LDL, a more sedentary lifestyle, weight gain and decreased muscle tone.

**Family history:** It is well known that there is genetic predisposition to developing IHD in certain families (Becker, 1987; Khaw, 1986; Hopkins and Williams, 1981).

**Menopause:** Studies have shown that following menopause, the incidence of IHD increases (Gordon et al.,



1978; Snowdon, 1989; Colditz, Walter, Willett, Stampfer, Rosner, Speizer and Hennekens, 1987; Stampfer, Colditz, Walter and Willett, 1985; Weinstein, Bewtra and Gallagher, 1990; Stampfer, Graham, Colditz, Walter and Willett, 1990).

Data from the Framingham study show the incidence of cardiovascular disease in women to be three times lower than in men prior to menopause and approximately equal to men in later years (Douglas, 1993; Murdaugh, 1990). There is also data to support an increase in risk of myocardial infarction two to threefold in premature menopause and sevenfold in surgically induced menopause, including oophorectomy (Douglas, 1993). Women with surgical menopause even without oophorectomy are also at a higher risk for IHD than are premenopausal women (Stampfer et al., 1990; Colditz et al., 1987; Rosenberg, Hennekend, Rosner, Belanger, Rothman and Speizer, 1981; Gordon, et al., 1978). There are no conclusive explanations why this increase in risk occurs, although it has been suggested that the increased rate of IHD may be due to estrogen deficiency. The Framingham study indicated 15% of post-menopausal women used replacement estrogen. Initially the risk of IHD was not improved in this group (Colditz et al., 1987; Gordon et al., 1978). However in a re-analysis of the data, in women 50-59 years of age, estrogen replacement was found to have a protective effect (Eaker and Castelli, 1986).

### 2.2.1 Iron As A Possible Risk Factor

High levels of iron as an independent risk factor for IHD is suggested in a number of studies (Magnussen, 1994; Sullivan, 1991; Salonen, Nyyssonen, Korpela, Tuomilehto, Seppanen and Salonen, 1992). As early as 1981, Sullivan observed that myocardial failure frequently occurred in patients with hemochromatosis, a disease in which there is an inappropriate increase in intestinal absorption of iron. He also observed that accumulation of stored iron increased with age in men; and after menopause the accumulation of stored iron in women approximated levels found in men (Sullivan, 1981; 1989).

Salonen (1992) studied 1,931 Eastern Finnish men over an eight year period. This study showed that men who had high levels of stored body iron as measured by serum ferritin had a significant 2.2 fold greater risk of acute myocardial infarction than men with lower levels of stored body iron. Similarly, a cross sectional study showed evidence that stored iron (measured by serum ferritin) was twice as high in post-menopausal women, compared to pre-menopausal women (Bartfay, 1993).

In the Framingham study, where 2,873 women were followed for 24 years, it was found that the incidence of heart disease increased in all women whether natural or surgical menopause had occurred, and whether ovaries were

removed or not (Sullivan, 1981). Sullivan (1981) argued against the hypothesis that lack of estrogen accounted for the increase in prevalence of CAD in post-menopausal women because there was evidence that following simple hysterectomy in pre-menopausal women, myocardial infarction incidence went up even with continued ovarian function and estrogen production. Therefore, despite estrogen production, the protection against heart disease was not seen (Sullivan, 1981). The influence of estrogen on the risk of CAD has been a controversial issue for many years. Although there are studies showing the potentially beneficial effects of estrogen replacement on CAD risk factors (Sullivan et al., 1988; Stampfer et al., 1991), the trend of estrogen replacement therapy is decreasing in recent years due to its association with endometrial carcinoma and strokes.

Recently it has been proposed that iron status may be a contributing factor to understanding the gender difference in death rates from heart disease. It is believed that regular menstrual blood loss resulting in lower iron levels in pre-menopausal women is the protective factor, rather than the estrogen levels alone (McCord, 1991; Sullivan, 1981; 1989). Support for the "iron hypothesis" is added by the finding that multiple and frequent blood transfusions given to anemic children cause a build-up of iron in the recipient's body. The build-up of iron causes the children

to die of heart failure in their mid to late teens unless the excess iron is removed (Crichton, 1971).

It has been postulated that iron plays a role in coronary artery disease through an oxidative modification of low density lipoproteins (LDL) and acting as a catalyst for oxygen free radical induced tissue damage (Lauffer, 1990). The iron causing oxidation of LDL occurs mostly in the subendothelial layer of the arteries where atherosclerosis is prone to develop. Since serum ferritin reflects the iron stores in the body, high ferritin is theorized to reflect a state of increased pathogenicity (Salonen et al., 1992; Magnusson et al., 1994). Salonen et al. (1992) found a synergistic association between serum ferritin and LDL cholesterol concentrations creating a risk for acute myocardial infarction. This supports the theory that iron overload increases the risk of myocardial infarction through promotion of oxidation of LDL cholesterol.

The identification of iron overload as a possible risk factor is important because it is a modifiable factor for those at risk such as men and post-menopausal women. Sullivan (1981) suggested that donation of blood three times a year would lower a man's serum ferritin level to that of a young woman and would therefore reduce his risk of IHD. "The finding that ferritin is a strong heart disease risk factor is especially relevant to the hypothesis that low iron stores protect young women from heart disease"

(Sullivan, 1992, p.1037). Most studies have excluded women, therefore further research involving women is necessary to establish stored body iron as a risk factor for IHD in women (Sullivan, 1992).

### **2.3 Iron Physiology: Function and Distribution**

Iron is found in the hemoglobin of red blood cells that are used to carry oxygen from the lungs to the tissues. Iron is also found in the muscle cells in the form of myoglobin and is an essential nutrient for humans (Herbert, 1987). Iron in myoglobin is used to store the oxygen necessary for muscle contraction. Iron is also found in plasma, being transported from place to place in the body by the carrier plasma protein transferrin. Iron is also present in certain tissue enzymes which help to oxidize carbohydrates, proteins and fats for energy metabolism (Bource, 1981).

Approximately 1 mg of iron is excreted daily in men and non-menstruating females and the rest is stored in the body as ferritin (Petersdorf et al., 1982). Iron metabolism occurs in such a way that body iron is conserved, so that the iron of hemoglobin degradation is continually re-utilized for erythropoiesis and stored iron is readily mobilized in response to increased demand. The amount of body iron present is largely dependent on the absorption in

the gut which is affected by diet and gastrointestinal secretions.

### 2.3.0 Absorption, Storage, Transport, Excretion

The primary site of iron absorption is in the duodenum and jejunum, however the amount of absorption depends on the bioavailability of dietary iron and is controlled by the gut mucosal "setting" (Petersdorf et al., 1982). Some factors in the gut affecting the absorption of iron are listed in Table 1 (Hughes, 1978).

**Table 1. Iron Absorption**

decreased by	increased by
phosphates	gastric juice
phytates	HCL
other metals (zinc, copper, manganese)	ascorbic acid
gastric and pancreatic	citric acid
iron-binding factors	fructose
	Heme complexes

Disturbance of the absorption of iron in the intestine is due to the competitive binding for the transport and storage proteins in the mucosal cell and also in the mucosal uptake of dietary iron (Bource, 1981; Hughes, 1978). Once the iron has been absorbed, it can remain in the intestinal mucosal cell in the form of storage iron, or it is transported to the blood where it binds to the plasma transport protein, transferrin (Hughes, 1978). The majority of our body iron is present in circulating hemoglobin which

contains over 2/3 of the total body iron. Although we are born with only 300 mg, it is estimated that as adults we hold 3 to 4 grams of total body iron (Crichton, 1971). Absorption depends on a sufficient quantity and quality of dietary iron, the correct physiochemical composition, absorptive cells in the small intestine, balanced intestinal secretions and intestinal motility (Bource, 1981).

Normally, very little iron is excreted, (approximately 1 mg/day), the majority through feces, and trace amounts through urine, hair, nails, sweat and skin cells (Hughes, 1981). The iron in the body is reused over and over again in a very efficient way and the functional iron as well as the stored iron is regulated through absorption (Stare and McWilliams, 1984; Hughes, 1981). Normally if the blood iron is low, the body absorbs more dietary iron, if iron levels are higher than normal, there is decreased absorption through the bowel.

All iron is bound to proteins with about 2/3 of it found in hemoglobin, smaller amounts in myoglobin, various enzymes and in transport as transferrin. The rest of the iron that is not immediately required is stored in ferritin (Salonen, 1992). Ferritin, in a sense, plays a "housekeeping" role in iron metabolism and provides iron when needed for growth or metabolic requirement (Beard, 1992).

There is an inverse relationship between the iron stores and the percentage actually absorbed, hence the higher the iron stores, the lower the percentage of iron absorbed (Monsen et al., 1978; Cook et al., 1974). Normal absorption of iron is regulated by the intestinal mucosa in accordance with the body needs (Cooke and Monsen, 1977). An abnormality in the mucosal tissues can cause excessive absorption (Finch, 1982). As a positive iron balance occurs, tissue storage pools of iron gradually increase. This causes a stimulus for apoferritin synthesis and subsequent increase in tissue and plasma ferritin levels, so the absorption of dietary iron decreases proportionally (Beard, 1992). In pre-menopausal women the amount absorbed varies and is dependent on the amount of iron lost during menstruation (Monsen et al., 1978).

### **2.3.1 Prevention of Absorption**

The absorption of non-heme iron decreases with age. Substances which inhibit iron absorption are phytate, phosphates, carbonates and strong chelating agents such as desferrioxamine (Cook and Monsen, 1975).

Dietary factors that decrease iron absorption are high fiber diets, high alkaline foods, milk and other dairy products, antioxidants and food preservatives (Bodinsky, 1987; Stare and McWilliams, 1984). One study showed iron



absorption to be reduced by about 52% when an antacid was given to subjects (Skine, 1981).

#### **2.4 Serum Ferritin**

Serum ferritin is a reliable and sensitive indicator for the assessment of body iron stores (Cook et al., 1974; Finch, 1982; Basset, 1979). Ferritin levels depend on tissue iron stores as well as on the rate of release of ferritin from the tissues. It acts as a type of body guard in iron metabolism, providing iron during periods of developmental growth and for metabolic requirements. An increased amount of iron in the cells will increase gene expression and exert regulatory control through an iron response element (Beard, 1992).

Although it is known that serum iron values may have analytical variability due to environmental contamination and hemolysis of red blood cells, the intra-individual day to day variability for serum ferritin is <15% (Salonen et al., 1992). The validity of serum ferritin has been questioned by some researchers because of intraindividual variability. Serum Ferritin values may at times show incorrect results, however there is usually a good explanation. An illness accompanied with a fever or inflammation of any kind may temporarily cause falsely elevated values for a few days to a few weeks (Wands, 1976; Risser, Risser and Goldberg, 1990).

Studies have shown that there is a significant positive correlation between serum ferritin and age in males and females; and a significant inverse relationship between serum ferritin and total iron binding capacity (TIBC) in females and males (Cook et al., 1974). There are differences reported in the literature in the mean serum ferritin values for females pre-menopause and post-menopause. Serum ferritin values increase with age in females over 40 years old (Vincente, Porto, de Sousa, 1990). A possible explanation for the increase in ferritin levels in older females could be the cessation of regular menstrual blood loss.

In male subjects, serum ferritin values over 200-300 ug/L indicates that some pathological process is present. Lethal iron levels as seen in hemochromatosis are approximately 200-400 mg/kg body weight or a serum ferritin concentration above 800-1000 ug/L (Halliday, 1982; Beard, 1992; Finch, 1982). The finding of low ferritin levels usually indicates iron deficiency. However, serum ferritin values may underestimate iron store in some patients with early hemochromatosis (Peterdorf et al., 1983).

Salonen and co-researchers (1992) concluded that the iron released from ferritin plays a causal role in the oxidative pathogenesis of cardiovascular disease (Beard, 1992).

#### **2.4.0 Hemoglobin and Hematocrit**

Serum iron levels may be low and hemoglobin and hematocrit can be normal in the presence of very high levels of stored iron (Salonen et al., 1992; Wilson et al., 1991). A hemoglobin value alone is not a good indicator of stored iron status in the body. As mentioned earlier, hemoglobin and hematocrit values could stay essentially unchanged while serum iron, TIBC and transferrin are elevated (Norrby, 1972).

#### **2.5 Iron: Dietary Sources**

The amount of iron that the body absorbs is dependent on the availability of heme and non-heme iron ingested from the diet (Nutrition Reviews, 1986). The recommended dietary allowance of iron is 18 mg/day (approximately 10% is absorbed) (National Research Council, 1974). As stated above, the amount of iron that is available from foods depends largely on the composition of the foods eaten together as well as the amount of iron supplied (Monsen, 1978; Nutrition Reviews, 1986). Eating a meal which includes beef, lamb, chicken or pork would raise the rate of non-heme iron absorption, while consuming milk, cheese, and eggs lowers the absorption of non-heme iron (Monsen, 1978). Certain substances in foods (tannic acid in tea, phosvitin of egg yolk, calcium and phosphate salts, EDTA preservative, and antacids) will suppress iron absorption (Disler et al.,

1975; Moore et al., 1951; Bjorn-Rasmussen, 1974; Monsen et al., 1976; Cook et al., 1976). Other dietary components such as oxalic acid have been reported to show enhancement of the bioavailability of iron from spinach (Van Campen and Welch, 1980; Nutrition Reviews, 1986). Studies indicate that iron availability from a diet is not necessarily the sum of iron absorption from individual meals (Nutrition Reviews, 1986). Table 2 lists the variation in iron content in foods.

**Table 2. Dietary Iron**

High content	Moderate content	Low content
Organ meat: liver, heart, kidney	muscle meat fish poultry	milk products white flour potatoes
egg yolk dried legumes cocoa shell fish	nuts green vegetables whole wheat flour cereal grains	fresh fruits

### 2.5.0 Vitamin C

In a study conducted by Cook and Monsen (1977), where 200 multiple radioiron absorption tests were performed in 63 male subjects, it was found that vitamin C, if taken with meals increased the iron absorption threefold. Other studies have supported the finding that absorption of non-heme iron is greatly enhanced by ingestion of vitamin C (Stare and McWilliams, 1984; Herbert, 1992; Monsen et al., 1978; Cook and Monsen, 1975; Nutrition Reviews 1987). Not

only does Vitamin C enhance iron absorption, but it also increases intracellular metabolism of iron-binding proteins (Nutrition Review, 1987). An average intake of 280 mg of vitamin C will increase iron absorption approximately fivefold. As little as 25 mg of Vitamin C can almost double the amount of dietary iron absorption and larger amounts of ascorbic acid will produce a progressive rise in iron absorption (Cook and Monsen, 1977).

Vitamin C may actually prove harmful in individuals who are not able to regulate iron absorption as in hemochromatosis and certain anemias (Cook and Monsen, 1977).

#### **2.5.1 Alcohol**

The amount of iron that is deposited in body organs is dependent on factors such as alcohol intake. Studies indicate that alcohol consumed with meals will increase iron absorption (Stare and McWilliams, 1984; Nutrition Reviews, 1980). Large amounts of alcohol consumption are known to cause disturbances to iron homeostasis and are associated with elevated levels of serum ferritin (Williams and Caliendo, 1984).

#### **2.5.2 Method of Preparation**

The method of preparing food can affect the availability of iron at the point of ingestion i.e. steamed

vegetables cooked for a short time will allow the iron to be retained (Stare and McWilliams, 1984).

