THE EFFECT OF RESISTANCE, ENDURANCE, AND COMBINATION EXERCISE ON LIPID METABOLISM AND NON-TRADITIONAL CARDIOVASCULAR DISEASE RISK MARKERS IN PREVIOUSLY UNTRAINED MEN

A Dissertation

by

STEVEN EDWARD MARTIN

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

August 2008

Major Subject: Kinesiology

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Approved by:

Chair of Committee,	Stephen F. Crouse
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ABSTRACT

The Effect of Resistance, Endurance, and Combination Exercise on Lipid Metabolism and Non-Traditional Cardiovascular Disease Risk Markers in Previously Untrained Men.

(August 2008)

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While adhering to an active lifestyle has been associated with a more favorable lipid profile and reduced risk of coronary heart disease (CHD), information regarding the optimal training modality is not well defined. This project examined the acute and chronic effects of endurance (ET), resistance (RT), and combination endurance / resistance (CT) exercise on lipid metabolism and non-traditional CHD risk markers in untrained men. Thirty-one subjects were randomly assigned to participate for 12 weeks in one of three exercise groups: ET, RT, or CT. To measure the effects of acute exercise on lipid metabolism, fasting blood samples were obtained before (baseline) and 24 hours after (24 h) acute exercise (treadmill jogging at 70% $\dot{V}O_{2peak}$, 350 kcals; weight lifting exercise at 70% of 1RM; combination of treadmill jogging and weight lifting at 70% maximal capacity, 350 kcals). Blood variables were adjusted for plasma volume shifts. This acute exercise protocol was completed on two different occasions corresponding to 0 and 12 weeks of training.

For acute exercise (pre-training), significant results of a 3 (Group) x 2 (Time) ANOVA, repeated for Time, ($p < 0.05$) were as follows: TC, HDL-C, $HDL_{2\&3}$-C were lower 24 h after exercise in the RT group. HDL_2-C was higher 24 h after exercise in the CT and ET groups. In the ET group, LDL_1-C was elevated 24 h after exercise. With all groups combined, LDL_3-C and the TC / HDL-C ratio were elevated and LDL_2-C decreased 24 h after exercise.

For exercise training, significant results of a 3 (Group) x 2 (Training Period) ANOVA, repeated for Training Period, ($p < 0.05$) were as follows: Body Fat, LDL_2-C, and apo A-I were lower after training. Changes in other lipid variables were similar in untrained males performing different types of exercise training.

For acute exercise (post-training), significant results of a 3 (Group) x 2 (Time) ANOVA, repeated for Time, ($p < 0.05$) were as follows: TC, HDL-C, HDL_2-C, LDL-C, NONHDL-C, VLDL-C, IDL-C, LDL_3-C, LDL density, and LPLa were all higher 24 h after exercise. Post-exercise changes in the dependent variables were similar in trained males performing different types of exercise.

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CHAPTER I

INTRODUCTION

This dissertation adheres to the guidelines of the journal article format method instead of the traditional 5-chapter method for dissertations. This document is organized into five chapters (with chapters II-IV intended to stand alone as manuscripts to be submitted for publication) and thirteen appendices. In accordance with these guidelines, a brief introduction to the dissertation topic will be presented in this chapter. Chapter II includes the first manuscript prepared from this investigation. Chapters III and IV include additional manuscripts which were developed as a part of this extensive project. Chapter V provides a general conclusion to the project as a whole, and it is followed by appendices that provide further detail to specific concepts. These include a pertinent review of the related literature, additional methodology, results, and supplemental materials.

Cardiovascular disease (CVD) claims more lives each year than the next seven prevalent causes of death combined. In 1999, CVD was responsible for 1 out of every 2.5 deaths in the United States. The direct and indirect economic costs of CVD and stroke in the United States this year alone - is estimated to be over $329.2 billion. This

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This dissertation follows the style of *Circulation.*

enormous figure includes health expenditures and lost productivity resulting from both morbidity and mortality.[1] Coronary heart disease (CHD), the coronary manifestation of CVD, is the single largest killer of American males and females. CHD was responsible for 529,659 deaths in the United States in 1999 – about 1 of every 5 deaths. About every 29 seconds an American will suffer a coronary event, and about every minute someone will die from one.[2] The private and public health impact of CHD is also indisputable. The direct and indirect costs attributable to CHD have been estimated at close to $95.6 billion in 1998. In 1986, The Framingham Study reported that by age 60, every 5th man and 17th woman would develop CHD.[3] It is imperative that clinical scientists and physicians work together to develop cost effective strategies to prevent, detect, and treat this debilitating disease.

Abundant evidence indicates that CHD is associated with high blood concentrations of total cholesterol (TC), low density lipoprotein (LDL) cholesterol (LDL-C), triglycerides (TG), and with low concentrations of high density lipoprotein (HDL) cholesterol (HDL-C). The risk for development of CHD may be reduced by increasing HDL-C, the less dense subfraction HDL_2-C, and by decreasing both LDL-C and TG concentrations.[4-10] Thus, an atherogenic lipid profile may be described as consisting of elevated TC, LDL-C, and TG and decreased concentrations of HDL-C.[2, 11]

It has also been suggested that other variables, in addition to the traditional lipoprotein-lipid profile, may be more beneficial in identifying individuals who are at an increased risk for developing CHD. Current research seems to suggest that high concentrations of non-HDL (NONHDL) cholesterol (NONHDL-C), intermediate density

lipoprotein (IDL) cholesterol (IDL-C), lipoprotein (a) (Lp (a)), apolipoprotein B (apo B), small, dense LDL particles (d = 1.040 – 1.063 g / cm^2), and the acute phase reactant, high-sensitivity c-reactive protein (hs-Crp) may be better indicators of CHD risk than information obtained from the traditional lipid panel.[12-22]

NONHDL- C includes all cholesterol present in lipoprotein particles that are considered to be atherogenic, including LDL, Lp (a), IDL, and very-low-density lipoprotein (VLDL). It has been suggested that the NONHDL- C fraction may be a better tool for risk assessment than LDL cholesterol.[23] Several studies have also shown that serum IDL-C concentrations can be predictive of an increased incidence of CHD[15] and an increased incidence of coronary events in those with CHD, independently of other risk factors.[12, 16] This relationship may be particularly strong in patients with normal TC concentrations.[24] In another study, normolipidemic men with CHD and subjects with dysbetalipoproteinemia had elevated levels of IDL-C when compared to controls; furthermore, the increased levels of IDL-C were not detected with conventional lipid screening.[25] Similar to LDL-C, IDL-C is taken up by macrophages and can cause foam cell formation and can impair endothelium-dependent vasomotor function in human coronary arteries.[16] The effects of elevated concentrations of Lp (a), the specialized form of LDL, on the atherosclerotic process remains somewhat controversial. Lp (a) recruitment of monocytes and their eventual binding to the wall of coronary vessels could lead to foam cell formation and localization of Lp (a) at the site of the developing atherosclerotic plaque.[22]

In normal individuals, at least four major LDL subfractions have been identified, each conferring a different risk for CHD.[26] LDL subfractions have been shown to identify CHD patients at higher risk for progression of coronary atherosclerosis. The "small, dense LDL" (d = 1.040 – 1.063 g / cm^2) particles have been shown to infiltrate the arterial wall, undergo oxidative modification, and exert atherogenic effects.[27] In the Familial Atherosclerosis Treatment Study (FATS), on-trial changes in LDL density, measured by density gradient ultracentrifugation, was the most important predictor of coronary progression.[21] Furthermore, significant changes in LDL subclass distribution have been shown to occur despite no change in total LDL mass or LDL-C.[28]

Experimental and clinical evidence accumulated since 1990 have established inflammatory processes as important contributors to atherogenesis as well as to the vulnerability of an atherosclerotic lesion to rupture. Based upon this evidence, protein markers of inflammation have been studied as noninvasive indicators of underlying atherosclerosis in apparently healthy individuals. The most extensively studied biomarker of inflammation in CHD is hs-Crp.[29-31] Some experts recommend routine measurement of hs-Crp at the time of traditional lipid screening to be used as adjunctive data in the overall assessment of cardiovascular risk.[18, 20] Among apparently healthy men, the baseline level of inflammation, as assessed by the serum hs-Crp, predicts the long-term risk of a first myocardial infarction (MI), ischemic stroke, peripheral vascular disease, and all-cause mortality.[19] Elevated blood hs-Crp > 3 μg / mL has also been identified as a cardiovascular disease risk marker at least as powerful as LDL-C concentration.[20, 32] Furthermore, evidence exists to suggest that hs-Crp may participate

as a causative agent in atherosclerosis.[33, 34] It is found in atherosclerotic plaques[30], and has been shown to induce LDL uptake by human macrophages.[31]

It is well established that high TC, TG, LDL-C and low HDL-C concentrations are indicative of an atherogenic lipid profile.[2, 11] However, most coronary events occur in people with normal LDL-C and HDL-C concentrations. Furthermore, nearly one half of all MI's occur in individuals who have no evidence of elevated LDL-C concentrations.[35] Thus, the traditional lipid panel may fail to detect almost 50% of people who are at an increased risk for CHD, possibly due to an inability to measure additional highly atherogenic biomarkers, such as Lp (a), IDL-C, NONHDL-C, LDL density, and hs-Crp.[36] A more comprehensive lipoprotein-lipid profile, including all lipoprotein classes as well as subfractions might lead to a more effective preventive treatment strategy for CHD.

In addition to lipoprotein-lipid risk markers, physical exercise and physical fitness are inversely associated with risk for development of CHD. Among the risk markers for this disease, physical inactivity carries a relative risk of 1.5 – 2.4, comparable to risks associated with high TC and high blood pressure.[2] In the United States, approximately 25 percent of the population does not participate in any leisure-time physical activity and only 22 percent report engaging in sustained physical activity for at least 30 minutes on 5 or more days a week.[37]

Over the last several years, the concept of preventing CHD through risk factor reduction has gained widespread popularity. Both pharmacologic and non-pharmacologic strategies have been employed to aid in risk factor reduction and

ultimately CHD prevention.[38-40] Non-pharmacologic strategies have included such areas as diet modification, smoking cessation, as well as physical activity / exercise programs. The role of exercise in reducing one's risk for developing CHD may be partly due to favorable alterations on the blood lipid profile.[41] Furthermore, research supports the fact that health benefits, including an improved lipid profile, may result from a single session of exercise.[42-44] The biological mechanisms by which these improvements occur with exercise are not fully understood, but it is apparent that the activities of some lipid-regulating enzymes (i.e., heparin-releasable lipoprotein lipase) are enhanced with exercise. However, while adhering to a physically active lifestyle has been associated with a more favorable lipid profile and a reduced risk of CHD,[41, 45] information regarding the optimal training modality (endurance, resistance, or combination endurance / resistance exercise) and volume (caloric expenditure) of exercise that will provide the most benefit has not been well defined.

Limited research has been done to explore the effects of resistance exercise on lipoprotein-lipid atherogenic risk markers, and almost no research has been published related to lipid metabolism and combined endurance and resistance exercise. If exercise programming is going to be effectively utilized as an intervention for CHD risk reduction, it is important to clearly define the role of each of these components (mode, volume) in order to provide physicians and exercise professionals with guidelines for developing and implementing safe and effective exercise programs for their patients.

Traditionally, research examining the effectiveness of physical activity on CHD risk reduction has been conducted using endurance exercise as the exercise stimulus. In

most cross-sectional studies endurance trained athletes display higher concentrations of HDL-C, apolipoprotein A-I (apo A-I), heparin-releasable lipoprotein lipase (LPL) activity (LPLa), and lower concentrations of LDL-C, apo B, TG, and hepatic triglyceride lipase (HTGL) activity (HTGLa) as compared with untrained individuals.[46-51] However, the results from longitudinal training studies have been inconsistent. A majority of the published research has reported that the concentrations of HDL-C and TG are more responsive to exercise training,[41] while the concentrations of TC and LDL-C are rarely altered.[41, 44] Elevations in LPLa have been shown to occur after exercise training.[52-57] Other lipoprotein enzymes such as HTGL and cholesterol ester transfer protein (CETP) have been studied although the results have been inconclusive.[56-61] The increased LPLa is associated with a reduction in TG, with subsequent elevations in HDL-C concentrations.[62, 63] The suppression of HTGLa and CETP activity, which may occur in response to exercise training, may lead to a reduced catabolism of HDL particles and a more favorable lipid profile.[64, 65] Explanations for the conflicting findings have been attributed to differences in exercise volume (caloric expenditure), duration of training, type of exercise, baseline subject characteristics, dietary influences, baseline lipid concentrations, and timing of blood sampling after the last session of exercise.[58, 66-68] It is also possible that subtle changes in lipoprotein metabolism may have gone undetected in a number of studies. For example, Crouse et al.[42] reported that 6 months of endurance training by men with elevated cholesterol resulted in a significant rise in HDL_2-C and fall in HDL_3-C, but no change in total HDL-C.

There is evidence that health benefits may occur in response to a single session of endurance exercise. Research supports the fact that a single session of endurance exercise may acutely alter lipoprotein-lipid concentrations for at least 48 hours after exercise (acute effect). LPLa has also been shown to increase[69, 70] after a single exercise session. HTGLa has been shown to decrease [60, 71] or remain unchanged [69] after prolonged exercise. The concentrations of HDL-C and both HDL subfractions are generally increased, [43, 69, 71-78] while TG, [72, 74, 76-85] TC, [72, 74, 79, 81, 84, 85] and LDL-C [69, 76, 79, 81] concentrations are reduced 24 to 48 hours after the single exercise session. Therefore, if the timing of blood sampling is not controlled and occurs $\leq$ 48 h after the last session of exercise, researchers may mistakenly attribute changes in the lipid profile to the effects of chronic exercise training when in fact the lipid alterations were induced by the last exercise session. Moreover, endurance training may alter the acute lipid response. Results from a cross-sectional investigation support the contention that endurance exercise training affects the acute lipoprotein-lipid response to a single session of exercise. Kantor et al. [69] reported that a measured increase in blood HDL-C concentrations after prolonged endurance exercise was due to elevated HDL_2-C concentrations in endurance trained subjects, but to elevated HDL_3-C in untrained subjects. Different acute changes in lipoprotein-lipids have been shown to occur after a single session of endurance exercise in trained compared to untrained normo – and hypercholesterolemic individuals.[43, 66, 69, 86] Crouse and colleagues [42] recently reported that 24 weeks of endurance training may suppress the rise in LDL-C noted in hypercholesterolemic men after a single session of endurance exercise. Additional well-

controlled studies are needed to verify these findings, and to determine the amount of change to be expected after a single session of exercise, both before and after a period of training.

It has been reported that men engaging in vigorous muscular activity had a lower incidence of sudden cardiac death when compared to men who were less active.[87] Research from the late 1970's indicates that lumberjacks, who perform activities similar to resistance exercise, had higher concentrations of HDL-C and lower TG concentrations when compared to a group of less active electricians.[88] Recently the American Heart Association and the Surgeon General have recommended resistance training as an integral part of a well-rounded physical activity program for health and disease prevention.[89, 90] Resistance exercise has been shown to aid in the prevention and rehabilitation of low back pain, osteoporosis, obesity, sarcopenia, and diabetes mellitus.[91] In addition, resistance training has also been shown to decrease heart rate, systolic blood pressure, and rate pressure product on a standard treadmill protocol.[92] With the increasing popularity of resistance exercise training, more people will likely adopt this type of activity, making it important to study the effects of this type of exercise on CHD risk factors.[89, 90] However, compared to the endurance exercise literature, there is a lack of information related to the effects of resistance exercise on circulating lipids and lipoproteins. Moreover, a review of the resistance training literature from the previous 22 years has produced contradictory results. In several studies, resistance training reduced blood LDL-C concentrations and increased HDL-C concentrations.[93-100] However, contrasting findings have also been reported.[101-106]

Interpreting the results from many of the resistance training studies is difficult, as they seem to suffer some of the same design problems present in many endurance training studies. Methodological differences, such as differences in training procedures, subject characteristics, dietary controls, and timing of blood sampling after exercise, may be responsible for some of the variability in the literature.[93-97, 100] For example, it has been suggested that resistance training using high repetitions and moderate resistance may promote favorable changes in the lipid profile, whereas resistance training consisting of low repetitions and heavy resistance does not.[107] Others have reported that neither low repetition nor high repetition resistance training effectively altered lipoprotein-lipids.[101] Although resistance exercise may be recommended to the general public for its proven skeletal muscle benefits, the beneficial influence of this mode of exercise on circulating lipids, lipoprotein enzymes, apolipoproteins, and non-traditional CHD risk markers remains to be established.

As with endurance exercise, it is possible that a single session of resistance exercise may alter the metabolism of circulating lipoprotein-lipids (acute effect). However, research in this area is currently lacking. There appears to be only a single, well-controlled investigation in which the lipid / lipoprotein response to a single session of resistance exercise was reported.[108] In this study increases in HDL-C occurred 24 h after a high-volume (800 kcal) resistance exercise session, but not after a low volume (200 kcal) session. Biochemical mechanisms responsible for this acute effect are not clear, and the influence of this form of exercise on LDL density and hs-Crp is unknown. Furthermore, the possibility that chronic resistance training may alter the acute lipid

response to a single session of resistance exercise in healthy, untrained men has not been published.

As the popularity of resistance training increases, more people are likely to develop total fitness programs, emphasizing both muscular strength and cardiovascular endurance. However, published research regarding the effects of combination exercise training on the lipoprotein-lipid profile are lacking. LeMura et al.[103] assessed the effects of various modes of training (endurance, resistance, and combination exercise) on changes in blood lipids after 16 weeks of training and 6 weeks of detraining in young untrained women. It was reported that 16 weeks of combination training did not result in any significant changes in blood lipids. Furthermore, research regarding the effects of a single session of combination exercise on the blood lipid profile has not been published. As with the resistance exercise literature, there has been nothing published regarding the possibility that the acute lipid response to a single session of combination exercise may be altered by chronic combination training. It is clear by the lack of published research in this area that additional studies are warranted.

It is also possible that resistance exercise, a high-intensity intermittent exercise involving small muscle groups, may produce unique changes in lipid metabolism compared to endurance exercise. A substantial portion of the energy requirement for resistance exercise is provided by stored phosphocreatine, blood glucose, and muscle glycogen. Pascoe and colleagues [109] have reported that strenuous resistance exercise has the potential to deplete muscle glycogen stores. It is believed that during recovery from resistance exercise lipids may be utilized as a primary source of energy (i.e., increased

oxidation of fats) thus sparing carbohydrate to be used for the resynthesis of glycogen stores.[110, 111] Increases in fat oxidation may also be attributed to elevated levels of catecholamines, resulting in increased rates of lipolysis.[112] Catecholamine levels have also been shown to be distinctly increased during heavy resistance exercise compared with cycling or running exercise of similar volumes.[113] On the other hand, energy for endurance exercise, a dynamic activity involving large muscle groups contracting rhythmically at low relative intensities, is provided primarily by oxidation of fats.[114] The energy demands associated with endurance exercise can eventually deplete intramuscular TG concentrations. It has been suggested that this depletion of intramuscular TG might stimulate secretion or synthesis of LPL in muscle capillaries. Greater LPLa is associated with increased TG clearance and HDL-C concentrations, changes indicative of decreased CHD risk.[115] The fact that resistance exercise results in a different metabolic stress in muscle compared to endurance exercise supports the argument that different acute and chronic changes in the lipoprotein-lipid profile might also result in response to resistance exercise training.

Other published data suggest that both resistance and endurance training act through similar mechanisms to produce beneficial effects on circulating lipids. For example, induction of LPL has been reported after intense local contractile activity in muscles of both rats [116] and humans, [117] suggesting that local contractile activity may be necessary for increased LPL expression during exercise training.[116] Furthermore, Kiens et al.[52] reported that 8 weeks of one-legged dynamic knee exercise resulted in an increase in muscle LPLa and the concentration of HDL_2-C in the trained leg, but not in

the untrained muscle. Since muscle is an important site of TG removal in humans, LPL induction and lipolysis in muscle may be essential for increasing HDL-C concentrations.[117] Given that strenuous muscle contraction accompanies both resistance and endurance exercise, both modes of exercise could, in theory, be capable of inducing an LPL response in skeletal muscle. However, while a single session of endurance exercise has been shown to reduce the postprandial rise in TG, the volume (caloric expenditure) of the exercise appears to affect the magnitude of the lipemic response.[118] In contrast, it has recently been reported that a single session of resistance exercise can also reduce the postprandial lipemic response despite a lower total energy expenditure during the exercise session.[119] This seems to suggest that the lipemic response after resistance exercise may not be related to the volume of exercise but to some other factor linked to strenuous muscle contraction associated with weight lifting. In spite of the prescriptive importance of data on this subject, research in this area is currently lacking.[102]

In addition, published literature regarding the interrelationships between non-traditional lipid variables, hs-Crp levels, LDL density, and other behavioral risk factors, such as exercise, are limited and urgently require verification by additional research.[120] Reduced hs-Crp has been shown to occur in association with leisure-time physical activity, [121, 122] after weight loss, [123, 124] and after marathon training.[125] The effects of chronic endurance exercise training on blood levels of hs-Crp is limited to a handful of studies.[125-127] Tisi et al. [127] have reported that blood hs-Crp levels were significantly reduced after 3 to 6 months of regular physical activity in individuals with intermittent

claudication. It is of clinical relevance that additional research be conducted to corroborate and expand upon these limited findings.

Research investigations have also reported that exercise may promote changes in HDL and LDL particle size, [58, 104] and there is clear evidence that LDL particle number can be increased when plasma TC and LDL-C levels are normal.[128] To our knowledge, no studies published to date dealing with hs-Crp and LDL densities have utilized combined resistance-endurance exercise as the exercise stimulus. It is imperative to address this lack of practical information since it is becoming more common for adult men and women, and especially the aged, to combine some form of resistance training with endurance training as part of their physical fitness practices.

The primary purpose of this investigation was to characterize the effects of both acute and chronic endurance, resistance, and combination exercise on circulating lipids, apolipoproteins, lipoprotein enzymes, lipoprotein subfractions, and blood levels of hs-Crp in previously untrained males. In order to examine this purpose, the following objectives were addressed:

Objective 1. Determine whether or not twelve weeks of endurance, resistance, or combination exercise training differentially affect the dependent variables measured.

Objective 2. Determine whether or not a single session of endurance, resistance, or combination exercise differentially affect the dependent variables measured.

CHAPTER II

A SINGLE SESSION OF RESISTANCE, BUT NOT ENDURANCE, OR COMBINATION EXERCISE, REDUCES SERUM LIPOPROTEIN-LIPIDS IN UNTRAINED MEN

Introduction

Coronary heart disease (CHD) is the single largest killer of American men and women.[4] Abundant evidence indicates that CHD is associated with high blood concentrations of total cholesterol (TC), low density lipoprotein (LDL) cholesterol (LDL-C), triglycerides (TG), and with low concentrations of high density lipoprotein (HDL) cholesterol (HDL-C).[4] The risk for development of CHD may be reduced by increasing HDL-C, the less dense subfraction HDL_2-C, and by decreasing both LDL-C and TG concentrations.[129, 130] In addition to traditional lipoprotein-lipid risk markers, physical exercise and physical fitness are inversely associated with risk for development of CHD. While adhering to a physically active lifestyle has been associated with a more favorable lipid profile and a reduced risk of CHD,[131] information regarding the optimal training modality (endurance, resistance, or combination endurance / resistance exercise) and volume (caloric expenditure) of exercise that will provide the most benefit has not been well defined.

Endurance-type exercise training has been utilized as the main exercise stimulus in the majority of research studies examining the effectiveness of physical activity on CHD risk reduction. Research suggests that an exercise stimulus of sufficient volume and duration may induce moderate increases in HDL-C, HDL_2-C, HDL_3-C, and reduce

TG concentrations.[72] The biological mechanisms by which these improvements occur are not fully understood, but it is apparent that the activities of some lipid-regulating enzymes (i.e., heparin-releasable lipoprotein lipase) are enhanced with exercise.

Some of the favorable lipoprotein-lipid modifications attributed to chronic exercise training may actually be stimulated by a single exercise session.[44, 131] The activity of lipoprotein lipase (LPL) and the concentration of HDL-C are often found to be acutely elevated and hepatic triglyceride lipase activity (HTGLa), TG, TC, and LDL-C concentrations reduced for at least 48 h after a single session of endurance exercise.[42, 69, 132, 133] Moreover, an individuals' training status may influence this acute lipoprotein-lipid response to prolonged exercise. Different acute changes in lipoprotein-lipids have been shown to occur after a single session of endurance exercise in trained compared to untrained normo – and hypercholesterolemic individuals.[43, 66, 69, 86] Kantor et al.[69] reported that a measured increase in HDL-C concentrations after prolonged endurance exercise was due to elevated HDL_2-C concentrations in endurance trained subjects, but to elevated HDL_3-C in untrained subjects. Additional well-controlled studies are needed to verify these findings, and to determine the amount of change to be expected after a single session of exercise in individuals of varying in fitness levels, and varying ages.

Resistance training has been recommended as an integral part of a well-rounded physical activity program for health and disease prevention.[89] Resistance training has been shown to aid in the prevention and rehabilitation of low back pain, osteoporosis, obesity, sarcopenia, and diabetes mellitus.[89] However, compared to the endurance exercise literature, there is a relative paucity of information related to the effects of

resistance exercise on circulating lipids and lipoproteins and almost nothing regarding combination endurance / resistance exercise. Studies that exist are often contradictory, and the published literature is almost completely lacking of reports comparing the effectiveness of endurance to either resistance or combination exercise designed for general health and fitness benefits in sedentary individuals.[95, 103, 134] It has been reported that resistance training favorably reduces blood LDL-C and increases HDL-C concentrations.[95, 98, 99] However, contrasting findings have also been published.[102, 103, 105]

Interstudy methodological differences, such as differences in training procedures, subject characteristics, dietary controls, and timing of blood sampling after exercise, may account for some of the variability in the published findings of both endurance and resistance training investigations.[58, 66, 67, 94, 95] For example, Hurley and associates[107] reported that athletes who trained using moderate resistance, high repetition exercise exhibited a more favorable lipid profile than those who trained using heavy resistance, low repetition exercise. Thus, although resistance exercise may be promoted to the general public for its proven skeletal muscle benefits, the beneficial influence of this mode of exercise on circulating lipids and lipoproteins remains to be established.

As with endurance exercise, it is possible that resistance exercise may exert an acute benefit on circulating lipids and lipoproteins. However, research in this area is currently lacking. There appears to be only a single, well-controlled investigation in which the lipoprotein-lipid response to a single session of resistance exercise was reported.[108] In this study increases in HDL-C occurred 24 h after a high-volume (800 kcal) resistance exercise session, but not after a low volume (200 kcal) session.

However, most sedentary individuals beginning an exercise program for general health and fitness gains would most likely not be able to tolerate this volume of work. In addition, the biochemical mechanisms responsible for this acute effect are not thoroughly understood. However, LPL induction has been measured after local contraction of muscles in both rats[116] and humans,[52, 117] suggesting that the response is localized to muscles involved in the exercise performed. As the popularity of resistance exercise increases, more people are likely to develop total fitness programs, emphasizing both muscular strength and cardiovascular endurance, making it important to study the effects of these types of exercise on CHD risk factors. Therefore, the purpose of this investigation was to characterize the short-term changes in circulating lipids and lipoprotein enzymes in untrained, college-aged men following a single session of endurance, resistance, and combination exercise.

Methods

Subjects

Subject recruitment began after the investigation was approved by the Texas A&M University Review Board for Human Subjects in Research, and was limited to Bryan/College Station, Texas. Potential volunteers responded to flyers which were posted on the Texas A&M University main campus. Thirty-six untrained male volunteers 18 – 40 years old were initially recruited for this investigation, asked to sign an informed consent approved by the Texas A&M Institutional Review Board for Research with Humans, and completed a health history questionnaire. Subjects were considered untrained if they had not participated regularly in endurance or resistance

training (less than 2 exercise sessions / week and ≤ 20 minutes per exercise session) for at least the last three months. Volunteers were screened to exclude those who exhibited evidence of medical contraindications to exercise and heparin, were taking drugs known to affect lipid/lipoproteins or blood clotting, used tobacco products, or consumed more than two ounces of alcohol per day. Five subjects did not complete the entire research protocol, four due to injury, and one for unknown reasons. Therefore, thirty-one subjects were included in the final data analysis.

Experimental Protocol

Following an orientation meeting (week 1), the subjects were randomly placed into one of three exercise groups (endurance, resistance, or combination endurance / resistance). The following week (week 2), all subjects, regardless of group assignment, were asked to report to the Applied Exercise Science Laboratory at Texas A&M University on two days for baseline physiological and performance measurements. After the week of pre-testing, all subjects completed a series of blood draw procedures over three consecutive days, which included an experimental exercise session (week 3). Diet and physical activity data were collected during all blood draw procedures. The subjects assigned to the exercise groups completed endurance, resistance, or combination exercise at an intensity of 70% maximal capacity. Blood was drawn the day before (baseline), and 24 hours (24 h) after exercise for assessment of dependent variables.

Physiological Testing

Each subject was measured for: 1) height and body weight; 2) waist and hip girth; 3) relative body fat 4) lung volumes 5) peak oxygen consumption ($\dot{V}O_{2peak}$), and; 6) one-repetition maximum strength assessments (1RM). Percent fat (% Fat) and lean body mass (LBM) were calculated from body density measured hydrostatically[135] at residual volume (RV). All subjects completed a standardized maximal graded exercise test (GXT) on a motor driven treadmill (Quinton Model # Q-65, Quinton Instrument Co., Seattle, WA) under the supervision of trained laboratory personnel.[136] Resting and maximum-exercise heart rate measurements were taken during the $\dot{V}O_{2peak}$ testing through the use of Polar® heart rate monitors. Blood pressure was determined manually, and ratings of perceived exertion were obtained during the last 30 seconds of every stage of the protocol. Respiratory gas exchange (minute ventilation ($\dot{V}_e$), oxygen consumption ($\dot{V}O_2$), and carbon dioxide production ($\dot{V}CO_2$) was measured on a breath-by-breath basis and averaged over 30-s intervals via open-circuit spirometry utilizing an automated metabolic cart (CPX / D Exercise Stress Testing System, Medical Graphics Corp., Minneapolis, MN) calibrated with gas mixtures of known composition before and after each test. The $\dot{V}O_{2peak}$ test was considered valid if at least two of the following criteria were met: 1) the maximum age-predicted maximum heart rate was achieved or; 2) the respiratory exchange ratio was greater than 1.1 or; 3) $\dot{V}O_2$ failed to rise with increasing workload.[137]

All subjects were tested for strength by determining the maximum weight that could be successfully lifted one time, with proper technique (1RM), after completion of a standardized warm-up. The warm-up consisted of 5 minutes of cycling, 5 minutes of stretching, and 4 light sets of each of the following exercises: leg press, leg curl, standing calf raise, barbell bench press, lat pull-down, dumbbell military press, and a barbell curl.

Experimental Exercise Session Calculations

Using data from the GXT for each participant in both EE and CE groups, the $\dot{V}O_2$ (L / min) and respiratory exchange ratio (RER) at 70% $\dot{V}O_{2peak}$ were used to estimate the exercise duration needed to elicit the target energy expenditure (kcal). The detailed procedures for estimating the duration of exercise needed to expend the target energy expenditures for all acute endurance exercise sessions have been previously reported by our laboratory.[42] With regards to the experimental session of resistance exercise, a regression equation was developed from pilot data to determine the rate of energy expenditure (kcal/min) of a similar resistance exercise workout. With respect to the experimental exercise sessions, subjects were instructed to abstain from any physical exercise for at least 72 h, before reporting to the laboratory (12-hour fast, water allowed *ad libitum*) to complete the submaximal, experimental exercise session. Specifically, for the acute bout of endurance exercise, subjects were asked to walk or jog on a motor-driven treadmill at 70% of their $\dot{V}O_{2peak}$ for the duration required to expend 350 kcal of

energy. The detailed methodological design of the acute exercise sessions has been previously reported by our laboratory.[42]

Subjects in the RE group completed a typical resistance exercise training session (duration = 58 min) similar to what might be recommended by the American Heart association (AHA) or the American College of Sports Medicine (ACSM) for sedentary individuals adopting an exercise program for general health and fitness benefits.[137] Weights used for each exercise were calculated as approximately 70% of the 1RM, and chosen so that the subject would be challenged, but yet able to complete all repetitions in each exercise set, and continue exercise until completion of the session. Subjects completed one warm-up set of ten repetitions at 50% of their 1RM followed by three sets of ten repetitions at 70% of their 1RM. The eight exercises consisted of leg press, leg curl, standing calf raise, barbell bench press, lat pull-down, dumbbell military press, barbell curl, and an abdominal crunch. Recovery time between sets and exercises were strictly controlled with two-minute turnovers. The results from our pilot study reinforced the notion that most young, untrained individuals would not have been able to tolerate any additional volume than our standard 58 minute protocol. Expired gases were measured for the first 16 minutes of resistance exercise with a portable metabolic system (Medical Graphics CPX / D) to spot check the results from our regression equation for determining the rate of energy expenditure (kcal/min).

For those in the combination group, subjects were asked to either walk or jog at an intensity equal to 70% of their maximal effort recorded on their earlier exercise test ($\dot{V}O_{2peak}$) for a length of time needed to burn 175 kcal of energy. After the subjects

finished with this activity, they performed several resistance exercises for a duration that required the expenditure of 175 kcal of energy. Weights used for each exercise were calculated as approximately 70% of the 1RM. Heart rate was monitored continuously and expired gases were measured every 10 minutes of endurance exercise and the first 16 minutes of resistance exercise with a portable metabolic system (Medical Graphics CPX / D) to determine the total O_2 uptake ($\dot{V}O_2$), and ultimately the rate of energy expenditure (kcal/min). Subjects were asked to stop lifting weights once the target caloric expenditure was achieved. The combined total energy expenditure for the combination exercise group was 350 kcal.

Blood Sampling

Blood samples were obtained 24 h before (baseline) and 24 h after the experimental exercise session. Each subject reported to the laboratory, time of day controlled, after a 12-hour fast (water allowed *ad libitum*) and having refrained from any exercise in the preceding 72 h. A more detailed description of our blood sampling procedures has been reported previoulsy.[42, 138] Serum and plasma from pre- and post-heparin blood was isolated by centrifugation at 1500 x g for 30 minutes at 4°C. Aliquots of pre- and post-heparin plasma and serum were sealed separately in 2 ml cryovials (no. 66008-284, VWR Scientific Inc., Westchester, PA) and stored at -80°C for later analysis. All blood variables were adjusted for plasma volume shifts that occurred as a result of acute exercise using hematocrit and hemoglobin measurements obtained from each sample.[139]

Biochemical Analysis

Frozen aliquots of serum were sent to Atherotech, Inc (Birmingham, AL) for complete lipoprotein-lipid analyses (TC, TG, LDL, HDL-C , HDL_2-C, and HDL_3-C) with the Vertical Auto Profile (VAP) method.[36] Atherotech is a fully certified and licensed clinical Laboratory. Atherotech is part of the "Cholesterol Reference Method Laboratory Network". Atherotech also participates in 3 highly recognized "Proficiency Testing Programs". These are *Northwest Lipid Research Laboratories (NWLRL),* one of five "CDC-NHLBI" cholesterol reference labs; *New York State Department of Health*, a "CLIA" approved program; and *"Accutest"*, a "CLIA" approved program. Total plasma lipase activity (TLa) and hepatic triglyceride lipase activity (HTGLa) were determined from post-heparin plasma using the methods described by Thompson et al.[140] and Belfrage and Vaughn.[141] The activity of endothelial-bound lipase (LPLa) was calculated as the difference between the TLa and that of HTGLa. Our lab intra-assay and inter-assay CVs for enzyme analysis were 7% and 10.4% for TLa and 3% and 10.6% for HTGLa.

Diet and Physical Activity Records

Self-reported dietary records were used to assess the nutritional composition and caloric intake in each subject's diet over the blood sampling period. Subject's recorded their diet over a 7 day period (4 days prior and 3 days during the blood sampling protocol). The dietary intake logs prompted each subject to record the date, time, type, portion size, and preparation methods for anything that was consumed during the period of interest. In addition, subjects were given verbal instruction on the proper techniques

for completing the dietary intake log. Also, each dietary intake log was accompanied by a written example of proper form completion and a summary of portion size estimation methods. All daily diet records were analyzed for caloric consumption and nutrient intake using the Food Processor SQL (Version 9.3, ESHA Research, Salem, OR) program. A seven–day physical activity questionnaire (PAQ) was used to assess routine daily activity over the same period in which the dietary intake logs were kept. The questionnaire was adapted from the seven-day record developed by Blair et al.[142] Subjects were also asked to refrain from any strenuous physical activity, including exercise, outside of that required by their job or as part of the research investigation.

Statistical Analysis

Baseline differences between the subjects assigned to the different exercise groups were determined for physiological, diet, physical activity, lipoprotein-lipid, and enzyme variables using one-way analysis of variance (ANOVA). Furthermore, relationships between the baseline physiological and blood variables were determined using Pearson product-moment correlation coefficients. The dependent variables of interest for this investigation were plasma volume adjusted concentrations of TC, TG, LDL-C, HDL-C, HDL_2-C, HDL_3-C, and the enzyme activities (LPLa and HTGLa). Furthermore, the following ratio variables were determined: TC / HDL-C, LDL-C / HDL-C, and HDL_2-C / HDL_3-C. A global test for significance was performed using a 3 (group) X 2 (time) ANOVA with repeats across time. Significant interactions were additionally explored using simple main effects analysis. In addition, mean separation

procedures were carried out using Duncan's New Multiple Range Test when appropriate. All data was analyzed using the Statistical Analysis System (SAS, version 9.13, Cary, NC). The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Baseline descriptive characteristics are presented in Table 1-1. In addition, significant relationships between selected physiological variables and baseline lipoprotein-lipids are displayed in Table 1-2. Statistical analysis of the lipid and lipoprotein enzyme data revealed that the type of exercise performed influenced the short-term lipid response in young, untrained men. The TC concentration was significantly reduced 24 h after exercise in the RE group compared to baseline values (Figure 1-1). In addition, the change in LDL-C followed a similar trend. However, the calculations for simple main effects did not reach significance for LDL-C concentration.

Table 1-1. Baseline Exercise Group Data

Variable	RE	EE	CE
Age, yrs	22 ± 1 [a]	24 ± 1 [a]	22 ± 1 [a]
Height, in	68.9 ± 0.66 [a]	69.7 ± 0.91 [ab]	71.7 ± 0.54 [b]
Weight, kg	73.8 ± 4 [a]	85.6 ± 5 [ab]	95.9 ± 4.7 [b]
BMI, kg/m^2	23.98 ± 1.04 [a]	27.4 ± 1.78 [a]	29.05 ± 1.64 [a]
% Fat, %	15 ± 1 [a]	19 ± 3 [a]	20 ± 3 [a]
$\dot{V}O_{2peak}$, mL/kg/min	43.6 ± 1.6 [a]	41.8 ± 2.7 [a]	42.7 ± 2.2 [a]
TC, mg/dL	165 ± 11 [a]	163 ± 7 [a]	163 ± 8 [a]
TG, mg/dL	103 ± 13 [a]	129 ± 15 [a]	90 ± 10 [a]
HDL-C, mg/dL	48 ± 3 [a]	42 ± 2 [a]	48 ± 2 [a]
EXKCAL	232 ± 22 [a]	355 ± 5 [b]	353 ± 1.2 [b]
EXDUR	57 ± 2 [a]	30 ± 2 [b]	43 ± 1 [c]

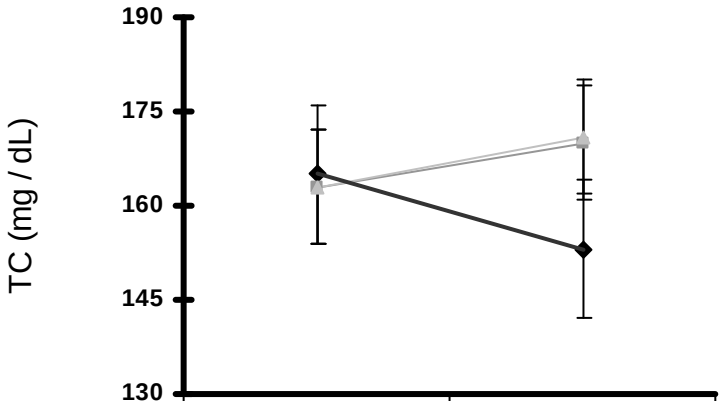
All data are presented as the mean ± SEM. RE = resistance exercise group, n = 9; EE = endurance exercise group, n = 10; CE = combination exercise group, n = 12;

BMI = body mass index; $\dot{V}O_{2peak}$ = peak oxygen consumption as measured during a standardized graded exercise test; TC = total cholesterol; TG = triglyceride; HDL-C = high density lipoprotein cholesterol; EXKCAL = caloric expenditure of acute exercise session; EXDUR = duration (minutes) of acute exercise session. Exercise group means within each row with same letters are not different ($p < 0.05$).

Table 1-2. Correlation Matrix for Selected Physiological, Lipid, and Enzyme Data at Baseline

Variable	HDL-C	HDL_2-C	HDL_3-C	$\dot{V}O_{2peak}$, mL/kg/min
LPLa		0.380		
TG	-0.547	-0.504	-0.533	
Weight, kg				-0.543

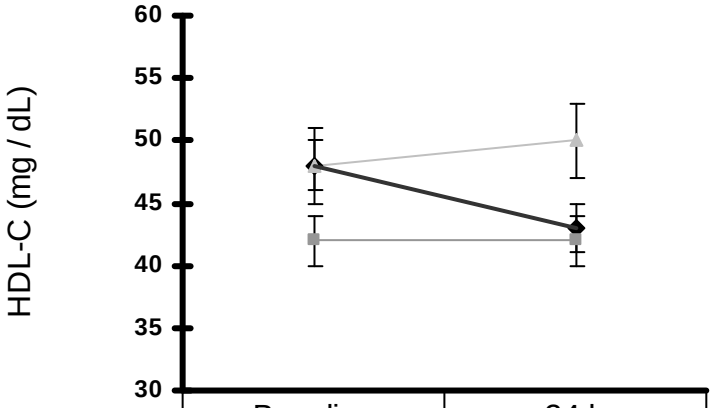
Relationships were determined after combining data from all exercise groups. All relationships shown are statistically significant ($p < 0.05$).



	Baseline	24 h
RE	165	153 *
EE	163	170
CE	163	171

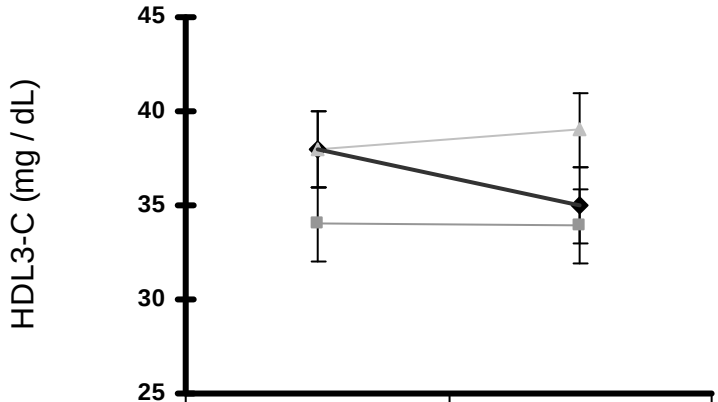
Figure 1-1. Average change in plasma volume-adjusted total cholesterol concentrations with exercise. Baseline, 24 h before exercise; 24 h = 24 hours after exercise. RE = resistance exercise group, n = 9; EE = endurance exercise group, n = 10; CE = combination exercise group, n = 12. Data are group means (mg / dL) ± SEM.
* Significant differences between times, within group ($p < 0.05$).

The HDL-C and HDL_3-C concentrations were significantly reduced 24 h after the acute exercise session in the RE group (Figures 1-2, 1-3). Furthermore, there was a significant difference in HDL-C and HDL_3-C concentrations between the exercise groups at the 24 h post-exercise blood draw time period. The concentrations of HDL-C and HDL_3-C were higher in the CE group compared to both EE and RE groups.



	Baseline	24 h
RE	48	43 * a
EE	42	42 a
CE	48	50 b

Figure 1-2. Average change in plasma volume-adjusted high-density-lipoprotein cholesterol concentrations with exercise. Baseline, 24 h before exercise; 24 h = 24 hours after exercise. RE = resistance exercise group, n = 9; EE = endurance exercise group, n = 10; CE = combination exercise group, n = 12. Data are group means (mg / dL) ± SEM. * Significant differences between times, within group ($p < 0.05$). [a,b] Significant difference within time, between groups ($p < 0.05$).

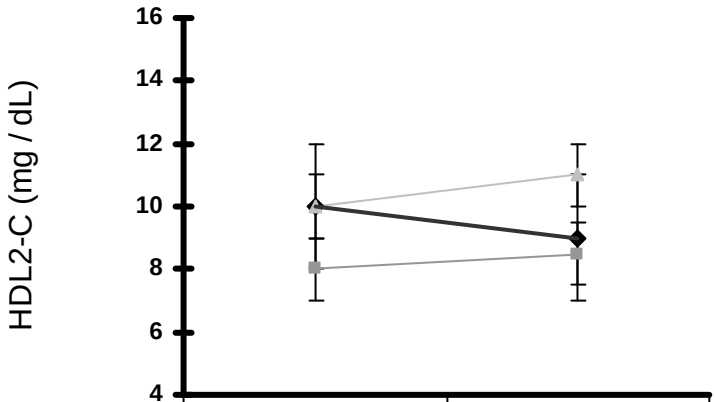


	Baseline	24 h	
RE	38	35 *	a
EE	34	33.9	a
CE	38	39	b

Figure 1-3. Average change in plasma volume-adjusted high-density-lipoprotein$_3$ cholesterol (HDL_3-C) concentrations with exercise. Baseline, 24 h before exercise; 24 h = 24 hours after exercise. RE = resistance exercise group, n = 9; EE = endurance exercise group, n = 10; CE = combination exercise group, n = 12. Data are group means (mg / dL) ± SEM. * Significant differences between times, within group ($p < 0.05$). [a,b] Significant difference within time, between groups ($p < 0.05$).

HDL_2-C concentrations were also differentially altered in response to the type of exercise performed by our subjects. The HDL_2-C concentration was significantly elevated 24 h after the exercise session within the CE and EE groups. Conversely, the HDL_2-C concentration was reduced 24h after acute exercise in the RE group (Figure 1-4).

No exercise group X time interactions were observed for any other lipoprotein-lipid or lipoprotein enzyme variables. A time main effect was noted for TG and the TC / HLD-C ratio ($p < 0.05$). The concentration of TG was significantly reduced at the 24 h post-exercise time period, regardless of exercise mode (Figure 1-5). The TC / HDL-C ratio was significantly elevated at the 24 h post-exercise time period. Both the



	Baseline	24 h
RE	10	9 *
EE	8	8.5 *
CE	10	11 *

Figure 1-4. Average change in plasma volume-adjusted high-density-lipoprotein$_2$ cholesterol (HDL_2-C) concentrations with exercise. Baseline, 24 h before exercise; 24 h = 24 hours after exercise. RE = resistance exercise group, n = 9; EE = endurance exercise group, n = 10; CE = combination exercise group, n = 12. Data are group means (mg / dL) ± SEM. * Significant differences between times, within group ($p < 0.05$).

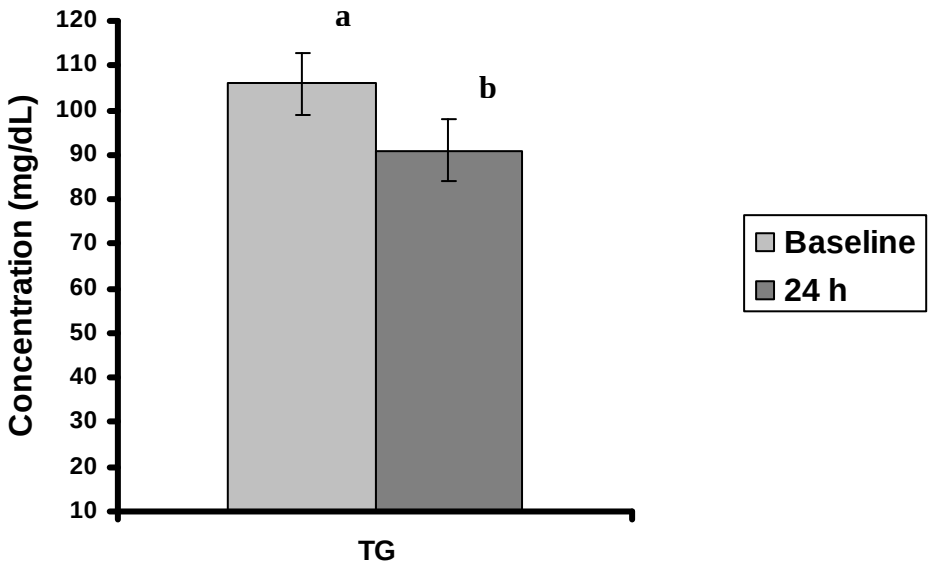


Figure 1-5. Average change in plasma volume-adjusted TG concentration with exercise. RE = resistance exercise group, n = 9; EE = endurance exercise group, n = 10; CE = combination exercise group, n = 12. Baseline, 24 h before exercise (light-gray bars); 24 h = 24 hours after exercise (dark-gray bars). Data are combined group means (mg / dL) ± SEM. TG concentration at each of the time-points were: Baseline = 106 ± 8; 24 h = 91 ± 7. [a,b] Significant difference between time ($p < 0.05$).

LDL-C / HDL-C and HDL_2-C / HDL_3-C ratios remained essentially unchanged after exercise. No time main effects were determined for any of the plasma volume adjusted lipoprotein enzyme activities. However, LPLa demonstrated a non-significant increase at the 24 h post-exercise time period ($p = 0.357$). The exercise-induced changes in plasma volume adjusted lipid and lipoprotein enzyme variables are presented in Table 1-3.

Table 1-3. Changes in Blood Lipid and Lipoprotein Enzyme Variables with Exercise

Variables	Baseline	24 h
LDL-C, mg/dL		
RE	98 ± 10	91 ± 9
EE	103 ± 8	109 ± 8
CE	99 ± 9	104 ± 9
LPLa, μmol FFA / mL / hr		
RE	6.1 ± 0.7	5.7 ± 0.5
EE	5.2 ± 0.3	6.0 ± 0.9
CE	5.9 ± 0.4	6.6 ± 0.5
HTGLa, μmol FFA / mL / hr		
RE	11.8 ± 1.4	12.0 ± 1.6
EE	12.2 ± 1.8	12.6 ± 1.9
CE	11.2 ± 1.1	11.6 ± 1.1

Values are group means at each time-point ± SEM. RE, n = 9; EE, n = 10; CE, n = 12; Baseline, 24 h before experimental exercise session; 24 h, 24 h after experimental exercise session.

Discussion

To our knowledge, this study is the first to compare lipoprotein-lipid changes in young, untrained men with normal cholesterol levels following a single session of resistance, endurance, and combination exercise modeled after the ACSM's guidelines for health and fitness benefits. The novel finding in this investigation was that the mode of exercise differentially affected the short-term lipid response to acute exercise in these subjects. The concentrations of TC and LDL-C were both reduced (-7%) in the RE group 24 h after a single session of exercise while slight elevations were noted for these lipids in both EE and CE groups. However, the reduction in LDL-C following resistance exercise did not reach statistical significance following simple main effects analysis. In

the majority of studies published, significant reductions in TC and LDL-C following acute exercise were reported in trained subjects performing endurance-type exercise of long-duration and requiring a large expenditure of calories.[72, 76, 85, 132] However, reductions in TC and LDL-C have also been noted in untrained subjects with normal[69, 86] and elevated[66] baseline cholesterol levels following lower volume, shorter duration exercise interventions.

The short-term TC and LDL-C response reported in our EE group has also been demonstrated previously. Crouse et al.[66] observed initial reductions in TC and LDL-C in untrained hypercholesterolemic men immediately after completing a single exercise session (350 kcal). However, the concentrations of these lipids continued to rise until LDL-C was significantly elevated (+ 5.8%) 24 h and TC (+ 4.7%) 48 h after the acute exercise session compared to baseline values. In addition, Kantor et al.[69] reported slightly elevated concentrations of both TC and LDL-C, although not significant, 24 h after untrained men completed a 1 h session of cycle ergometer exercise.

Research studies examining the effects of a single session of resistance exercise on short term changes in lipoprotein-lipids are sparse,[108, 143, 144] and to our knowledge, nothing has been published regarding a single session of combination endurance / resistance exercise. Our study is the first to show that the concentration of TC can be significantly reduced following a single session of resistance exercise. Previous studies that have evaluated acute resistance exercise resulted in no change in TC and LDL-C concentrations immediately and in the days following a single exercise session.[108, 143, 144] Reductions in TC concentrations following endurance exercise are rare unless the

volume of exercise is quite large. It has been suggested that resistance exercise may not be as effective as endurance exercise in modifying blood lipids, because the caloric expenditure is lower than what would be attained during endurance exercise.[131] Thus, the reductions in TC and LDL-C following resistance exercise in the present study were unexpected. The estimated total energy expenditure for the volume of resistance exercise in the present study was about 230 kcal, comparable to that of the low volume group reported in Wallace et al.,[108] and that estimated (225 kcal) in Jürimäe et al.[144] It is difficult to make comparisons between these resistance training studies due to differences in the type of resistance exercise performed and volume of the exercise session. The exercise stimulus employed by Jürimäe and colleagues[144] consisted of low volume circuit weight training, whereas a low volume non-circuit approach was performed in the present study. Wallace and coworkers[108] employed both a low and high volume non-circuit approach in their investigation. Clearly, future studies are needed to expand upon the limited body of knowledge in this area.

In the current investigation subjects performing a single session of resistance exercise demonstrated unfavorable changes in HDL cholesterol concentrations compared to a single session of endurance and combination exercise. The concentrations of HDL-C and HDL_3-C were reduced (- 10.4% and - 7.9%, respectively) in the RE group 24 h after a single session of resistance exercise while these lipids were not significantly altered in our EE and CE groups. In addition, the concentration of HDL_2-C was significantly reduced in the RE group (- 10%) 24 h after a single session of resistance exercise while HDL_2-C was significantly elevated following both endurance (+ 12.5%)

and combination exercise (+ 10%). Previous work in this area, although limited, supports the findings that exercise, of this volume, is not sufficient to induce favorable changes in HDL-C and the HDL subfractions. Jürimäe et al.[144] reported that concentrations of HDL-C were not significantly altered in untrained subjects 5 min after completion of a 30 minute single-circuit weight-training session. Wallace et al.[108] reported that the concentrations of HDL-C were not significantly altered immediately after a single session of both low and high volume resistance exercise in trained males. However, increases in the concentrations of HDL-C (+ 11%) and HDL_3-C (+ 12 %) reached significance 24 h after the single, high volume, resistance exercise session (800 kcal), but not after the low volume exercise session (200 kcal).

As with the endurance training literature, it is generally believed that in order to consistently elevate HDL-C concentrations, a certain volume of exercise needs to be performed.[131] In both normocholesterolemic and hypercholesterolemic untrained men, reports indicate that a single session of endurance exercise ranging from 350 to 500 kcal has resulted in significant increases in the concentration of HDL-C 24 h after the exercise bout.[66, 138] In contrast, research has shown that in trained subjects, a caloric expenditure of at least 1000 kcal may be required in order to elevate plasma HDL-C concentrations.[132] Our data suggest that regardless of exercise mode, an energy expenditure of 232 - 350 kcal is not sufficient to induce significant elevations in HDL-C in young, untrained men.

It is also possible that subtle changes in lipoprotein metabolism may have gone undetected in a number of studies reporting that HDL-C was unresponsive to a single

acute exercise session. In studies reporting a lack of change in HDL-C levels following acute endurance exercise did not even measure HDL subfractions (HDL_2-C and HDL_3-C).[82, 145] Reports indicate that HDL-C and both HDL subfractions are responsive to a single session of endurance exercise for up to 48 h after the stimulus.[44] It is generally held that the increase in HDL-C in sedentary subjects is due to increases in the HDL_3-C subfraction, whereas HDL_2-C increases in trained individuals following endurance exercise, at least in normocholesterolemic individuals.[44] However, our EE group demonstrated a slight, but statistically significant, rise (0.5 mg / dL) in HDL_2-C 24 h after the exercise stimulus. The elevation in HDL-C (2 mg / dL) in our CE group was attributed to equal increases (1 mg / dL) in both HDL subfractions. Indeed, research has shown that both subfractions can be elevated following an acute endurance exercise session.[42, 72, 132]

An inverse relationship between HDL-C and TG concentrations has been widely established.[146] Indeed, TG concentrations in the present investigation were inversely related to HDL-C, HDL_2-C, and HDL_3-C at baseline. The peak in LPLa usually occurs about 18 - 24 hours after exercise. Following the actions of LPL, surface remnants from TG hydrolysis appear to be converted into nascent HDL-C, and lipids are transferred to existing HDL, thus raising HDL-C.[146] In the present investigation, it was determined that the mode of exercise did not influence the short-term TG response in young, healthy untrained men. However, when all group data was combined, a significant reduction in TG (- 14.2%) was observed.