The type of cooking pot also has an effect on iron content of foods. For example, cooking spaghetti in a ceramic pot will provide 3 mg of iron whereas cooking an egg in an iron pot will increase the iron content to 87 mg (Bodinski, 1987; Hamilton and Whitney, 1982). Bantu siderosis, a pathological form of acquired iron overload may occur where a combination of foods prepared in iron cooking pots and home-brewed beer are consumed. (Nutrition Reviews, 1990). Heating inactivates the absorptive capacity of ascorbic acid but not of meat. Certain methods of food preparation and storage will cause oxidation (Monsen et al., 1978).

### **2.5.3 Heme and Non-heme Iron**

Heme iron, found in hemoglobin and myoglobin, is most readily available from meat sources and is absorbed directly as the intact iron, porphyrin complex, is freed in the intestinal mucosal cell (Monsen, 1978; Turnbull et al., 1962; Conrad et al., 1967; Layrisse et al., 1972). Heme iron is much better absorbed from the diet than non-heme iron (Monsen, 1978; Bjorn-Rasmussen, 1974; 1976). However, absorption depends on the body's status of stored iron.

Most dietary iron exists as non-heme and comes from foods such as vegetables, grains, fruits, eggs, and dietary

products. The composition of the foods ingested in a meal greatly affects how well non-heme iron is absorbed. Ascorbic acid for example, enhances the absorption of non-heme iron by as much as fourfold (10 to 30%). Meat products, poultry and fish eaten along with vegetables also enhance absorption of non-heme iron. Enhancing factors are so important that if they are not present, absorption of non-heme iron would be very low (Finch, 1982). Gastric secretion also facilitates non-heme iron absorption (Zhang et al., 1990).

## **2.6 Iron Overload**

"Iron overload exists when total iron stores are in excess of about 4 g or about 50 mg per kilogram" (Finch 1982, p.1525). Iron overload can result due to disease or due to gradual accumulation of excess iron from dietary or environmental factors (Leggett et al., 1990). Iron overload can occur as a result of multiple blood transfusions causing extremely high serum ferritin levels. Iron overload can also be caused because the body lacks readily available mechanisms for excreting large amounts of iron.

### **2.6.0 Hemochromatosis**

This congenital disorder refers to the presence of excessive amounts of iron in parenchymal tissues. It is due to genetic enhancement of iron absorption from the gut.

Secondary hemochromatosis is caused by different environmental factors including transfusional iron overload and excessive iron ingestion over many years (Nutrition Reviews, 1990; Petersdorf et al., 1983). The iron slowly accumulates in many tissues of the body such as the liver, heart and pancreas and causes cardiac manifestations, blood disorders, and hepatic damage among other things. Cardiac failure is one of the leading causes of death in patients with hemochromatosis (Ashinsky, 1992). It is characterized by a low transferrin saturation and a progressive increase in serum ferritin (Finch, 1982).

The iron toxicity which occurs in hemochromatosis may cause destruction of parenchymal tissues and increase the risk of infection (Finkelstein, Sciortino and McIntosh, 1983).

#### **2.6.1 Thalassemia**

Thalassemia is a condition of iron overload caused by high levels of iron absorption related to the high rate of erythropoiesis. The treatment for thalassemia and other forms of chronic anemia consists of frequent blood transfusions, unfortunately causing excess iron to accumulate in different organs leading to cell destruction. There is also a hemolytic component of the disorder which occurs because of the high turnover of iron from red cells with a shortened lifespan (Nutrition Reviews, 1990).



People with thalassemia who are dependent on blood transfusions, acquire massive iron overload and usually die of intractable congestive heart failure or cardiac arrhythmias (Sullivan, 1988). Children with thalassemia present on average with 28 g of iron and have symptoms of slow growth and retarded puberty (Letsky, Miller, Worwood, Flynn, 1974; Nutrition Reviews, 1990).

### **2.6.2 Oral Contraceptives**

A study comparing the serum ferritin levels in two groups of menstruating women (Frassinelli-Gunderson et al., 1985), reported that the serum ferritin levels were higher for oral contraceptive users ( $39.5 \pm 21.5$  ng/ml) than for non-users of oral contraceptives ( $25.4 \pm 15.96$  ng/ml). Other studies show that the use of contraceptive pills elevates serum iron, total iron binding capacity (TIBC), serum transferrin, but does not alter the levels of hemoglobin and hematocrit (Norrby, 1972; Frassinelli-Gunderson et al., 1985).

It is not well understood why women who use oral contraceptives have increased body iron stores, however it is hypothesized that the cause is due to a reduction in menstrual blood loss (Frassinelli-Gunderson, 1985; Sullivan, 1989).

## 2.7 Iron Losses

It is estimated that there are some physiological losses of iron (1 mg/day) which are excreted in urine, feces, sweat and skin (Bource, 1981). Iron depletion and iron deficiency can protect against potentially fatal oxygen radical injury. It is thought that the protection is effective even with mild iron depletion due to the associated increase in the antioxidant apotransferrin (Sullivan, 1989).

### 2.7.0 Blood Donation

Donation of one unit of blood per year reduces serum ferritin by approximately half in healthy adult male blood donors. Giving three units per year reduces stored iron further to about the level found in pre-menopausal women (Sullivan, 1981, p.1294)

Phlebotomy or blood donation has been used to treat iron overload (Cook et al., 1977; McCord, 1991; Sullivan, 1991; Milman and Kirchhoff, 1991). In a population survey comprising 1433 Danish male subjects, the effect of blood donation on iron status was studied. It was found that donors had lower serum ferritin, (median 95 ug/L), than non-donors, (median 136 ug/L) (Milman and Kirchhoff, 1991). A second study investigating a large cohort of Danish women also found blood donors to have lower serum ferritin values than non-donors. Pre-menopausal donors were found to have

serum ferritin values of 31 ug/L compared to 39 in non-donors. Post-menopausal donors had serum ferritin values of 47 ug/L compared to 72 ug/L in non-donors. Women who were using oral contraceptives had higher serum ferritin values, 33 ug/L than nonusers, 22 ug/L (Milman and Kirchhoff, 1991).

Between phlebotomies, the loss of iron due to the bleeding causes a decrease in the mobilization of iron stores, leading to an increased iron absorption from dietary sources. With regular blood donation, the body would reach an equilibrium at lower levels of iron stores (Garry et al., 1992; Milman and Kirchhoff, 1991).

### **2.7.1 Anemia**

Anemia can be defined as iron deficiency with a circulating hemoglobin level of less than 129 g/L, transferrin saturation less than 15%, hematocrit less than 35% and serum ferritin level less than 15 ug/L (Milman and Kirchhoff, 1991). With persistent anemia, there is a depletion of body iron stores and the following trends can be seen: a decrease in serum ferritin, a decrease in percent saturation of serum transferrin (a protein that binds and transports iron) (Hughes, 1978). In normal individuals who become anemic, iron absorption through the mucosa is increased to restore hemoglobin levels (Nutrition Reviews, 1985). Some causes of iron deficiency can be poor

dietary intake, blood losses i.e. menstrual blood loss, frequent blood donations, pregnancy.

## 2.8 Free Radicals

Free radicals are considered the most powerful and destructive chemical reactor agents that occur in the body. Free radicals are capable of widespread oxidation and peroxidation of proteins and lipids causing cellular and tissue destruction such as massive loss of heart tissue in myocardial infarctions. Although radicals are constantly being formed inside the cells by the body's own metabolism, if allowed to accumulate inside the cell, they will quickly destroy it. Free radicals are highly reactive agents that contain one or more unpaired electrons (Emery, 1991). A commonly known potent radical is called the hydroxyl radical ( $\cdot\text{OH}$ ) which has one free electron attached to it that can react explosively if allowed to accumulate. Fortunately there are enzymes in the body that destroy the hydroxyl radicals preventing cell death and organ failure. If the enzyme production cannot keep up with the formation of hydroxyl radicals, the body tissues will begin to decompose. Examples of radical producing contributors are smoking, nitrites, pollution and (one of the worst producers of radicals) **iron**. Ionic metals such as iron are powerful oxidation catalysts which increase the formation of free radicals, potent oxidizing agents, thereby promoting

atherosclerosis through LDL-cholesterol oxidation (Cross, Halliwell, Borish, Pryor, Ames, Saul, McCord and Harman, 1987). It has been hypothesized recently that free iron can induce lipid peroxidation, a chain reaction providing a continuous supply of free radicals and promote ischemic myocardial injury (Salonen et al., 1992). The reaction of oxygen radicals with polyunsaturated lipids present in the plasma and the arterial wall seems to irritate the arterial wall and cause lesions and injury in the myocardium (Cross et al., 1987). It is hypothesized that aging is associated with an increase in the level of free radical reactions (Harman, 1968; 1986; 1983; 1984).

#### **2.8.0 Antioxidants**

Antioxidants appear to help the body get rid of free radicals by repairing oxidative damage or preventing free radicals from forming. Antioxidants are sometimes referred to as "free radical scavenging enzymes". Antioxidants such as vitamin C, vitamin E, and beta carotene appear to decrease the level of free radical reactions and hence can protect against heart disease and possibly increase our span of life by 5 or more years (Cross, et al., 1987; Heart and Stroke, January 1994).

Within our own cells, antioxidant defenses are provided by specific enzymes (i.e. catalase, superoxide dismutase) which bind with iron and decrease lipid peroxidation (Emery,

1991). The protein lactoferrin, may act as an antioxidant by binding the iron and stopping it from participating in radical reactions; transferrin may act as a major antioxidant by keeping metal ions from participating in radical reactions (Cross et al., 1987). Regular aerobic exercise is thought to increase levels of high-density lipoproteins thereby acting as an antioxidant because higher levels of HDL scavenge free radicals (Chander, 1990).

### **2.8.1 Iron Chelators**

There is no physiological mechanism for the excretion of excess iron, hence in certain abnormal conditions there is a pathological accumulation of iron. Regular chelation therapy has been successfully used to decrease serum iron in patients with diseases such as hemochromatosis and transfusional iron excess (Barry, 1974; Nutrition Reviews, 1990). Metal chelating agents such as desferrioxamine have been reported to have antioxidant effects by inhibiting the formation of oxygen-free radicals and lipid peroxidation (McCord, 1991; Campbell, 1993). Desferrioxamine has been shown to increase the survival time and decrease the side effects seen in patients with iron overload. In animal studies, desferrioxamine has been shown to be protective against reperfusion damage in ischemic hearts (Cross et al., 1987).

Other studies have shown that iron chelator therapy can arrest tissue damage in thalassemia (Barry et al., 1974; Halliday et al., 1980).

## **2.9 Iron, Menopause and IHD**

Pre-menopausal women in western society are largely protected from heart diseases which afflict large numbers of men and post-menopausal women (Gordon et al., 1978). The cause of the gender difference and the loss of protection with the onset of menopause is not completely understood. One hypothesis suggests that the higher incidence of coronary heart diseases in men and post-menopausal women is due to higher levels of stored iron in both these groups (Sullivan et al., 1981). Data from this study showed that pre-menopausal women have significantly lower levels of stored iron.

In the past, other studies suggested the increased incidence of coronary heart disease in older women was due to lack of estrogen (Stampfer et al., 1975), however, Sullivan argued against this theory saying it is unlikely that the estrogen is responsible for the gender difference in heart disease and the effect of menopause because younger women with hysterectomies and oophorectomies who are still producing estrogen have an equal incidence of coronary heart disease as older women with natural menopause (Sullivan et al., 1981; Gordon et al., 1978).

There is a parallel increase in risk and iron stores in post-menopausal women to levels found in men, hence the support for Sullivan's hypothesis that iron has an important role in the etiology of IHD (Sullivan 1981).

## **2.10 Exercise and the Incidence of IHD**

A number of studies support the hypothesis that physical exercise reduces the risk of IHD (Statistics Canada, 1981; Health and Welfare Canada, 1981; Shangold, 1990; Notelovitz, 1991; Kaplan, Casperson and Powell, 1989; Blair, Kohl, Paffenbarger et al., 1986; Salonen, Puska and Tuomilehto, 1982; Oka, 1990). With the increased use of technology and automation, our population in general leads a lifestyle of sub-maximal physical activity and therefore experiences a generally higher level of coronary heart disease. In a culture where the population has a more active lifestyle such as walking or running, the prevalence of IHD is much less than in areas with less active lifestyles (i.e. TV watching, driving instead of walking, etc.). Most studies link physical activity, not fitness, to a lower risk of coronary heart disease, thus it may be possible to achieve many of the cardioprotective benefits of exercise via participation in moderate activities, such as walking (Sharkey, 1990, p.188). Exercise is known to play an important part in weight control and muscular strength as well as leading to improved mental well-being and stress



reduction. Due to the complexity of the cardiovascular response to exercise, it is not known how much exercise training is needed to gain the most benefit. There is evidence from small-scale studies of elderly volunteers that suggests exercise has to be intensive and frequent for any benefits in physical capacity to occur (Ebrahim and Williams, 1992). Some studies maintain that regular aerobic exercise (exercise done continuously at a sustained elevated heart rate) can help to reduce the risk of CVD (Shangold, 1990). Studies have shown that in spite of age, older endurance runners proved to be more fit than young sedentary men (Pollock, 1978). It was determined that men who exercise for 45 minutes per day gain more fitness benefit than those who exercise 30 minutes per day. Exercise done five times a week was associated with more improvement in fitness than three times a week, and three times was better than once a week (Pollock, 1978).

Results from a Canadian Fitness Survey demonstrated that over 50% of adult Canadians may be classified as sedentary (energy expenditure less than 1.5 kcal/kg/day). It appeared that women were less active than men at all ages and that only one in four Canadians are adequately active for cardiovascular benefit (energy expenditure over 3 kcal/kg/day) (Stephens et al., 1986).

Menopausal women often blame the cumulative effects of an adverse lifestyle on hormonal changes or the "aging"

process. A program of regular exercise can prevent or minimize many of these problems, obesity, muscle weakness, osteoporosis, and depression (Shangold, 1990, p.53s). Blair, Kohl, Paffenbarger et al. (1986) investigated 3,120 women over 8 years, and documented that physical fitness was inversely associated with morbidity and mortality from several chronic diseases.

Researchers such as Notelovitz, Fields and Caramelli (1985) hypothesized that age related decrease in cardiorespiratory fitness seen in sedentary women can be reversed with initiation and maintenance of physical activity. Other studies have noted that active women have a cardioprotective effect of one decade when compared to sedentary women (Profant, Nilson and Nilson et al., 1972). In a study comparing maximal oxygen consumption ( $VO_2$ ) in active and sedentary women, it was found that the mean  $VO_2$  max of active 40-49 year old women was higher than that of sedentary 30-39 year old women, and active 50-59 year old women had values similar to those of sedentary 40-49 year old women (Profant et al., 1972). Another study investigating the effects of moderate exercise (walk-jogging three times a week for 12 weeks) found there was a significant increase in the  $VO_2$  max and time on the treadmill when compared with age controlled females who did not exercise (Gill, Veigl and Shuster et al., 1984).

Older women often maintain low activity levels and are not motivated to start an intense aerobic training program. Walking, however, has been suggested as an excellent exercise for the older person because of its utilization of large muscle groups and low associated risk of injury (Notelovitz, 1991, p.210). Group walking programs also provide social interaction and enhance compliance which can in turn enhance well-being (Notelovitz, 1991).

### **2.11 Exercise and the Effect on Iron**

It has been established that exercise causes a change in iron status, however the mechanisms by which this occurs is largely unknown (Moore et al., 1993). While there is little information specific to older individuals in the literature, a number of studies report that exercise results in decreased serum ferritin concentration in young people in general and athletes in particular. In most cases decreased serum ferritin is reflective of diminished iron stores found after exertion. In other studies, it was demonstrated that while endurance training decreased serum ferritin significantly, iron and iron saturation were unaltered. It is hypothesized that the reduction in ferritin levels induced by exercise may be responsible for the decreased morbidity and mortality rates and the overall beneficial effects (Lauffer, 1991; Blair et al., 1990). " The iron hypothesis is consistent with the graded reductions in

mortality observed as a function of fitness level, and it is the first unified mechanism which can explain the reductions in both heart disease and cancer" (Lauffer, 1990, p.103).

A study to compare the iron status between sedentary and active women (ages 22-51) engaged in a fitness-type exercise was carried out by Blum, Sherman and Boileau in 1986. The exercise classes lasted 35 minutes and were scheduled four days per week for 13 weeks.

Blood levels assessing serum ferritin, transferrin, TIBC and hemoglobin were collected at 0, 6 and 13 weeks for both the exercise group and the sedentary group (See Tables 3 and 4).

**Table 3. Mean Blood Values for the Exercise Group**

	week 0	week 6	week 13
serum ferritin	30.7 ± 2.8	24.6 ± 4	24.9 ± 3.6
transferrin	31.1 ± 2.8	30.2 ± 2.4	27.8 ± 2.5
TIBC	386 ± 14	379 ± 16	378 ± 15.7
hemoglobin	14.2	15.0	14.1

**Table 4. Mean Blood Values for the Sedentary Group**

	week 0	week 6	week 13
serum ferritin	26.1 ± 4.7	27.3 ± 5.0	28.2 ± 4.6
transferrin	33.3 ± 4.8	26.2 ± 3.8	25.5 ± 2.9
TIBC	399.6 ± 18	419.7 ± 17.5	438.1 ± 23.5
hemoglobin	13.8 ± 0.3	14.2 ± 0.3	13.8 ± 0.3

adapted from Blum, Sherman and Boileau (1986)

The exercise group showed serum ferritin concentrations to be lower at week 6 and week 13 than they were initially. In the sedentary control group, there were no significant changes in the ferritin concentrations for the duration of the study. The transferrin, TIBC and Hemoglobin were essentially unchanged for the exercise group. The sedentary group showed TIBC to be higher by week 6 and even higher by week 13. Transferrin gradually decreased over the 13 week period. Hemoglobin was unchanged by week 13 for the sedentary group.

This study indicated that thirteen weeks of moderate fitness-type exercise decreased iron stores as measured by serum ferritin levels in previously untrained adult women but had no effect on hematological status (Blum et al., 1986).

## **2.12 Summary**

In summary, a review of the literature suggests that exercise, diet, gender, menopause, menstrual status, certain diseases, blood donation and blood transfusion have an effect on iron status. Individuals who are physically active or women who are pre-menopausal tend to have lower levels of stored body iron. Individuals who are sedentary, women who are post-menopausal and males tend to have higher stored body iron. It has been shown that ferritin levels are decreased by exercise in young athletes. However,

little research has been directed towards observing changes in iron status in a controlled experimental environment involving moderate forms of exercise in sedentary post-menopausal women.

It has been suggested that stored iron promotes IHD and that iron depletion protects against IHD (Sullivan, 1981; 1989; 1992; Salonen, 1988). It has also been suggested that more research is required to elucidate the role of iron as a potential risk factor for IHD especially in post-menopausal women. The extent to which exercise decreases stored body iron and the degree to which cardiovascular risk is modified by exercise after controlling for the other known risk factors, also warrants study.

## CHAPTER THREE: METHODOLOGY

### 3.0 Background Information

The purpose of this study was to examine the effects of a 24 week brisk walking program on stored body iron as measured by serum ferritin in post-menopausal women. A comparison was made between the effect of brisk walking 3 days per week versus 5 days per week and not walking for 60 minutes per day at an equivalent intensity of 60 % VO<sub>2</sub> max.

The design and methodology for this quantitative study are outlined in chapter three. The sample size, criteria for inclusion and exclusion, the setting, instruments used, procedures and methods of data collection and analysis are reported. The data collected for this study was part of a larger study involving a multi-disciplinary team including researchers from the Faculties of Nursing, Physical Education, Human Ecology and Medicine studying the effects of exercise on cardiovascular and psychosocial parameters.

### 3.1 Design

A randomized controlled experimental time-frame design was used to determine the effect of exercise on stored body iron as measured by serum ferritin levels in post-menopausal women. The study lasted 24 weeks and serum ferritin levels were taken at the beginning of the study and at the completion of the walking program.

Seventy-nine subjects were randomly selected into three groups. The random selection procedure involved putting all participant names in a hat and making a random assignment to the three treatment groups. Statistical analysis was used to determine if the walking program caused a significant difference in the mean ferritin values within and between the three groups. Statistical analysis was also used to determine if walking 5 times per week would significantly lower the ferritin levels more than walking 3 times per week. Comparison of the clinical data was also made between the grouped 3 and 5 day walkers and the non-walkers.

### **3.1.0 Independent and Dependent Variables**

The treatment (independent) variable in this study was the walking program with frequency of walking being either 3 times per week for a minimum of 150 minutes or 5 times per week for a minimum of 240 minutes per week. Duration of walking was 60 minutes per session and the walking intensity was 60% VO<sub>2</sub> max. The outcome measure (dependent variable) was the product of iron metabolism measured as serum ferritin. Other variables measured included weight, body mass index (BMI), waist-hip ratio (WHR), percent fat loss, maximal oxygen consumption (VO<sub>2</sub> max), hemoglobin and hematocrit.



Pre- and post-test measures for the dependent variables were measured at time 1 and time 2 as illustrated in Figure 2.

### **3.2 Population and Sample**

To achieve a power of 90% with alpha set at 0.05 in testing between three groups, it was calculated that a minimum of 20 subjects per group would be required to determine a significant difference (Cohen, 1988, p.55). A sample of 80 women were selected to begin the study.

Subjects participating in this research were healthy, sedentary, post-menopausal women not on estrogen therapy between the ages of 51 and 75 years. All participants were volunteers who gave informed written consent.

#### **3.2.0 Recruitment**

Participant recruitment took place from September to December 1993. Participants were recruited using local newspapers, television interviews, radio, posters and word of mouth (see Appendix A). Researchers involved in the study appeared on radio and local television programs to recruit volunteers. Hospitals and physicians were mailed a letter describing the study and were asked to distribute copies of the letter to middle aged women who expressed an interest in participating in the walking study (see Appendix B).

### 3.2.1 Screening

Women interested in participating in the study were given the number of a dedicated phone line at the University of Manitoba. They left their name and phone number on the answering machine and the researcher returned the calls and did a preliminary screening interview over the phone (see Appendix C). The researchers received over 700 inquiries from interested women. A phone interview was conducted to explain the study to potential participants and to determine if the candidates met the following selection criteria: a) 55 years of age or older, b) post-menopausal (defined as a period of amenorrhea for 12 months), c) not on estrogen replacement therapy, d) sedentary with no recent changes in their activity patterns, e) physically capable of exercising, f) nonsmoker for the past year. The women passing the phone interview were then further screened to ensure that they a) did not consume more than 7 oz of alcohol per week, b) were clinically healthy (no signs of cardiovascular, pulmonary or metabolic diseases that would preclude safe participation in an exercise program), c) not on medications that would affect iron metabolism, d) agreed to maintain their regular eating habits throughout the study and not begin a new dietary regime.

Criteria excluding potential participants were: a) women who were too physically active, (did 15 minutes of exercise more than 3 times per week) b) hypercholesteremia,

c) occasional menstrual periods, d) walked regularly, e) would be unavailable for over one month between January 1994 and October 1994, f) smoked or took medications which could affect results. Once the participants met the above criteria and agreed to random selection to be in one of the aforementioned exercise groups or the sedentary control group, they were mailed a medical questionnaire and an informed consent form. Approximately 500 women were excluded during the phone interview for being too active, smokers, on estrogen replacement therapy or had donated or received blood in the last year. Medical questionnaires were mailed to 230 women who passed the phone screening (see Appendix F). Approximately 150 women returned the completed questionnaires; of these, 30 were screened out for medical reasons (taking medications for hyperlipidemia, not able to walk long distances, high risk for cardiac problems, etc.).

Women who met the criteria after a cardiologist reviewed their medical forms were invited to attend one of two information meetings (January 6 and March 3, 1994) at the University of Manitoba. Sixty-seven women attended the first meeting on January 6, 1994 and 19 women attended the meeting on March 3, 1994. Team members explained the study in detail at the information meetings. The women were asked to read a letter of invitation to participate in the study, (see Appendix I); and to sign a consent form (see Appendix J). The participants were encouraged to ask questions

during the orientation evening. They were assured of complete confidentiality concerning their results. Only one woman decided not to continue at this point, because she did not want to take the chance of possibly being selected into the control group, therefore 85 women were left to begin the study.

### **3.2.2 Setting**

The participants agreed to walk on the indoor track at the Max Bell Centre at the University of Manitoba at least once a week. The blood tests, anthropometric measurements and treadmill tests were conducted on the second floor of the Max Bell Centre.

### **3.2.3 Assumptions**

Due to the nature of the study, there were certain assumptions made about the participants' ability to accurately record and monitor their physical activity and dietary intake. Participants were counselled a) not to change their dietary habits or go on a diet during the six month program, b) to accurately complete their weekly activity log sheets. Participants were counselled on how to accurately complete their 3 day food frequency records and how to accurately monitor their own pulse rates while exercising. Participants were told to fast for 12 hours

prior to the blood testing and to report any symptoms of infection.

### 3.3 Data Collection

Participants were tested for a number of measurements at the beginning and at the end of the study. Twenty-seven of the women were randomly selected to begin testing in January 1994, twenty-eight in February and thirty in March 1994. All pre-testing was completed by March; measurements included:

- a) blood pressure
- b) 12 lead EKG
- c) anthropometric measurements (see Appendix L)
- d) body weight and height
- e) body mass index (BMI)
- f) treadmill stress test (involves walking on a treadmill to a maximum heart rate)
- g) VO2 max testing (involves testing exercise intensity)
- h) fasting venous blood samples for serum ferritin, hematocrit, hemoglobin

Women who were anemic (serum ferritin less than 10 ug/L) or who had triglyceride levels greater than 4.2 mmol/L or total cholesterol levels greater than 8.0 mmol/L were excluded from the study. Data collection involved completing a physical activity and lifestyle

questionnaire (see Appendix D), an exercise participation questionnaire (see Appendix E), a 3 day food frequency questionnaire (see Appendix H).

There were 85 women tested; three were screened out on the treadmill test due to EKG abnormalities; one for abnormally high serum ferritin values (hemochromatosis); one did not complete the pre-tests and one withdrew voluntarily. This left 79 women to begin the study. Participants were randomly (names picked out of a hat) assigned to walk 5 days per week (N=27), 3 days per week (N=27), or to remain sedentary in the control group (N=25).

### **3.3.0 Serum Ferritin**

The subjects had blood samples drawn between 0700 and 0900 after 12 hours of fasting. In addition, they were asked to refrain from exercise for 24 hours prior to the blood test. Approximately 15 to 20 ml was collected into Vacutainer tubes (Beaton Dickinson, EDTA) after the subjects had been sitting for 20 minutes. Blood was drawn from the antecubital vein with an 21 gauge 1 1/2 inch sterile vacutainer needle after the rubber tourniquet was released. Samples drawn included 5 ml of blood for serum ferritin analysis {camouflage red top tube}, and 5 ml for hemoglobin and hematocrit {heparinized lavender tube}. Blood samples for hemoglobin and hematocrit were kept in the fridge at -5 degrees centigrade and then transported to St Boniface

Hospital for analysis. Samples for the serum ferritin were centrifuged at 3,500 revolutions per minute (RPM) for 20 minutes using a table top centrifuge. The plasma was transferred by pipette to a plastic capped container (3 ml). Determination of serum transferrin concentration was carried out at St. Boniface Hospital using a radial immunodiffusion method (Frassinelli-Gunderson et al., 1985).

### **3.3.1 General Principals of Immunoradiometric Assay**

Immunoradiometric assay (IRMA) was the method used to determine serum ferritin levels for this study (Cook et al., 1974; Frassinelli-Gunderson et al., 1985). The quantimune Ferritin IRMA is based on the principles of two-site immunoradiometric assays which are often referred to as "sandwich assays" because the antigen (ferritin) becomes "sandwiched" between labelled and immobilized antibodies (Bio-Rad Laboratories, 1992). This two site assay "uses highly purified  $^{125}$  I-labelled antibody to ferritin as the tracer, and ferritin antibodies immobilized on polyacrylamide beads as the solid phase" (Bio-Rad Laboratories, 1992). The ferritin standard consists of human liver ferritin in a solution of phosphate buffer and bovine serum albumin which comes supplied in a kit. St. Boniface laboratory followed the eight steps in accordance with the instruction manual provided by the Bio-Rad Laboratories (1992, p.5).

### **3.3.2 Blood Pressure**

After 5 minutes in the recumbent position, blood pressure was measured by the researcher, using a mercury sphygmomanometer. A normal adult size blood pressure cuff was used to measure at the level of the mid-upper arm approximately 3 cm above the crease of the elbow with the bladder centered over the brachial artery.

### **3.3.3 Body Weight and Height**

Body weight was measured on a lever balance and recorded to the nearest 0.1 kg. Height was measured to the nearest centimeter.

### **3.3.4 Body Mass Index (BMI)**

Body mass index was calculated as weight (kg) divided by the square of the height (m<sup>2</sup>).

### **3.3.5 Anthropometric Measurements**

Using calipers, skinfold measurements (triceps, biceps, subscapular, pectoral, iliac crest, abdominal, front thigh, medial calf), girths, breadths, and lengths were taken in duplicate in accordance with procedures outlined by Ross and Marfell-Jones (1982) and Lohman et al., (1988) (See Appendix L). Measurements were made in triplicate. From the above measurements, waist to hip ratio (WHR) was calculated. Percent body fat was calculated from skinfold measurements.



### 3.3.6 Diet Analysis and Counselling

Diet analysis and counselling was done by a nutritionist. Prior to week 1 of the study, and following the completion of the study, participants completed a record of all foods consumed during a three day period, including two weekdays and one weekend day. Prior to the start of the study, the nutritionist met individually and in groups with all the participants involved in the study and taught them how to properly complete the 3-day food frequency questionnaires. The data was entered in a special database program derived from the 1991 Canadian Nutrient File, Version 1.2. The dietary analysis software used for micro-computers was Demeter, Version 1.06. Food intake was further analyzed to determine mean heme iron consumption, dietary fiber, vitamin C and vitamin supplements over a three day period. The mean amount of heme iron content consumed by each individual participant and by each group was estimated according to the method of Monsen et al., (1978) e.g. (mg of iron/day X.4 factor). Dietary consumption of total iron, heme iron, fibre and vitamin C was correlated with the serum ferritin and log of serum ferritin values.

### 3.3.7 Treadmill Testing

Participants underwent a Balke treadmill test to rule out any cardiac abnormalities, to measure their VO<sub>2</sub> max and

to determine if subjects could safely participate in the exercise program (Pollock et al., 1976). Each test was supervised by a cardiologist who documented any abnormalities. A familiarization session was held with each subject prior to the treadmill test to decrease anxiety and to eliminate a learning effect. The "trial run" of the Balke test included familiarization with the headgear and mouthpiece used in measuring oxygen uptake. On the day of the actual treadmill test, the subjects walked on the treadmill at a constant speed of 5.4 km/Hr (3.3 miles/hr). Elevation began at 0% grade at 0 minutes, and increased by 1% per minute. Expired gases were measured using a Metabolic Measurement cart (sensoredmedics). Blood pressure measurements (sitting and supine) and a 12-lead EKG were taken prior to the test. EKG tracings and blood pressure were monitored each minute during the test. The test was terminated if EKG abnormalities were apparent, or if the subject became exhausted. Criteria for achievement of VO2 max included a heart rate approaching the age predicted maximum. In order to test cardiovascular fitness levels (VO2 max) and to monitor the changes, the subjects in the walking group and the control group were tested just prior to the walking program and again at the end of the 24 weeks.