The magnitude of this reduction is similar to what has been previously reported for untrained normo-and hypercholesterolemic subjects.[66, 138] The magnitude of the TG response within the EE group (- 24.8 %) is also similar to what has been previously reported for untrained hypercholesterolemic men following acute endurance exercise.[66, 138] Conversely, others have not observed a reduction in TG concentrations following acute endurance exercise in sedentary subjects.[69, 145] It has been suggested that individuals with the highest baseline TG values tend to show the greatest post-exercise reductions.[66, 69, 138] Lamon-Fava and coworkers[85] reported that male subjects who had the highest pre-race TG concentrations demonstrated the greatest post-race TG reductions compared to their other subjects. Furthermore, the reductions in TG concentrations were extremely large (approximately 160 mg / dL). In contrast, several studies using untrained subjects with low baseline TG concentrations (89 - 123 mg / dL), similar to those individuals in the present study, did not report favorable reductions in TG following acute endurance exercise.[69, 145] However, alterations in TG concentrations have been documented in sedentary subjects following an exercise session that was moderate, with respect to caloric expenditure;[66, 82, 138] results in agreement with our own observations.

Recently, Wallace et al.[108] reported that the concentrations of TG were not significantly altered 5 minutes after a single session of both low and high volume resistance exercise. However, decreases in the concentrations of TG reached significance 24 h after the single, high volume, resistance exercise session (800 kcal), but not after the low volume exercise session (200 kcal). The estimated total energy

expenditure for the volume of resistance exercise in the present study was about 232 kcal, comparable to that of the low volume group reported in Wallace et al.[108] Clearly, future investigations are needed to expand upon the limited body of knowledge in this area.

It was determined that the type of exercise performed in the present study did not influence the magnitude or direction of the lipoprotein enzyme response to an acute exercise session. HTGLa has been shown to be reduced[132, 133] after prolonged endurance exercise. However, more often than not, the activity of this enzyme has remained unaltered following a single session of endurance exercise.[69, 76, 138] In the present study, HTGLa remained essentially unchanged following a single session of endurance, resistance, and combination exercise.

Researchers have reported increases in plasma,[69, 71, 76, 132, 138] skeletal muscle,[147] and adipose tissue LPLa[147] following a single session of endurance exercise. Increases in LPLa have been observed in both sedentary and trained subjects following a single session of exercise on a cycle ergometer.[69] However, the results of the present study are in agreement with the findings reported by Gordon and coworkers.[71] In that particular investigation, researchers did not observe a significant increase in LPLa after trained men performed acute sessions of both low and high intensity exercise of equal caloric volume (800 kcals). However, the trend was for an increase in LPLa following the high intensity exercise session. Conversely, Grandjean and coworkers[138] reported a significant increase in LPLa 24 h following an acute bout of treadmill walking (500

kcal) in normo - and hypercholesterolemic men. Moreover, this increase was still evident 48 h later.

It is difficult to make comparisons between investigations due to differences in study design, subject characteristics, and the timing of blood sampling, all which can affect the LPL response to acute exercise. The volume of exercise employed in the current investigation (230 - 350 kcal) was significantly lower than that used by both Gordon and Grandjean. It is generally held that significant alterations in LPLa may occur if the exercise intervention is of sufficient volume and intensity to deplete intramuscular TG stores.[146] The lack of a statistically significant change in LPLa and HTGLa in the current study may be due, in part, to employing an exercise intervention that was of insufficient volume to stimulate a response from our subjects.

It has recently been reported that a single session of strenuous resistance exercise can reduce the postprandial lipemic response despite employing a lower total energy expenditure during the exercise session.[119] However, contrasting findings have been reported.[148] The induction of LPL has been reported after intense local contractile activity in muscles of both rats[116] and humans,[146] suggesting that local contractile activity may be necessary for increased LPL expression during exercise.[116] This seems to suggest that the lipemic response after resistance exercise may not be related to the volume of exercise but to some other factor linked to strenuous muscle contraction associated with weight lifting. However, the caloric expenditure for the resistance exercise session used in that investigation (400 kcal)[119] was still higher than what was employed in the current study (230 kcal).

While every effort was taken to ensure that subjects randomly assigned to the three exercise groups were similar with respect to age, weight, and relative body fat, baseline analysis of the physiological data indicated that significant differences were noted for body weight (RE < CE; $p < 0.05$). Furthermore, baseline dietary data indicated that there were also significant differences between the groups with respect to the average daily intake of protein, saturated fat (RE > CE), and cholesterol (RE > EE & CE). Increased cholesterol intake can elevate cholesterol concentrations in all the lipoprotein fractions.[131] However, it is important to note that there were no baseline differences among the three groups with respect to any of the lipoprotein-lipids measured. Furthermore, day to day dietary intake during the blood sampling protocol was not different. In addition, the subject's diets were not altered for this investigation. Subjects were asked to adhere to their normal dietary habits. Thus, dietary influences are probably not responsible for the alterations noted during this acute exercise investigation.

In conclusion, our results demonstrate that post-exercise changes in TC, HDL-C, HDL_2-C, and HDL_3-C across time were different for the RE group. Furthermore, favorable post-exercise changes in HDL_2-C across time occurred in both CE and EE groups (10% to 12.5% increase). Except for the change in TC, unfavorable reductions in HDL metabolism were observed following a single session of resistance exercise. However, these unfavorable changes were not seen following an acute bout of combination exercise, which included equal volumes of both resistance and endurance exercise. Despite the unfavorable lipid response following an acute resistance exercise

session in this particular study, resistance exercise has been shown to aid in the prevention and rehabilitation of osteoporosis, obesity, sarcopenia, and diabetes mellitus;[89] health benefits that can lead to a reduced risk for CHD. In spite of the prescriptive importance of data on this subject, research in this area is currently lacking and additional studies are warranted.

CHAPTER III

THE EFFECTS OF RESISTANCE, ENDURANCE, AND COMBINATION EXERCISE TRAINING ON SERUM LIPOPROTEIN-LIPIDS IN PREVIOUSLY UNTRAINED MEN

Introduction

It is well documented that coronary heart disease (CHD) is associated with high concentrations of total cholesterol (TC), low density lipoprotein (LDL) cholesterol (LDL-C), triglycerides (TG), and with low concentrations of high density lipoprotein (HDL) cholesterol (HDL-C).[4] The risk for development of CHD may be reduced by increasing HDL-C, the less dense subfraction HDL_2-C, and by decreasing both LDL-C and TG concentrations.[4, 8] Among the risk markers for CHD, physical inactivity carries a relative risk comparable to risks associated with high TC and high blood pressure.[131] However, while maintaining a physically active lifestyle has been associated with a more favorable lipid profile and a reduced risk of CHD,[131] information regarding the optimal training modality (endurance, resistance, or combination endurance / resistance exercise) and volume (caloric expenditure) of exercise that will provide the most benefit has not been well defined.

Exercise training may provide protection against the development of CHD partly through improvements in the lipoprotein-lipid profile.[4] The majority of research examining the effectiveness of physical activity on CHD risk reduction has been conducted using endurance exercise as the exercise stimulus. Current research suggests that exercise of sufficient volume may deplete intramuscular TG, consequently

stimulating the synthesis of lipoprotein lipase (LPL) in muscle capillaries. Greater lipoprotein lipase activity (LPLa) is associated with increased TG clearance and HDL-C concentrations, changes associated with decreased CHD risk.[115]

Athletes and individuals with a long history of endurance training tend to have higher concentrations of HDL-C, LPLa, and lower concentrations of LDL-C, TG, and hepatic triglyceride lipase activity (HTGLa) as compared with sedentary individuals.[48, 131] However, the results from longitudinal training studies have been inconsistent. It is generally accepted that while the concentrations of TC and LDL-C are rarely altered in longitudinal exercise training studies,[44, 131] HDL-C and TG concentrations may be more responsive to regular exercise training.[131] However, more research is needed to clarify this finding. Methodological differences such as exercise volume (caloric expenditure), duration of training, exercise modality, baseline subject characteristics, diet, and time of blood sampling after the last session of exercise may explain the divergent reports in the literature.[66, 67, 131, 149] It is also possible that subtle changes in lipid metabolism may have gone undetected in a number of investigations. For instance, Crouse et al.[42] reported that 6 months of endurance training by men with elevated cholesterol resulted in a significant rise in HDL_2-C and fall in HDL_3-C, but no change in total HDL-C.

Evidence is now emerging to show the importance of resistance exercise for health and disease prevention.[89] Resistance training has been shown to aid in the prevention and rehabilitation of low back pain, osteoporosis, obesity, sarcopenia, and diabetes mellitus.[89] However, compared to the endurance training literature, there is a relative paucity of information related to the effects of resistance training on circulating

lipids and lipoproteins and almost nothing regarding combination endurance / resistance training. Studies that exist are often contradictory, and the published literature is almost completely lacking of reports comparing the effectiveness of endurance to either resistance or combination exercise.[95, 103, 134, 150] It has been reported that resistance training favorably reduces blood LDL-C and increases HDL-C concentrations.[95, 98, 99] Contrasting findings have also been reported with some regularity.[102, 103, 105]

Interpreting the results from many of the published resistance training studies is difficult, as they seem to suffer some of the same design problems present in many endurance training studies.[67, 93-96] For example, it has been suggested that resistance training using high repetitions and moderate resistance may promote favorable changes in the lipid profile, whereas resistance training consisting of low repetitions and heavy resistance does not.[107] Others have reported that neither low repetition nor high repetition resistance training effectively altered lipoprotein-lipids.[101] Although resistance exercise may be recommended to the general public for its proven skeletal muscle benefits, the beneficial influence of this mode of exercise on circulating lipids and lipoprotein enzymes remains to be established.

Research investigations evaluating the effects of combination exercise training on the lipoprotein-lipid profile are scarce.[103, 134, 150, 151] With the increasing popularity of resistance training, more people are will likely adopt this type of activity , making it important to study the effects of these types of exercise on CHD risk factors.[89] It is clear by the lack of published research in this area that additional studies are warranted. Therefore, the purpose of this investigation was to characterize the effects of a chronic

endurance, resistance, and combination exercise training program, similar to what the ACSM might recommended to sedentary individuals for health and fitness benefits, on serum lipoprotein-lipids and lipoprotein enzymes in previously untrained males.

Methods

Subjects

Subject recruitment began after the investigation was approved by the Texas A&M University Review Board for Human Subjects in Research and was limited to Bryan / College Station, Texas. Potential volunteers responded to flyers which were posted in a majority of the buildings on the Texas A&M University main campus. Thirty-six untrained male volunteers 18 – 40 years old were initially recruited for this investigation, asked to sign an informed consent approved by the Texas A&M Institutional Review Board for Research with Humans, and completed a health history questionnaire. Subjects were considered untrained if they had not participated regularly in endurance or resistance training (less than 2 exercise sessions / week and ≤ 20 minutes per exercise session) for at least the last three months. Volunteers were screened to exclude those who exhibited evidence of medical contraindications to exercise and heparin, were taking drugs known to affect lipid/lipoproteins or blood clotting, used tobacco products, or consumed more than two ounces of alcohol per day. A total of four subjects did not complete the study due to various injuries obtained from the exercise training program and one subject dropped out for unknown reasons. Therefore, the final subject selection included a total of 31 subjects.

Experimental Protocol

Following an orientation meeting (week 1), the subjects were randomly placed into one of three exercise training groups (endurance, resistance, or combination endurance / resistance). The following week (week 2), all subjects, regardless of group assignment, were asked to report to the Applied Exercise Science Laboratory at Texas A&M University on two days for baseline physiological and performance measurements. After the week of pre-testing, and before the start of their exercise training programs, all subjects reported to the laboratory for baseline blood sampling procedures (week 3). Diet and physical activity data were also collected during this week.

Physiological Testing

Each subject was measured for: 1) height and body weight; 2) waist and hip girth; 3) relative body fat 4) lung volumes 5) peak oxygen consumption ($\dot{V}O_{2peak}$), and; 6) one-repetition maximum strength assessments (1RM). Percent fat (% Fat) and lean body mass (LBM) were calculated from body density measured hydrostatically[135] at residual volume (RV). All subjects completed a standardized maximal graded exercise test (GXT) on a motor driven treadmill (Quinton Model # Q-65, Quinton Instrument Co., Seattle, WA) under the supervision of trained laboratory personnel.[136] Resting and maximum-exercise heart rate measurements were taken during the $\dot{V}O_{2peak}$ testing through the use of Polar® heart rate monitors. Blood pressure was determined manually, and ratings of perceived exertion were obtained during the last 30 seconds of

every stage of the protocol. Respiratory gas exchange (minute ventilation ($\dot{V}_e$), oxygen consumption ($\dot{V}O_2$), and carbon dioxide production ($\dot{V}CO_2$) was measured on a breath-by-breath basis and averaged over 30-s intervals via open-circuit spirometry utilizing an automated metabolic cart (CPX / D Exercise Stress Testing System, Medical Graphics Corp., Minneapolis, MN) calibrated with gas mixtures of known composition before and after each test. The $\dot{V}O_{2peak}$ test was considered valid if at least two of the following criteria were met: 1) the maximum age-predicted maximum heart rate was achieved or; 2) the respiratory exchange ratio was greater than 1.1 or; 3) $\dot{V}O_2$ failed to rise with increasing workload.[137]

All subjects were tested for strength by determining the maximum weight that could be successfully lifted one time, with proper technique, after completion of a standardized warm-up. The warm-up consisted of 5 minutes of cycling, 5 minutes of stretching, and 4 light sets of each exercise. Subjects were required to perform a 1RM test in all of the exercises that were incorporated into the resistance-training program (leg press, leg curl, standing calf raise, barbell bench press, lat pull-down, dumbbell military press, barbell curl, and an abdominal crunch).

Blood Sampling

Blood samples were obtained before (pre-training) and after the twelve week exercise training program (post-training). Each subject reported to the laboratory, time of day controlled, after a 12-hour fast (water allowed *ad libitum*) and having refrained from any physical activity in the preceding 72 h. A more detailed description of our

blood sampling procedures has been reported previoulsy.[42, 138] Serum and plasma from pre- and post- heparin blood was isolated by centrifugation at 1500 x g for 30 minutes at 4°C. Aliquots of pre- and post-heparin plasma were sealed separately in 2 ml cryovials (no. 66008-284, VWR Scientific Inc., Westchester, PA) and stored at -80°C for later analysis.

Exercise Training Program

Upon completion of the preliminary testing described above, all subjects initiated their training programs. The exercise training varied for each of the three groups. Members of each group took part in a training program that lasted twelve weeks, allowing for one week of mid-training re-testing during week seven. The resistance-training group participated in a basic resistance-training program conforming to the guidelines by the American College of Sports Medicine.[137] Every odd number week this group trained two times per week, and every even number week this group trained three times per week. This training schedule was adopted in order to accommodate the schedules of all the subjects as well as the availability of the fitness trainers and equipment.

The resistance-training program entailed a total body workout consisting of 4 sets of 6-10 repetitions on 8 exercises that trained all the major muscle groups. The exercises included leg press, leg curl, standing calf raise, barbell bench press, lat pull-down, dumbbell military press, barbell curl, and abdominal crunches. A percentage of each subject's 1RM was used to determine the intensity for each week. Recovery time between sets was determined by two-minute turnovers. The intensity and number of

repetitions performed for each exercise changed bi-weekly. A more detailed description of the progression of the resistance-training program has been reported elsewhere.[152] The endurance group's training consisted of walking / jogging on a motor-driven treadmill 2-3 times per week. This group followed the same pattern of the resistance-training group by training twice on odd number weeks and three times on even number weeks. The running intensity was determined using a percentage of the heart rate reserve through use of the Karvonen formula.[153] Resting and exercise maximum heart rate measurements were taken during $\dot{V}O_{2peak}$ testing through the use of Polar® heart rate monitors. The duration of the training sessions lasted between 20-40 minutes. The intensity and duration of each session increased bi-weekly as the training progressed. A more detailed description of the progression of the endurance-training program has been previously reported.[152] The combination-training group trained five times per week. Every odd number week this group performed the resistance program three times and the endurance program twice. Every even number week the combination group performed the endurance program three times and the resistance program twice. During training all subjects were asked to avoid making any dietary changes and maintain their habitual diet. Compliance was assessed through the use of dietary records during the first and last week of training. Ninety percent subject compliance (27 out of 30 workouts for the RT and ET subjects and 54 out of 60 for CT subjects) was required for a subject's data to be included in the final statistical analysis. All exercise protocols complied with the 7th edition of the American College of Sports Medicine's "Guidelines for Exercise Testing and Prescription."[137]

Mid- and Post-Testing

% Fat, $\dot{V}O_{2peak}$, and 1RM tests were re-tested during week seven of the study. All testing was conducted using the same methods and procedures that were used during the preliminary testing. This re-testing allowed 1RMs to be adjusted for the remaining weeks of the resistance-training program. Resting and exercise maximum heart rates were also reassessed in order to adjust the intensity of the endurance-training program for the remainder of the program. The week following the completion of the training program, all variables measured during preliminary testing were repeated for the final time. This post-training testing followed the same methods and procedures as the preliminary testing.

Diet and Physical Activity Records

Subjects were instructed to maintain their normal dietary habits throughout the study. Self-reported dietary records were used to assess the nutritional composition and caloric intake in each subject's diet. Subjects recorded their diet over a 7 day period. The dietary intake logs prompted each subject to record the date, time, type, portion size, and preparation methods for anything that was consumed during the period of interest. In addition, subjects were given verbal instruction on the proper techniques for completing the dietary intake log. Also, each dietary intake log was accompanied by a written example of proper form completion and a summary of portion size estimation methods. Dietary intake logs were analyzed for: 1) total daily caloric intake; 2) total daily grams of carbohydrate, fat, protein, saturated fat, polyunsaturated fat, and total daily milligrams of cholesterol; 3) and the ratio of polyunsaturated to saturated fat using

the Food Processor SQL (Version 9.3, ESHA Research, Salem, OR) program. A seven–day physical activity questionnaire (PAQ) was used to assess routine daily activity over the same period in which the dietary intake logs were kept. The questionnaire was adapted from the seven–day record developed by Blair et al.[142] Subjects were also asked to refrain from any strenuous physical activity, including exercise, outside of that required by their job or as part of the research investigation.

Biochemical Analysis

Frozen aliquots of serum were sent to Atherotech, Inc (Birmingham, AL) for complete lipoprotein-lipid analyses (TC, TG, LDL, HDL-C, HDL_2-C, and HDL_3-C) with the Vertical Auto Profile (VAP) method.[36] Atherotech is a fully certified and licensed clinical Laboratory. Atherotech is part of the "Cholesterol Reference Method Laboratory Network". Atherotech also participates in 3 highly recognized "Proficiency Testing Programs". These are *Northwest Lipid Research Laboratories (NWLRL),* one of five "CDC-NHLBI" cholesterol reference labs; *New York State Department of Health*, a "CLIA" approved program; and *"Accutest"*, a "CLIA" approved program. The methods for determining total plasma lipase activity (TLa) and hepatic triglyceride lipase activity (HTGLa) have been reported previously by our lab.[138] The activity of LPL was calculated as the difference between the TLa and that of HTGLa. Our lab intra-assay and inter-assay CVs were 7% and 10.4% for TLa and 3% and 10.6% for HTGLa.

Statistical Analysis

The dependent variables of interest in this study were the concentrations of TC, TG, LDL-C, HDL-C, HDL_2-C, HDL_3-C, and the lipoprotein enzyme activities (LPLa and

HTGLa). Furthermore, the following ratio variables were determined: TC / HDL-C, HDL_2-C / HDL_3-C, and LDL-C / HDL-C. Baseline differences between the subjects assigned to the different exercise training groups were determined for physiological, diet, blood lipid and lipoprotein enzyme activities using one-way analysis of variance (ANOVA). Furthermore, relationships between the baseline physiological and blood variables were determined using Pearson product-moment correlation coefficients. The physiological, diet, and exercise training data were analyzed using a 3 (group) X 2 (training period) ANOVA (repeated for training period) as a global test for significance. Significant interactions were additionally explored using simple main effects analysis. In addition, mean separation procedures were carried out using Duncan's New Multiple Range Test when appropriate. Training-induced changes in physiological data, blood lipids, and lipoprotein enzymes were also calculated (post training value – pre training value). Relationships between these change variables were determined using simple linear correlation analysis. All data was analyzed using the Statistical Analysis System (SAS, version 9.13, Cary, NC). The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Diet and Physiological Variables

Baseline descriptive physiological characteristics are presented in Table 2-1. Significant relationships between selected physiological variables and baseline lipid and lipoprotein enzymes are displayed in Table 2-2. Significant group X training period

interactions were noted for average daily cholesterol intake, lean body mass (LBM), maximal upper body strength (BPMAX), and lower body strength (LPMAX) determined from the leg and bench press 1RMs ($p < 0.05$). There was a significant difference in average daily cholesterol intake among the training groups only at the pre-training time-point. Average daily dietary cholesterol was greater in the RT group compared to both ET and CT groups. There was also a significant difference in average daily cholesterol

Table 2-1. Baseline Exercise Training Group Data.

Variable	RT	ET	CT
Age (yrs)	22 ± 1 [a]	24 ± 1 [a]	22 ± 1 [a]
Height (in)	68.9 ± 0.66 [a]	69.7 ± 0.91 [ab]	71.7 ± 0.54 [b]
Weight (kg)	73.8 ± 4 [a]	85.6 ± 5 [ab]	95.9 ± 4.7 [b]
BMI (kg/m^2)	23.98 ± 1.04 [a]	27.4 ± 1.78 [a]	29.05 ± 1.64 [a]
% Fat (%)	15 ± 1 [a]	19 ± 3 [a]	20 ± 3 [a]
$\dot{V}O_{2peak}$ (mL/kg/min)	43.6 ± 1.6 [a]	41.8 ± 2.7 [a]	42.7 ± 2.2 [a]
TC (mg/dL)	165 ± 11 [a]	163 ± 7 [a]	163 ± 8 [a]
TG (mg/dL)	94 ± 13 [a]	123 ± 16 [a]	85 ± 10 [a]
HDL-C (mg/dL)	48 ± 3 [a]	42 ± 2 [a]	48 ± 2 [a]

All data are presented as the mean ± SEM. RT = resistance training group, n = 9; ET = endurance training group, n = 10; CT = combination training group, n = 12; BMI = body mass index; % Fat = relative body fat percentage; $\dot{V}O_{2peak}$ = peak oxygen consumption as measured during a standardized graded exercise test; TC = total cholesterol; TG = triglyceride; HDL-C = high density lipoprotein cholesterol. Exercise group means within each row with same letters are not different ($p < 0.05$).

Table 2-2. Correlations for Selected Physiological, Lipid, and Lipoprotein Enzyme Data at Baseline.

Variable	HDL-C	HDL_2-C	HDL_3-C	$\dot{V}O_{2peak}$ (mL/kg/min)
LPLa		0.380		
TG	-0.547	-0.504	-0.533	

Relationships were determined after combining data from all exercise groups. All relationships shown are statistically significant ($p < 0.05$).

intake, with respect to 12 weeks of training, in the CT and RT groups. The average daily dietary cholesterol intake was significantly higher post-training compared to pre-training values in the CT group. Furthermore, average daily dietary cholesterol intake was significantly lower post-training compared to pre-training values in the RT group.

There was a significant difference in LBM among the training groups at both pre-training and post-training time-points. LBM was significantly higher in the CT group compared to both ET and RT groups at the pre-training time-point. Furthermore, the increase in LBM following 12 weeks of training was significant for the CT and RT groups compared to the ET group. There was a significant difference in LPMAX, with respect to training period, in all the training groups. The maximum weight lifted on the leg press was significantly higher post-training compared to the pre-training values in all exercise training groups.

There was a significant difference in BPMAX, with respect to training period, in the CT and RT training groups. The maximum weight lifted on the bench press was significantly higher post-training compared to pre-training in both training groups. Training-induced changes in selected physiological variables are illustrated as individual

group means in Table 2-3. Significant group main effects were determined for body weight and waist girth ($p < 0.05$). Each of these variables was greater in the CT group compared to the RT group.

Table 2-3. Changes in Physiological Variables with Training.

Variables	Pre-Training	Post-Training
Weight (kg)		
RT	73.8 ± 4 [a]	75.7 ± 4
ET	85.6 ± 5 [a,b]	84.7 ± 5
CT	95.9 ± 5 [b]	96.8 ± 4
% Fat (%)		
RT	14.7 ± 1	13.6 ± 1
ET	18.8 ± 3	17.6 ± 2
CT	19.9 ± 3	18.5 ± 3
$\dot{V}O_{2peak}$ (mL/kg/min)		
RT	43.6 ± 1.6	45.7 ± 1.3
ET	41.8 ± 2.7	45.2 ± 2.2
CT	42.7 ± 2.2	42.9 ± 1.9
BPMAX (lbs)		
RT	158 ± 15	200 ± 14 [*]
ET	183 ± 15	189.5 ± 14
CT	187 ± 14	223 ± 12 [*]
LPMAX (lbs)		
RT	515.5 ± 35	717.8 ± 45 [a,*]
ET	601 ± 51	723 ± 60 [a,*]
CT	617 ± 37	884 ± 49 [b,*]

Values are group means at each training period ± SEM. Pre-Training, before exercise training; Post-training, after 12-weeks of exercise training; W / H ratio = waist girth / hip girth; BPMAX = 1RM on bench press; LPMAX = 1RM on leg press. * Significant differences between training periods, within group ($p < 0.05$). [a,b] Significant differences within training period, between groups ($p < 0.05$).

As shown in Table 2-4, significant training period main effects were determined for waist girth (Waist) and hip girth (Hip), waist-to-hip ratio (W / H ratio), % Fat, fat mass (FMass), and $\dot{V}O_{2peak}$ ($p < 0.05$).

Each of the values for Waist, Hip, % Fat, and FMass were significantly lower after 12 weeks of training when compared to pre-training values. The values for W / H ratio and $\dot{V}O_{2peak}$ were all significantly higher after 12 weeks of training when compared to pre-training values.

Table 2-4. Training Period Main Effects.

Variable	Pre-Training	Post-Training
Waist (in)	36 ± 1	35 ± 1*
Hip (in)	41 ± 1	40 ± 1*
W / H ratio	0.86 ± 0.01	0.87 ± 0.01*
% Fat (%)	18.1 ± 1	16.7 ± 1*
FMass (kg)	16.5 ± 1.8	15.4 ± 1.7*
$\dot{V}O_{2peak}$ (mL/kg/min)	42.7 ± 1.3	44.5 ± 1.1*

Values are the training means ± SEM. Values are collapsed across training groups (RT, ET, and CT). * Significant differences between training periods ($p < 0.05$).

Lipids and Lipoprotein Enzymes

Statistical analysis of the lipoprotein-lipid and lipoprotein enzyme data revealed that the type of exercise training did not differentially influence the lipid profiles in young, previously untrained men. No significant group X training period interactions,

group main effects, or training period main effects were determined for any of the serum lipid or lipoprotein enzyme variables (Table 2-5).

Table 2-5. Changes in Serum Lipid and Lipoprotein Enzyme Variables with Training.

Variables	Pre-Training	Post-Training
TC (mg/dL)		
RT	165 ± 11	164 ± 10
ET	163 ± 7	156 ± 8
CT	163 ± 8	160 ± 10
TG (mg/dL)		
RT	94 ± 13	83 ± 12
ET	123 ± 16	113 ± 16
CT	85 ± 10	87 ± 8
LDL-C (mg/dL)		
RT	98 ± 10	101 ± 9
ET	103 ± 8	97 ± 7
CT	99 ± 9	98 ± 9
HDL-C (mg/dL)		
RT	48 ± 3	45 ± 2
ET	42 ± 2	41 ± 2
CT	48 ± 2	45 ± 3
HDL_2-C (mg/dL)		
RT	10 ± 1	9 ± 1
ET	8 ± 1	8 ± 1
CT	10 ± 1	9 ± 1
HDL_3-C (mg/dL)		
RT	38 ± 2	36 ± 2
ET	34 ± 2	33 ± 2
CT	38 ± 2	36 ± 2
LPLa (μmol FFA / mL / hr)		
RT	6.1 ± 0.7	6.0 ± 0.5
ET	5.2 ± 0.3	5.2 ± 0.2
CT	5.9 ± 0.4	5.7 ± 0.3

Values are group means at each training period ± SEM. Pre-Training, before exercise training; Post-training, after 12-weeks of exercise training. * Significant differences between training periods, within group ($p < 0.05$). [a,b] Significant differences within training period, between groups ($p < 0.05$).

With data from all three training groups combined, the change in HDL-C was related to the change in HDL_2-C ($r = 0.91$, $P < 0.05$) and to the change in HDL_3-C ($r = 0.987$, $P < 0.05$). The change in LPLa was correlated positively with the change in % Fat ($r = 0.374$, $P < 0.05$). In addition, the change in HTGLa was correlated positively with the change in body weight ($r = 0.501$, $P < 0.05$), % Fat ($r = 0.431$, $P < 0.05$), and to the change in Waist ($r = 0.577$, $P < 0.05$). None of the changes in lipoprotein enzyme activities or serum lipid concentrations were related to any of the dietary variables or to the changes in body weight, lean body mass, fat mass, or $\dot{V}O_{2peak}$ (Table 2-6).

Table 2-6. Correlation Matrix for 12-Week Changes in Selected Physiological, Lipid, and Enzyme Data.

Variable	% Fat (%)	BPMAX	HDL-C	HTGLa	$\dot{V}O_{2peak}$ (mL/kg/min)
LPLa	0.374				
Weight (kg)	0.516	0.461		0.501	-0.546
% Fat (%)				0.431	-0.598
LBM (kg)		0.628			
FMass (kg)					-0.637
Waist (in)	0.405	0.376		0.577	-0.462
HDL_2-C			0.910		
HDL_3-C			0.987		

Relationships were determined after combining data from all exercise groups. All relationships shown are statistically significant ($p < 0.05$).

Discussion

Differences in subject characteristics, such as diet composition, may affect the lipoprotein-lipid profile in some individuals. For example, ingestion of a high carbohydrate diet has been shown to increase fasting TG concentrations and may reduce LPLa and HDL-C.[154, 155] In contrast, a diet high in fat or cholesterol may increase the cholesterol concentrations in all the lipoprotein fractions as well as lower TG concentrations.[155] However, these findings are not universal. Other researchers have reported that dietary manipulation does not influence the lipoprotein-lipid profile.[156] Thus, the purposes of the diet records were to ensure stable caloric and nutrient intake during the pre-training and post-training blood sampling periods.

Analysis of the daily dietary records from both pre-training and post-training blood sampling periods revealed no differences in the daily average caloric intake or the nutrient composition of the subject's diets between the two training periods, with the exception of the average daily cholesterol intake. Dietary cholesterol was significantly higher post-training compared to the pre-training period in the CT group, while the opposite was observed for the RT group. As mentioned previously, increased cholesterol intake can elevate cholesterol concentrations in all the lipoprotein fractions.[155] However, the lipoprotein-lipids measured for this investigation were essentially unaltered in response to the training protocol. In addition, there were no differences in lipoprotein-lipids among the three groups at the start of training and the subject's diets were not altered for this investigation. Subjects were asked to adhere to

their normal dietary habits. Thus, dietary influences are probably not responsible for any alterations noted during this exercise training investigation.

All subjects in this present study did not exercise on a regular basis, at least not in the previous three months. In addition, subjects were repeatedly instructed to avoid any strenuous physical activity, outside of the exercise intervention, while participating in this investigation. Analysis of the physical activity questionnaires revealed that the average daily energy expenditures were not different between the two blood sampling periods.

In this investigation, all three exercise training groups demonstrated significant improvements in maximum leg-press strength after 12 weeks of training in their respective disciplines. The increases in LPMAX after training by the RT (+ 39%) and CT (+ 43%) groups were similar to strength measures that have been previously reported in the literature.[157] Our ET group significantly improved their LPMAX by a respectable 20%. Other researchers have reported similar gains in leg strength in previously untrained subjects completing an endurance training program similar to the one used in this investigation.[158] Furthermore, LPMAX after training was significantly greater in the CT group compared to the measures in both the ET and RT groups. These results are in contrast with findings reported by researchers supporting the "interference phenomenon" theory.[159]

Similar to the strength measures reported for LPMAX, the average increase in BPMAX in our RT (+26%) and CT (+19%) groups were similar in magnitude and significantly higher than pre-training strength measures. These results are comparable to

those previously reported in the literature.[157, 159] In comparison, only a small increase in BPMAX was noted in our ET group (+ 3.8%). However, increases in BPMAX were not expected in this group of subjects.[137] Modest increases have been reported in the literature. Hass and colleagues[158] reported significant increases in 1RM chest press after subjects completed a 12-week endurance training program similar to the one used in this investigation.

In this study, the mode of exercise training did not differentially affect changes in body weight, % Fat, FMass, or $\dot{V}O_{2peak}$ in young, healthy untrained men. However, an increase in LBM following 12 weeks of training was significant for both CT and RT groups but not for the ET group. A main effect for training period was determined for % Fat, FMass, and $\dot{V}O_{2peak}$. When data from all groups were combined, statistically significant reductions in % Fat (- 1.4%) and FMass (- 6.9%) were observed after training compared to pre-training values. Similar findings have been previously reported.[160]

Twelve weeks of resistance, endurance, and combination exercise training resulted in a significant elevation (+ 4.2%) in relative $\dot{V}O_{2peak.}$ (combined data from all groups). This increase is slightly lower than what is usually reported after endurance training.[111, 137] The smaller change noted in this investigation might be the result of a lower total volume of training completed by our subjects. The principle of training specificity would predict no, or very little, increase in $\dot{V}O_{2peak}$ with a traditional resistance training program.[111] Other researchers have reported increases in $\dot{V}O_{2peak}$ with resistance training, when performed in a circuit fashion.[100] However, our training

program was a traditional resistance training protocol and did not resemble a circuit training design. Moreover, resistance training usually induces physiological adaptations (muscle hypertrophy and decreased mitochondrial volume) that may hinder any improvements in maximal aerobic capacity.[137] Thus, we had speculated that the ET and CT groups would demonstrate significant increases in aerobic capacity when compared to the RT group. We have no explanation for our findings. However, Stone et al.[161] suggest that an increase in $\dot{V}O_{2peak}$ with resistance training may be the result of increased strength. These researchers believe that improved strength may allow a "truer" expression of a subject's maximal aerobic capacity.[161] Indeed, all groups demonstrated significant increases in lower body strength (LPMAX) after 12 weeks of training in addition to an increased treadmill duration during $\dot{V}O_{2peak}$ post-testing. In spite of the lack of statistical significance between groups, the more than 3-fold greater improvement in $\dot{V}O_{2peak}$ in the ET and RT groups may be considered to be functionally important.

In this investigation, the modality of exercise did not influence the lipoprotein enzyme response to 12-weeks of exercise training in young, previously untrained men. The activity of HTGL has been shown to be unchanged,[162] but more often lower activities have been reported after endurance training.[160, 163] In the present study, HTGLa was basically unaltered following the training program.

In the present study, the activity of LPL, similar to that of HTGL, was essentially unchanged following 12 weeks of exercise training of varying modalities. Other

researchers have reported increases in plasma,[160, 164] skeletal muscle,[70] and adipose tissue[56] LPLa following endurance exercise training. However, these results are not without opposition.[162] The effect of resistance training on the activities of LPL and HTGL has rarely been addressed. To our knowledge, only one study has examined the effects of LPLa and HTGLa in response to a 20 week resistance training program. Kokkinos et al.[102] concluded that 20 weeks of resistance training in middle-aged men with elevated lipoprotein-lipid profiles did not substantially alter the activities of LPL and HTGL; results similar to the present findings.

In this investigation, the mode of exercise did not differentially affect serum lipids in response to 12-weeks of training in young, previously sedentary men. Typically, changes in serum lipids following longitudinal exercise training studies have been inconsistent. While the concentrations of TC and LDL-C are rarely altered,[131] reductions in response to training have been reported.[56, 165] In addition, a majority of the published research has reported that the concentrations of HDL-C and HDL_2-C may be increased while TG is lowered in response to exercise training.[56, 68, 160, 164] However, contrasting findings have been reported on occasion.[162] Explanations for the conflicting findings have been attributed to differences in exercise training volume (caloric expenditure), duration of training, type of exercise, baseline subject characteristics, dietary influences, baseline lipid concentrations, and timing of blood sampling after the last session of exercise.[43, 131, 166]

It has been proposed that exercise training is most effective at increasing HDL-C and reducing TG concentrations in individuals with initially high TC or TG and low

HDL-C.[131] The mean baseline HDL-C concentration in each of our training groups was considered to be in the "normal" range (≥ 42 mg / dL).[4] In addition, greater reductions in TG concentrations following exercise training are typically observed in sedentary subjects with elevated baseline concentrations.[67, 160] In the current study, TG concentrations were essentially unaltered in response to training when all group data was combined. It is important to point out that the baseline lipid profiles of our training subjects were fairly low.

Some researchers have suggested that a subject's baseline body composition or perhaps changes in body composition as a result of exercise training are responsible for the favorable changes in blood lipids following exercise training regimens. In support of this, correlations between body weight and / or body fat reductions in response to exercise training and changes in lipoprotein-lipids have been reported.[56, 167, 168] In the current study, body weight was not significantly altered, while % Fat was slightly reduced following 12-weeks of exercise training. It is possible that a more substantial change in body composition would have produced favorable alterations in the lipoprotein-lipids measured in our study. However, there are those who have reported an independent effect of exercise training on changes in lipoproteins.[14, 160, 164] Typically, reductions in TC and LDL-C are more frequently observed when a substantial loss of body weight and / or % Fat occurs in response to the exercise intervention.[131] It is also important to point out that changes in body weight, FMass, LBM, % Fat, and $\dot{V}O_{2peak}$ in our subjects were not correlated with changes in any of the lipoprotein-lipid concentrations measured.

The training intensity of an exercise program has been reported to be an integral factor in inducing favorable changes in lipoprotein-lipids.[166] The majority of published longitudinal exercise training studies reporting reductions in TC, TG, and LDL-C with elevated HDL-C have utilized training intensities ≥ 60% of maximum heart rate or $\dot{V}O_{2peak}$.[131] However, while subjects in the current study did indeed train at intensities ranging from 65% to 80% of heart rate reserve, serum lipids remained unaltered. What seems to be more important in order for favorable alterations in lipids to occur is the volume of the exercise intervention. It is believed that lipoprotein-lipid changes most often occur when the exercise regimen is one that consists of a large volume (caloric expenditure) of work, at least 1200-2200 kcal / week.[44, 131] The lack of change in serum lipids and lipoprotein enzymes in our investigation may be partly due to the lower total volume of training performed by our subjects. Our study was designed so that the frequency and volume of endurance training would be balanced between the ET and CT groups. Hence, our ET subjects alternated between three-day- and two-day-per-week frequencies of training sessions over the 12 week training program for a total of 30 workout sessions. Given our research design, the weekly caloric expenditure for the ET group ranged from 486 kcal to 1846 kcal / week. The weekly caloric expenditure for these subjects reached and / or surpassed 1500 kcals only three times during the 12 week study. Thus, it could be that the weekly training volume in the present study was not sufficient to elicit significant changes in these lipoprotein-lipids.

In addition, it has been suggested that favorable alterations in serum lipids may not be independent of the duration of the training program.[169] In light of this, beneficial

changes in these lipids might have occurred if the duration of our training program was prolonged. A majority of the research reporting reductions in the concentrations of TC and LDL-C included training durations ≥ 6 months.[151, 170] Elevations in the concentrations of HDL-C in response to exercise training usually occur in a dose-dependent manner.[131] When alterations in HDL-C are reported, the exercise intervention usually lasts longer than the 12 weeks employed in the current study, but contrasting findings have also been reported.[60, 171] As previously mentioned, elevations in HDL-C, are infrequently reported when the weekly training volume does not reach 1200 kcals.[131]

It is possible that subtle changes in lipoprotein metabolism may have gone undetected in a number of studies. For example, Crouse et al.[43] reported that 6 months of endurance training by men with elevated cholesterol resulted in a significant rise in HDL_2-C and fall in HDL_3-C, but no change in total HDL-C. HDL subfractions were measured in the current investigation, but were not significantly altered in response to any of the training programs. Similar findings regarding HDL subfractions have also been observed.[172]

With respect to the effects of 12 weeks of resistance training, we failed to show significant training changes in any of the lipoprotein-lipid variables. These findings are consistent with the reports of several other groups.[101, 102, 105] In contrast to our results, reductions in the concentrations of LDL-C[94-96] and increases in HDL-C[93, 95, 96, 98] after resistance training have been reported. It is important to note that in investigations in which favorable changes in the lipoprotein-lipid profile were reported, the effect of the most recent bout of exercise was not controlled.[93-96] Hence, changes in lipoprotein-lipid

concentrations may have been spuriously altered as a consequence of changes induced by the most recent training session. In an effort to avoid this design flaw in our current investigation, blood samples were obtained 72 h after the last exercise training session.

The weekly resistance training volume may be an important factor in affecting alterations in blood lipoprotein-lipids. In some instances, the largest change in blood lipoprotein-lipids occurred during periods of high volume resistance training.[93] In one of these studies large muscle mass, Olympic Type resistance exercise, was employed as the exercise stimulus.[93] The caloric expenditure in these exercises is about twice that of smaller muscle mass exercises,[173] as was performed in the present investigation and in several other studies.[101-103] The endurance training literature also lends support to this finding. Moore et al.[174] reported higher levels of HDL-C among female runners who increased their running volume compared to a control group consisting of sedentary women. More recently, the threshold of exercise required to produce favorable alterations in HDL-C has been defined as 1000 to 1500 kcals / week.[131] Given the alternating frequency of exercise sessions with our research design, the weekly caloric expenditure for the RT group ranged from 450 to 863 kcals / week. Thus, it could be that the weekly training volume in the present study was not sufficient to elicit significant changes in lipoprotein-lipids.

There is a clearly a paucity of published research relating to lipid metabolism and combined endurance and resistance exercise. To our knowledge, only a few studies have been published with contrasting results.[103, 134, 151] Direct comparisons between these investigations and our own study cannot be made due to differences in subject

characteristics and study design. Boardley and coworkers[134] examined the effects of different exercise modes (resistance training, endurance training, and a combination of resistance and endurance training) on lipids in sedentary older adults after 16 weeks of training. Body weight did not change with training. While the exercise training resulted in significant improvements in strength and aerobic capacity, blood lipids were not altered. In fact, all groups (even sedentary control) experienced similar reductions in the concentrations of TC, TG, LDL-C, and HDL-C over time. Thus, the authors concluded that these results were probably due to seasonal effects on blood lipids.

Similar to the previous findings, Tokmakidis et al.[151] observed that the concentrations of TC and TG were significantly reduced and HDL-C and apo A-I were significantly elevated following 8 months of combination training in middle-aged men with CHD. It is important to point out that these two research investigations did not control for the effects of the last training session. Thus, alterations in lipid metabolism that were attributed to training may in fact have been in response to the last session of exercise.

In contrast, LeMura et al.[103] did not observe any significant changes in any of the lipid variables for their resistance and combination exercise groups following 16 weeks of training in young women. However, HDL-C was significantly higher (+ 28%) and TG significantly lower in the endurance training group after training. The authors concluded that the lack of changes in lipoprotein-lipids in the resistance and combination exercise groups was most likely attributable to the type and intensity of the training programs in those groups.

As previously mentioned, changes in lipoprotein-lipids most often occur when the exercise regimen is one that consists of a large volume (caloric expenditure) of work, at least 1200 – 1500 kcals / week.[44, 131] In light of this information, the lack of lipoprotein-lipid changes in our CT group was an unexpected finding. The weekly caloric expenditure in this particular group ranged from 1380 to 2526 kcals. As previously mentioned, it is possible that the low baseline lipid profiles of all our subjects prevented any further alterations in response to the training intervention.

In summary, the results from the current study demonstrate that 12 weeks of endurance, resistance, and combination exercise training employed in this study can improve cardiovascular and muscular fitness levels in previously untrained men. Regardless of the modality of exercise, training did not alter lipoprotein-lipids in young, healthy previously untrained men.

CHAPTER IV

A SINGLE SESSION OF RESISTANCE, ENDURANCE, AND COMBINATION EXERCISE DOES NOT DIFFERENTIALLY AFFECT THE LIPOPROTEIN-LIPID RESPONSE TO ACUTE EXERCISE IN TRAINED MEN

Introduction

Atherosclerotic coronary heart disease (CHD) claims more lives each year than the next seven prevalent causes of death combined.[4] It is generally accepted that high blood concentrations of total cholesterol (TC), low density lipoprotein (LDL) cholesterol (LDL-C), triglycerides (TG), and low concentrations of high density lipoprotein (HDL) cholesterol (HDL-C) are associated with CHD.[4] The risk for development of CHD may be reduced by increasing HDL-C, the less dense subfraction HDL_2-C, and by decreasing both LDL-C and TG concentrations.[130] Individuals who maintain a regular regimen of physical activity have been shown to have a reduced risk of CHD, which may be due, in part, to favorable alterations to the lipoprotein-lipid profile.[131] However, information regarding the most effective type (endurance, resistance, or combination endurance / resistance exercise) and volume (caloric expenditure) of exercise needed to induce favorable alterations in these CHD risk variables has not been well defined.

The majority of research examining the effectiveness of physical activity on CHD risk reduction has been conducted using endurance exercise. Research suggests that exercise of sufficient volume may deplete intramuscular TG, stimulating the synthesis of lipoprotein-lipase (LPL) in muscle capillaries. Increased LPL activity

(LPLa) is associated with increased TG clearance and HDL-C concentrations, changes associate with decreased CHD risk.[115]

Some of the favorable lipoprotein-lipid modifications thought to occur in response to chronic exercise training may actually be stimulated by an acute bout of exercise.[44, 131] The activity of LPL and the concentration of HDL-C are often found to be acutely elevated and hepatic triglyceride lipase activity (HTGLa), TG, TC, and LDL-C concentrations reduced for at least 48 h after a single session of endurance exercise.[42, 69, 132, 133] Moreover, endurance training may alter this acute lipid response. Different acute changes in lipoprotein-lipids have been shown to occur after a single session of endurance exercise in trained compared to untrained normo–and hypercholesterolemic individuals.[42, 69, 86] Crouse and colleagues[42] recently reported that 24 weeks of endurance training may suppress the rise in LDL-C noted in hypercholesterolemic men after a single session of endurance exercise. In addition, Kantor et al.[69] reported that a measured increase in HDL-C concentrations after prolonged endurance exercise was due to elevated HDL_2-C concentrations in endurance trained subjects, but to elevated HDL_3-C in untrained subjects. Additional well-controlled studies are needed to verify these findings, and to determine the amount of change to be expected after a single session of exercise, both in trained and sedentary individuals.

Recently resistance training has been recommended as an integral part of a well-rounded physical activity program for health and disease prevention.[89] Resistance training has been shown to aid in the prevention and rehabilitation of low back pain, osteoporosis, obesity, sarcopenia, and diabetes mellitus.[89] However, compared to the

endurance exercise literature, there is a relative dearth of information related to the effects of resistance exercise on circulating lipoprotein-lipids and almost nothing regarding combination endurance / resistance exercise. Studies that exist are often contradictory, and the published literature is almost completely lacking of reports comparing the effectiveness of endurance to either resistance or combination exercise.[95, 103, 134] It has been reported that resistance training favorably reduces blood LDL-C concentration and increases HDL-C concentrations.[95, 98, 99] Contrasting findings have also been reported with some regularity.[102, 103, 105]

Interpreting the results from many of the resistance training studies is difficult, as they seem to suffer some of the same design problems present in many endurance training studies. Methodological differences, such as differences in training procedures, subject characteristics, dietary controls, and timing of blood sampling after exercise, may account for some of the variability in published findings.[66, 67, 94, 95, 131] For example, it has been suggested that resistance training using high repetitions and moderate resistance may promote favorable changes in the lipid profile, whereas resistance training consisting of low repetitions and heavy resistance does not.[107] Others have reported that neither low repetition nor high repetition resistance training effectively altered lipoprotein-lipids.[101]

As with endurance exercise, it is possible that resistance exercise may exert an acute benefit on circulating lipids. However, research in this area is currently lacking. Wallace and coworkers[108] reported elevations in HDL-C 24 h after a high-volume (800 kcal) resistance exercise session, but not after a low volume (200 kcal) session. The

biochemical mechanisms responsible for this acute effect are not entirely clear and additional research in this area is warranted. However, LPL induction has been measured after local contraction of muscles in both rats[116] and humans,[52, 117] suggesting that the response is localized to muscles involved in the exercise performed. As the popularity of resistance training increases, more people are likely to develop total fitness programs, emphasizing both muscular strength and cardiovascular endurance. Research regarding the effects of a single session of combination exercise on the blood lipid profile has not been published. With the increasing popularity of resistance and combination exercise training, more people will likely include these activities in their exercise programs, making it important to study the effects of these types of exercise on CHD risk factors. Therefore, the purpose of this investigation was to characterize the short-term changes in circulating lipoprotein-lipids and lipoprotein enzymes in young, healthy trained men following a single session of endurance, resistance, and combination exercise.

Methods

Subjects

Subjects for this particular investigation recently completed twelve weeks of either endurance training (EE, N = 9), resistance training (RE, N = 9), or combination endurance / resistance (CE, N = 9) training in our laboratory and volunteered for this subsequent investigation. Twenty-seven trained male volunteers agreed to participate in this investigation, which was approved by the Texas A&M University Review Board for Human Subjects in Research. All volunteers were asked to sign an informed consent

approved by the Texas A&M Institutional Review Board for Research with Humans and completed a health history questionnaire. Volunteers were screened to exclude those who exhibited evidence of medical contraindications to exercise and heparin, were taking drugs known to affect lipid / lipoproteins or blood clotting, used tobacco products, or consumed more than two ounces of alcohol per day.

Experimental Protocol

Following completion of the training study, all subjects were asked to report to the Applied Exercise Science Laboratory at Texas A&M University, one week later, for baseline physiological and performance measurements. After the week of pre-testing, all subjects completed a series of blood draw procedures over three consecutive days, which included the experimental exercise session. Diet and physical activity data were collected during all blood draw procedures. The subjects then completed endurance, resistance, or combination exercise at an intensity of 70% maximal capacity. Blood was drawn the day before (baseline), and 24 hours (24 h) after exercise for assessment of dependent variables.

Physiological Testing

Each subject was measured for: 1) height and body weight; 2) waist and hip girth; 3) relative body fat 4) lung volumes 5) peak oxygen consumption ($\dot{V}O_{2peak}$), and; 6) one-repetition maximum strength assessments (1RM). Percent fat (% Fat) and lean body mass (LBM) were calculated from body density measured hydrostatically [135] at residual volume (RV). All subjects completed a standardized maximal graded exercise test (GXT) on a motor driven treadmill (Quinton Model # Q-65, Quinton Instrument Co.,

Seattle, WA) under the supervision of trained laboratory personnel.[136] Resting and maximum-exercise heart rate measurements were taken during the $\dot{V}O_{2peak}$ testing through the use of Polar® heart rate monitors. Blood pressure was determined manually, and ratings of perceived exertion were obtained during the last 30 seconds of every stage of the protocol. Respiratory gas exchange (minute ventilation ($\dot{V}_e$), oxygen consumption ($\dot{V}O_2$), and carbon dioxide production ($\dot{V}CO_2$) was measured on a breath-by-breath basis and averaged over 30-s intervals via open-circuit spirometry utilizing an automated metabolic cart (CPX / D Exercise Stress Testing System, Medical Graphics Corp., Minneapolis, MN) calibrated with gas mixtures of known composition before and after each test. The $\dot{V}O_{2peak}$ test was considered valid if at least two of the following criteria were met: 1) the maximum age-predicted maximum heart rate was achieved or; 2) the respiratory exchange ratio was greater than 1.1 or; 3) $\dot{V}O_2$ failed to rise with increasing workload.[137]

All subjects were tested for strength by determining the maximum weight that could be successfully lifted one time, with proper technique (1RM), after completion of a standardized warm-up. The warm-up consisted of 5 minutes of cycling, 5 minutes of stretching, and 4 light sets of each of the following exercises: leg press, leg curl, standing calf raise, barbell bench press, lat pull-down, dumbbell military press, barbell curl, and an abdominal crunch.

Experimental Exercise Session Calculations

Using data from the GXT for each participant in both EE and CE groups, the $\dot{V}O_2$ (L / min) and respiratory exchange ratio (RER) at 70% $\dot{V}O_{2peak}$ were used to estimate the exercise duration needed to elicit the target energy expenditure (kcal). The detailed procedures for estimating the duration of exercise needed to expend the target energy expenditures for all acute endurance exercise sessions have been previously reported by our laboratory.[42] With regards to the experimental session of resistance exercise, a regression equation was developed from pilot data to determine the rate of energy expenditure (kcal/min) of a similar resistance exercise workout. With respect to the experimental exercise sessions, subjects were instructed to abstain from any physical exercise for at least 72 h, before reporting to the laboratory (12-hour fast, water allowed *ad libitum*) to complete the submaximal, experimental exercise session. Specifically, for the acute bout of endurance exercise, subjects were asked to walk or jog on a motor-driven treadmill at 70% of their $\dot{V}O_{2peak}$ for the duration required to expend 500 kcal of energy. The detailed methodological design of the acute exercise sessions has been previously reported by our laboratory.[42]

Subjects in the RE group completed a typical resistance exercise training session (duration = 58 min) similar to what might be recommended by the AHA or the ACSM for individuals adopting an exercise program for general health and fitness benefits.[137] Weights used for each exercise were calculated as approximately 70% of the 1RM, and chosen so that the subject would be challenged, but yet able to complete all repetitions in each exercise set, and continue exercise until completion of the session. Subjects

completed one warm-up set of ten repetitions at 50% of their 1RM followed by three sets of ten repetitions at 70% of their 1RM. The eight exercises consisted of leg press, leg curl, standing calf raise, barbell bench press, lat pull-down, dumbbell military press, barbell curl, and an abdominal crunch. Recovery time between sets and exercises were strictly controlled with two-minute turnovers. The results from our pilot study reinforced the notion that most young, moderately trained individuals would not have been able to tolerate any additional volume than what was included in our standard 58 minute protocol. Expired gases were measured for the first 16 minutes of resistance exercise with a portable metabolic system (Medical Graphics CPX / D) to spot check the results from our regression equation for determining the rate of energy expenditure (kcal/min).

For those in the combination group, subjects were asked to either walk or jog at an intensity equal to 70% of their maximal effort recorded on their earlier exercise test ($\dot{V}O_{2peak}$) for a length of time needed to burn 250 kcal of energy. After the subjects finished with this activity, they performed several resistance exercises for a duration that required the expenditure of 250 kcal of energy. Weights used for each exercise were calculated as approximately 70% of the 1RM. Heart rate was monitored continuously and expired gases were measured every 10 minutes of endurance exercise and the first 16 minutes of resistance exercise with a portable metabolic system (Medical Graphics CPX / D) to determine the total O_2 uptake ($\dot{V}O_2$), and ultimately the rate of energy expenditure (kcal/min). Subjects were asked to stop lifting weights once the target

caloric expenditure was achieved. The combined total energy expenditure for the combination exercise group was 500 kcal.

Blood Sampling

Blood samples were obtained 24 h before (baseline) and 24 h after the experimental exercise session. Each subject reported to the laboratory, time of day controlled, after a 12-hour fast (water allowed *ad libitum*) and having refrained from any exercise in the preceding 72 h. A more detailed description of our blood sampling procedures has been reported previoulsy.[42, 138] Serum and plasma from pre- and post-heparin blood was isolated by centrifugation at 1500 x g for 30 minutes at 4°C. Aliquots of pre- and post-heparin plasma and serum were sealed separately in 2 ml cryovials (no. 66008-284, VWR Scientific Inc., Westchester, PA) and stored at -80°C for later analysis. All blood variables were adjusted for plasma volume shifts that occurred as a result of acute exercise using hematocrit and hemoglobin measurements obtained from each sample.[139]

Biochemical Analysis

Frozen aliquots of serum were sent to Atherotech, Inc (Birmingham, AL) for complete lipoprotein-lipid analyses (TC, TG, LDL, HDL-C, HDL_2-C, and HDL_3-C) with the Vertical Auto Profile (VAP) method.[36] Atherotech is a fully certified and licensed clinical Laboratory. Atherotech is part of the "Cholesterol Reference Method Laboratory Network". Atherotech also participates in 3 highly recognized "Proficiency Testing Programs". These are *Northwest Lipid Research Laboratories (NWLRL),* one of five "CDC-NHLBI" cholesterol reference labs; *New York State Department of Health*,

a "CLIA" approved program; and *"Accutest"*, a "CLIA" approved program. The procedures used in determining total plasma lipase activity (TLa) and hepatic triglyceride lipase activity (HTGLa) by our lab have been reported previously.[138] The activity of endothelial-bound lipase (LPLa) was calculated as the difference between the TLa and that of HTGLa. Our lab intra-assay and inter-assay CVs for enzyme analysis were 7% and 10.4% for TLa and 3% and 10.6% for HTGLa.

Diet and Physical Activity Records

Self-reported dietary records were used to assess the nutritional composition and caloric intake in each subject's diet over the blood sampling period. Subject's recorded their diet over a 7 day period (4 days prior and 3 days during the blood sampling protocol). The dietary intake logs prompted each subject to record the date, time, type, portion size, and preparation methods for anything that was consumed during the period of interest. In addition, subjects were given verbal instruction on the proper techniques for completing the dietary intake log. Also, each dietary intake log was accompanied by a written example of proper form completion and a summary of portion size estimation methods. All daily diet records were analyzed for caloric consumption and nutrient intake using the Food Processor SQL (Version 9.3, ESHA Research, Salem, OR) program. A seven–day physical activity questionnaire (PAQ) was used to assess routine daily activity over the same period in which the dietary intake logs were kept. The questionnaire was adapted from the seven–day record developed by Blair et al.[142] Subjects were also asked to refrain from any strenuous physical activity, including exercise, outside of that required by their job or as part of the research investigation.