### **3.3.8 Activity Records and Interim Questionnaire**

A physical activity and lifestyle questionnaire was completed by each subject prior to the beginning the exercise intervention (See Appendix D). Walkers recorded their weekly activity, including a record of walking in a log book throughout the study (see Appendix M). The control group also kept weekly profiles of all physical activity. An interim questionnaire was given at weeks 12 and 24 to monitor changes in medication, activity level, injuries and illnesses (See Appendix K).

## **3.4 Walking Program**

Supervised walking classes were offered five times per week (including warm-up, group stretch, one-hour walking and a cool-down). The women were required to walk at least once a week at the indoor track (Max Bell Centre) at the University of Manitoba, and to complete the remainder of their program on their own. Participants were instructed to keep additional endurance activity to a minimum. Each week the log books were examined and signed by the investigators.

### **3.4.0 Compliance**

The walking program required that the 3-day per week group walk a minimum of 150 minutes per week and a maximum of 180 minutes per week. The 5-day per week group was required to walk a minimum of 240 min per week and a maximum

of 300 minutes per week. Lack of adherence to the walking program required the researchers to eliminate 3 participants from the 3-day group and 4 participants from the 5-day group in the final data analysis.

#### **3.4.1 Exercise Progression**

Increased distance and not intensity was used to build progression into the exercise program. As subjects became more fit, the distance completed within the designated time (60 minutes) increased, thereby ensuring progression.

#### **3.5 Facilities and Equipment**

All treadmill testing, blood samples, and anthropometric measurement were done at the Health, Leisure and Human Performance Research Institute, Max Bell Centre, University of Manitoba. Serum ferritin, TIBC, serum iron, hemoglobin and hematocrit was done at St. Boniface General Hospital Hematology and Biochemistry Laboratories.

#### **3.6 Ethical Considerations**

Informed voluntary written consent was obtained from all participants in the study (see Appendix J). All participants were informed of the possible risks of injury that could result from the training program. All participants were provided with a letter explaining the nature and purpose of the study, the potential risks and

benefits, procedures, and the name of the investigator and contact phone numbers (see Appendix I). Participants were informed that they could withdraw from the study at any point without prejudice.

The data collected were kept in a locked area to assure confidentiality and anonymity. Subjects were informed that only the researchers, members of the thesis committee and testers would have access to the data. All participants received their results at the end of the study.

Participants with abnormal results were contacted immediately by phone and encouraged to contact their physician about the results. With the participants' agreement, the abnormal results were sent to their physician.

### **3.7 Summary**

This study was a prospective experimental design to determine the relationships between serum ferritin and exercise in post-menopausal women. The effects of a 24 week walking program on iron levels was assessed to determine the minimum levels of exercise required to achieve improvements in health.

## CHAPTER FOUR: RESULTS

### 4.1 Statistical Analysis

All data were analyzed using Statistical Analysis System (SAS) Institute software on the mainframe located at the University of Manitoba. Descriptive data were reported for all participants and then separately in the control group, 3 day walking group and the 5 day walking group. Summary statistics expressed as mean values with standard deviation were used for preliminary investigation. One way analysis of variance (ANOVA) was used to determine if there were any differences between the means of each group at time 1 and six months later at time 2. Anova is parametric analysis with specific distributional assumptions and was used for analysis of the normally distributed log of ferritin. Logarithmic transformation was used to induce normality and reduce the effect of outlying observations for ferritin. Nonparametric statistics (Kruskal-Wallis and Wilcoxon signed rank test) were used with the non-normal distributions such as the raw ferritin levels.

Analysis of covariance (ANCOVA) was used to adjust the post-test results using the pre-test figures as a covariate. The level of the serum ferritin was the covariate and the change in the ferritin level was the outcome variable. In this way, the affect of the walking program on changes in

ferritin level could be determined while controlling for other variables.

Correlation coefficients were used to test the relationships between independent variables (age, weight, BMI, WHR, %fat, VO2 max, hgb, hct and diet) and the dependent variable ferritin. Pearson's product-moment correlation coefficient ( $r$ ) was used, after determining a normal distribution, to assess the degree of linear relationship between the dependent variables ferritin and the log of ferritin with the independent variables mentioned above. Spearman Rank correlation coefficient ( $\rho$ ) was used, whenever a non-normal distribution was observed, to measure the degree of linear association between the dependent variables ferritin and log of ferritin with the independent variables mentioned above.

A step-wise multiple linear regression was used to determine if a predictive model could be built out of the statistically significant associations for the values of the dependent variable ferritin. Scatter plots were developed to determine if there was a linear relationship between age and ferritin before and after the walking program and to give visual representation of the relationship.

#### **4.1.0 Calculation of the Power Index**

The power level of a study describes how likely the study will detect a genuine treatment effect between the

experimental group and the control group. The power level of a study depends on several factors including the size of the alpha level. The power level is also dependent on the sample size. The power index was set at ( $p < 0.05$ ) for the study considering the sample size of 56. Setting  $\alpha = 0.05$ , the power to detect a significant difference among the means of the three groups is as follows:

<u>power</u>	<u>effect size</u>
10%	small
50%	moderate
88%	large

The power level was based on the assumption that between a moderate and a large effect size, there should be sufficient power to detect differences among the means. Since a clinically significant effect corresponds to a moderate effect size, this design is sufficient to answer the research question with a reasonable level of confidence (Cohen, 1988).

#### **4.2 Summary Statistics**

In total, 85 post-menopausal women met the inclusionary criteria and were selected to participate in the 24 week study. During the first testing phase, one subject withdrew voluntarily and five were screened out for medical reasons. The remaining 79 women were randomly selected into three



groups, non-walkers (control n=25), three day walkers (n=27) and five day walkers (n= 27).

Eighty percent (n=20) of the control subjects completed the study (see Table 5). Five control subjects were excluded for a number of reasons (medical n=2; noncompletion of final testing n=1; moved away n=1; loss of interest n=1). In the three day/week walking group 70% (n=19) completed the 6 month program (see Table 5). Subjects were excluded because of noncompliance (walking less than 150 minutes per week) n=3; injury n=2; positive stress test n=1; illness n=1; menstrual period n=1. Sixty-three percent (n=17) of the subjects in the 5 days/week exercise group (n=27) completed the walking program (see Table 5). Ten subjects were excluded due to: noncompliance (n=4), defined as walking less than 240 minutes per week and/or changing of diet; injury (n=4); illness (n=1); lack of final testing data (n=1).

**Table 5. Compliance of Post-Menopausal Women Who Completed the 24 Week Walking Study**

GROUPS	COMPLETED	
	n=	%
CONTROL	20	80
3 DAY/WEEK treatment group	19	70
5 DAY/WEEK treatment group	17	63
TOTAL	56	71

Table 6 shows body composition characteristics and blood values for all subjects measured prior to walking.

**Table 6. Physical Characteristics of Participants (N=56)**

PARAMETERS	MEAN $\pm$ SD	RANGE
AGE (yrs)	61.3 $\pm$ 5.8	51.3 - 74.5
HEIGHT (cm)	161.9 $\pm$ 5.8	147.0 - 174.0
WEIGHT (kg)	69.7 $\pm$ 10.8	51.7 - 98.6
BMI	26.5 $\pm$ 3.6	19.6 - 34.2
WHR	0.78 $\pm$ 0.1	0.65 - 0.96
% Fat	33.4 $\pm$ 5.8	20.6 - 43.8
VO2 max (ml/kg/min)	22.3 $\pm$ 3.7	13.7 - 31.5
VO2 max (l/min)	1.5 $\pm$ 0.3	0.9 - 2.2
FERRITIN (ug/kg)	110.8 $\pm$ 81.4	12.0 - 388.0
LOG OF FERRITIN	4.4 $\pm$ 0.8	2.5 - 6.0
HEMOGLOBIN	137.1 $\pm$ 7.3	122.0 - 155.0
HEMATOCRIT	0.40 $\pm$ 0.0	0.36 - 0.46

Table 6 shows the sample population of post-menopausal women had an average BMI of 26.5  $\pm$  3.6. Mean serum ferritin is slightly above the average range of 10-95 ug/L for females, while mean hemoglobin (hgb) and mean hematocrit (hct), are within the normal range. Mean height, weight and percent body fat closely approximates the average height (160 cm), weight (60.9 kg) and body fat (34.2%) for older women between 43-68 years of age (McArdle, Katch and Katch, 1994).

Mean WHR was within normal limits, as ratios above 0.85 for women are considered an added health risk (Lea and Febiger, 1991). The observed mean maximal oxygen uptake ( $22.3 \pm 3.7$  ml/kg/min) of the participants is rated as fair compared with a national average based on gender and age. The average predicted VO<sub>2</sub> max for females 50-65 years old is 27-34 (McArdle, Katch and Katch, 1994).

#### **4.2.0 Physical Characteristics of Participants by Group**

Table 7 describes the physical characteristics of the subjects completing the study in the control group (N=20), 3 days/week group (N=19) and 5 days/week group (N=17).

In the beginning of the program, there were no significant differences in age, weight, height, BMI, WHR, % fat, VO<sub>2</sub> max, ferritin, log of ferritin, hemoglobin and hematocrit between the 3 groups.

**Table 7. Physical Characteristics by Group Prior to the Walking Intervention (n=56)**

PARAMETERS	CNTRL	3X/WK	5X/WK	p value	
	n=20	n=19	n=17	Anova	K-W
AGE (yrs)	62.2 ± 5.7	59.6 ± 4.7	62.0 ± 6.8	0.3224	0.3063
HEIGHT (cm)	161.6 ± 6.9	162.2 ± 5.1	161.1 ± 6.0	0.7876	0.7413
WEIGHT (kg)	70.7 ± 10.9	71.7 ± 12.9	67.2 ± 9.4	0.7108	0.7704
BMI (kg/m <sup>2</sup> )	26.6 ± 3.8	26.8 ± 4.3	26.2 ± 2.5	0.8609	0.9014
WHR	0.80 ± 0.07	0.79 ± 0.06	0.76 ± 0.06	0.1254	0.1529
%FAT	33.3 ± 5.1	33.2 ± 7.1	33.9 ± 5.4	0.9272	0.9393
VO <sub>2</sub> max (ml/kg/min)	21.6 ± 2.8	23.0 ± 4.3	22.3 ± 4.3	0.5052	0.6933
VO <sub>2</sub> max (l/min)	1.5	1.6	1.5	0.5191	0.4787
FERRITIN (ug/L)	104.7 ± 86.0	102.5 ± 88.2	127.4 ± 69.5	0.6096	0.2739
Log of Ferritin	4.3 ± 0.84	4.3 ± .83	4.7 ± 0.58	0.2710	0.2739
HEMOGLOBIN (g/L)	138.2 ± 8.2	135.4 ± 7.2	137.9 ± 6.1	0.4283	0.3455
HEMATOCRIT	0.40	0.40	0.40	0.4027	0.1960

p value = level of significance for analysis of variance; a probability <.05 is considered significant.

One way ANOVA analysis of variance and Kruskal-Wallis tests conducted to assess differences in ferritin levels among the 3 groups.

#### 4.2.1 Walking Characteristics

Weekly walking characteristics for subjects completing either the 3 day or 5 day per week program are shown in Table 8.

**Table 8. Weekly Walking Characteristics (X±SD)\***

GROUP	N=36	FREQUENCY	DURATION (min)	DISTANCE (km)	VELOCITY** (m/sec)
3-DAY	n=19	2.9 ± 0.1	171 ± 7	16.5 ± 2.1	1.66 ± 0.22
5-DAY	n=17	4.9 ± 0.4	279 ± 20	26.3 ± 4.2	1.65 ± 0.15

\* = mean and standard deviation

\*\* = average walking velocity during 24 week program

The participants adhered to the assigned frequency of walking, that is, the 3 day/week group walked an average of 2.9 ± 0.1 times per week for a total of 171 ± 7 minutes, and the 5 day/week group, 4.9 ± 0.4 times per week for a total of 279 ± 20 minutes.

#### 4.3 Changes in Serum Ferritin and Log of Ferritin

The normal range of ferritin is 10-175 ug/L and often shows a non-normal distribution of values within groups. To control for the observed non-normal distribution curve, a log transformation of ferritin was used to induce a normal distribution. Parametric procedures were used for analysis of the normally distributed log of ferritin and nonparametric statistics were used to describe the non-normal distribution of ferritin.

Table 9 shows mean serum ferritin levels and log of ferritin demonstrating differences of means between the pre- and post-exercise program measurements.

The mean serum ferritin was reduced by 19% in the 5 day walkers and by 16% in the 3 day walkers. Mean serum ferritin increased by 5% in the control group (see Table 9). The difference of means between the three groups over time shows a statistically significant difference between pre- and post-exercise values ( $p=0.0136$ ) for serum ferritin and ( $p=0.0428$ ) for log of ferritin. The Anova  $p$  value is referred to for normal distribution of values and Kruskal-Wallis  $p$  value is used for non-normal distribution of values. To maintain clinical interpretation by the reader, the raw ferritin scores were reported along with the log of ferritin results.

A more precise estimation of group differences was then conducted using a combination of variance and regression. Analysis of covariance (Ancova) was conducted among the three groups to determine the difference of the effectiveness of walking between time 1 and time 2 (see Table 10). This allowed for each participant's individual pre-test ferritin levels to be used as a covariate as well as assessing differences among the three groups in post-test ferritin levels.

Table 9. Differences of Means for Se Ferritin and Log of Ferritin for 3 Groups

Parameters	Control	3/week	5/week	Anova	K-W
	n= 20	n= 19	n= 17		
Se Ferritin					
PRE	104.7 ± 86.0	102.5 ± 88.2	127.4 ± 69.5	0.6096	0.2739
POST	110.1 ± 103.0	90.0 ± 68.9	107.5 ± 62.9	0.7223	0.6029
Difference of Means	5.5	- 13.8	- 19.9	0.0814	0.0136*
Log of Fer					
PRE	4.3 ± 0.8	4.4 ± 0.8	4.7 ± 0.6	0.2730	0.2739
POST	4.4 ± 0.8	4.2 ± 0.9	4.5 ± 0.7	0.7223	0.6029
Difference of Means	0.05	- 0.14	- 0.21	0.0428*	0.0248*

\* p value significant at < 0.05

**Table 10. Effectiveness of Walking Among 3 Groups: Post-Test (Ancova)**

Variables	Cntrl vs 3Day	Cntrl vs 5Day	3Day vs 5Day
Se Ferritin 0.1018	0.0920	0.0514*	0.7601
Log of Ferritin 0.0562	0.0707	0.0255*	0.6168

\* p value significant at  $p < 0.05$

Table 10 shows no statistical difference between the control groups versus the 3 day group, nor between the 3 day group versus the 5 day group, however data show a statistical difference between the control group versus the 5 day group for log of ferritin ( $p=0.0255$ ) and for serum ferritin ( $p=0.0514$ ).

Table 11 shows mean serum ferritin levels (ug/L) for the non-walkers ( $n=20$ ) and the pooled walkers ( $n=35$ ) pre- and post- walking program.



**Table 11. Differences of Means in Serum Ferritin Levels and Log of Ferritin for Walkers vs Non-Walkers**

Parameters	non-walkers	walkers	Anova	K-W
N=	20	35		
Se Ferritin (ug/L)				
PRE	104.7 ± 86.0	114.3 ± 79.8	0.6756	0.5495
POST	110.1 ± 103.4	98.5 ± 65.6	0.6139	0.8818
Difference of Means (ug/L)	5.5	- 16.7	0.0284*	0.0082*
Log of Ferritin				
PRE	4.3 ± 0.8	4.5 ± 0.7	0.4618	0.5495
POST	4.4 ± 0.8	4.3 ± 0.8	0.7835	0.8818
Difference of Means	0.05	- 0.18	0.0145*	0.0133*

\* p = significant at the 0.05 value

Significant differences were evident in the difference of means of the ferritin levels for the control group and the walkers when data from both walking groups (N=35) were pooled (p=0.0082). The log of ferritin showed significant difference between the control group and the pooled walking groups (p=0.0145). The data in Table 11 show ferritin levels increased by 5 % for non-walkers and decreased by 17 % for walkers.

A more precise estimate of group differences was seen when analysis of covariance (ANCOVA) was used (see Table 12).

**Table 12. Comparison of Ferritin Levels Between Walkers and Non-Walkers using Analysis of Covariance (Ancova)**

Variables	Non-Walkers n= 20	Walkers n= 35	p=
Se Ferritin	110.1 ± 103.4	98.5 ± 65.6	0.0335*
Log of Ferritin	4.4 ± 0.8	4.3 ± 0.8	0.0184*

\* p value significant at  $p < 0.05$

Table 12 shows statistically significant differences in serum ferritin (p=0.0335) and log of ferritin (p=0.0184) between walkers and non-walkers demonstrating the effect of walking.

#### 4.4 Changes in Body Composition

Table 13 shows body composition and fitness levels for the 3 day and 5 day per week walking groups and the controls prior to and following the 24 weeks of exercise (mean  $\pm$  SD).

**Table 13. Body Composition and Fitness Variables: Pre- and Post-24 Week Walking Program (ANOVA)**

Parameters		Control	3 days/wk	5 days/wk	p value
N=		20	19	17	
WEIGHT(kg)	pre	69.8	71.1	68.0	0.7108
	post	70.6	70.5	68.0	0.7507
Dif of Means		+ 0.8	+0.6	0.0	0.0727
BMI(kg/L)	pre	26.6	26.8	26.2	0.8609
	post	27.0	26.8	26.3	0.8159
Dif of Means		+ 0.4	0.0	+ 0.1	0.0754
%FAT	pre	33.3	33.2	33.9	0.9272
	post	33.5	32.1	32.6	0.7482
Dif of Means		+ 0.2	-1.1	-1.3	0.0383*
WHR	pre	0.80	0.78	0.76	0.1254
	post	0.81	0.79	0.77	0.1724
Dif of Means		0.0	0.0	0.0	0.1371
VO2 max (ml/kg/min)	pre	21.6	23.0	22.3	0.5052
	post	21.8	26.0	25.4	0.0163*
Dif of Means		0.2	+ 3.0	+ 3.1	0.0020*
VO2 max (L/min)	pre	1.52	1.62	1.53	0.5191
	post	1.53	1.80	1.7	0.0604*

\* = significant at .05 level

The analysis of variance showed no significant differences observed in mean weight, BMI and WHR within the three groups at post-test. However the data show there were significant differences of means post-exercise in % Fat and VO2 max ( $p=0.0383$ ) and ( $p=0.0020$ ) respectively.

In the 3 and 5 times per week walkers, there was a significant increase in maximum oxygen uptake (VO2 max). There was no significant difference in the VO2 max pre- and post-test in the control group. There was a significant increase in the VO2 max expressed in weight relative units (ml/kg/min) ( $p=0.0163$ ) for the walking groups, whereas the VO2 max remained virtually unchanged in the control group post-exercise. VO2 max increased 12% in both the 3 day walkers and the 5 day walkers, a value significantly greater than in the control group.

Table 14 shows analysis of covariance for body composition variables post-exercise program, comparing three groups over time showing the effect of the experimental intervention.

**Table 14. Identification of Significant Differences in Body Composition and Fitness Variables Comparing Groups (ANCOVA)**

Variables	Cntr/3-day	Cntrl/5-day	3-day/5-day
WEIGHT (0.0766)	0.0243*	0.2294	0.3135
BMI (0.0792)	0.0314*	0.1102	0.6095
WHR (0.2182)	0.1492	0.8642	0.1245
%FAT (0.0389)*	0.0326*	0.0248*	0.8585
VO2 max (ml/kg/min) ) (0.0024)*	0.0078*	0.0010*	0.4845
VO2 max (ml/min) (0.1040)	0.0475*	0.0985	0.7349

\* p value significant at  $p < 0.05$

Table 14 shows there is a significant difference in weight, BMI, % Fat and VO2 max post-exercise in the control versus the 3-day group. In the control versus 5-day group, only % Fat and VO2 max showed any significant difference post-walking program. There were no significant differences between the 3-day versus 5-day groups.

Table 15 shows body composition and fitness levels for the walkers and non-walkers prior to and following the 24 weeks of exercise (Mean  $\pm$  SD).

**Table 15. Differences of Means for Body Composition: Walking vs Non-Walking Group (X $\pm$ SD)**

PARAMETERS		Non-Walkers	Walkers	p value
	N= 55	n= 20	n= 36	
WEIGHT (kg)	pre	69.8 $\pm$ 10.9	69.7 $\pm$ 10.9	0.9583
	post	70.6 $\pm$ 11.1	69.4 $\pm$ 11.0	0.6853
	Dif of means	+ 0.8	-0.3	0.0397*
BMI (kg/L)	pre	26.6 $\pm$ 3.8	26.5 $\pm$ 3.6	0.9548
	post	27.0 $\pm$ 3.8	26.5 $\pm$ 3.6	0.6450
	Dif of means	+ 0.4	0.0	0.0267*
% FAT	pre	33.3 $\pm$ 5.1	33.5 $\pm$ 6.2	0.8680
	post	33.5 $\pm$ 4.7	32.4 $\pm$ 6.3	0.4750
	Dif of means	+ 0.2	-1.2	0.0107*
WHR	pre	0.80 $\pm$ 0.07	0.77 $\pm$ 0.06	0.1232
	post	0.80 $\pm$ 0.06	0.77 $\pm$ 0.05	0.0840
	Dif of means	0.0	0.0	0.9713
VO2 max (ml/kg/min)	pre	21.59 $\pm$ 2.75	22.69 $\pm$ 4.20	0.2972
	post	21.83 $\pm$ 3.31	25.68 $\pm$ 4.90	0.0043*
	Dif of means	0.0	+ 0.2	0.0005*
VO2 max (L/min)	pre	1.51 $\pm$ 0.33	1.57 $\pm$ 0.24	0.4595
	post	1.54 $\pm$ 0.39	1.75 $\pm$ 0.26	0.0223*
	Dif of means	0.0	+ 0.2	

\* p value significant at  $p < 0.05$

The analysis of variance shows significant differences of means (see Table 15) between walkers and non-walkers for weight ( $p=0.0397$ ), BMI ( $p=0.0267$ ), % Fat ( $p=0.0107$ ) and VO2 max ( $p=0.0005$ ). The data also show a significant increase in VO2 max (ml/kg/min) for the walkers ( $p=0.0043$ ) and VO2 max (L/min) ( $p=0.0223$ ). The non-walkers showed virtually no change in their VO2 max levels. The WHR decreased for the walkers but it did not reach the 0.05 level of significance.

Table 16 shows analysis of covariance showing the effect of walking on body composition variables between walkers and non-walkers.

**Table 16. Effectiveness of Walking on Body Composition Variables Among Walkers and Non-Walkers (Ancova)**

Variables	Non-Walkers n=20		Walkers n=36		p=
	PRE	POST	PRE	POST	
Weight (kg)	69.8	70.6	69.7	69.4	0.0415*
BMI (kg/l)	26.6	26.9	26.5	26.5	0.0276*
%FAT	33.3	33.5	33.5	32.4	0.0107*
WHR	0.80	0.81	0.77	0.77	0.4136
VO2 max (ml/kg/min)	1.52	1.54	1.57	1.75	0.0348*

\* p value significant at  $p < 0.05$

Analysis of covariance in Table 16 shows the decrease in weight, BMI and % Fat was small but none the less statistically significant between walkers and non-walkers (weight,  $p=0.0415$ , BMI,  $p=0.0276$ , % Fat,  $p=0.0107$ ).

#### 4.5 Correlational Analysis

Table 17 provides a summary of correlation coefficients (r) for independent variables and the dependent variable serum ferritin in post-menopausal women in the control group, 3 days/week or 5 days/week group. An r of 0.1 to 0.3 is considered a weak relationship, a 0.3 to 0.5 is a moderate relationship and above 0.5 is a strong relationship.

**Table 17. Correlation Coefficients (rho) for Serum Ferritin and Independent Variables: 3 Groups**

Independent Variables		control	3 days/wk	5 days/wk
N=		20	19	17
AGE	pre	- 0.35	0.26	0.59*
	post	- 0.26	- 0.01	0.58*
BMI	pre	0.29	0.20	0.21
	post	0.20*	- 0.34	0.15
WHR	pre	0.14	0.10	0.49*
	post	0.10	0.12	0.49*
%FAT	pre	0.16	0.14	0.34
	post	0.15	- 0.38	0.17
HCT	pre	0.32	0.32	0.33
	post	0.32	0.15	0.29
HGB	pre	0.41	0.43	0.35
	post	0.44*	0.22	0.24
VO2 max (ml/kg/L)	pre	0.38	- 0.25	- 0.48*
	post	0.26	0.14	- 0.30
VO2 max (l/kg)	pre	0.27	0.26	- 0.60*
	post	0.15	0.41*	- 0.52*

\* = significant at 0.05 level

Table 17 shows positive correlations with serum ferritin for both pre- and post-exercise for age and WHR,



for the 5 day walkers but not for the other groups. VO2 max was negatively correlated with ferritin pre- and post-walking program only for the women in the 5 day group.

**Table 18. Correlation Coefficients for Serum Ferritin and Independent Variables: Walkers vs Non-Walkers**

Independent Variables		non-walkers	walkers
N=		20	36
AGE	pre	- 0.35	0.35*
	post	- 0.26	0.32*
BMI	pre	0.29	- 0.16
	post	0.20*	- 0.14
WHR	pre	0.14	0.20
	post	0.10	0.32*
%FAT	pre	0.16	- 0.11
	post	0.15	- 0.11
HCT	pre	0.32	0.12
	post	0.32	0.18
HGB	pre	0.41*	0.06
	post	0.43*	0.18
VO2 max (ml/kg/min)	pre	0.38	- 0.27
	post	0.26	- 0.16
VO2 max (L/min)	pre	0.27	- 0.16
	post	0.15	- 0.10

\* p value = 0.05 significance

Table 18 shows the relationships between the dependent variable ferritin and the independent body composition variables, age, BMI, WHR, % Fat, HCT, HGB, VO2 max expressed in relative units (ml per kg per minute) and VO2 max as the absolute value of oxygen consumption expressed in (L/min).

The correlations show that age is positively related with ferritin both pre- and post-walking program for the

women in the walking groups. The data shows a significant positive relationship between BMI and ferritin, and between HGB and ferritin in the non-walkers. WHR is positively related with ferritin following the exercise program.

To further investigate the relationship among the variables and ferritin, model building was attempted by stepwise multiple linear regression, however no variables were found to be predictive of ferritin values and so no model could be built.

#### **4.6 Dietary Consumption**

Table 19 shows dietary consumption of vitamin C, alcohol, fibre, total iron and heme iron all of which may affect serum ferritin values. A significant difference is shown in vitamin C consumption between the three groups in the post-walking program indicating that 5 day walkers consumed the most vitamic C at post-test (see Table 19).

**Table 19. Mean Dietary Consumption: 3 Groups**

Variables		control n=20	3 day n=19	5 day n=17	p
VITAMIN C (mg)	Pre	185.6	292.0	253.1	0.5352
	Post	87.6	124.2	165.3	0.0144*
ALCOHOL (gm)	Pre	1.9	4.4	2.0	0.5087
	Post	2.0	6.4	3.3	0.3660
FIBRE (mg)	Pre	66.3	152.7	112.5	0.6426
	Post	13.3	36.3	22.1	0.5225
TOTAL IRON (mg)	Pre	11.8	13.2	11.7	0.4318
	Post	10.8	12.3	11.9	0.6279
HEME IRON (mg)	Pre	5.8	6.1	6.4	0.8368
	Post	5.5	5.3	5.4	0.9788

p value significant at  $p < 0.05$

Table 20 shows a combination analysis of variance and regression used to control any extraneous variables. This analysis of covariance adjusted for any initial differences in dietary consumption.

**Table 20. Analysis of Covariance for Dietary Consumption: 3 Groups Post-Exercise Program**

variables	CNTRL vs 3DAY	CNTRL vs 5DAY	3DAY vs 5DAY
VITAMIN C 0.0135*	0.1342	0.0035*	0.0960
ALCOHOL 0.6434	0.3502	0.6390	0.6656
FIBRE 0.4265	0.3257	0.2224	0.7628
TOTAL IRON 0.6916	0.5270	0.4191	0.8266
HEME IRON 0.9900	0.8960	0.9840	0.9158

p value significant at  $p < 0.05$

Table 21 shows dietary consumption of vitamin C, alcohol, fibre, total iron and heme iron between walkers and non-walkers. The data shows walkers consumed significantly more vitamin C than the non-walkers throughout the study.

**Table 21. Dietary Consumption Comparing Grouped Walkers and Non-Walkers (ANOVA)**

Independent Variables		n=20 Non-Walkers	n=36 Walkers	p value
VITAMIN C (mg)	pre	185.6	275.5	0.2929
	post	87.4	141.6	0.0158*
ALCOHOL (gm)	pre	1.9	3.4	0.5066
	post	2.0	5.0	0.2951
FIBRE (mg)	pre	66.3	135.7	0.3984
	post	13.3	30.3	0.2887
TOTAL IRON (mg)	pre	11.8	12.6	0.5134
	post	10.8	12.1	0.3420
HEME IRON (mg)	pre	5.8	6.2	0.6105
	post	5.5	5.3	0.8596

\* = significant p value

Three day diet records indicated that both walkers and non-walkers consumed significantly more vitamin C pre-exercise than they did post-exercise program. Diet records also indicated that pooled 3 day and 5 day walkers consumed significantly more vitamin C than the non-walkers (p=0.0158).

Non-Walkers consumed less alcohol than the walkers, however consumption differences were not significant. Both walkers and non-walkers consumed more fibre at the pre-exercise diet testing than at the end of the 24 weeks.

There were no statistical differences between the walkers and the non-walkers for total iron and heme iron consumed.

**Table 22. Dietary Consumption Comparing Grouped Walkers and Non-Walkers (ANCOVA)**

variables	non-walkers		walkers		p=
	pre	post	pre	post	
VITAMIN C	185.6	87.4	275.5	141.6	0.0154*
ALCOHOL	1.9	2.0	3.4	5.0	0.4025
FIBRE	66.3	13.3	135.7	16.6	0.2017
TOTAL IRON	11.8	10.8	12.6	12.1	0.4040
HEME IRON	5.8	5.5	6.2	5.3	0.9252

\* p value significant at  $p < 0.05$

The data (using analysis of covariance) again show that considerably less vitamin C was consumed at the post-exercise time (August, 1994) than at the pre-exercise time (January, 1994) by all participants.