Statistical Analysis

Baseline differences between the subjects assigned to the different exercise groups were determined for physiological, diet, physical activity, lipoprotein-lipid, and enzyme variables using one-way analysis of variance (ANOVA). Relationships between the baseline physiological and blood variables were determined using Pearson product-moment correlation coefficients. The dependent variables of interest for this investigation were plasma volume adjusted concentrations of TC, TG, LDL-C, HDL-C, HDL_2-C, HDL_3-C, and the enzyme activities (LPLa and HTGLa). Furthermore, the following ratio variables were determined: TC / HDL-C, LDL-C / HDL-C, and HDL_2-C / HDL_3-C. A global test for significance was performed using a 3 (group) X 2 (time) ANOVA with repeats across time. Significant interactions were additionally explored using simple main effects analysis. In addition, mean separation procedures were carried out using Duncan's New Multiple Range Test when appropriate. All data was analyzed using the Statistical Analysis System (SAS, version 9.13, Cary, NC). The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Baseline descriptive characteristics are presented in Table 3-1. Statistical analysis of the lipoprotein-lipid and lipoprotein enzyme data revealed that the type of exercise performed did not influence the short-term lipid response in young, trained men. No group X time interactions or group main effects were determined for the exercise-induced plasma volume shifts. However, a time main effect ($p < 0.05$) was

determined indicating that a significant plasma volume shift occurred over the blood sampling period. Plasma volume was expanded 4.8 % ± 1 above baseline values by the 24 h time-point.

Table 3-1. Post-Training Acute Exercise Baseline Group Data.

Variable	RE	EE	CE
Age (yrs)	22 ± 1 [a]	23 ± 1 [a]	22 ± 1 [a]
Height (in)	68.9 ± 0.66 [a]	70.2 ± 0.84 [a]	71.3 ± 0.61 [a]
Weight (kg)	75.7 ± 4 [a]	87.7 ± 4 [ab]	99.7 ± 5 [b]
% Fat (%)	14 ± 1 [a]	17 ± 3 [a]	21 ± 3 [a]
$\dot{V}O_{2peak}$ (mL/kg/min)	45.7 ± 1.2 [a]	46.1 ± 2.2 [a]	40.1 ± 1.5 [b]
TC (mg/dL)	164 ± 10 [a]	158 ± 9 [a]	166 ± 13 [a]
HDL-C (mg/dL)	45 ± 2 [a]	42 ± 2 [a]	45 ± 4 [a]
EXKCAL	254 ± 18 [a]	500 ± 1 [b]	500 ± 2 [b]
EXDUR	58 ± 0.0 [a]	35 ± 0.58 [b]	64 ± 2 [c]

All data are presented as the mean ± SEM. RE = resistance exercise group, n = 9; EE = endurance exercise group, n = 9; CE = combination exercise group, n = 9; $\dot{V}O_{2peak}$ = peak oxygen consumption as measured during a standardized graded exercise test; TC = total cholesterol; HDL-C = high density lipoprotein cholesterol; EXKCAL = caloric expenditure of acute exercise session; EXDUR = duration (minutes) of acute exercise session. Exercise group means within each row with same letters are not different ($p < 0.05$).

No group X time interactions or group main effects were determined for any of the plasma volume adjusted lipid and lipoprotein enzyme activities or lipid ratios (Table 3-2). Thus, the influence of acute exercise on blood lipoprotein-lipids, lipoprotein enzyme activities, and lipid ratios (time main effect) are reported. A significant time main effect was observed for TC, LDL-C, HDL-C, HDL_2-C, and LPLa ($p < 0.05$). An increase in plasma volume adjusted TC concentration occurred at the 24 h post exercise time-point. The concentration of LDL-C followed the same response pattern as TC. An increase in plasma volume adjusted HDL-C concentration occurred at the 24 h post exercise time-point. HDL_2-C concentrations followed a similar trend. HDL_3-C concentrations were elevated from 35.2 ± 1.2 to 36.7 ± 1 mg / dL 24 h after the exercise session. This change in plasma volume adjusted HDL_3-C did not reach statistical significance ($p = 0.0564$). LPLa was elevated (+ 10.7%) at the 24 h post exercise time-point. No other time main effects were noted for any other dependent variables.

Table 3-2. Post-Training Acute Exercise Changes in Blood Lipid and Lipoprotein Enzyme Variables

Variables	Baseline	24 h
TC, mg/dL		
RE	164 ± 10	176 ± 12
EE	158 ± 9	168 ± 6
CE	166 ± 13	177 ± 12
TG, mg/dL		
RE	83 ± 12	96 ± 12
EE	93 ± 10	89 ± 12
CE	94 ± 8	104 ± 14
LDL-C, mg/dL		
RE	101 ± 9	109 ± 11
EE	98 ± 8	104 ± 6
CE	104 ± 11	111 ± 11
HDL-C, mg/dL		
RE	45 ± 2	47 ± 2
EE	42 ± 2	46 ± 2
CE	45 ± 4	47 ± 4
HDL_2-C, mg/dL		
RE	9 ± 1	9 ± 1
EE	9 ± 1	10 ± 1
CE	9 ± 1	10 ± 1
HDL_3-C, mg/dL		
RE	36 ± 2	38 ± 2
EE	33 ± 2	36 ± 1
CE	36 ± 3	37 ± 2
LPLa, µmol FFA / mL / hr		
RE	6 ± 0.5	6 ± 0.3
EE	5.2 ± 0.2	6.4 ± 0.6
CE	5.8 ± 0.3	6.1 ± 0.4
HTGLa, µmol FFA / mL / hr		
RE	12 ± 1.2	12.5 ± 1.5
EE	12.1 ± 1.6	13 ± 1.6
CE	10.3 ± 1.2	9.8 ± 0.9

Values are group means at each time point ± SEM. RE, n = 9; EE, n = 9; CE, n = 9; Baseline, 24 h before experimental exercise session; 24 h, 24 h after acute exercise.

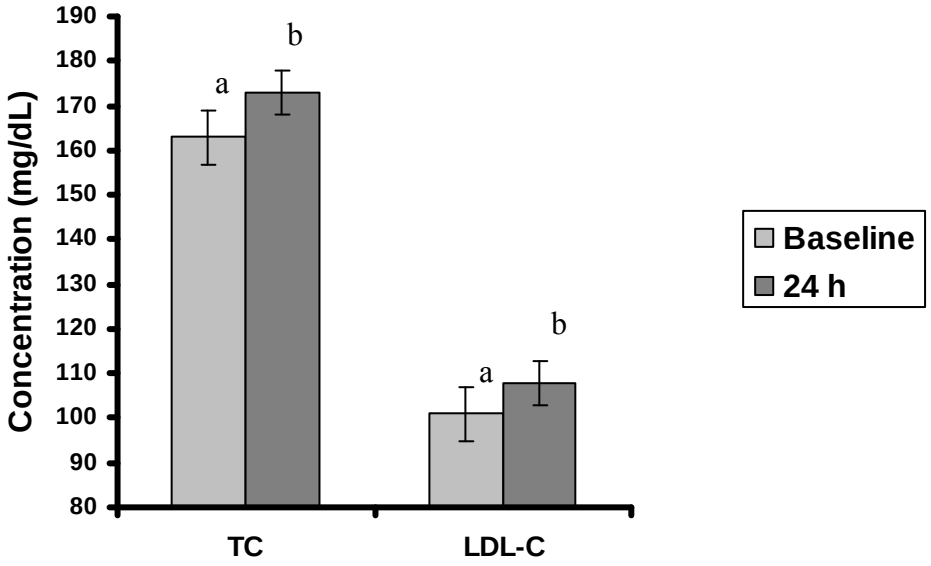


Figure 3-1. Average change in plasma volume-adjusted total cholesterol and low-density lipoprotein cholesterol concentrations with exercise. Data are combined group means ± SEM. Baseline, 24 h before exercise (light-gray bars); 24 h = 24 hours after exercise (dark-gray bars). TC concentrations at each of the time-points were: Baseline = 163 ± 6; 24 h = 173 ± 6. LDL-C concentrations at each of the time-points were: Baseline = 101 ± 5; 24 h = 108 ± 5. [a,b] Significant difference between times ($p < 0.05$).

The exercise-induced changes in plasma volume adjusted lipids and lipoprotein enzyme activities are presented in Figures 3-1 through 3-3.

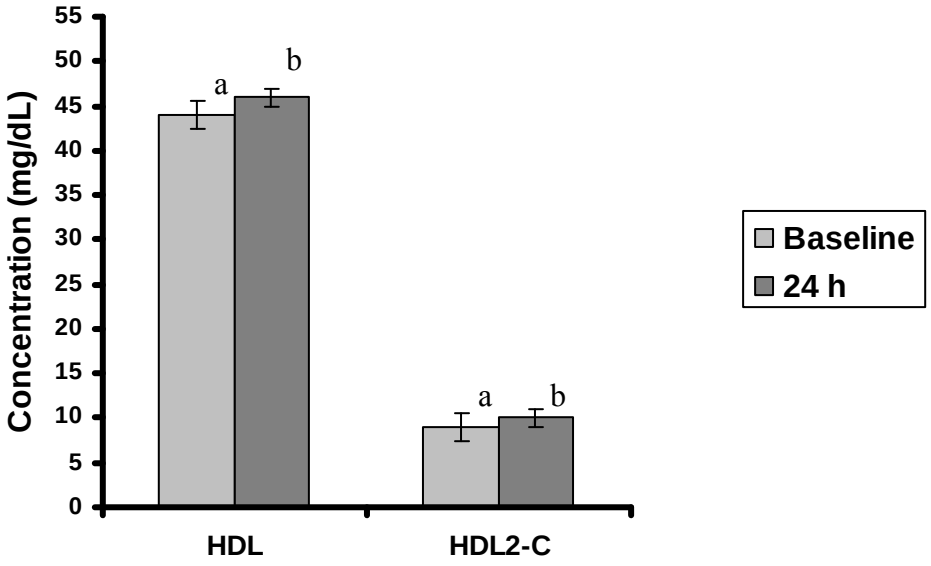


Figure 3-2. Average change in plasma volume-adjusted high-density-lipoprotein cholesterol (HDL-C) and HDL_2-C concentrations with exercise. Data are combined group means ± SEM. Baseline, 24 h before exercise (light-gray bars); 24 h = 24 hours after exercise (dark-gray bars). HDL-C concentrations at each of the time-points were: Baseline = 44 ± 1.5; 24 h = 46 ± 1.4. HDL_2-C concentrations at each of the time-points were: Baseline = 9 ± 0.4; 24 h = 10 ± 0.5. [a,b] Significant difference between times ($p < 0.05$).

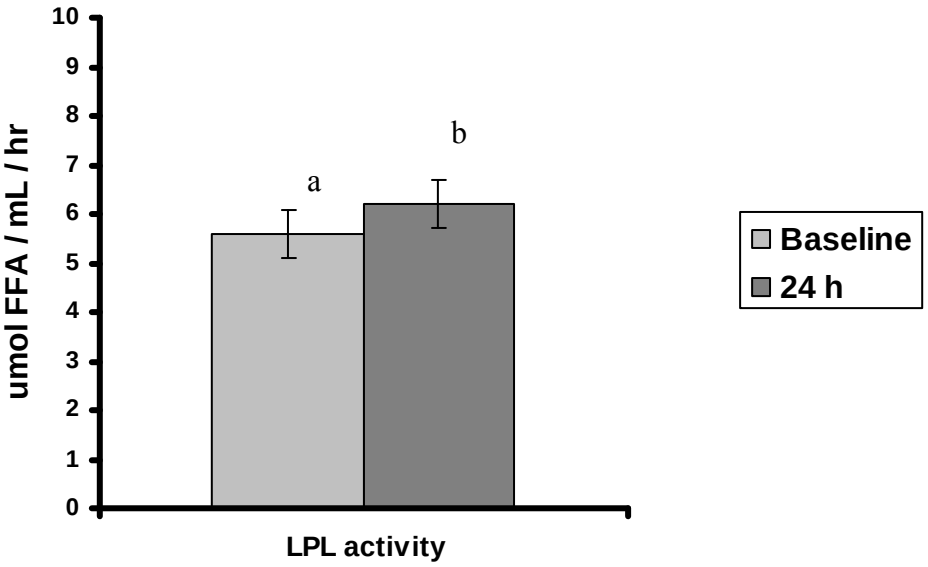


Figure 3-3. Average change in postheparin plasma lipase activity. Values are plasma volume adjusted means (μmol FFA / mL / hr) ± SEM. Baseline, 24 h before exercise (light-gray bars); 24 h = 24 hours after exercise (dark-gray bars); FFA, free fatty acid. Baseline = 5.6 ± 0.2; 24 h = 6.2 ± 0.3. [a,b] Significant difference between times ($p < 0.05$).

Discussion

Our purpose in the current study was to examine the short-term lipoprotein-lipid response to a single session of resistance, endurance, and combination exercise in young, trained men with normal baseline cholesterol levels. These exercise sessions were consistent with what would be recommended by both the AHA and the ACSM for

general health and fitness benefits. The novel finding in this investigation was that the modality of exercise did not differentially affect the short-term lipid response to acute exercise in young, healthy trained men. When data from all groups were combined, both TC and LDL-C were significantly elevated (+ 6% and + 7%, respectively) 24 h after the exercise session. Previous research indicates that blood lipid changes following a single endurance exercise session will often, but not always, include reductions in the concentrations of TC,[72, 85, 86] and LDL-C.[69, 76, 78] However, these findings are not universal, as several investigations have reported that a single endurance exercise session was unable to induce favorable alterations in TC and LDL-C concentrations.[133, 138, 145, 175] In the majority of studies published, reductions in TC and LDL-C were reported in trained subjects following prolonged exercise requiring a large expenditure of calories.[76, 78, 85, 132] However, reductions in TC and LDL-C have also been reported in untrained subjects with normal[69, 86] and elevated[66] baseline cholesterol levels.

The elevated TC and LDL-C concentrations reported in the present study are in agreement with previous findings from our laboratory. Crouse et al.[42] observed initial reductions in TC and LDL-C in hypercholesterolemic men immediately after completing an acute bout of exercise (350 kcal). However, the concentrations of these lipids continually increased until LDL-C was significantly elevated (+ 5.3%) 24 h and TC (+ 1.6%) 48 h after the acute exercise session compared to baseline values. In addition, Gordon et al.[176] reported elevated concentrations of both TC and LDL-C, although not significant, 24 h after moderately trained men completed a single exercise session which consisted of treadmill running (800 kcal).

Research studies examining the effects of a single session of resistance exercise on lipoprotein-lipids are rare,[108, 143, 144] and to our knowledge, nothing has been published regarding a single session of combination resistance / endurance exercise. The concentrations of both TC and LDL-C are reportedly unaltered immediately and in the days following an acute bout of resistance exercise.[108, 143, 144] It is difficult to make comparisons between these resistance training studies due to differences in the type of resistance exercise performed and volume (caloric expenditure) of the exercise session. The exercise stimulus employed by Jürimäe and colleagues[144] consisted of low volume circuit weight training, whereas a low volume non-circuit approach was performed in the present study. Wallace and coworkers[108] employed both a low and high volume non-circuit approach in their investigation. Clearly, future studies are needed to expand upon the limited body of knowledge in this area.

The present investigation provides evidence that the post-exercise TG response is the same in young, healthy trained men following a single exercise session of varying modalities. Reductions in the concentrations of TG in trained subjects are most often reported when the caloric expenditure of the exercise stimulus is large (i.e., triathlon / marathon running).[76, 78, 85, 132] One reason for the lack of significant change in TG concentrations in the current study could be the relatively low baseline lipid profiles of the trained subjects. It has been suggested that individuals with the highest baseline TG values tend to show the greatest post-exercise reductions.[66, 69, 138, 145] Lamon-Fava and coworkers[85] reported that male subjects who had higher pre-triathlon concentrations of TG demonstrated greater post-triathlon reductions compared to the other subjects. In

addition, several studies using untrained subjects with low baseline TG concentrations (89 - 123 mg / dL), similar to those individuals in the present study, did not report favorable reductions in TG following acute exercise.[69, 145]

In the present investigation, TG concentrations were essentially unaltered following low-volume (250 kcal), non-circuit resistance exercise. The limited published work in this area supports the findings of the present study. Jürimäe et al.[144] reported that concentrations of TG were not significantly altered in untrained subjects 5 min after completion of a 30 minute single-circuit weight-training session. Hill et al.[143] observed a slight increase in TG immediately following both a low and high intensity resistance exercise session in untrained men. Wallace and coworkers[108] reported significant reductions in TG concentrations 24 h after a single, high volume, resistance exercise session (800 kcal), but not after a low volume exercise session (200 kcal). The estimated total energy expenditure for the volume of resistance exercise in the present study was approximately 250 kcals, comparable to that of the low volume group reported in Wallace et al.,[108] and that estimated (225 kcal) in Jürimäe et al.[144]

With regards to HDL metabolism, the mode of exercise did not differentially affect the short-term HDL-C, HDL_2-C, and HDL_3-C response to acute exercise in young, healthy trained men. When data from all groups were combined, both HDL-C and HDL_2-C were significantly elevated 24 h after the exercise session. The concentration of HDL_3-C followed a similar trend, but did not reach statistical significance. The slight elevation in HDL-C (+ 4.5%) was primarily due to an 11% increase in HDL_2-C, followed by a 4% rise in HDL_3-C.

It has been suggested that an individual's training status may influence the HDL subfraction response to acute exercise. Different acute changes in lipids have been shown to occur after a single session of endurance exercise in trained compared to untrained normo – and hypercholesterolemic individuals.[43, 66, 69] It is generally held that the increase in HDL-C in sedentary subjects is due to increases in the HDL_3-C subfraction, whereas HDL_2-C increases in trained individuals following endurance exercise, at least in normocholesterolemic individuals.[44] The findings of the present investigation are in agreement with this relationship. However, research has shown that both subfractions can be elevated following a prolonged exercise session.[42, 44, 132]

Lipoprotein lipase is known to hydrolyze TG in chylomicrons and VLDL to replenish intramuscular TG stores which may have been depleted during prolonged exercise. The peak in LPLa usually occurs about 18 - 24 hours after exercise.[146] Surface remnants from TG hydrolysis appear to be converted into nascent HDL-C, and lipids are transferred to existing HDL, thus raising HDL-C.[146] However, this reduction in TG with concomitant rise in HDL-C following prolonged exercise in trained individuals has not been reported on a regular basis.[72, 76] For instance, it is not uncommon for reductions in TG to occur without any significant elevations in HDL-C concentrations in trained subjects.[78, 85] Conversely, increases in HDL-C have also been reported in trained subjects without significant alterations in TG concentrations.[71, 177] The TG and HDL-C data in the present investigation are in agreement with the latter findings.

While increases in HDL-C in young, moderately-fit individuals have been reported in studies using a caloric expenditure similar to the one used in this

investigation,[178] this is not always the case.[175] As with the endurance training literature, it is generally believed that in order to consistently elevate HDL-C concentrations, a certain volume of exercise needs to be performed.[131] In untrained hypercholesterolemic men, reports indicate that a single session of endurance exercise ranging from 350 to 500 kcal has resulted in significant increases in the concentration of HDL-C 24 h after the exercise bout.[66, 138] Conversely, research has shown that in trained subjects, a caloric expenditure of at least 1000 kcal may be required in order to elevate plasma HDL-C concentrations.[132] Regardless of the mode of exercise, our data suggest that in young, trained men an energy expenditure of 500 kcal is sufficient to induce elevations in HDL-C.

The effects of an acute session of resistance exercise on HDL metabolism have not been thoroughly studied.[108, 143, 144] To our knowledge, nothing has been published regarding the HDL-C response to a single session of combination resistance / endurance exercise. Jürimäe et al.[144] reported that concentrations of HDL-C were not significantly altered in untrained subjects 5 min after completion of a 30 minute single-circuit weight-training session. Recently, Wallace et al.[108] reported increases in the concentrations of HDL-C (+ 11%) and HDL_3-C (+ 12 %) 24 h after a single, high volume, resistance exercise session (800 kcal), but not after a low volume exercise session (200 kcal). Hill and coworkers[143] also noted significant elevations in HDL-C in untrained men following a high intensity resistance exercise session. The estimated total energy expenditure for the volume of resistance exercise in the present study was about 254 kcal, comparable to that of the low volume group reported in Wallace et al.,[108] and that estimated (225 kcal)

in Jürimäe et al.[144] Clearly, in order to significantly increase HDL-C and HDL subfractions after a single session of resistance exercise, a certain volume of work (caloric expenditure) has to be reached.

It was determined that the type of exercise performed in the present study did not influence the magnitude or direction of the lipoprotein enzyme response to an acute exercise bout in young, trained men. The activity of HTGL was essentially unaltered following each acute exercise session. HTGLa has been shown to be reduced[132, 133] after prolonged exercise. However, more often than not, the activity of this enzyme has remained unchanged following a single exercise session.[69, 76, 138]

When data from all the exercise groups were combined, a delayed increase in plasma LPLa was observed 24 h after the acute exercise. Other researchers have reported increases in plasma,[69, 76, 132, 138] skeletal muscle,[52] and adipose tissue LPLa[147] following a single session of endurance exercise. Greater LPLa is associated with an increased TG clearance and HDL-C concentrations, changes indicative of decreased CHD risk.[115] Increases in LPLa have been observed in both sedentary and trained subjects following a single session of exercise on a cycle ergometer.[69] It is difficult to make comparisons amongst investigations due to differences in study design, subject characteristics, and the timing of blood sampling, all which can affect the LPL response to acute exercise. It is generally held that alterations in LPLa may occur if the exercise intervention is of sufficient volume and intensity to deplete intramuscular TG stores.[146] The minimal elevation in LPLa and lack of change in HTGLa in the current study may be due, in part, to employing an exercise intervention that was of insufficient volume to

stimulate a response from our subjects. However, statistically significant increases in HDL-C (2 mg / dL) and HDL_2-C (1 mg / dL) were observed in our study.

It has recently been reported that a single session of strenuous resistance exercise can reduce the postprandial lipemic response despite employing a lower total energy expenditure during the exercise session.[119] The induction of LPL has been reported after intense local contractile activity in muscles of humans, [117] suggesting that local contractile activity may be necessary for increased LPL expression during exercise.[116] This seems to suggest that the lipemic response after resistance exercise may not be related to the volume of exercise but to some other factor linked to strenuous muscle contraction associated with weight lifting. However, the caloric expenditure for the resistance exercise session used in that investigation (400 kcals)[119] was still higher than what was employed in the current study (250 kcals). In spite of the prescriptive importance of data on this subject, research in this area is currently lacking.[102]

In summary, the results from this investigation show that the mode of exercise did not differentially affect the lipoprotein-lipid and lipoprotein enzyme response to acute exercise in young, trained men. Regardless of the mode of exercise, the activity of LPL and the concentrations of TC, LDL-C, HDL-C, and HDL_2-C were significantly elevated 24 h after a single exercise session in trained college-aged men. The favorable alterations in LPLa, HDL-C, and HDL_{2-3}-C following exercise may help reduce the risk of CHD.

CHAPTER V

CONCLUSIONS

Exercise Training

The Responses of Serum Lipids, Non-Traditional CHD Risk Markers, Enzyme Activities, and Physiological Variables to Exercise Training

Individuals who maintain a regular regimen of physical activity have been shown to have a reduced risk of CHD, which may be due, in part, to favorable alterations to the lipoprotein-lipid profile.[41, 45] It has also been suggested that other variables, in addition to the traditional lipoprotein-lipid profile, may be more beneficial in identifying individuals who are at an increased risk for developing CHD. While it is well established that high TC, TG, LDL-C, and low HDL-C concentrations constitute an atherogenic lipid profile,[11] most coronary events occur in people with normal LDL-C and HDL-C concentrations. It is possible that the traditional lipid profile may fail to detect almost 50% of people who are at an increased risk for developing CHD by not including measurements of certain non-traditional atherogenic biomarkers. Thus, a more comprehensive lipoprotein-lipid profile may lead to more effective preventive treatment strategies for CHD.

Information regarding the most effective type and volume of exercise training needed to induce favorable alterations in these CHD risk variables has not been well defined. In recent years, resistance training has been recommended as an integral part of a well-rounded physical activity program for health and disease prevention.[89] However, compared to the endurance training literature, there is a relative paucity of information

related to the effects of resistance training on circulating lipids and lipoproteins and almost nothing regarding combination endurance / resistance exercise training. As the popularity of resistance training increases, more people are likely to develop fitness programs emphasizing both muscular strength and cardiovascular endurance. Thus, more people will likely include these activities in their exercise programs, making it important to study the effects of these types of exercise on CHD risk factors.[90] It was our purpose to characterize the effects chronic endurance, resistance, and combination resistance / endurance exercise training on serum lipids, non-traditional CHD risk markers, and lipoprotein enzymes in previously untrained males.

Our results demonstrate that the 12 weeks of endurance, resistance, and combination endurance / resistance exercise training employed in this study can improve cardiovascular and muscular fitness levels in previously untrained men. However, the type of exercise training did not differentially affect the serum lipid, non-traditional CHD risk marker, or lipoprotein enzyme response to chronic exercise training in young, healthy untrained men. The biological mechanisms by which improvements in blood lipids occur with exercise are not fully understood, but it is apparent that the activities of some lipid-regulating enzymes (LPL and HTGL) are altered with exercise. The activity of HTGL has been shown to be unchanged,[162] but more often lower activities have been reported after endurance training.[56, 57, 160] The effect of resistance training on the activities of LPL and HTGL has rarely been addressed. To our knowledge, only one study has examined the effects of LPLa and HTGLa in response to a 20 week resistance training program. Kokkinos et al.[102] concluded that 20 weeks of resistance training in

middle-aged men with elevated lipoprotein-lipid profiles did not substantially alter the activities of LPL and HTGL. In the present study, the activity of LPL, similar to that of HTGL, was essentially unchanged following 12 weeks of exercise training of varying modalities, results which are in agreement with Kokkinos and colleagues. Other researchers have reported increases in plasma,[55, 57, 160, 164] skeletal muscle,[52, 117] and adipose tissue[55, 56] LPLa following endurance exercise training. However, these results are not without opposition.[162]

Typically, changes in serum lipids following longitudinal exercise training studies have been inconsistent. While the concentrations of TC and LDL-C are rarely altered,[58, 131, 179] reductions in response to training have been reported.[55, 56, 60, 165, 168, 171, 180] In addition, a majority of the published research has reported that the concentrations of HDL-C and HDL_2-C may be increased while TG is lowered in response to exercise training.[55-57, 60, 68, 134, 160, 164, 165, 180, 181] However, contrasting findings have been reported on occasion.[60, 162, 182, 183] Explanations for the conflicting findings have been attributed to differences in exercise training volume (caloric expenditure), duration of training, type of exercise, baseline subject characteristics, dietary influences, baseline lipid concentrations, and timing of blood sampling after the last session of exercise.[58, 66-68]

It is possible that the "normal" baseline lipid profiles of our subjects were partly responsible for the failure of the training programs to induce beneficial changes in the dependent variables measured. It has been proposed that exercise training is most effective at increasing HDL-C and reducing TG concentrations in individuals with initially high TC or TG and low HDL-C.[180] The mean baseline HDL-C concentration in

each of our training groups was considered to be in the "normal" range (≥ 42 mg / dL).[4] In addition, greater reductions in TG concentrations following exercise training are typically observed in sedentary subjects with elevated baseline concentrations.[60, 67, 160] In the current study, TG concentrations were essentially unaltered in response to training when all group data was combined. It is interesting to note that the mean baseline TG concentrations of our groups were fairly low.

Some researchers have suggested that a subject's baseline body composition or perhaps changes in body composition as a result of exercise training were responsible for the favorable changes in blood lipids following exercise training regimens. In support of this, correlations between body weight and / or body fat reductions in response to exercise training and changes in lipoprotein-lipids have been reported.[49, 56, 167, 168, 184] In the current study, body weight was not significantly altered, while % Fat was only slightly reduced following 12 weeks of exercise training. It is possible that a more substantial change in body composition would have produced favorable alterations in the lipoprotein-lipids measured in our study. The lack of change in hs-Crp in the present study is not surprising given the minimal reduction in relative body fat. The majority of published literature supporting reductions in hs-Crp levels with chronic exercise training also reported substantial reductions in both body weight and % Fat.[124, 185-189]

However, there are those who have reported an independent effect of exercise training on changes in lipoproteins.[14, 57, 160, 164, 190, 191] Increases in HDL-C,[57, 166, 192] and decreases in LDL-C,[166, 182] and TG[57] have been reported to occur following exercise training without changes in either body weight or % Fat. Thus, the independent effect of

exercise training on lipoprotein-lipid metabolism can't be discounted. Typically, reductions in TC and LDL-C are more frequently observed when a substantial loss of body weight and / or % Fat occurs in response to the exercise intervention.[41, 193] It is also important to point out that changes in body weight, FMass, LBM, and % Fat in our subjects were not correlated with changes in any of the lipoprotein-lipid concentrations measured.

Changes in lipoprotein-lipids most often occur when the exercise regimen is one that consists of a large volume (caloric expenditure) of work, at least 1200 – 1500 kcals / week.[41, 44, 194] In light of this information, the lack of changes in the dependent variables in our ET and RT groups was not an unexpected finding. Given the alternating frequency of exercise sessions with our research design, the weekly caloric expenditure for the RT group ranged from 450 to 863 kcals / week. In addition, the weekly caloric expenditure for the ET subjects reached and / or surpassed 1500 kcals only three times during the 12 week study. Thus, it could be that the weekly training volume in the present study was not sufficient to elicit significant changes in lipoprotein-lipids. However, the results regarding the CT group was unexpected according to the training volume logic. The weekly caloric expenditure in this particular group ranged from 1380 to 2526 kcals. As previously mentioned, it is possible that the baseline lipid levels of all our subjects prevented any further alterations in response to the training intervention. It is clear that additional research is warranted to expand upon the limited body of work in this particular area.

Other Factors of Potential Influence on Lipid Metabolism

Daily Variation in Lipid Metabolism, and Lipoprotein Enzyme Activities

It is generally accepted that both daily and seasonal fluctuations in lipid metabolism occur and may be in response to hormonal fluctuations. However, in an acute exercise study, Gordon and coworkers[177] were able to differentiate exercise-induced lipid alterations from those due to daily variations. Researchers often employ a separate control group in order to control for the normal day-to-day variation of lipids and lipoproteins. In the present study, normal daily variation was not assessed. In light of this, specific methodological procedures were employed to minimize the factors which might potentially confound the results. First, each subject reported to the laboratory, time of day controlled, after a 12 h fast and having refrained from any physical activity in the preceding 72 h. Prior to each blood draw, the subjects completed a form reporting their physical activity and dietary adherence over the last 24 h and the time of their last meal. After examination of these forms, it was apparent that all blood samples were obtained as specified under the established guidelines of this investigation. Thus, to the best of our knowledge, daily variation in lipid metabolism was minimized.

Summary

From this investigation, there was no interaction between the type of exercise training and the 12-week training period. Thus, the lipoprotein-lipid, non-traditional CHD risk marker, and lipoprotein enzyme response to chronic exercise training was similar in untrained males performing varying types of exercise. Regardless of the exercise group, LDL_2-C and apo A-I were lower after 12 weeks of training compared to

pre-training values. Furthermore, regardless of the exercise group, % Fat and resting heart rate were lower while $\dot{V}O_{2peak}$, LPMAX, and BPMAX were higher following 12 weeks of exercise training, changes indicative of improved health and wellness.

Pre-Training Acute Exercise

The Responses of Serum Lipids, Non-Traditional CHD Risk Markers, and Enzyme Activities to Acute Exercise in Untrained Men

The role of exercise in reducing one's risk for developing CHD may be partly due to favorable alterations on the lipoprotein-lipid profile.[41] The majority of research examining the effectiveness of exercise training on CHD risk reduction has been conducted using endurance exercise. However, some of the favorable lipid alterations attributed to exercise training may actually be stimulated by a single exercise session. The activity of LPL and the concentration of HDL-C are acutely elevated and hepatic triglyceride lipase activity (HTGLa), TG, TC, and LDL-C concentrations reduced for at least 48 h after a single session of endurance exercise.[43, 69, 71, 72, 76, 79, 133, 195] In light of the fact that nearly one half of all myocardial infarctions (MI's) occur in individuals who have normal LDL-C concentrations,[35] the traditional lipid panel may fail to detect almost 50% of people who are at an increased risk for developing CHD by not including measurements of additional non-traditional atherogenic biomarkers. Thus, a more comprehensive lipoprotein-lipid profile may lead to more effective preventive treatment strategies for CHD. Furthermore, information regarding the optimal training modality (endurance, resistance, or combination endurance / resistance exercise) and volume (caloric expenditure) of exercise that will provide the most benefit has not been well

defined. With the increasing popularity of resistance and combination exercise training, more people will likely include these activities in their exercise programs, making it important to study the effects of these types of exercise on CHD risk factors.[90] Therefore, the purpose of this investigation was to characterize the short-term changes in lipids, non-traditional CHD risk markers, and lipoprotein enzymes in untrained, college-aged men following a single session of endurance, resistance, and combination exercise.

The biological mechanisms by which improvements in blood lipids occur following exercise are not fully understood, but alterations in the activities of some lipid-regulating enzymes (LPL and HTGL) have been shown to occur following exercise. It was determined that the type of exercise performed in the present study did not influence the magnitude or direction of the lipoprotein enzyme response to an acute exercise bout. In this investigation, the activity of LPL, similar to that of HTGL, was essentially unchanged after an acute session of endurance, resistance, and combination exercise.

To our knowledge, this study is the first to show that the mode of exercise did not differentially affect changes in LDL density, lipoprotein particle number, and hs-Crp levels in young, sedentary men following acute exercise. Of the acute exercise studies that have been published to date, only a small percentage have included IL-6 and hs-Crp measurements. While studies have reported elevations in both IL-6 and hs-Crp following prolonged exercise,[196-202] they are not without opposition.[198, 203, 204] Almost all of the investigations reporting elevated IL-6 and hs-Crp following acute exercise included trained subjects completing extremely strenuous activities such as marathons and / or triathlons.[196, 197, 199-202] It is possible that increases in inflammatory biomarkers

(IL-6 and hs-Crp) are more likely to occur after extremely prolonged and strenuous activities than in response to a single session of a moderate intensity, lower volume exercise. A few studies seem to support this theory.[198, 203, 204]

Compared to the endurance training literature, there is a relative paucity of information related to the effects of a single exercise session on LDL particle size and LDL density; reports that have been published are often contradictory. Moreover, almost all of the investigations reporting increased LDL size and lower LDL densities following acute exercise included trained subjects completing strenuous, long-duration activities.[85, 205] In addition, a review of the related literature did not reveal any published studies pertaining to the effects of a single session of resistance and / or combination exercise on LDL size, LDL density, and lipoprotein particle number.

One reason for the lack of change in LDL density and lipoprotein particle number in the current study could be the relatively low baseline lipid profiles of our sedentary subjects. It has been suggested that pre-exercise lipid levels, especially TG concentrations, may determine both the magnitude of change in lipid concentrations following acute exercise.[66, 69, 138, 145, 180] Subjects with initially high TC or TG and low HDL-C concentrations tend to respond more favorably to a prolonged exercise session. Indeed, Lamon-Fava and coworkers[85] reported that the male subjects who significantly increased their LDL size following a triathlon, had higher pre-race concentrations of TG, a greater post-race reduction in TG, as well as a lower pre-race plasma HDL-C compared to the other subjects. Furthermore, the reductions in plasma TG concentrations were extremely large (approximately 160 mg / dL) on average. Similar

to the work of Lamon-Fava,[85] a reduction in dense LDL occurred in subjects who experienced large reductions in serum TG following a 30 km cross-country race.[206] In addition, the initial TG concentrations in the previous studies were significantly higher than those reporting no changes in LDL size with exercise;[207, 208] similar to the baseline TG levels in the present study.

The primary finding of this investigation was that the mode of exercise differentially affected the short-term lipid response to acute exercise in young, healthy untrained men. The concentrations of TC and LDL-C were reduced in the RE group 24 h after a single session of exercise while slight elevations were noted for these lipids in both ET and CT groups. However, the reduction in LDL-C following resistance exercise did not reach statistical significance following simple main effects analysis. The concentrations of HDL-C and HDL_3-C were significantly reduced in the RT group (- 10.4% and - 7.9%, respectively) 24 h after a single session of resistance exercise while these lipids were not significantly altered in our ET and CT groups. In addition, the concentration of HDL_2-C was significantly reduced in the RT group (- 10%) 24 h after a single session of resistance exercise. Conversely, the concentration of HDL_2-C was significantly elevated in the ET group (+ 12.5%) and the CT group (+ 10%) 24 h after a single session of endurance and combination resistance/ endurance exercise, respectively. It is important to point out that the volume of work (caloric expenditure) completed by both ET and CT groups was calorically balanced (350 kcal).

In the present investigation, significant reductions in HDL-C (- 10.4%), HDL_2-C (- 10%), and HDL_3-C (- 7.9%) were observed in the RT group following low-volume

(232 kcal), non-circuit resistance exercise. Previous unpublished observations from our laboratory have also shown that the concentration of HDL_3-C was significantly reduced (- 10.6%) immediately after a single resistance exercise session (212 kcal) when compared to baseline values. It is interesting to note that after 8 weeks of resistance training, this decrease was not evident when subjects were retested following the same protocol. Previous work in this area, although limited, supports the findings that exercise, of this volume, is not sufficient to induce favorable changes in HDL-C and the HDL subfractions. Jürimäe et al.[144] reported that concentrations of HDL-C were not significantly altered in untrained subjects 5 min after completion of a 30 minute single-circuit weight-training session. Wallace et al.[108] reported that the concentrations of HDL-C were not significantly altered immediately after a single session of both low and high volume resistance exercise in trained males. However, increases in the concentrations of HDL-C (+ 11%) and HDL_3-C (+ 12 %) reached significance 24 h after the single, high volume, resistance exercise session (800 kcal), but not after the low volume exercise session (200 kcal).

As with the endurance training literature, it is generally believed that in order to consistently elevate HDL-C concentrations, a certain volume of exercise needs to be performed.[58, 131, 179, 193] In hypercholesterolemic men, reports indicate that a single session of endurance exercise ranging from 350 to 500 kcal has resulted in significant increases in the concentration of HDL-C 24 h after the exercise bout.[66, 138] In addition, research has shown that in trained subjects, a caloric expenditure of at least 1000 kcal may be required in order to elevate plasma HDL-C concentrations.[132, 209] Our data

suggest that in young, healthy untrained men, an energy expenditure of 350 kcal is not sufficient to induce significant elevations in HDL-C.

In previously mentioned endurance studies,[69, 72] large muscle mass, dynamic exercise was performed. Conversely, in the present study, smaller muscle masses were engaged during resistance exercise. It has been reported that the rate of caloric expenditure of large muscle mass, dynamic exercise is about twice the rate of small muscle mass exercise (12 vs 7 kcals $\cdot$ min^{-1}).[173] Morris et al.[210] reported that physical activities with an intensity above 7 kcal / min are associated with higher HDL-C levels and a lower atherogenic index. Clearly, in order to significantly increase HDL-C and HDL subfractions after a single session of resistance exercise, a certain volume of work (caloric expenditure) has to be reached.

In summary, our results demonstrate that a single session of endurance, resistance, and combination exercise did not differentially affect the non-traditional CHD risk marker response to acute exercise in young, sedentary men. Regardless, of exercise mode, a single session of moderate volume (230 – 350 kcal) exercise failed to induce beneficial alterations in several CHD risk markers. However, our results demonstrate that post-exercise changes in TC, HDL-C, HDL_2-C, and HDL_3-C across time were different for the RT group. Furthermore, favorable post-exercise changes in HDL_2-C across time occurred in both CT and ET groups (10% to 12.5% increase). Except for the change in TC, unfavorable changes in HDL metabolism were observed following a single session of resistance exercise. Despite the unfavorable lipid response following resistance exercise in this particular study, the fact remains that resistance

exercise is highly recommended as an integral part of a well-rounded physical activity program for health and disease prevention.[89, 90, 211] Resistance exercise has been shown to aid in the prevention and rehabilitation of low back pain, osteoporosis, obesity, sarcopenia, and diabetes mellitus;[212] health benefits that can lead to a reduced risk for CHD. If exercise therapy is going to be effectively utilized as an intervention for CHD risk reduction, it is important to clearly define the role of each of these components (mode, volume) in order to provide physicians and exercise professionals with guidelines for developing and implementing safe and effective exercise prescriptions for their patients. Furthermore, research in this area is currently lacking and additional studies are warranted.

Other Factors of Potential Influence on Lipid Metabolism

Dietary Intake and Physical Activity

Analysis of the baseline self-reported dietary and physical activity records revealed significant differences between the exercise groups with respect to the average daily intake of protein, saturated fat, cholesterol, as well as daily energy expenditure. Specifically, the average daily intake of protein and saturated fat were lower (45% and 62%) in the CT group compared to the RT group. The average daily cholesterol intake was higher in the RT group compared to both ET and CT groups. Differences in subject characteristics, such as diet composition and recreational physical activity, may affect the lipoprotein profile in some individuals. For example, ingestion of a high carbohydrate diet has been shown to increase fasting TG concentrations and may reduce LPLa and HDL-C levels.[135-137] In contrast, a diet high in fat or cholesterol may increase

the cholesterol concentrations in all the lipoprotein fractions as well as lower TG concentrations.[155] However, these findings are not universal. Other researchers have reported that dietary manipulation does not influence the lipoprotein-lipid profile.[156, 213] Furthermore, subject participation in strenuous activities of daily living, in addition to the prescribed exercise intervention, may also influence the lipoprotein-lipid profile. Thus, the previously mentioned literature reinforces the need to control factors such as diet and physical activity when studying the response of lipid metabolism to a single session of exercise. The "ideal research situation" would be to have an entire project conducted within a closed, controlled setting. Thus, all food consumption would come from prepared meals (i.e. metabolic kitchen) created by registered dieticians. However, the manpower, finances, and research facilities needed to completely control these variables are beyond the capabilities of this, and most other, laboratories. In addition, the intent of this investigation was to examine the effects of resistance, endurance, and combination exercise on lipid metabolism and non-traditional CHD risk markers in untrained men in a natural setting.

Dietary cholesterol and saturated fat intake was higher in the RT group compared to the other two exercise groups. As mentioned previously, increased cholesterol intake can elevate cholesterol concentrations in all the lipoprotein fractions.[155] However, the RT exercise group demonstrated decreases and not increases in TC, HDL-C, HDL_3-C, and HDL_2-C concentrations in response to prolonged exercise. In addition, the subject's diets were not altered for this investigation. Subjects were asked to adhere to their

normal dietary habits. Thus, dietary influences are probably not responsible for the alterations noted during this acute exercise investigation.

All subjects in this present study did not exercise on a regular basis, at least not in the previous three months. In addition, subjects were repeatedly instructed to avoid any strenuous physical activity, outside of the acute exercise intervention, while participating in this investigation. Thus, daily physical activity, in addition to the exercise intervention, probably was not responsible for the alterations in lipid metabolism.

Daily Variation in Lipid Metabolism, and Lipoprotein Enzyme Activities

It is generally accepted that both daily and seasonal fluctuations in lipid metabolism occur and may be in response to hormonal fluctuations. However, in an acute exercise study, Gordon and coworkers[177] were able to differentiate exercise-induced lipid alterations from those due to daily variations. Researchers often employ a separate control group in order to control for the normal day-to-day variation of lipids and lipoproteins. In the present study, normal daily variation was not assessed. In light of this, specific methodological procedures were employed to minimize the factors which might potentially confound the results. First, each subject reported to the laboratory, time of day controlled, after a 12 h fast and having refrained from any physical activity in the preceding 72 h. Prior to each blood draw, the subjects completed a form reporting their physical activity and dietary adherence over the last 24 h and the time of their last meal. After examination of these forms, it was apparent that all blood

samples were obtained as specified under the established guidelines of this investigation. Thus, to the best of our knowledge, daily variation in lipid metabolism was minimized.

Post-Training Acute Exercise

The Responses of Serum Lipids, Non-Traditional CHD Risk Markers, and Enzyme Activities to Acute Exercise in Trained Men

Subjects for this particular investigation recently completed twelve weeks of either endurance training (ET, N = 9), resistance training (RT, N = 9), or combination endurance / resistance (CT, N = 9) training in our laboratory and volunteered for this subsequent "post-training acute exercise" investigation. Some of the favorable lipoprotein-lipid modifications attributed to chronic exercise training may actually be stimulated by an acute bout of exercise.[44, 131] The activity of LPL and the concentration of HDL-C are acutely elevated and HTGLa, TG, TC, and LDL-C concentrations reduced for at least 48 h after a single session of endurance exercise.[43, 69, 71, 72, 76, 79, 133, 195] Therefore, if the timing of blood sampling is not controlled and occurs ≤ 48 h after the last session of exercise, researchers may mistakenly attribute changes in the lipid profile to the effects of chronic exercise training when in fact the lipid alterations were induced by recent exercise. Moreover, endurance training may alter this acute lipid response. Kantor et al.[69] reported that a measured increase in HDL-C concentrations after prolonged endurance exercise was due to elevated HDL_2-C concentrations in endurance trained subjects, but to elevated HDL_3-C in untrained subjects. Different acute changes in lipoprotein-lipids have been shown to occur after a single session of endurance exercise in trained compared to untrained normo – and hypercholesterolemic

individuals.[43, 66, 69, 86] Additional well-controlled studies are needed to verify these findings, and to determine the amount of change to be expected after a single session of exercise, both in trained and sedentary individuals. Therefore, the purpose of this investigation was to characterize the short-term changes in circulating lipids, non-traditional CHD risk markers, and lipoprotein enzymes in trained, college-aged men following a single session of endurance, resistance, and combination exercise.

It was determined that the type of exercise performed in the present study did not influence the magnitude or direction of the lipoprotein enzyme response to an acute exercise bout in young, trained men. When data from all the exercise groups were combined, a delayed increase in plasma LPLa was observed 24 h after the acute exercise. Increases in LPLa have been observed in both sedentary and trained subjects following a single session of exercise on a cycle ergometer.[69] It is difficult to make comparisons amongst investigations due to differences in study design, subject characteristics, and the timing of blood sampling, all which can affect the LPL response to acute exercise. It is generally held that alterations in LPLa may occur if the exercise intervention is of sufficient volume and intensity to deplete intramuscular TG stores.[146] The minimal elevation in LPLa and lack of change in HTGLa in the current study may be due, in part, to employing an exercise intervention that was of insufficient volume to stimulate a response from our subjects.

After a review of the related literature, our investigation appears to be the first to show that the type of exercise did not differentially affect changes in hs-Crp levels in young, trained men following acute exercise. A large majority of the investigations

which observed a significant rise in IL-6 and hs-Crp following acute exercise included trained subjects completing extremely strenuous activities such as marathons and / or triathlons.[196, 197, 199-202] It may be possible that increases in inflammatory biomarkers (IL-6 and hs-Crp) are more apt to occur following prolonged and strenuous activities than in response to a single session of a moderate intensity, lower volume exercise. This theory has garnered recent support.[198, 203, 204] Plaisance and coworkers[204] evaluated the inflammatory response following an acute session of endurance exercise (500 kcals; 70% $\dot{V}O_{2peak}$) between individuals of high and moderate fitness levels. The subjects in the high fit group were significantly leaner compared to the moderately fit group. While the hs-Crp levels were 76% lower at baseline in the high fit group compared to moderately fit group, hs-Crp, fibrinogen, and WBC count remained unaltered in the days after exercise. The authors suggested that the "lower volume" exercise stimulus could have produced less tissue damage and glycogen depletion compared to other investigations.

There is evidence that exercise training can enhance the body's antioxidative defense mechanisms after physical exercise.[214] It is possible that after a period of training the production of IL-6 in exercising muscle is reduced due to enhanced antioxidative protection.[125] For example, IL-6 release from adipose tissue is augmented by increased sympathetic stimulation, which has been shown to be suppressed by exercise training.[215] Thus, trained individuals would theoretically have a reduced IL-6 response to an acute exercise session due to a training-induced suppression of sympathetic activity, ultimately leading to a diminished production of hs-Crp. In

support of this, Dufaux et al.[216] noted lower hs-Crp levels in swimmers when compared to sedentary control subjects. The results from a previous study in our lab, which enlisted the same subjects as in the current study, also support this theory. These subjects were sedentary and about to begin a 12-week training program. Before training, both ET and CT groups demonstrated increases in hs-Crp levels following a single session of strenuous exercise. However, after training, a blunted inflammatory response to acute exercise was observed in these individuals. Clearly more research is needed to evaluate the inflammatory response in previously sedentary subjects after training.

Changes in the other non-traditional CHD risk markers were not statistically different between three groups of trained men following acute exercise of varying modalities. However, when data from all groups were combined, significant elevations in NONHDL-C, VLDL-C, LDL_3-C, IDL-C, and LDL density were observed 24 h after the exercise stimulus. While favorable alterations in NONHDL-C and VLDL-C may not normally occur following acute exercise in young, trained men, prolonged exercise interventions consisting of large volumes of work (kcal) may need to be utilized in order to consistently reduce these lipid concentrations. IDL is under strong genetic control, thus diet and exercise interventions rarely alter this lipoprotein.[217]

One potential explanation for the lack of favorable alterations in LDL density in the current study could be the relatively low baseline lipid profiles of our trained subjects. It has been suggested that pre-exercise lipid levels, especially TG concentrations, may determine both the magnitude of change in lipid concentrations following acute exercise.[66, 69, 138, 145, 180] Subjects with initially high TC or TG and low

HDL-C concentrations have been observed to respond more favorably to a single session of exercise. In support of this, Lamon-Fava and coworkers[85] reported that male subjects who significantly increased their LDL size following a triathlon, had higher baseline TG concentrations, a greater post-race reduction in TG, as well as lower baseline HDL-C compared to the other subjects. Similar to the work of Lamon-Fava,[85] a reduction in dense LDL occurred in subjects who experienced large reductions in serum TG following a 30 km cross-country race.[206] In addition, the initial TG concentrations in the previous studies were significantly higher than those reporting no changes in LDL size with exercise;[207, 208] similar to the baseline TG levels in our investigation.

The mode of exercise did not influence the short-term lipid response to acute exercise in young, healthy trained men. When data from all groups were combined, both TC and LDL-C were significantly elevated (+ 6% and + 7%, respectively) 24 h after the exercise session. The elevated TC and LDL-C concentrations reported in the present study are in agreement with previous findings from our laboratory. Crouse et al.[42] observed initial reductions in TC and LDL-C in hypercholesterolemic men immediately after completing an acute bout of exercise (350 kcal). However, the concentrations of these lipids continually increased until LDL-C was significantly elevated (+ 5.3%) 24 h and TC (+ 1.6%) 48 h after the acute exercise session compared to baseline values. In addition, Gordon et al.[176] reported elevated concentrations of both TC and LDL-C, although not significant, 24 h after moderately trained men completed a single exercise session which consisted of treadmill running (800 kcal).

With regards to HDL metabolism, the mode of exercise did not differentially affect the short-term HDL-C, HDL_2-C, and HDL_3-C response to acute exercise in young, healthy trained men. When data from all groups were combined, both HDL-C and HDL_2-C were significantly elevated 24 h after the exercise session. The concentration of HDL_3-C followed a similar trend, but did not reach statistical significance. It has been suggested that an individual's fitness status may influence the HDL subfraction response to acute exercise. Different acute changes in lipids have been shown to occur after a single session of endurance exercise in trained compared to untrained normo – and hypercholesterolemic individuals.[43, 66, 69] It is generally held that the increase in HDL-C in sedentary subjects is due to increases in the HDL_3-C subfraction, whereas HDL_2-C increases in trained individuals following endurance exercise, at least in normocholesterolemic individuals.[44] The findings of the present investigation are in agreement with this relationship. However, research has shown that both subfractions can be elevated following a prolonged exercise session.[42, 44, 72, 132, 218]

From this investigation, there was no interaction between the type of exercise and the temporal changes in the dependent variables. Thus, changes in lipoprotein-lipids, non-traditional CHD risk markers, and lipoprotein enzymes were similar in trained males performing different types of acute exercise. Regardless of the exercise group, the activity of LPL and the concentrations of TC, VLDL-C, IDL-C, HDL-C, HDL_2-C, NONHDL-C, LDL-C, LDL_3-C, and LDL density were significantly elevated 24 h after a single exercise session in trained men. The favorable alterations in LPLa, and HDL-C, HDL_3-C, and LDL_3-C in response to exercise may help reduce the risk of CHD. The

majority of published research regarding the acute effects of exercise on lipoprotein-lipids have involved extremely prolonged exhaustive exercise such as triathlons and marathon running. However, recommended physical activity which would be appropriate and reasonably achievable by the general population doses not exactly fall into this category. Less intense, shorter duration activities may be more desirable and effective for the general population especially with regards to long-term compliance. Thus research studies involving the effects of this type of exercise on CHD risk factors are indeed warranted.

Other Factors of Potential Influence on Lipid Metabolism

Dietary Intake and Physical Activity

Analysis of the self-reported dietary records revealed that there were no differences between groups for any of the dietary variables measured. Differences in subject characteristics, such as diet composition and recreational physical activity, may affect the lipoprotein profile in some individuals. For example, ingestion of a high carbohydrate diet has been shown to increase fasting TG concentrations and may reduce LPLa and HDL-C levels.[135-137] In contrast, a diet high in fat or cholesterol may increase the cholesterol concentrations in all the lipoprotein fractions as well as lower TG concentrations.[155] However, these findings are not universal. Other researchers have reported that dietary manipulation does not influence the lipoprotein-lipid profile.[156, 213] Furthermore, subject participation in strenuous activities of daily living, in addition to the prescribed exercise intervention, may also influence the lipoprotein-lipid profile. Thus, the previously mentioned literature reinforces the need to control factors such as

diet and physical activity when studying the response of lipid metabolism to a single session of exercise. The "ideal research situation" would be to have an entire project conducted within a closed, controlled setting. Thus, all food consumption would come from prepared meals (i.e., metabolic kitchen) created by registered dieticians. However, the manpower, finances, and research facilities needed to completely control these variables are beyond the capabilities of this, and most other, laboratories. In addition, the intent of this investigation was to examine the effects of resistance, endurance, and combination exercise on lipid metabolism and non-traditional CHD risk markers in trained men in a natural setting.

As previously mentioned, differences in the composition of our subject's diet can potentially influence lipid metabolism. Analysis of the daily dietary records revealed no significant differences between the three groups for caloric intake or the nutrient content of their respective diets. In addition, the subject's diets were not altered for this investigation. Subjects were asked to adhere to their normal dietary habits. These findings indicate that dietary factors were not responsible for the lipoprotein-lipid alterations noted during the post-exercise time period. All subjects in this present study were repeatedly instructed to avoid any strenuous physical activity, outside of the exercise intervention, while participating in this investigation. Thus, daily physical activity, in addition to the exercise intervention, probably was not responsible for the alterations in lipid metabolism.

Daily Variation in Lipid Metabolism, and Lipoprotein Enzyme Activities

It is generally accepted that both daily and seasonal fluctuations in lipid metabolism occur and may be in response to hormonal fluctuations.[216-218] However, in an acute exercise study, Gordon and coworkers[177] were able to differentiate exercise-induced lipid alterations from those due to daily variations. Researchers often employ a separate control group in order to control for the normal day-to-day variation of lipids and lipoproteins. In the present study, normal daily variation was not assessed. In light of this, specific methodological procedures were employed to minimize the factors which might potentially confound the results. First, each subject reported to the laboratory, time of day controlled, after a 12 h fast and having refrained from any physical activity in the preceding 72 h. Prior to each blood draw, the subjects completed a form reporting their physical activity and dietary adherence over the last 24 h and the time of their last meal. After examination of these forms, it was apparent that all blood samples were obtained as specified under the established guidelines of this investigation. Thus, to the best of our knowledge, daily variation in lipid metabolism was minimized.

Suggestion for Further Research

The results of this investigation have generated several related suggestions for potential areas of future research:

1. It is recommended that future studies include measurements of additional intravascular enzymes, such as LCAT and CETP. Furthermore, analysis of the tissue specific sources of LPL is warranted.

2. It is recommended that future studies examine the influence of exercise training on the blood lipid response to different types of acute exercise. In addition, it is important to keep the total volume of work for the acute studies identical (pre-training acute and post-training acute) in order to appropriately answer this research question. Furthermore, additional studies are needed to determine potential training thresholds (caloric expenditures) needed to favorably alter traditional and non-traditional lipoprotein-lipid profiles among different training modalities.
3. It is recommended that future studies include subjects who are "at risk" for CHD. This would include recruitment of older subjects as well as subjects with lipid profiles which are considered to be out of the "normal" range. In addition, including a non-exercising control group would be beneficial for evaluating daily variations in lipid metabolism.
4. It is finally recommended that future studies try to determine if there are distinguishing characteristics for "responders" versus "non-responders". (A responder would be defined as someone who demonstrated increases in HDL-C and reductions in TC, LDL-C, and TG).