#### **4.7 Hypothesis Testing**

##### **Hypothesis 1**

Hypothesis 1 stated that walking for three days per week would significantly lower levels of stored body iron (measured by serum ferritin). This hypothesis is not supported by measurement of serum ferritin ( $p=0.0920$ ) nor by log of ferritin ( $p=0.0707$ ).

**Hypothesis 2**

Hypothesis 2 stated walking for five days a week would significantly decrease levels of stored body iron more so than walking three days a week. This hypothesis is supported by measurement of serum ferritin ( $p=0.0514$ ) and log of ferritin ( $p=0.0255$ ).

## CHAPTER 5: DISCUSSION

### 5.1 Introduction

The hypothesis that stored body iron is a potential risk factor for IHD is a relatively recent one. It has been argued that excess iron deposited in the parenchyma cells of the heart tissue can cause substantial damage. Tissue injury results from disruption of iron laden lysosomes and lipid peroxidation of subcellular organelles. The "iron" hypothesis has been supported in several studies in men, however older women are either absent or underrepresented in these studies. This is surprising since women in the post-menopausal years are particularly vulnerable to IHD.

The hypothesis of this study is that if iron is a risk factor for IHD, then an intervention such as exercise may reduce the risk of IHD by lowering levels of stored iron that are common in many post-menopausal women. This investigation is the first randomized controlled exercise study of previously sedentary post-menopausal women.

The study determined that a 24 week walking program of regular walking five times per week for 60 minutes at 60-70% VO<sub>2</sub> max decreased stored body iron as measured by serum ferritin. There was in addition a small but significant decrease in body weight and % fat, and an increase in fitness level measured by VO<sub>2</sub> max during treadmill testing.

## 5.2 Hypotheses

### Hypothesis # 1:

The findings of the present study do not support the hypothesis that walking three days per week will significantly lower levels of stored body iron compared to a control group.

### Hypothesis # 2:

The findings of the present study support the hypothesis that walking 5 times per week lowers stored body iron significantly, more so than walking 3 times per week.

## 5.3 The Study Population

The study population consisted of a representative sample of healthy post-menopausal women. Overall, there was good compliance to the treatment intervention (71%). The control group had the least trouble complying at 80%, followed by the 3 day/week groups at 70% and then the 5 day/week group at 63%. Walking 5 times per week may have been too drastic a lifestyle change for elderly women who had previously been sedentary. A lower activity rate may be more easily incorporated into one's life-style and may be better maintained over time.

The overall sample of post-menopausal women was an excellent group for this experimental study. The participants were keen, cooperative, compliant and reliable.



They were committed to keep walking as instructed for the duration of the walking program.

#### **5.4 Changes in Ferritin Level**

The results of this study found a trend of higher than normal se ferritin levels in post-menopausal women who were inactive. This study demonstrated that moderate exercise decreased stored body iron in sedentary post-menopausal women. The small but significant reduction in serum ferritin is an important finding as it demonstrates that an exercise program alone, without alteration in diet can significantly reduce the stored body iron in this population and possibly reduce the risk for ischemic heart disease. The clinical importance of this finding is supported by reports from other studies that report the preventative effect of exercise stem in part from lower body iron levels associated with physical exertion (Lauffer, 1990, 1991; Sullivan, 1989; Blum, 1986).

The findings in this study are consistent with trends of an increased level of serum ferritin reported in the literature for post-menopausal females (Cooke et al., 1976; Vincente, Porto & de Sousa, 1980). The average serum ferritin for post-menopausal women in this study was higher than the normal range for all females. There were no statistical differences in ages between the three groups.

When the groups were combined, there was no relationship between age and ferritin.

### **5.5 Body Composition (Body Weight, % Fat, WHR)**

Twenty-four weeks of moderate exercise reduced body weight and % fat by a small but significant amount. Reducing weight was evidenced in other studies as a result of physical exercise, although there is no direct evidence that weight loss reduces the risk of coronary heart disease as yet due to the small number of subjects who are able to maintain a reduced level of weight (Edwards-Rich, Manson, Hennekens, and Buring, 1995). Changes in VO<sub>2</sub> max expressed in absolute terms (ml/min) were not significant, suggesting that weight loss may have accounted for a large part of the improvement in cardiovascular fitness.

Studies suggest the risk of coronary heart disease rises among women whose WHR is higher than 0.8, however the mean WHR for the women in this study was 0.78 pre-walking program. Although the WHR was lower in the walkers compared to the non-walkers, it did not reach a level of significance. Although there was a positive relationship between WHR and ferritin, there was no significant difference in the WHR for the walkers following the 24 week walking program. Another interesting finding verbally reported by the women was that although they had not

evidenced a drastic weight loss, their clothes seemed to fit better and they generally felt healthier.

### **5.6 Fitness Level Changes**

The results of this study demonstrate that a program of regular walking three or five times per week is associated with significant improvement in functional capacity in this group of older women. Twenty-four weeks of moderate exercise improved VO<sub>2</sub> max of the sedentary subjects by 5.5% for 3day/week walkers and by 12.0% for the 5day/week walkers. This magnitude of change in max VO<sub>2</sub> is consistent with other studies of the same length (Blumenthal et al., 1991; Nieman et al., 1993). Other studies with longer periods of exercise reported higher improvements in max VO<sub>2</sub> (Seals, Hagberg, Hurley, Ehsani and Holloszy, 1984).

### **5.7 Dietary Consumption**

The participants' diet including nutrients that tend to alter iron absorption did not change significantly during the 24 week walking program except for vitamin C. There was more intake of vitamin C in winter (January) by all three groups. It is possible the participants felt that more vitamin C was warranted during the cold winter months. There was also more intake of vitamin C by the walkers throughout the study. Vitamin C is known to enhance the absorption of iron in the body, however there were no

significant differences in se ferritin between the walkers and non-walkers at the beginning of the study. Se ferritin levels for the walkers were significantly lower than the non-walkers at post test despite their greater vitamin C consumption.

Dietary changes, such as decreasing iron intake and increasing fibre is known to decrease iron absorption in the gut. Fibre such as bran diminishes iron absorption but how much fibre has not been quantified yet (Hallberg, 1987).

Although large amounts of alcohol is known to increase the absorption of dietary iron and the concentration of ferritin in serum among healthy men (Leggett et al., 1990), the participants in this study consumed a minimal amount of alcohol (less than 10 gm per day).

The participants were asked to keep 3 day food records. The method used to calculate dietary intake of iron was an effective way to determine the effects of diet on serum ferritin and to monitor the changes in dietary intake over time. There was only a small amount of dietary iron intake per day by the participants, and there was no a correlation of mean dietary intake of iron per day with serum ferritin. Longitudinal studies to investigate the effects of dietary iron on serum ferritin need to be undertaken.

## 5.8 Summary

In summary, the findings of this study indicate that different walking intensities influence ferritin levels, various aspects of body composition and cardiovascular fitness.

## 5.9 Conclusion

This study demonstrated that a 24 week walking program induces small but significant reductions in stored body iron (measured as serum ferritin) in women, post-menopause. The related benefits, however small but significant, were loss of weight and percent fat and an increase in fitness evidenced by an improvement in VO<sub>2</sub> max.

This moderate exercise program proved to be a beneficial and inexpensive health promotion intervention for women, post-menopause. Although the magnitude of change in ferritin level appears modest, from a public health perspective, even small improvements in coronary risk factors, if established on a population-wide basis, could lower cardiovascular related mortality.

Walking an average of 5 hours per week for approximately 60 minutes at an intensity of 50-60% maximum heart rate reserve resulted in a significant increase in VO<sub>2</sub> max, decrease in serum ferritin and a small but significant loss of weight and body fat. Walking at an intensity of 60% maximum heart rate reserve for 3 hours per week may be

sufficient to induce improvements in VO2 max and therefore cardiovascular fitness. However, it appears that walking 5 times a week is needed to significantly decrease ferritin levels. Decreases in ferritin level associated with increased activity is in keeping with other studies showing increased physical activity in young athletes.

A trend was visible and an association between exercise and a decrease in ferritin level was established. If it is true that iron is a risk factor for heart disease, then walking is a prevention strategy for heart disease by decreasing iron levels.

This study has extended the existing areas of research related to stored body iron by examining the relationship between stored body iron and exercise in post-menopausal women. Further research needs to be done to investigate the long term patterns of exercise that the participants engaged in, following the end of the study as well as their long term cardiovascular status. It is suggested that a further longitudinal study be done to determine if any correlations exist between exercise, stored body iron status and risk of IHD in this sample population.

#### **5.10 Limitations**

The length of this study was only 24 weeks, so a longer time period may be necessary before more consistent and dramatic changes are seen in the serum ferritin level. A

more vigorous exercise training may also be necessary to evidence more changes in this population. Diet alteration in conjunction with exercise may be needed to further reduce ferritin levels. Weight and fat loss were small in this population.

A larger sample size may show more consistent trends in the relationship between exercise and reduction in stored body iron. Although the design of this study was well controlled, results may still have been confounded by variables that interfered with the internal validity such as change producing events not reported by the participants. Examples of events beyond the control of the researcher are unreported change in diet, unreported donation of blood or other sources of iron loss, intake of medications affecting ferritin levels i.e. large doses of vitamin C, aspirin or iron supplements, unreported non-adherence to the walking program and unexpected changes in body composition however closely monitored.

Monitoring dietary intake may have been a particularly difficult task for the women because of the subjectivity involved in describing their usual dietary patterns. There is always the possibility that they had tendencies to over or under estimate portion sizes of food.

Clinical significance is difficult to prove in the absence of any symptoms. The results of this study must be carefully interpreted, because when statistically

significant correlations or regression coefficients are obtained, it does not follow that the results are necessarily clinically significant. The fact that serum ferritin levels dropped by 20 or 30 ug/l may be statistically significant but not necessarily clinically significant.

It remains to be determined whether the changes in ferritin levels observed in this present study are applicable to populations outside of Manitoba, to women in a higher age category, to women with higher or lower BMIs, % fat and fitness levels. It is unknown whether women who are at a high risk of developing cardiovascular disease or who already have cardiovascular disease would respond in a similar manner as observed among the healthy post-menopausal women who participated in this study. Further research is needed to clarify these issues.

The decrease in ferritin values were small and inconsistent with large standard deviations. It is possible that a program of longer duration would show declining trends in body iron status and eventually a decrease in CVD risk. The findings must be interpreted cautiously due to the small sample size. Ferritin levels have a large variability in values and are affected by a number of factors such as infection, viruses, medication and foods thereby masking the true relationship between ferritin and



independent variables. Most variables were carefully monitored and controlled for.

### **5.11 Implications for Nursing and Future Research**

Successful improvement in health in our aging population will depend in part on the reduction of CVD and other related disabilities. Physical inactivity is an independent risk factor for CVD. Moderate exercise has the potential to enhance the health of many sedentary individuals and nurses should recommend it.

This study demonstrated that a moderate exercise program of walking 5 times per week for one hour successfully reduced serum ferritin when comparing sedentary women of the same age group.

Little is known concerning factors which influence participation and compliance rate in exercise such as a regular walking program. Participants in this study appeared to benefit from the social and group dynamics of the walking sessions. This was evidenced by their camaraderie observed by the researcher. It appeared that the group format provided motivation and an opportunity for socialization. Decreasing excess body iron by exercising is an opportunity to make a healthy lifestyle choice. Maintenance of a regular exercise program for an extended time interval is associated with greater cardiovascular benefits among older adults (Blumenthal, Emery, Madden,

Coleman, Riddle, Schniebolk, Cobb, Sullivan, and Higginbotham, 1991). Continuance of a walking program for a period of time extended beyond 24 weeks may also be associated with a further decrease in stored body iron. The association between lack of physical activity and risk of heart disease is clear. The results of studies such as this one will help to establish more effective programs for the primary prevention of coronary heart disease in women. Nurses can educate the public by relaying the results of studies such as this one and making people aware that sedentary lifestyles can have considerable detrimental effects on people's wellbeing. Educating the public on self care by increasing physical activity and reducing modifiable potential risk factors of heart disease may result in a substantial reduction of deaths from cardiovascular disease. An important public health message delivered by nurses may persuade sedentary women to become a little more active even at low levels. This supports other epidemiologic studies that suggest women who regularly participate in physical activities, even at low levels, may experience lower all-cause mortality rates compared with a cohort of sedentary women (Blair, Kohl, Paffenbarger, Clark, Cooper, Gibbons, 1989).

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# MAJOR CAUSES OF DEATH IN 1991

Number of deaths: 195,568  
Statistics Canada 1991

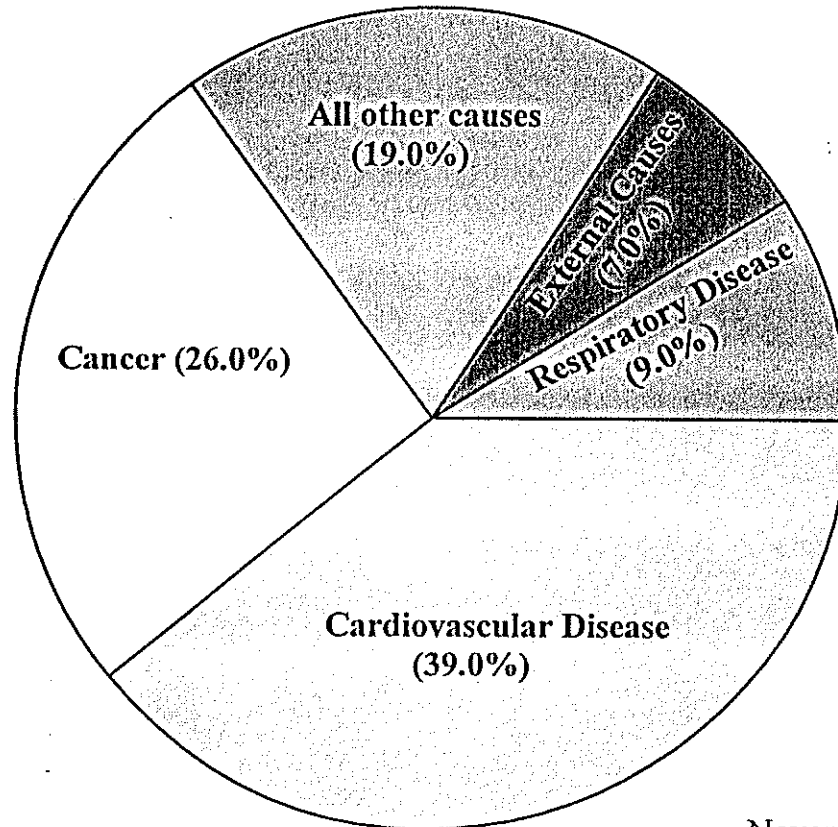


Figure 1

November 9, 1993 Free Press

Figure 2 Study Design

Week*	0	<u>24</u>
<b>Group</b>		
R Non-Walkers	<u>XT</u>	<u>YT</u>
R Walkers (3X/WEEK)	<u>XT</u>	<u>YT</u>
R Walkers (5X/week)	<u>XT</u>	<u>YT</u>

X : testing: ferritin pre- walking program

Y : testing: ferritin post-walking program

T : treadmill testing

R : random assignment

Walking was started at week 0 and completed at week 24.

Walking intervention is indicated by the underline.

\* entry into study was staggered by one month intervals, for each group.