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APPENDIX A

REVIEW OF RELATED LITERATURE

Initially in this review, an overview of the atherosclerotic process will be presented. Following this discussion, relationships between atherosclerosis, CHD, and blood lipids will be presented. Next, the physiologic structure and function of lipoprotein-lipids will be discussed along with an overview of intravascular lipid transport and basic lipoprotein metabolism. The lipoprotein-lipid and non-traditional CHD risk marker response to chronic exercise training as well as a single exercise session will be discussed for both endurance and resistance exercise. Lastly, the potential mechanisms whereby exercise may beneficially influence lipoprotein metabolism will be presented.

Atherosclerosis, Cardiovascular Disease, and Blood Lipids

The Atherosclerotic Process

Atherosclerosis is a disease characterized by the accumulation of lipids, lipid-laden immune cells and apoptic cells within the arterial wall. [219, 220] The luminal diameters of the affected arteries become diminished due to plaque / lipid build-up in the intima, or inner lining of the arterial wall. This gradual occlusion limits blood flow to the particular tissue the vessel is serving. Various clinical manifestations of CHD, including angina pectoris, congestive heart failure, myocardial infarction, and sudden cardiac death may occur if this pathological event involves the coronary vasculature.[2] The precursors of atherosclerotic lesions, the fatty streaks, are observed in humans even during early childhood. The advanced lesions of the disease of atherosclerosis are found

in the larger arteries such as the abdominal aorta, coronary arteries, cerebral arteries and others.[221]

The arterial wall contains three distinctive layers—the intima, media and adventitia. The intima is the innermost layer of the arterial wall. It is characterized by a monolayer of endothelial cells (EC) that form the crucial interface between the arterial wall and the blood flow, a thin basal membrane on which the endothelial cells rest and a subendothelial layer of smooth muscle cells (SMCs), proteoglycans, and fine collagen fibrils. The endothelial cells serve several purposes that include providing a smooth surface for fluid flow, secretion of anticoagulants to maintain the fluid state of the blood and chemical signaling of immune cells. The tunica media lies under the media and internal elastic lamina. The media of elastic arteries such as the aorta have well developed concentric layers of smooth muscle cells, interleaved with layers of elastin-rich extracellular matrix. The external elastic lamina bounds the tunica media abluminally, forming the border with the adventitial layer. The outermost layer, the adventitia, consists of fibroblasts, fibrocytes (collagen- and elastin-producing cells) and thick bundles of collagen fibers. The fibers are aligned nearly in the axial direction. They provide reinforcement of the arterial wall and, at high pressures, prevent overstretch and rupture of the vessel.[219, 222-224]

The atherosclerotic process can be broken down into 3 stages; fatty streak development, fibrous plaque / atheroma formation, and the formation of the complicated lesion with its fibrous cap and encroachment of the lumen. According to recent theory,[220] the lesions of atherosclerosis that form in the intimal layer constitute a chronic

inflammatory response to injury. The first step involves endothelial dysfunction and subsequent formation of the "fatty streak". A number of factors have been considered as possible causes of endothelial dysfunction. These include CVD risk factors such as cigarette smoking, diabetes mellitus, hypercholesterolemia, hypertension, and possibly even infection by microorganisms (e.g. herpes viruses or Chlamydia pneumonae).[219, 222-224] This process is characterized by a change in the permeability of the endothelial layer that allows lipids to migrate into the subendothelial layer followed by an influx of the cells that comprise the immune response. These lipoprotein particles have an increased susceptibility to oxidative or other chemical modifications. The change in permeability is also accompanied by an increase in the adhesiveness of the endothelial layer and a change from anticoagulant to procoagulant properties. Expression of different leukocyte adhesion molecules (Vascular cell adhesion molecule-1 (VCAM-1), Intercellular adhesion molecule-1 (ICAM-1)) on the surface of the endothelium regulates the adherence of monocytes and other substances to the endothelium.[224, 225] Platelets adhere to the EC while monocytes, leukocytes, and T- lymphocytes are dispatched to the injured area to try to repair the damage. Once adherent to the endothelium, leukocytes receive a signal to penetrate the endothelium and enter the arterial wall. Chemoattractant cytokines (Chemokines) are protein molecules thought to be involved in directing this migration. Monocyte Chemoattractant protein-1 (MCP-1) is produced by the endothelium in response to oxidized lipoprotein and other stimuli. The endothelium can also produce this chemokine when stimulated by inflammatory mediators. MCP-1 selectively promotes the directed migration (or chemotaxis) of monocytes. After

adhering to the endothelium, monocytes and leukocytes move between cell junctions to enter the intima, where they begin to accumulate lipids and become foam cells. LDL can become oxidized (oxLDL) by the EC and platelets. This oxLDL, as well as other monocytes and platelets, can produce chemotaxic agents (platelet derived growth factor (PDGF)) that will eventually attract more platelets, monocytes, and lymphocytes to the area.[226, 227] Monocytes that have invaded the intimal layer are susceptible to activation by EC or oxLDL and form macrophages. These macrophages have a scavenger receptor (SRB1) that can take up oxLDL at an unregulated rate, eventually forming lipid laden foam cells. Once macrophages move into the intima and become foam cells, a macrophage colony stimulating factor (co-mitogen) can stimulate macrophage cell division. Other candidates include interlukin-3 and granulocyte-macrophage colony stimulating factor. In the established lesion, macrophage foam cells provide a source of proinflammatory mediators, both proteins such as cytokines and chemokines and various eicosanoids and lipids such as platelet-activating factor. These inflammatory mediators can promote inflammation in the plaque and contribute to the progression of the lesions (fibrous plaque formation).

As the formation of the atherosclerotic lesion advances, smooth muscle cells (SMC) are also attracted to the intima and invade though gaps in the internal elastic lamina. Macrophages continue their accumulation of oxLDL and SMC also take up lipids to become lipid filled foam cells. Besides chemotaxic agents, proliferation agents are also secreted, leading to SMC and macrophage proliferation in the intima. Extracellular matrix rather than cells themselves makes up much of the volume of an

advanced atherosclerotic plaque. The major extracellular matrix molecules that accumulate in atheroma include interstitial collagens (types I and III) and proteoglycans such as versican, biglycan, aggrecan, and decorin. Elastin fibers can also accumulate in plaques. Biglycan has been shown to bind and trap various lipoproteins such as VLDL remnants, LDL, and HDL.[226, 227] Vascular SMC can also produce these matrix molecules in disease. Stimuli for excessive collagen production include PDGF and transforming growth factor (TGF-B). The SMC that invaded the intima eventually loose their ability to contract (through loss of contracting proteins) and some cells die (leading to increased necrotic tissue build-up). The shoulders of the plaque can even become vascularized. Endothelial migration and replication also occur as plaques develop in microcirculation, characterized by newly formed vessels. These microvessels form in response to angiogenic peptides overexpressed in the atheroma. These include acidic and basic fibroblast growth factors, vascular endothelial growth factor, and placental growth factor. These microvessels may allow growth of the plaques, overcoming diffusion limitations on oxygen and nutrient supplies. A rupture of these microvessels may cause local SMC proliferation and matrix accumulation in the area near the disruption. The process of SMC and macrophage proliferation as well as extracellular matrix deposition continue with the progressing lesion. Calcification occurs and a fibrous connective tissue cap is formed. It consists mainly of SMC and matrix material. Underneath are the foam cells, SMC, necrotic material and extracellular lipid. After the plaque burden exceeds the capacity of the artery to remodel outward, encroachment on

the arterial lumen begins. Lesions that produce stenoses of greater than 60 percent can cause flow limitations under conditions of increased demands.[219-224]

Blood Lipids and Cardiovascular Disease

CHD is the single largest killer of American males and females. In 1913, Russian experimentalists Anitchkow and Chalatow observed that rabbits fed an egg-rich diet developed lipid-laden arterial lesions that were similar to human atheromas. It was later discovered that cholesterol was the constituent of the eggs that produced these atherogenic lesions.[228] Currently, the relationship between cholesterol levels and CHD is widely accepted.[2-4, 229] Abundant evidence indicates that CHD is associated with high blood concentrations of TC, LDL-C, TG, and with low concentrations of HDL-C. The risk for development of CHD may be reduced by increasing HDL-C, the less dense subfraction HDL_2-C, and by decreasing both LDL-C and TG concentrations.[4-10] Thus, an atherogenic lipid profile may be described as consisting of elevated TC, LDL-C, and TG and decreased concentrations of HDL-C.[2, 11] Recent research seems to suggest that high concentrations of NONHDL-C, IDL-C, Lp (a), apo B, dense LDL particles, and the acute phase reactant, hs-Crp may be better indicators of CHD risk than information obtained from the traditional lipid panel.[12-22]

Castelli and coworkers[8] assessed the association between CHD and fasting lipid concentrations in men and women as part of the Cooperative Lipoprotein Phenotyping Study. TC, LDL-C, and TG were directly related to the prevalence of CHD. Conversely, subjects with known CHD had the lowest HDL-C concentrations. Furthermore, Gordon et al.[230] examined the relationship between fasting concentrations

of LDL-C and the incidence of CHD using data obtained in The Framingham Study. The researchers reported a direct relationship between LDL-C and the incidence of CHD in both male and female subjects. The Kuopio Ischemic Heart Disease Study[231] was a cross-sectional study examining 412 men from eastern Finland. Subjects ranged in age from 42 to 60 years. High resolution B-mode ultrasound was used to evaluate the presence of carotid atherosclerosis. Fasting serum lipids and lipoproteins were also measured. The probability of carotid atherosclerosis in subjects with HDL-C < 39 mg / dL was nearly four times greater than in those with HDL-C > 58 mg / dL. The subjects were divided into four sub-groups in order of increasing atherosclerotic disease: normal, intimal-medial thickening, nonstenotic plaque, and > 20% stenosis. A linear trend was found that associated greater severity of carotid atherosclerosis with decreasing HDL-C levels. As part of the Multiple Risk Factor Intervention Trial (MRFIT), Stamler et al.[10] examined the lipid profiles of approximately 350,000 healthy men. The ages for subjects ranged from 35 to 57 years. For each five-year age group, a relationship between CHD mortality and serum TC concentration was strongly indicated. The researchers also reported that the risk of nonhemorrage stroke death increased with increasing cholesterol concentrations.

A cause and effect relationship between low HDL-C levels and CHD is supported by epidemiological, animal, and human clinical studies. Rubin and coworkers[232] reported that when mice were genetically manipulated to overproduce apo A-I, they were protected against diet-induced atherosclerosis compared to control mice.

In another animal model, rabbits which were infused with HDL-C were shown to exhibit regression of atherosclerotic lesions.[233]

Clinical studies during the 1980s were the first to establish a protective effect of pharmacological cholesterol reduction on coronary morbidity. The Lipid Research Clinic Study showed that bile acid-binding resins could lower cholesterol levels in individuals with high baseline levels. A decrease in coronary morbidity accompanied the drop in serum cholesterol.[228] The Lipoprotein and Coronary Atherosclerosis Study (LCAS) was an angiographic trial comparing treatments with fluvastatin to subjects receiving a placebo. After 2.5 years, patients treated with the placebo (HDL-C < 35 mg / dL) had an average decrease in coronary artery luminal diameter of 0.250 mm (i.e., progression), whereas those subjects with HDL-C > 35 mg / dL had only a 0.083-mm progression.[38] Thus, those subjects with low HDL-C had significantly more angiographic progression than those with higher HDL-C.

The Framingham Heart Study was designed to obtain long-term information about different factors associated with the development of CHD in healthy men and women. Investigators reported a significant inverse relationship between HDL-C and the incidence of CHD in older men and women.[9] Furthermore, HDL-C was also identified as the most powerful lipid risk factor, independent of LDL-C concentrations. Since this time, several primary and secondary prevention studies have further examined the role of HDL-C as an independent risk factor for CHD, and have demonstrated that a strong inverse association does indeed exist.[9, 129, 130, 234] The Helsinki Heart Study (HHS) was a 5-year, double-blinded, primary prevention trial which randomized

approximately 4,000 dyslipidemic men to treatment with either fibrate, gemfibrozil, or placebo.[129] It was reported that subjects with low HDL-C in combination with high TG concentrations were more than twice as likely to have a cardiac event compared with those subjects with normal lipid levels. Furthermore, gemfibrozil treatment resulted in changes in TC, LDL-C, HDL-C, and TG that were maintained over the duration of the study. A 34% reduction in risk for developing CHD also occurred. The Veterans Affairs HDL Intervention Trial (VA-HIT) was a secondary prevention trial involving men with documented CHD, low HDL-C, and low LDL-C levels. Researchers examined the role of gemfibrozil treatment in raising low levels of HDL-C and its impact on long-term clinical events.[130] The data suggest that increasing HDL-C with a reduction in TG levels may be a cost-effective means of decreasing the incidence of coronary events in secondary prevention without any alterations in LDL-C levels. A 6% increase in HDL-C was associated with a 22% reduction in event rates. The Air Force / Texas Coronary Atherosclerosis Prevention Study (AFCAPS / TexCAPS) was a double-blinded, randomized, placebo-controlled, primary prevention study designed to examine the effects of lovastatin treatment in subjects with average TC and LDL-C concentrations, below average HDL-C, and no evidence of CHD.[234] It was reported that in subjects treated with lovastatin and whose HDL-C was in the lowest tertile at baseline; there was a reduction in cardiovascular events of about 45%. Thus, increasing HDL-C could lower the incidence of coronary events. Taken together, the results of the HHS and VA-HIT suggest that an increase of 1% in HDL-C is associated with a 3% decrease in risk of CHD.[235]

The existing evidence from epidemiological studies, transgenic animal studies, and subgroup analysis of human intervention trials supports the contention that the aforementioned lipoprotein-lipids are strongly associated with the development of CHD. Because of the strong inverse relationship between HDL-C levels and CHD risk, HDL-C has become a popular target for intervention to decrease the risk of future disease events. Since it is believed that pharmacological therapy is neither cost-effective nor medically appropriate in primary prevention in younger populations, it is imperative that intensive life-style modifications to reduce CHD risk due to lipid disorders should become a top priority in today's society.

Lipoproteins

Composition and Function

Because of their insolubility in water, triglycerides, cholesterol, and cholesterol esters can't be transported freely in the blood or lymph. In order to accomplish this, assembly is required with additional lipids and specialized proteins, forming a lipoprotein molecule. Plasma lipoproteins are spherical macromolecular particles consisting of lipids and specific protein molecules (apolipoproteins).[236-238] The hydrophobic core of the lipoprotein is made up of neutral lipids (triglycerides and cholesterol esters). The core is surrounded by a hydrophilic monomolecular surface layer of polar lipids such as phospholipids, unesterified cholesterol, and specialized apolipoproteins. The primary function of lipoproteins is to transport these water-insoluble lipids (cholesterol, triglycerides, and cholesterol esters) to various tissues for

energy utilization, lipid deposition, steroid hormone production, and bile acid formation.[238-240] The structure of a lipoprotein is represented in Figure A-1.

The major lipids which are mainly transported in plasma lipoproteins are phospholipids, triglycerides, and cholesterol. Phospholipids contain one or more fatty acid and one phosphoric acid radical and usually contain a nitrogenous base. Phospholipids are considered amphipathic molecules, meaning they are soluble in aqueous and non-aqueous solutions. They contain a hydrophilic head (phosphate group) with a hydrophobic tail (2 fatty acid chains). These amphipathic molecules span the majority of the surface layer of the lipoprotein, and provide stability to the molecule during transit.[236, 237] Most of the energy stored in the body is in the form of triglycerides, which because of their hydrophobic nature, are transported within the core of the lipoprotein molecule. Cholesterol exists in cell membranes of all tissues and is present in all of the lipoproteins, to a certain degree. Cholesterol is a sterol, made up of 4 fused carbon rings (A-D), where the D ring is attached to a hydrocarbon chain. Cholesterol is primarily transported within the hydrophobic core of the lipoprotein molecule as cholesterol esters. Seventy percent of plasma cholesterol exists in this form. However, free cholesterol can be found on the hydrophilic surface of the lipoprotein particle. Peripheral tissues rely on cholesterol for the synthesis of membranes, bile acids, as well as the formation of adrenocortical hormones in the adrenal glands.[236-238]

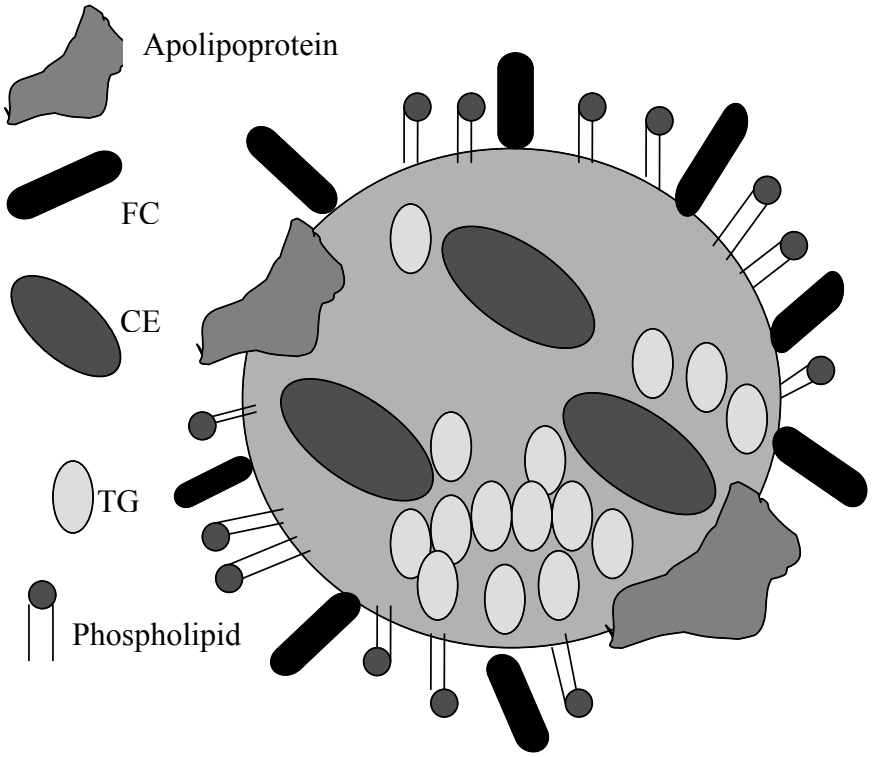

Figure A-1. Structure of a lipoprotein particle. FC = free cholesterol; CE = cholesterol esters; TG = triglyceride.

Classification of Lipoproteins

Plasma lipoproteins have traditionally been classified according to their hydrated density (g / mL). These classifications are usually determined by gradient ultracentrifugation.[236, 238] The major classes of lipoproteins are also characterized by differences in particle size, lipid / protein composition within the core of the particle, as well as their hydrated density. The largest and most buoyant lipoproteins contain a higher percentage of hydrophobic core lipids and a relatively smaller protein mass. As

the physical size of the lipoprotein decreases, the hydrated density increases. This is characterized by a lower lipid content in the hydrophobic core in association with an increase in protein mass. Table A-1, adapted from Fielding and Fielding [237] and Ginsberg[239] represents the most commonly found lipoproteins in plasma according to hydrated density, diameter, and relative lipid composition.

Each lipoprotein class has a characteristic apolipoprotein composition which plays a role in the structure and function of the lipoprotein. It is the apolipoprotein portion of the particle that solubilizes and stabilizes the lipoprotein during transit. The more prominent apolipoproteins also regulate the interaction of the lipoprotein complex with various tissue receptors and lipolytic enzymes. Therefore, the protein composition of the lipoprotein particle plays the vital role in determining the metabolism of the lipid components.[236-238] Table A-2, adapted from Fielding and Fielding [237] and Ginsberg, [239] lists the characteristics and functions of the primary apolipoproteins.

Table A-1. Classification of the Major Lipoproteins.

Lipoprotein	Density (g / mL)	Diameter (nm)	TG	CE	PL
Chylomicrons	$d < 0.95$	100-1000	805	2-7	6
VLDL	$d < 1.006$	35-50	53	14	15
IDL	$1.006 < d < 1.019$	28-35	31	23	22
LDL	$1.019 < d < 1.063$	20-26	4	42	21
HDL	$1.063 < d < 1.21$	8-12	3	23	29
HDL_2	$1.063 < d < 1.12$	8-10	2	20	30
HDL_3	$1.120 < d < 1.21$	6-7	1	16	25

Lipid (%) = % of total lipid and protein content. PL = phospholipid; CE = cholesterol ester; TG = triglyceride; VLDL = very low-density lipoprotein; IDL = intermediate-density lipoprotein; LDL = low-density lipoprotein; HDL = high-density lipoprotein; $HDL_{2\&3}$ = high-density lipoprotein subfractions.

Lipoprotein Metabolism

Dynamics of Lipid Transport

The major function of plasma lipoproteins is to transport lipids from tissues where they are synthesized to those tissues which will metabolize or store them. There are three major interconnected pathways involved in lipoprotein metabolism. The first pathway involves the transport of dietary or exogenous lipids, to peripheral tissues for

Table A-2. Characteristics of the Major Apolipoproteins.

APOLIPOPROTEIN	ORIGIN	LIPOPROTEINS	FUNCTION
apo A-I	Liver, Intestine	HDL, Chylomicrons	Cofactor of LCAT
apo A-II	Liver	HDL	LCAT inhibitor; phospholipid binding
apo A-IV	Liver, Intestine	HDL, VLDL, Chylomicrons	Unknown
apo B-100	Liver	VLDL, LDL	Assembly and secretion of VLDL; cell receptor binding
apo B-48	Intestine	Chylomicrons	Assembly and secretion of Chylomicrons
apo C-I	Liver, Intestine	Chylomicrons, VLDL, HDL	Cofactor adipose tissue LPL
apo C-II	Liver, Intestine	Chylomicrons, VLDL, HDL	Activator of LPL
apo C-III	Liver, Intestine	Chylomicrons, VLDL, HDL	Inhibitor of LPL; LCAT activator
apo D	Many Tissues	HDL	Transfer lipoprotein for core lipids
apo E	Many Tissues	Chylomicrons, VLDL, HDL	Cell receptor binding

CE = cholesterol ester; TG = triglyceride; VLDL = very low-density lipoprotein; IDL = intermediate-density lipoprotein; LDL = low-density lipoprotein; HDL = high-density lipoprotein; $HDL_{2\&3}$ = high-density lipoprotein subfractions; LPL = endothelial-bound lipoprotein lipase; HTGL = hepatic triglyceride lipase; LCAT = lecithin: cholesterol acyltransferase.

utilization or storage. The second pathway involves the transport of hepatic or endogenous lipid, to the peripheral tissues for catabolism. These first two pathways are referred to as forward cholesterol transport.[237, 238, 241, 242] The third pathway is reverse cholesterol transport. Reverse cholesterol transport is the pathway where peripheral cell cholesterol can be transported back to the liver for catabolism.[64, 242-244] It is important to remember that these three distinct pathways are dynamically interrelated. While the protein composition of the lipoprotein molecule largely determines the metabolism of its

lipids, it is the apolipoprotein content that is often altered during circulation in plasma. The interaction of these processes largely determines the lipid distribution amongst the different tissues.[237]

Chylomicron Formation and Exogenous (Dietary) Lipid Transport

Dietary cholesterol and fat are secreted from intestinal cells on chylomicrons in a process requiring apolipoprotein B-48. Cholesterol and fat from the diet are absorbed into the mucosal cells of the small intestine as fatty acids and cholesterol. Before this can occur, bile acids must emulsify the large fat particles so they can be attacked by lipases (pancreatic lipase). Bile salts also help in the absorption of fatty acids and cholesterol by forming minute complexes referred to as micelles. Micelles also transport monoglycerides & free fatty acids to the brush borders of intestinal epithelial cells where these particles diffuse through the enterocyte cell membrane. Fatty acids and monoglycerides can then be taken up by the smooth endoplasmic reticulum and recombined to form new triglyceride. Some monoglycerides are further digested into glycerol and fatty acids by intracellular lipase. Triglycerides aggregate within the endoplasmic reticulum and then eventually reach the Golgi apparatus forming globules that contain absorbed cholesterol, phospholipids, and newly synthesized cholesterol and phospholipids. Small amounts of apolipoproteins (apo) coat part of the surface of each globule. The chylomicron surface consists of the apo C lipoproteins, apo E, and apo B-48. Apo B-48 is essential for cellular exocytosis of chylomicrons to occur.[237, 240, 242, 244]

Chylomicrons enter the lymph and travel upward through the thoracic duct and empty into the great veins of the neck. Once they reach the plasma, the apo E content

increases, and chylomicrons receive apo C-II and apo C-III from HDL and VLDL. The addition and removal of the various apolipoproteins is an ongoing process occurring between HDL and the triglyceride-rich lipoproteins, VLDL and chylomicrons.[238, 239] The addition of apo C-II activates the chylomicron for lipolysis (see Table A-2). The TG content of chylomicrons is rapidly hydrolyzed by both muscle and adipose tissue lipoprotein lipase, releasing fatty acids and glycerol. Chylomicrons recirculate until about eighty percent of the initial TG content has been catabolized in the peripheral tissues. The TG-poor chylomicron remnants formed as a result of the lipolytic process are then removed from the circulation by the liver via low-density lipoprotein-like receptors (LRP, 65%), or by hepatic apo B / E receptors (35%) through receptor-mediated endocytosis.[237, 239, 241, 242] The half-life of a chylomicron is less than one hour, so they are rarely detected in a fasted state.[237] A graphic representation of this pathway, and the lipolytic enzymes associated with it are presented in Figure A-2.

Endogenous Lipid Transport

The liver is the source of TG-rich VLDL which contains apo B-100 and smaller amounts of cholesterol, phospholipids, as well as apo A-1, and the apo C proteins.[244, 245] VLDL particles contain a core of TG (60 percent by mass) and cholesterol esters (20 percent by mass). The TG is synthesized from fatty acids produced from acetate units of dietary carbohydrates. Microsomal triglyceride transfer protein is essential for the transfer of the bulk of triglycerides into the endoplasmic reticulum for VLDL assembly and for the secretion of apo B-100 from the liver. Once VLDL is secreted into the plasma, apo A-I is lost and the apo E and apo C protein content increases through

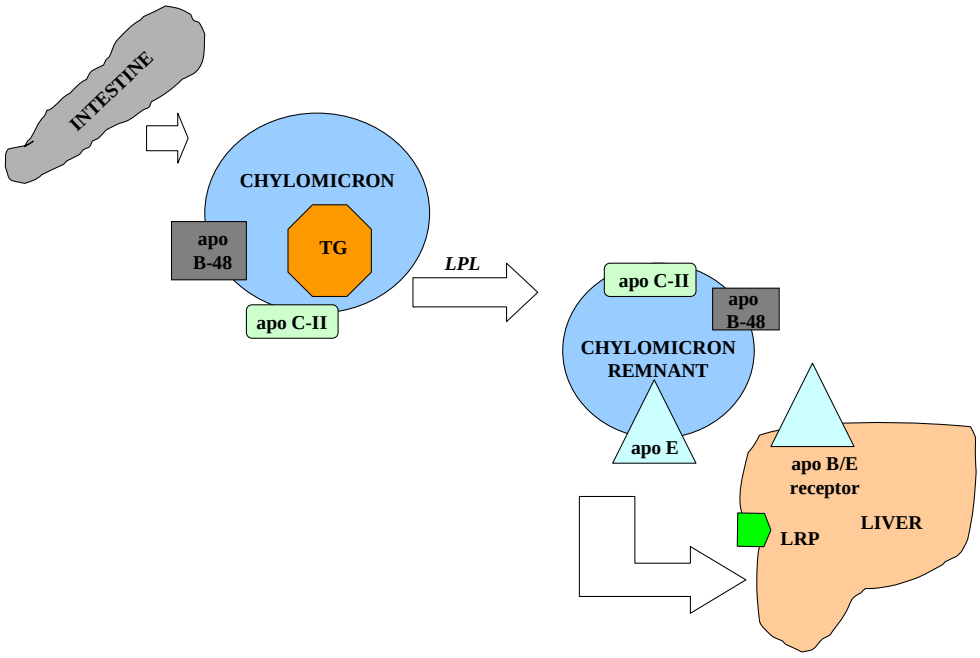

Figure A-2. Exogenous lipid transport. TG = triglyceride; apo = apolipoprotein; LRP = low-density lipoprotein-like receptor; LPL = endothelial-bound lipoprotein lipase.

interactions with HDL. This usually occurs within the first five minutes of entry into the plasma.[236, 237, 245] Fully activated VLDL contain between 10 and 20 apo C-II molecules.