## Appendix A:

## RECRUITMENT CONTACTS

Winnipeg Free Press  
697-7000

University of Manitoba Information Centre  
474-8346

University of Manitoba Bulletin  
474-8111

Manitoba Society of Seniors Journal  
942-3147

Manitoba Society of Seniors Recreation Coordinator  
942-3147

Age and Opportunity  
304-323 Portage Ave.  
947-1276

Creative Retirement Manitoba  
Health Promotion Dept.,  
811-294 Portage Ave.  
949-2558

Gov't of Manitoba - Seniors Directorate  
400-500 Portage Ave.  
945-2127

City of Winnipeg, Parks and Recreation  
Seniors Programs

Radio and Television  
CKSB, St. Boniface

Physicians and Clinics Offices

## Appendix B:

### Walking program for Women aged 55 Years and Older

Women aged 55 years and older are needed to take part in a six month study to determine the benefits of regular walking. Volunteers must be non-smokers who have been inactive during the past year. They must be healthy and able to walk regularly, and must not be taking estrogen replacement therapy.

#### What the Study is About

This study will compare the benefits of brisk walking 60 minutes per day, 3 days per week versus 5 days per week, for 6 months. The effect of each program on cardio-vascular fitness, as well as on several physical and mental health indicators including (cholesterol, stored body iron, blood pressure, % body fat, weight, incidence of illness, self-esteem, and stress), will be measured. One third of participants will be placed in a non-walking group and will be counselled to begin walking after the 6 month study.

#### Reasons Why We are Conducting the Study

Regular exercise has been shown to improve many risk factors for heart disease including body fat, blood pressure and cholesterol. It may also help decrease stored body iron, another possible risk factor. It is also believed that exercise helps people to reduce stress and to feel better about themselves. Although we know that physical activity has many potential health benefits, we don't know how much is necessary to bring about these improvements. Risk for heart disease increases following menopause, yet few of the studies which look at exercise and risk factors have involved women. Walking was selected because it has been linked with health benefits, and is a safe and popular activity suitable for use with most people.

#### Why You Should Consider Taking Part

All participants will receive free blood testing, nutritional counselling, and fitness and body fat assessments at the beginning and end of the program. You will also be helping us to understand more about prevention of heart disease in women. Walkers will have the motivation of being in a study, and of meeting other women to exercise with. Finally, you will have fun!

#### Who is Conducting the Study

The study is taking place at the Health, Leisure and Human Performance Research Institute at the University of Manitoba.

For more information, please call: 474-8638

Preliminary Screening Interview Incoming Call: Date \_\_\_\_\_ # \_\_\_\_\_

Name of caller: \_\_\_\_\_ Phone #: \_\_\_\_\_ Best Time: \_\_\_\_\_

Interviewer: \_\_\_\_\_ Date: \_\_\_\_\_

"Hello, this is \_\_\_\_\_ from the Walking Study at the University of Manitoba. I understand that you are interested in taking part in the study? Do you have approximately 5 to 10 minutes to talk now, or is there a better time for me to call?"

(Call back: \_\_\_\_\_)

"Before I tell you about the study I would like to ask you a few questions. You are free not to answer, however we will not then be able to consider you for the study because we need this information to see whether you might be able to take part. Shall I proceed?":

	Yes	No
May I ask your age? _____ (under 55?)	<input type="radio"/>	<input type="radio"/>
Do you smoke, or have you been a smoker during the past year?	<input type="radio"/>	<input type="radio"/>
Do you take any medications (drugs) to lower your cholesterol level?	<input type="radio"/>	<input type="radio"/>
Do you still have menstrual periods?	<input type="radio"/>	<input type="radio"/>
Are you taking Estrogen Replacement Therapy, or have you taken it in the past year?	<input type="radio"/>	<input type="radio"/>
In the past year, have you walked regularly for exercise? (ie. for more than 15 minutes, 2 days+ a week, brisk pace)	<input type="radio"/>	<input type="radio"/>
In the past year have you taken part in any type of regular exercise? (eg. aquacise, badminton, 1x/wk+)?	<input type="radio"/>	<input type="radio"/>
Is there any medical or physical reason that you could not walk for one hour several times per week?	<input type="radio"/>	<input type="radio"/>
Will you be out of town for any long periods between January and October (ie. over a month?)	<input type="radio"/>	<input type="radio"/>

(If the response to any of the above questions is YES, the woman is NOT ELIGIBLE to take part):

Caller is: Eligible  Not eligible

If not eligible: "I am sorry, but we are looking for women who .....(eg. are non-smokers) so I am afraid you do not qualify to take part. Thank you very much for your interest, and please pass our phone number along to any friends or relatives who may also be interested. Good-bye".

Physical Activity And Lifestyle Questions

1. What physical activity do you currently do?

Type of activity	Time/Distance	How often?	# of Years	How hard?
------------------	---------------	------------	------------	-----------

Eg. Walking	30 minutes	3x/wk	2	Moderate
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____

2. If you are not currently active, were you active in the past?

YES  NO

If yes: i) how long ago did you stop being active? \_\_\_\_\_ years ago

ii) please indicate what activities you did and for how long:

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

3. Which of the following best describes your average consumption of alcohol (check one answer)?:

- Never \_\_\_\_\_
- Occasionally (1 to 3 drinks per month) \_\_\_\_\_
- From 1 to 3 drinks per week \_\_\_\_\_
- From 4 to 7 drinks per week \_\_\_\_\_
- Over 8 drinks per week \_\_\_\_\_

(One drink is the equivalent of one oz. of alcohol, one beer, or one 6 oz. glass of wine)

4. Have you been to see any of the following health care providers in the past year? (List # of times and reason for visit):

Your own doctor	_____	Walk in clinic	_____
Specialist	_____	Hospital emergency	_____
Physiotherapist	_____	Nurse practitioner	_____
Dentist	_____	Chiropractor	_____
Other	_____		



HOW ACTIVE ARE YOU?

**Instructions:** Did you do any of these physical activities in the past week? If so, HOW MUCH TIME IN MINUTES did you spend on each occasion? Add your own activities at the end if they are not listed here.

EXERCISE PARTICIPATION IN THE PAST WEEK

WORK ACTIVITIES

	Time spent in minutes on each occasion							(For office use only)	
	Mon.	Tues.	Wed.	Thurs.	Fri.	Sat.	Sun.	MET	x HOURS
Work in the home (sweaty)	___	___	___	___	___	___	___	5.5	___
Work in the home (light)	___	___	___	___	___	___	___	3.0	___
Outdoor work (sweaty)	___	___	___	___	___	___	___	6.0	___
Outdoor Work (light)	___	___	___	___	___	___	___	3.0	___
Other physical work?? TYPE: _____	___	___	___	___	___	___	___		___

LEISURE ACTIVITIES

	Time spent in MINUTES on each occasion							(For office use only)	
	Mon.	Tues.	Wed.	Thurs.	Fri.	Sat.	Sun.	MET	x HOURS
Aerobic Fitness Class	___	___	___	___	___	___	___	6.0	___
Aquacize class	___	___	___	___	___	___	___	6.0	___
Badminton	___	___	___	___	___	___	___	5.5	___
Bicycling outdoors (sweaty)	___	___	___	___	___	___	___	6.0	___
Bicycling outdoors (light)	___	___	___	___	___	___	___	5.5	___
Bicycling indoors (sweaty)	___	___	___	___	___	___	___	6.0	___
Bicycling indoors (light)	___	___	___	___	___	___	___	5.5	___
Bowling (5 Pin)	___	___	___	___	___	___	___	3.0	___
Bowling (Lawn)	___	___	___	___	___	___	___	3.0	___
Bowling (Carpet)	___	___	___	___	___	___	___	3.0	___
Calisthenics	___	___	___	___	___	___	___	4.5	___
Canoeing or kayaking	___	___	___	___	___	___	___	3.0	___
Curling	___	___	___	___	___	___	___	3.0	___
Dancing (Square, Tap, Folk)	___	___	___	___	___	___	___	6.0	___
Dancing (Ballroom, Ballet)	___	___	___	___	___	___	___	5.0	___
Dancing (Line, Hawaiian)	___	___	___	___	___	___	___	4.0	___

Leisure Activity...	Mon.	Tues.	Wed.	Thurs.	Fri.	Sat.	Sun.	MET	x HOURS
Darts	—	—	—	—	—	—	—	2.5	—
Golf	—	—	—	—	—	—	—	3.5	—
Gymnastics, Rhythmic	—	—	—	—	—	—	—	6.0	—
Hiking hilly terrain	—	—	—	—	—	—	—	8.0	—
Horseshoes	—	—	—	—	—	—	—	3.0	—
Jogging (warmth inducing)	—	—	—	—	—	—	—	10.0	—
Jogging (sweat inducing)	—	—	—	—	—	—	—	12.0	—
Rebounding (mini-trampoline)	—	—	—	—	—	—	—	10.0	—
Rope skipping	—	—	—	—	—	—	—	12.0	—
Rowing (machine or boat)	—	—	—	—	—	—	—	8.0	—
Skating (Ice or Roller)	—	—	—	—	—	—	—	6.0	—
Stair Climbing (continuous)	—	—	—	—	—	—	—	8.0	—
Stretching exercises	—	—	—	—	—	—	—	3.0	—
Swimming (gentle)	—	—	—	—	—	—	—	7.0	—
Swimming (non-stop)	—	—	—	—	—	—	—	10.0	—
Table Tennis (ping pong)	—	—	—	—	—	—	—	4.0	—
Tai Chi	—	—	—	—	—	—	—	3.0	—
Tennis	—	—	—	—	—	—	—	6.0	—
Walking (slow strolling)	—	—	—	—	—	—	—	3.0	—
Walking (warmth inducing)	—	—	—	—	—	—	—	4.0	—
Walking (race or speed)	—	—	—	—	—	—	—	5.0	—
Other _____	—	—	—	—	—	—	—	—	—
Other _____	—	—	—	—	—	—	—	—	—
Other _____	—	—	—	—	—	—	—	—	—

THANK YOU VERY MUCH FOR COMPLETING THIS SURVEY.

(FOR OFFICE USE ONLY)

TOTAL HOURS OF PAST WEEK EXERCISE = \_\_\_\_\_

TOTAL ENERGY = \_\_\_\_\_ KG. x \_\_\_\_\_ (MET x HOURS TOTAL)

**Walking Study II**  
**Health, Leisure and Human Performance Research Institute**

**Medical Questionnaire**

Name: \_\_\_\_\_ Phone Number: \_\_\_\_\_

Date of Birth: \_\_\_\_\_ (mm/dd/yy)

---

1. Do you take any MEDICATIONS? YES  NO

a) If you answered yes to the above question please list all pills prescribed (name and dose):

1) \_\_\_\_\_

2) \_\_\_\_\_

3) \_\_\_\_\_

4) \_\_\_\_\_

5) \_\_\_\_\_

2. Do you SMOKE? YES  NO

a) If you have quit, please indicate the month and year:

\_\_\_\_\_ (mm/yy)

3. Do you have HIGH BLOOD PRESSURE? YES  NO

UNKNOWN

a) If you answered yes to the above question, are you on medication?

YES  NO

4. Do you have DIABETES? YES  NO

UNKNOWN

a) If you answered yes to the above question, are you on medication?

YES  NO

5. Do you have HIGH CHOLESTEROL? YES  NO   
 UNKNOWN

a) If you answered yes to the above question, are you on medication?  
 YES  NO

b) If possible, please indicate your most recent cholesterol level:

\_\_\_\_\_ (date tested: \_\_\_\_\_)

6. Do you have a FAMILY HISTORY OF HEART DISEASE?  
 (immediate family only ie. mother, father, brother, or sister)  
 YES  NO   
 UNKNOWN

For those members with heart disease, fill in the following:

	<u>Age Disease Appeared</u>	<u>Current Age</u>	<u>Age Died</u>
Mother	_____	_____	_____
Father	_____	_____	_____
Brother	_____	_____	_____
Brother	_____	_____	_____
Brother	_____	_____	_____
Sister	_____	_____	_____
Sister	_____	_____	_____
Sister	_____	_____	_____

7. Do you have?
- |                     |     |                          |    |                          |
|---------------------|-----|--------------------------|----|--------------------------|
| a) HEART DISEASE    | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| b) STROKE           | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| c) POOR CIRCULATION | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| d) LUNG DISEASE     | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| e) KIDNEY DISEASE   | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| f) BOWEL DISEASE    | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| g) LIVER DISEASE    | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| h) BLOOD DISEASE    | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
8. Have you ever been told you were ANEMIC?
- |  |     |                          |    |                          |
|--|-----|--------------------------|----|--------------------------|
|  | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|--|-----|--------------------------|----|--------------------------|
- a) Have you been given a blood transfusion in the past year?
- |  |     |                          |    |                          |
|--|-----|--------------------------|----|--------------------------|
|  | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|--|-----|--------------------------|----|--------------------------|
- b) Have you donated blood in the past year?
- |  |     |                          |    |                          |
|--|-----|--------------------------|----|--------------------------|
|  | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
|--|-----|--------------------------|----|--------------------------|
9. Do you notice or experience the following when WALKING?
- |                      |     |                          |    |                          |
|----------------------|-----|--------------------------|----|--------------------------|
| a) CHEST DISCOMFORT  | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| b) TROUBLE BREATHING | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| c) LEG CRAMPS        | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
10. Have you
- |   |     |                          |    |                          |
|---|-----|--------------------------|----|--------------------------|
| a) had previous exercise tests (eg. bike or treadmill)? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| b) seen a cardiologist?                                 | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
11. What was the date of your last MENSTRUAL PERIOD?
- \_\_\_\_\_ (mm/yy)

Walking Study II  
Health, Leisure and Human Performance Institute

Menstrual History Questionnaire

Name: \_\_\_\_\_ Phone Number: \_\_\_\_\_  
Date of Birth : \_\_\_\_\_ (mm/dd/yy)

---

1. When was your last menstrual period? \_\_\_\_\_ (mm/yy)
2. Which of the following best describes you (check one):
  - i) not yet reached menopause \_\_\_\_\_
  - ii) undergoing menopause \_\_\_\_\_
  - iii) past menopause \_\_\_\_\_
3. a) If you are undergoing or past menopause, please list the most common symptoms you experienced (eg. hot flashes, spotting):
 

-----  
-----  
-----

b) Which of the above symptoms, if any, do you still experience?

-----  
-----
4. If you believe you are past menopause, please estimate the length of time (in months) from the time you think menopause began to the time it ended (your periods stopped completely and you no longer experienced any of the symptoms of menopause):
 

----- months
5. Have you had any medical treatments or surgical procedures such as a hysterectomy which would have resulted in early menopause?
 

YES  NO

6. If you answered yes to question 5, please indicate your age at the time of surgery or treatment. \_\_\_\_\_ years

7. Do you now, or have you ever taken any hormones? (This includes oral contraceptives ie. "the pill")

YES  NO

8. If you answered yes to question 7, which hormones or oral contraceptives were taken (brand name) and during what time period?

-----  
-----  
-----

9. a) Have you ever been on estrogen replacement therapy?

YES  NO

b) If you have been on estrogen replacement therapy, please indicate when it began and ended (month and year) and the brand name of the medication.

Medication -----  
Began -----  
Ended -----

10. Have you ever been pregnant?

YES  NO

Other Comments:

Interviewed by: \_\_\_\_\_

Date: \_\_\_\_\_

---

**FOOD FREQUENCY RECORD FOR THREE DAYS ONLY**

This record will give you an estimate of your energy, protein, fat, carbohydrate, calcium and alcohol intake.

PLEASE TAKE YOUR TIME FILLING IN THE DETAILS, SO THE RESULTS CAN BE AS ACCURATE AS POSSIBLE.

Student #: \_\_\_\_\_ Age: \_\_\_\_\_ Sex: \_\_\_\_\_

To decide your frame size, place your fingers of one hand around the wrist of your other hand. If thumb and middle finger meet, fill in "medium frame", if they overlap, write "small frame" and if they do not meet, write "large frame".

Height: cm \_\_\_\_\_ or ft. in \_\_\_\_\_

Weight: kg \_\_\_\_\_ or lbs \_\_\_\_\_

Frame size: \_\_\_\_\_

Dates Recorded: \_\_\_\_\_

**INSTRUCTIONS:**

- Starting with breakfast, go down the list of foods on the following pages and for each item decide how many times you have eaten it **IN THE LAST THREE DAYS**.
- At each meal, on average, did you eat more or less than the portion size given in the list? If you ate less, write for example 1/2 or 1/3 of the portion size. If more, write for example 2 or 3 portions.
- Repeat for other meals and snacks.

Example: 2 slices of toast eaten at 2 out of 3 breakfasts, and 1 slice of bread at supper every night, and 1/2 cup of macaroni and cheese for lunch one day, is written as:

FOOD	EXAMPLE OF PORTION SIZE	BREAKFAST		LUNCH		SUPPER		SNACKS	
		Number of breakfasts with this food in the last three days	How many example portions per breakfast	Number of lunches with this food in the last three days	How many example portions per lunch	Number of suppers with this food in the last three days	How many example portions per supper	Number of snacks with this food in the last three days	How many example portions per snack
BREAD(all types)	1 slice	2	2			3	1		
Macaroni+Cheese	1 cup			1	.5				



FOOD	EXAMPLE OF PORTION SIZE	BREAKFAST		LUNCH		SUPPER		SNACKS	
		Number of breakfasts with this food in the last three days	How many example portions per breakfast	Number of lunches with this food in the last three days	How many example portions per lunch	Number of suppers with this food in the last three days	How many example portions per supper	Number of snacks with this food in the last three days	How many example portions per snack
<b>DAIRY AND EGGS</b>									
FOR ITEMS 1, 2, AND 3 - INCLUDE MILK USED IN TEA AND/OR COFFEE.									
1	Milk (skim or 1%)	1 cup							1
2	Milk (2%)	1 cup							2
3	Milk (whole, homo)	1 cup							3
4	Chocolate Milk	1 cup							4
5	Milkshake	1 cup							5
6	Cottage Cheese/tofu	1/2 cup							6
7	Hard Cheese	1" cube/1/2 oz.							7
8	Processed Cheese Slice/Spread	1 slice/1 Tbsp.							8
9	Low fat Cheese (eg. low fat mozzarella)	1" cube/1/2 oz.							9
10	Cream Cheese	1 Tbsp.							10
11	Yoghurt	1 small tub							11
12	Cream in tea/coffee	1 Tbsp.							12
13	Eggs (boiled, poached)	1 egg							13
14	Eggs (fried, scrambled)	1 egg							14
<b>BREADS AND CEREALS</b>									
15	Breads (all types) DO NOT INCLUDE SANDWICHES	1 slice							15
16	English Muffin/Bagel	1 medium							16
17	Croissant/Dorut/Danish	1 medium							17
18	Pancakes/Waffles	3 medium							18
19	Muffin	1 medium							19
20	Cooked Cereal (eg. oatmeal/cream of wheat)	3/4 cup							20
21	Granola-type Cereal (eg. Harvest Crunch)	1/2 cup							21
22	Sweetened Cereal (eg. Honeycomb/Frosted Flakes/Froot Loops)	3/4 cup							22
23	Ready-to-Eat Cereal (Group A) (eg. Shreddies/Raisin Bran/Life/Bran Flakes/Fruit 'n fibre)	3/4 cup							23
24	Ready-to-Eat Cereal (Group B) (eg. Special K/Corn Flakes/Rice Krispies/Puffed Wheat/Cheerios)	3/4 cup							24
25	Crackers/Pretzels	4 crackers/ 25 sticks							25

FOOD	EXAMPLE OF PORTION SIZE	BREAKFAST		LUNCH		SUPPER		SNACKS	
		Number of breakfasts with this food in the last three days	How many example portions per breakfast	Number of lunches with this food in the last three days	How many example portions per lunch	Number of suppers with this food in the last three days	How many example portions per supper	Number of snacks with this food in the last three days	How many example portions per snack
<b>FRUITS AND JUICES</b>									
53	Apples/Pears	1 medium							53
54	Apricots/Plums	3 small							54
55	Banana	1 medium							55
56	Nectarine/Peaches	1 medium							56
57	Melon/Pineapple	1/2 cup							57
58	Strawberries/Raspberries/Blueberries	1/2 cup							58
59	Cherries/Grapes	15 medium							59
60	Orange	1 medium							60
61	Grapefruit	1/2 medium							61
62	Canned Fruit (water pack)	1/2 cup							62
63	Canned Fruit (juice pack or light syrup)	1/2 cup							63
64	Canned Fruit (heavy syrup)	1/2 cup							64
65	Dried Fruit (eg. raisins/dates)	1/4 cup							65
66	Fruit Juice (type 1) (eg. grape/cranberry/pineapple)	1/2 cup							66
67	Fruit Juice (type 2) (eg. grapefruit/apple/orange)	1/2 cup							67
68	Vegetable Juice (eg. tomato, V-8)	1/2 cup							68
<b>VEGETABLES</b>									
69	Broccoli/Spinach	1/2 cup							69
70	Squash/Turnip	1/2 cup							70
71	Brussel Sprouts/Cabbage/Cauliflower/Peppers	1/2 cup							71
72	Peas	1/2 cup							72
73	Corn	1/2 cup							73
74	Asparagus/Wax or String Beans	1/2 cup							74
75	Carrots	1/2 cup							75
76	Cole Slaw	1/2 cup							76
77	Mixed Green Salad	1 cup							77
78	French Fries	15 pieces							78
79	Potatoes (mashed/baked/boiled) or perogies	1/2 cup 2 perogies							79

The Relationship Between Serum Ferritin and Exercise  
in Postmenopausal women  
INVITATION TO PARTICIPATE

The risk of heart disease increases after menopause and it has been suggested that increase in levels of stored iron in the body associated with the cessation of menstruation is linked to this increased risk. It has also been suggested that stored iron levels are lower in postmenopausal women who participate in a regular aerobic exercise regimen. The amount of exercise necessary to bring about a significant change in the stored iron is not clear. Accordingly, we plan to determine the effect of a 24 week walking program on the level of stored iron in the blood. There will be two groups of walkers, one group will walk three times per week and one group will walk five times per week. A third group will not be put on a walking program, and will follow their usual activities of daily living.

Participants must be non-smokers and postmenopausal (cessation of regular menstrual cycle for a period of one year), 55 years and older who are non-users of alcohol or moderately so (less than 7 ounces per week), are clinically healthy, have no cardiovascular, pulmonary, or metabolic diseases that would preclude safe participation in an exercise program), and are not on medications that will affect serum iron levels. Participants must not be on any estrogen replacement therapy.

If you agree to participate in the study, you will be asked questions relating to your health and lifestyle using a questionnaire; your weight, and height will be recorded; you will be asked to keep a 3 day record of you diet; and have 10 ml (approximately 1/3 ounce) of blood drawn at the beginning and end of the 24 week exercise period. You may experience brief mild discomfort or slight bruising at the site of the needle poke. A 12 hour fast will be required prior to the blood test, however you may continue to drink water during the fasting period.

Fitness Assessment:

Prior to entering the study you will also undergo a treadmill exercise test to make sure that you can safely enter the exercise program. During the treadmill test your blood pressure will be monitored by a cuff wrapped around your upper arm and connected to a pressure gauge and the rate and rhythm of your heart beat (monitored by electrodes placed on your chest and connected to an electrocardiograph) will be recorded. The test will involve a "warm up" period lasting for 3 minutes. The walking pace will then be increased with an accompanying increase in the incline of the treadmill. The test will end when your heart rate reaches a level appropriate for your age. If you become tired before that end-point you may stop. It is highly unlikely that you will experience untoward effects during the test. Potential risks include dizziness, fainting, leg cramps, nausea, chest discomfort, and in extremely rare

instances abnormalities in heart rhythm. It is anticipated that testing will take approximately 1 hour of your time.

DIET ANALYSIS:

Prior to the study, you will be asked to record all foods consumed during a 3 day period. The investigator will then meet with you, and will counsel you to maintain a normal diet throughout the study. You will also complete a three day diet recall form at the end of the study to monitor energy intake and proportion of calories as carbohydrate, fat, iron and protein. The nutrition session will take approximately 1 hour.

TRAINING PROGRAM:

Over a 24 week period you will participate in a program of endurance exercise, where you will be asked to walk at a moderate intensity for 60 minutes. Depending on your group assignment you will be expected to walk either 3 or 5 days per week. During the first two weeks of the study you will be asked to walk at the Max Bell track at the University of Manitoba two times per week with the investigators; thereafter you will be asked to walk at least once per week at the university. As you become more fit the distance you walk will increase. A log book will be provided in which exercise heart rates, attendance, and additional activity will be recorded. A detailed record describing your usual level of physical activity will also be completed during the study. This will involve the reporting of daily activities (leisure and job-related) during a representative one-week

period. It is important that outside endurance activity is kept to a minimum throughout the duration of the study.

It is highly unlikely that injury or illness will result from the training program or from the assessments. You will be evaluated by a cardiologist prior to inclusion in the program, and all tests will be conducted by qualified individuals.

While there may be no direct benefits to your personal participation in this study, the information obtained will provide a better understanding of the possible role of exercise in reducing stored iron and thereby reducing the risk of heart disease.

It is perfectly acceptable to refuse to participate in this study at any time without prejudice. The questionnaires and results of the blood test will be kept in a locked cabinet and only accessible to the researcher.

The results may be published in the form of a journal article. Your name will not appear on any published documents. A summary of the study results will be provided to those requesting it. If you have any questions or concerns that you would like addressed, please contact Ms. Sylvia Oosterveen at 261-4547 (home) or 477-3134 (Victoria Hospital). Thank you for your cooperation.

Sincerely,



Sylvia Oosterveen RN

## Consent Form

### Influence of Energy Expenditure on Fitness and Health Benefits: Comparison of Two Walking Programs

I have read the description of the study and understand the measurement procedures involved.

I also understand that my participation in this study is voluntary and that I may withdraw from it at any time without prejudice. I am free to question the investigators at any time about any aspect of the study.

All information will be kept confidential, and my results will be released to me at the completion of the study.

-----  
Date

-----  
Participant

-----  
Date

-----  
Witness

Name: \_\_\_\_\_

Address: \_\_\_\_\_

Phone number: \_\_\_\_\_

**Walking Study II**  
**Health, Leisure and Human Performance Research Institute**

**Health Status and Lifestyle Questionnaire**

Name: \_\_\_\_\_ Phone Number: \_\_\_\_\_

Date of Birth: \_\_\_\_\_ (mm/dd/yy)

1. a) Are you currently on medication (include non-prescription drugs)?  
 YES  NO

b) If yes: Medication: \_\_\_\_\_  
 Dose: \_\_\_\_\_  
 Reason: \_\_\_\_\_

Medication: \_\_\_\_\_  
 Dose: \_\_\_\_\_  
 Reason: \_\_\_\_\_

c) Has your medication changed in the past three months?  
 YES  NO

d) If yes: Medication: \_\_\_\_\_  
 Dose: \_\_\_\_\_  
 Reason: \_\_\_\_\_

Medication: \_\_\_\_\_  
 Dose: \_\_\_\_\_  
 Reason: \_\_\_\_\_

2. a) Has your activity level changed in the past three months (apart from participation in this walking study)?  
 YES  NO

b) If yes, how?  
 \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_



3. a) Have you had any illnesses in the past three months?  
YES  NO

b) If yes, what and how severe?

-----  
-----  
-----

c) Have you been to see any of the following health care providers in the past three months (indicate the number of times)?

Your own doctor:	-----	Specialist:	-----
Walk in clinic:	-----	Physiotherapist:	-----
Nurse:	-----	Hospital emergency:	-----
Dentist:	-----	Chiropractor:	-----
Athletic therapist:	-----	Other:	-----

4. a) Have you had any injuries related to walking in the past three months?  
YES  NO

b) If yes, what?

-----  
-----  
-----

c) Have you seen a therapist for any injuries related to walking in the past three months?  
YES  NO

d) If yes, who did you see (physiotherapist? doctor? athletic therapist?)?

-----  
-----

e) If you went to Athletic Therapy Clinic here at U of M, do we have your permission to see your records for your visit?  
YES  NO

5. a) Have you had any injuries in the past that might affect your walking?

YES  NO

b) If yes, what?

-----  
-----

6. a) Has your diet or alcohol intake changed in the past three months?

YES  NO

b) If yes, how?

-----  
-----

7. a) Have you ever been under any excess stress these past three months (such as deaths, retirements, weddings, etc.)?

YES  NO

b) If yes, what?

-----  
-----

8. Have you had an increase, decrease, or no change in your energy level in the past three months? \_\_\_\_\_

9. a) Have your sleeping habits changed in the past three months?

YES  NO

b) If yes, how?

-----  
-----  
-----

Interviewed by: \_\_\_\_\_

Date: \_\_\_\_\_

Anthropometric Proforma

Name \_\_\_\_\_  
(last) (first & initial)

ID# \_\_\_\_\_

Birth Date     /    /      
(month / day / year)

Measurement Date     /    /      
(month / day / year)

Measured by \_\_\_\_\_

Body Size:

height [stature] (cm).....	_____	_____	_____		_____
weight (kg).....	_____	_____	_____		_____

Skinfolds (mm):

biceps.....	_____	_____	_____		_____
triceps.....	_____	_____	_____		_____
subscapular.....	_____	_____	_____		_____
iliac crest.....	_____	_____	_____		_____
abdominal/umbilical (vertical).....	_____	_____	_____		_____
front thigh.....	_____	_____	_____		_____
medial calf.....	_____	_____	_____		_____

Girths (cm):

arm.....	_____	_____	_____		_____
forearm.....	_____	_____	_____		_____
wrist.....	_____	_____	_____		_____
chest.....	_____	_____	_____		_____
waist.....	_____	_____	_____		_____
gluteal.....	_____	_____	_____		_____
upper thigh.....	_____	_____	_____		_____
mid thigh.....	_____	_____	_____		_____
calf.....	_____	_____	_____		_____
ankle.....	_____	_____	_____		_____
neck.....	_____	_____	_____		_____

Name: \_\_\_\_\_ Phone #: \_\_\_\_\_ Walking Group: \_\_\_\_\_

Week of \_\_\_\_\_ to \_\_\_\_\_ Training Heart Rate: \_\_\_\_\_ Time for 4 laps (sec) \_\_\_\_\_

Time Walking (min)	Distance* (laps MaxBell/ km)	Exercise Heart Rate (at 30/60 min)	Comments/Class Attendance
Mon _____	_____/____	_____/____	_____
Tue _____	_____/____	_____/____	_____
Wed _____	_____/____	_____/____	_____
Thu _____	_____/____	_____/____	_____
Fri _____	_____/____	_____/____	_____
Sat _____	_____/____	_____/____	_____
Sun _____	_____/____	_____/____	_____

TOTAL: \_\_\_\_\_ min \_\_\_\_\_ km Average: \_\_\_\_\_ bpm # Classes attended: \_\_\_\_\_

Other physical activity done this week: \_\_\_\_\_

Weekly check-in: Exercise leader's signature: \_\_\_\_\_ Check in date: \_\_\_\_\_

PLEASE HAND IN ONCE PAGE IS COMPLETED !!

\* NOTE: 4.2 laps of Max Bell track outer lane is equal to one km.

LOG BOOK PAGE  
REVISED JANUARY 13, 1994