The TG in the core of the VLDL particles is hydrolyzed into free fatty acids and glycerol by lipoprotein lipase, using apo C-II as a cofactor. Lipoprotein lipase hydrolyses 1(3)-ester linkages of the TG contained in the core of the VLDL molecule, generating 2-monoacylglycerol and unesterified fatty acids. Like the hydrolysis of chylomicron TG, VLDL catabolism also occurs in the capillary beds of both muscle and

adipose tissue. The free fatty acids produced during the lipolysis are either taken up for energy utilization or stored for future energy requirements.[240, 242, 244] After the initial TG hydrolysis, the lipoprotein molecule also loses surface lipids and the density of the remnant lipoprotein is increased and it is now termed IDL. IDL still contains some TG as well as apo B-100 and apo E. Some of the IDL particles are removed through the interaction of apo E with the LDL receptor on the surface of the liver, while a larger portion (50-70%) of the IDL particles are hydrolyzed further by hepatic lipase, subsequently producing LDL.[237, 238, 242, 246] The IDL to LDL conversion involves the loss of 80-90% of IDL TG, removal of some phospholipid, and the dissociation of the remaining apo E and apo C proteins. LDL is solely formed by the hydrolysis of the VLDL and IDL particles in the circulation. LDL is the main cholesterol-containing particle in human plasma containing one molecule of apo B-100 and no other apolipoproteins. Half of the LDL particles are metabolized through the apo B / E receptor pathway or they can be taken up by extrahepatic tissues through LDL receptor endocytosis.[237, 241, 242] A graphic representation of each pathway, and the lipolytic enzymes associated with it are presented in Figure A-3.

Reverse Cholesterol Transport

Reverse cholesterol transport refers to the process whereby unesterified cholesterol is removed from peripheral cells and atherosclerotic plaques through the transfer of cholesterol across the cell membrane by the ABC1 transporter.[247] This free cholesterol is picked up by nascent HDL particles and esterified by the enzyme lecithin:cholesterol acyltransferase (LCAT), forming cholesterol esters. These

cholesterol esters are then returned to the liver for clearance or reutilization via three distinct pathways which are described in the following paragraphs.[240, 243, 246, 248]

In 1973, Glomset [249] initially proposed the theory of the reverse cholesterol transport pathway. This theory detailed the protective effects of HDL. A cross-sectional study of men of Japanese ancestry living in Hawaii demonstrated that there is an inverse relationship between plasma HDL levels and coronary heart disease.[250] HDL is considered a chaperon that oversees lipid metabolism.

Origin of HDL and HDL Apolipoproteins

Intestine and hepatic cells are believed to be the major sources of the A apolipoproteins. Apo A-I content in intestinal absorptive cells and apo A-I transport in the lymph increases considerably during fat absorption.[251] The apo A-I pool represents the amount of protein available for HDL formation. This pool is derived from 2 sources: 1) secretion of free apolipoproteins by cells that synthesize and secrete apolipoproteins; and 2) apolipoproteins released from lipolyzed triglyceride-rich lipoproteins.

Three processes must be considered as sources of HDL precursors: 1) direct secretion of discoidal high density structures from hepatic and intestinal cells ("nascent" HDL particles); 2) lipid and protein surface remnants released from lipolyzed triglyceride-rich lipoproteins; and 3) phospholipid-apolipoprotein associations (apo A-I or apo A-II).[237-239, 243, 252] Phospholipids, free cholesterol, and apolipoprotein C molecules are displaced from the surface of lipolyzed VLDL and can associate with high density proteins. It is believed that surface remnants originating from the outer surface

of lipolyzed triglyceride-rich lipoproteins constitute the major, if not the only, source of HDL precursors.[253]

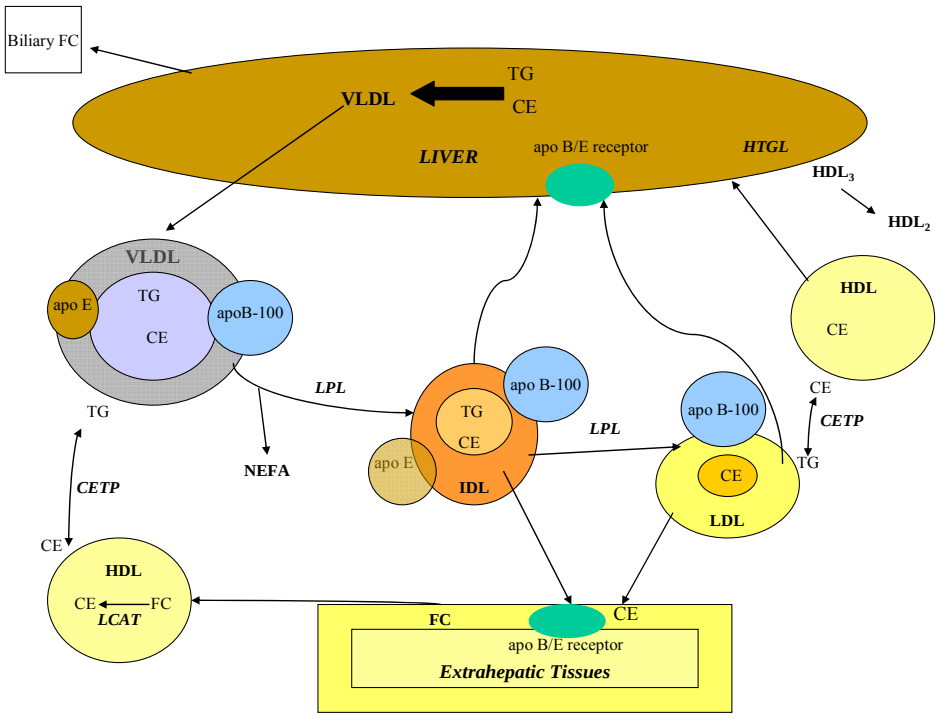

Figure A-3. Endogenous lipid transport. FC = free cholesterol; CE = cholesterol ester; TG = triglyceride; VLDL = very low-density lipoprotein; IDL = intermediate-density lipoprotein; LDL = low-density lipoprotein; HDL = high-density lipoprotein; $HDL_{2\&3}$ = high-density lipoprotein subfractions; LPL = endothelial-bound lipoprotein lipase; HTGL = hepatic triglyceride lipase; LCAT = lecithin: cholesterol acyltransferase; CETP = cholesterol ester transfer protein; apo = apolipoprotein.

HDL Phospholipids and Free Cholesterol

Four potential sources contribute phosphatidylcholine (PC) molecules to HDL. Newly secreted chylomicrons contain surplus phospholipids (PL), which are rapidly transferred to HDL even before any metabolic events take place. The lipolysis of

triglyceride-rich lipoproteins is another major source of HDL-phospholipids. VLDL lipolysis also contributes PL to the HDL molecule.[237, 243, 248]

The sources of free cholesterol (FC) are similar to phospholipids, nascent particles, the surface coat of lipolyzed triglyceride-rich lipoproteins, and cell membranes. The FC generated during lipolysis remains in the vascular system, and none is taken up by the peripheral cells. Thus, VLDL and LDL are important sources of FC for the HDL lipoprotein, and this process is accelerated by lipolysis.

The transformation of discoidal HDL precursors to spherical HDL is dependent on the activity of LCAT.[237, 243, 248] The LCAT reaction forms cholesterol esters from PC and FC molecules obtained from peripheral cells and from the surface layer of triglyceride-rich lipoproteins following lipolysis. The CE formed at the surface of the newly formed spherical particles is displaced into the hydrophobic core.[238, 239, 252] It is believed that the utilization of free cholesterol by LCAT allows the movement of additional cholesterol molecules from cell membranes to HDL.[243]

The accumulation of CE in the hydrophobic core contributes to the conversion of nascent HDL to HDL_3, and then to the larger, more buoyant, HDL_2 particle.[237, 239, 243, 246, 252] In order for the conversion from HDL_3 to HDL_2 to take place, it is necessary to increase the number of CE molecules in HDL_3 by 2 to 3 fold and to provide HDL_3 with one molecule of apo A-I and sufficient amounts of surface lipids (phospholipids and free cholesterol). HDL_3 readily accepts phospholipids, free cholesterol, and apolipoproteins (predominantly apo C) released from the surface layer of the lipolyzed VLDL.[254]

Mature HDL particles are characterized by the presence of apo A-II, apo C-II, apo C-III, and apo E with a greater CE and TG concentration.[239]

The HDL_2 particles are eventually depleted of their lipids and proteins and form smaller HDL_3. HTGL will hydrolyze HDL phospholipids and TG. It has been shown that HTGL hydrolyzes phospholipids and TG in VLDL, LDL, and HDL with a preference towards both VLDL and HDL. As a result of the activity of HTGL, HDL_2 is converted back into HDL_3.[255] In order for a true conversion from HDL_2 to HDL_3 to occur, there must be a loss of CE from the HDL_2 particle.

It has been shown that when VLDL and LDL have been added to plasma there is an induced transfer of CE from HDL to VLDL and LDL while the TG from VLDL and LDL is transferred back to HDL. This transfer is mediated by a cholesterol ester transfer protein (CETP). Therefore, the study demonstrated that particles similar to HDL_3 can be formed from HDL_2 when the activity of the CETP is combined with lipolysis of the transferred TG.[254] The bidirectional transfer of TG and CE is always related to the amount of transfer protein, the time of exposure between donor and acceptor particles, and the relative mass of the two. It is believed that the most important single factor that determines the amount of TG in HDL is the ratio between the mass of TG-rich lipoproteins (chylomicrons & VLDL) and of HDL in the plasma.[237, 238, 243, 254]

The HDL CE can be returned to the liver by 3 distinct pathways: 1) HDL cholesterol esters are transferred to TG-rich lipoproteins (VLDL, IDL, and LDL) through the actions of CETP, and then CE-enriched apo B lipoproteins are removed from the circulation by apo B / E receptors in the liver; 2) there is also a selective uptake

of HDL CE's without the degradation of the HDL protein. This pathway is mediated by the scavenger receptor BI (SR–B1); and 3) there is the uptake of holo-HDL particles and the degradation of HDL associated proteins such as apo A-I. This pathway may involve the formation of large HDL, enriched in apo E.[248] A graphic representation of this pathway, and the lipolytic enzymes associated with it are presented in Figure A-4.

Remnant Lipoproteins (RLP) and Remnant like Particles

There are two types of remnant lipoproteins: Chylomicron remnants derived from chylomicrons synthesized in the small intestine and VLDL remnants derived from VLDL synthesized in the liver. The Food and Drug Administration (FDA) of the United States of America (USA) has recognized that an increase in the concentrations of RLP constitute a risk factor for CHD. The Framingham Heart Study reported that an increase in RLP cholesterol (RLP-C) is a significant risk factor for CHD, especially in women.[256] Remnant lipoproteins are easily taken up into macrophages in the arterial wall, leading to foam cell formation of the macrophages and initiation of atherosclerotic lesions. RLP have also been shown to promote platelet aggregation, impair endothelial function, promote adhesion of monocytes to endothelial cells, and promote proliferation of vascular smooth muscle cells.[257-261]

Lipoprotein Enzymes

Lipoprotein Lipase

Lipoprotein lipase (LPL) is a key enzyme in the regulation of lipoprotein and fatty acid metabolism. The main physiological function of LPL is to hydrolyze TG in chylomicrons and VLDL to provide free fatty acids as an energy source in muscle tissue

and for re-esterification and storage in adipose tissue. The activity of LPL is dependent on apo C-II, which acts as an enzyme activator. Apo C-II does not activate any other enzyme, so its effect is specific to LPL.[64, 237-239, 252, 262]

LPL is a glycoprotein whose synthesis occurs in parenchymal cells, primarily adipose tissue and skeletal muscle. It has been noted that red muscle fibers tend to have higher LPL activity when compared to white muscle fibers.[263] After secretion, LPL is transported to the vascular surface of the capillary endothelium of muscle and adipose tissues where it is ultimately bound to heparin sulphate proteoglycans.[237, 239] Active LPL hydrolyzes 1(3)-ester linkages of TG in chylomicrons and VLDLs, generating 2-monoacylglycerol and unesterified fatty acids. These molecules are now available for uptake and utilization by the surrounding peripheral tissues.[237, 239]

The synthesis and secretion of LPL is highly regulated, showing distinct tissue specificity[52, 237, 264-266] The best-studied example of tissue specific LPL regulation occurs with adipose tissue LPL and muscle tissue LPL during periods of fasting and refeeding.[267] In adipose tissue, food intake raises LPL activity (LPLa), while during

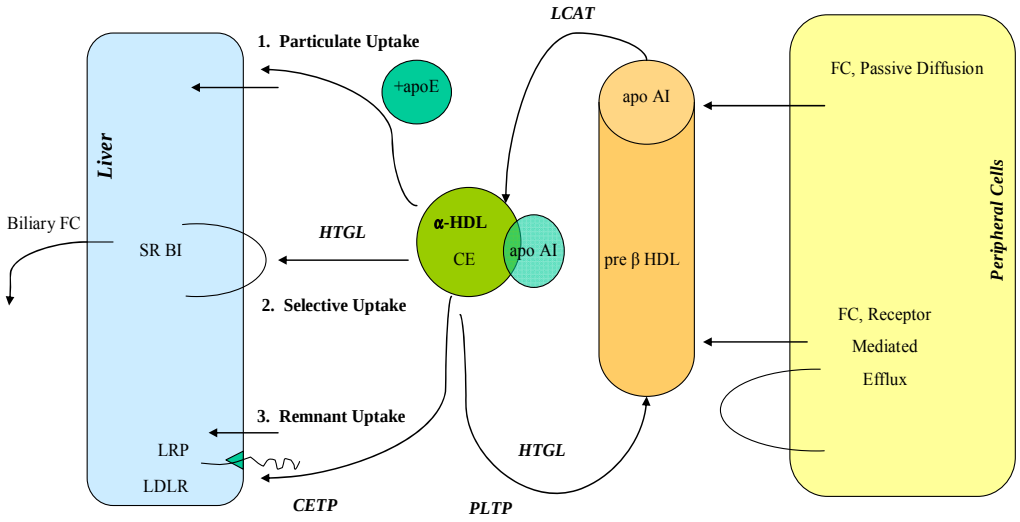

Figure A-4. Reverse cholesterol transport. FC = free cholesterol; CE = cholesterol ester; HDL = high-density lipoprotein; HTGL = hepatic triglyceride lipase; LCAT = lecithin: cholesterol acyltransferase; CETP = cholesterol ester transfer protein; apo = apolipoprotein; SR BI = scavenger receptor BI; LRP = low-density lipoprotein-like receptor; LDLR = low-density lipoprotein receptor; PLTP = phospholipid transfer protein.

periods of fasting a down-regulation of LPLa occurs. This physiological response provides large amounts of free fatty acids for fat deposition in adipose tissue during the postprandial state. The opposite is true for muscle tissue LPL.[268] LPL has also been known to act as a ligand in binding lipoproteins to receptors as well as cell surfaces.[237, 243, 262, 267, 269]

Research has shown that insulin will stimulate adipose tissue LPLa in a dose-dependent manner. Conversely, increased plasma insulin concentrations will down regulate LPLa in human skeletal muscle.[52] The effects of different compositions of one's diet on LPLa have also been investigated.[270] In human subjects, skeletal muscle LPLa has been shown to decrease by up to 50% in response to increases in muscle glycogen concentrations after consuming a high carbohydrate (CHO) diet.[52, 70, 264, 266] One investigation reported that decreasing CHO from 48% to 31% of the daily caloric intake increased skeletal muscle LPLa by 83% without affecting fasting insulin or the insulin response to infused glucose.[271]

It is generally accepted that endurance exercise increases LPLa in postheparin plasma.[115] With exercise, insulin is decreased and glucagon is increased, leading to activation of muscle L-HSL and inhibition of adipose tissue LPL. Animal studies report increases in skeletal muscle LPLa and decreases in adipose tissue LPLa with exercise. However, human studies have reported exercise-induced increases in LPLa in both tissues. Interestingly, the regulation of LPL in skeletal muscle of young animals has been shown to be different between muscle fiber types. Furthermore, LPL protein mass and LPLa were low in white glycolytic muscles and high in red oxidative skeletal muscles.[272] In addition, different responses of LPLa have been reported between white glycolytic and red oxidative muscles with exercise and physical inactivity.[116] Skeletal muscle is a major site for TG removal in humans. LPL is an integral part of this process and the LPL-induced lipolysis of TG in muscle may be a major contributor to the generation of HDL-C. This association may be viewed as anti-atherogenic due to the

favorable increase in HDL-C.[62] A decrease in LPLa is associated with high plasma concentrations of VLDL-TG, delayed and elevated postprandial lipids, and low HDL-C concentrations, leading to an increased risk for the development of CAD.[262, 263, 266, 268]

Hepatic Triglyceride Lipase

Hepatic triglyceride lipase (HTGL) is synthesized in the liver, and binds to the luminal surface of endothelial cells in the hepatic vasculature.[239, 262] HTGL is an enzyme that hydrolyzes TG as well as ditriglycerides and monotriglycerides, but is more efficient than LPL in hydrolyzing phospholipids in all lipoproteins. HTGL differs from LPL in that it is not dependent on apo C-II for activation.[237, 243, 262] HTGL also plays a role in the regulation of plasma HDL levels. HTGL has been shown to participate in the conversion of HDL_2-C particles into the smaller and denser HDL_3-C. This occurs through the hydrolysis of TG and phospholipids from the HDL_2-C substrate and the subsequent transfer of cholesterol esters to other lipoproteins.[273]

It has been reported that concentration of HDL-C is inversely correlated to postheparin plasma HTGL activity (HTGLa).[262, 269] Thus, a decrease in HTGLa should result in an increase in HDL_2-C due to a slower catabolism thereby promoting a favorable lipid profile. In contrast, an increase in HTGLa is associated with the lowering of plasma HDL_2-C.[262] The activity of HTGL is also influenced by steroid hormones. Intake of anabolic steroids by athletes can lead to an increase in HTGLa accompanied by low levels of HDL-C. On the other hand, estrogen has been shown to decrease the activity of HTGL.[262, 269]

Lecithin: Cholesterol Acyltransferase

Lecithin: Cholesterol Acyltransferase (LCAT) is a glycoprotein which is secreted from the liver into the plasma. The active sites on the LCAT molecule share similarities with those from LPL and HTGL. Once it reaches the plasma, LCAT is transported mainly bound to high-density lipoproteins.[237, 239] LCAT catalyzes a transesterification reaction in which an acyl group from the 2-position of phosphatidylcholine (PC) is transferred to the 3-hydroxyl group of cholesterol, converting PC to lyso-PC and cholesterol to cholesterol ester.[237, 239] The lysolecithin that is also produced from this reaction is taken up by albumin and carried back to the liver.[237, 243] Apo A-I acts as a cofactor for LCAT in the esterification of free cholesterol. The optimal substrate for LCAT is discoidal HDL. The activity of LCAT decreases as CE accumulates in the core of the spherical molecule. With the increase in the uptake of CE, HDL will increase in size to form the HDL_3 particle. A continual transfer of cholesterol esters into the hydrophobic core eventually yields the larger HDL_2 particle.[239, 244, 254] It is generally accepted that high cholesterol esterification rates promote efflux of cholesterol from peripheral tissues, and that LCAT activity presumably protects against atherosclerosis.

Cholesterol Ester Transfer Protein

Cholesterol ester transfer protein (CETP) is a hydrophobic glycoprotein that is secreted mainly from the liver and circulates in plasma, bound mainly to the HDL molecules.[274] CETP is not considered an enzyme, but a protein that has an affinity for non-polar lipid transfer.[237] CETP mediates the transfer of CE (produced from the LCAT reaction) from HDL to VLDL or LDL and of TG from VLDL and LDL to HDL. The

CETP mediated transfer of these non-polar lipids is reversible; however, this net transfer is driven by preexisting concentrations gradients. The rate and direction of the net lipid transfer is established by gradients maintained by LPL and LCAT.[237] CETP accounts for the entire neutral lipid transfer activity of human plasma but only part of the phospholipid transfer activity.[239, 248, 274]

The CETP reaction is a complex process, with the exact mechanism of neutral lipid exchange remaining a controversial topic.[274] One method for the proposed action of CETP is a carrier-mediated mechanism of CE transfer where CETP binds to the donor lipoprotein (HDL), takes up certain lipids (phosphatidylcholine and CE or TG), then collides with the acceptor lipoprotein (VLDL), exchanges its bound lipids and then dissociates from the acceptor.[275] Another hypothesis is that CETP may mediate the formation of a "collision complex" involving CETP, the donor, and the acceptor lipoproteins together.[274, 275]

The CETP reaction increases the capacity of the plasma to clear CE, by reusing VLDL, IDL, and LDL molecules to transfer the CE back to the liver for catabolism. Thus, the CETP-mediated transfer of neutral lipids is a process that works in concert with the LCAT reaction. Furthermore, the utilization of HDL to transfer TG back to the liver provides an additional pathway involving HTGL.[237] The level of CETP activity may have an important role in determining the CE distribution between LDL and HDL. The extent of CETP mediated CE distribution is dependent on both the reactivity and the quantity of particles in the donor and acceptor fractions.[275] Thus, CETP activity is

increased postprandially, where an increase in the TG content of the apo B lipoproteins occurs.[237, 274]

The atherogenicity of CETP activity has been consistently debated. It has been suggested that CETP can potentially inhibit atherogenesis by enhancing the rate of reverse cholesterol transport. CETP mediated transfers from HDL to VLDL and LDL provide a potential indirect pathway by which HDL CE's can be delivered to the liver for catabolism.[242, 243] Human subjects with a homozygous CETP deficiency have elevated concentrations of HDL cholesterol, apo A-I, apo A-II, and apo E. The increased HDL concentration is primarily due to a reduction in the rate of catabolism, with a markedly delayed catabolism of apo A-I and apo A-II. However, if elevated HDL_2-C levels occur due to a CETP deficiency a reduced capacity for cholesterol efflux occurs.[274] The HDL_2-C from CETP-deficient patients has a reduced ability for cholesterol efflux compared to normal HDL_2. Conversely, species with high or moderate levels of CETP activity are susceptible to atherosclerosis, and do not develop prominent HDL-C. Enhanced CETP activity may promote increased cholesterol-rich IDL particles and cholesterol-poor HDL particles, which may lead to promoting premature atherosclerosis.[276]

Non-Traditional CHD Risk Markers

hs-Crp

Experimental and clinical evidence have indicated that inflammatory processes play a key role not only in the initiation and progression of atherosclerosis but also in the stability of the established atherosclerotic plaques.[225] Based in part on these findings,

protein markers of inflammation have been studied as noninvasive indicators of underlying atherosclerosis.[120, 220] The most extensively studied inflammatory biomarker in CHD has been high-sensitivity C-reactive protein (hs-Crp). However, it must be pointed out that hs-Crp is a nonspecific marker of inflammation.[277]

This acute phase protein is produced predominantly by hepatocytes in response to stimulation from cytokines such as interleukin (IL) – 6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha). An acute phase protein has been recently defined as a protein whose plasma concentration increases by at least 25% in response to inflammation induced by either trauma, immunologic, or infectious processes anywhere in the human body.[277] It was thought that the production of hs-Crp was limited to the liver, but recent studies have shown that hs-Crp may be produced by other tissues, such as human atherosclerotic lesions, coronary artery smooth muscle cells, aortic endothelial cells, and adipocytes.[278, 279]

Hs-Crp has recently been shown to possess proatherogenic properties. Pasceri et al.[280] have reported that hs-Crp activates endothelial cells to express adhesion molecules, intracellular adhesion molecule-1, vascular cell adhesion molecule-1, selectins, and the chemokine, monocyte chemotactic protein-1. Hs-Crp has also been shown to enhance the uptake of LDL by macrophages.[31] Moreover, hs-Crp has been shown to be deposited in human atherosclerotic plaques, and the amount has been determined to be sufficient to promote the development of atherosclerosis.[281]

It must be pointed out that the value that constitutes an elevated hs-Crp level has not been clearly defined. The Centers for Disease Control and Prevention and the

American Heart Association (CDC / AHA) recommend averaging two assays, taken two weeks apart, in order to provide a more stable estimate compared to obtaining a single blood sample. Blood levels of hs-Crp < 1, 1 to 3, and > 3 mg / L correspond to low, moderate, and high vascular risk across all levels of LDL-C, the Framingham Risk Score, and the metabolic syndrome.[120] Hs-Crp usually exists at very low concentrations in plasma, with 90% of individuals having hs-Crp levels < 3 mg / L. A value above 10 mg / L should alert clinicians to initiate a search for a source of infection or inflammation with the measurement being repeated in two weeks.

Data from numerous research studies have shown a significant association between elevated serum or plasma concentrations of hs-Crp and the prevalence of underlying atherosclerosis and the incidence of first cardiovascular events among individuals at risk for atherosclerosis.[120] Furthermore, hs-Crp levels > 6 mg / L were associated with a 75% higher risk of restenosis compared to subjects with values < 1 mg / L during a 5-year follow-up study in patients with CVD.[282] Among patients with stable angina and established CHD, levels of hs-Crp have consistently demonstrated an association with the recurrent risk of cardiovascular events.[282]

The most relevant use of hs-Crp has been in the primary prevention setting. Several studies have shown baseline levels of hs-Crp to independently predict future MI, stroke, and cardiovascular death.[19, 20] Ridker et al.[20] reported that hs-Crp was a better predictor of the risk of cardiovascular events than LDL-C in a prospective study comprising 28,000 women. In a cohort of 22,000 middle-aged men with no clinical evidence of CHD, those with elevated baseline hs-Crp in the highest quartile had a 3-

fold increase in risk of MI and the effect was independent of all other lipid and non-lipid risk factors.[19] However, not everyone is convinced that hs-Crp is a valuable CHD risk marker. Kereiakes[283] has stated that only half of all patients who experience an acute MI in the absence of an unstable angina prodrome will have an elevated hs-Crp level. Furthermore, approximately 35% of all patients who present with unstable angina will have a "normal" hs-Crp level. Wilson et al.[284] determined that elevated hs-Crp levels provided no additional predictive value in estimating risk of new cardiovascular events in a cohort from The Framingham Study.

While lifestyle and pharmacological interventions have proven to be successful in reducing traditional CHD risk factors, they may also have favorable effects on non-traditional risk factors such as hs-Crp. Several drugs that are used in the treatment of cardiovascular disease have been shown to reduce serum hs-Crp levels. Thus, it is possible that reduced inflammation contributes to the favorable effects of these medications. Multiple statins have been shown to significantly decrease serum hs-Crp in people with hyperlipidemia. Furthermore, this reduction seems to be independent of decreases in LDL-C.[285] It is believed that the effect of statins on hs-Crp may be mediated in part by reduced monocyte expression of IL-6 and TNF-alpha.[286]

Non-pharmacological methods have also been shown to favorably alter hs-Crp levels. Tchernof et al.[124] reported that weight loss in obese postmenopausal women reduced hs-Crp levels. Heilbronn and coworkers[123] also reported that hs-Crp was significantly reduced in obese, healthy women after a 12 week weight loss program. Furthermore, Tisi et al.[127] evaluated several markers for disease severity in a randomized

trial of therapeutic exercise training in 49 patients with intermittent claudication. It was reported that both serum amyloid A and hs-Crp levels were significantly reduced after 3-6 months of regular physical activity.

Hs-Crp is an excellent biomarker for inflammation. It can provide clinicians a valuable tool for identifying people at risk for cardiovascular events in primary prevention in addition to lowering LDL-C.[32] Hs-Crp screening is readily available and relatively inexpensive. Thus, hs-Crp may be a beneficial adjunct in addition to traditional risk factor analysis regarding the progression of CHD. If anything, this risk marker may motivate certain individuals with moderate to high risk levels to make important lifestyle modifications (i.e. smoking cessation, diet modification, exercise, and weight loss).

LDL and HDL Subfractions

Increasing evidence suggests that several LDL subfractions, which are characterized by variations in size, flotation rate, density, and chemical composition, have important clinical significance in relation to CHD risk reduction. LDL subfraction distribution has been determined by two different methods, analytic ultracentrifugation (ANUC) and gradient gel electrophoresis (GGE). ANUC provides separation of lipoprotein particles based on density and Svedberg flotation intervals. GGE determines multiple LDL peaks and the diameter of each peak in angstroms.[26] One of the benefits of measuring lipoprotein-lipid subfractions is that they can provide additional cardiac risk information, (i.e. detecting changes in concentrations of the subfractions in response to an intervention), even when the standard lipid panel remains unaltered.[286, 287] It has

even been reported that close to eighty percent of patients who develop CHD have similar TC concentrations as those who do not develop CHD.[288]

According to a certain level of LDL-C, the risk for developing CHD can differ depending primarily on the LDL particle number as well as the density of the lipoprotein particle.[286, 287] One's risk for developing CHD is increased if they have larger numbers of LDL particles and smaller rather than larger LDL diameters.[289] The HDL lipoprotein class can be further subdivided into the following classes: (H_5-H_1) with H_5, H_4, and H_3 being the larger particles. H_5, H_4, and H_3 are negatively associated with CHD, whereas H_2-H_1 are positively associated with CHD. H_5, H_4, H_3 subclasses correspond roughly to HDL_2-C whereas H_2 and H_1 correspond to HDL_3-C.

In normal subjects, up to four major LDL subspecies, distinguished by size and density, have been identified.[290] LDL-1 is the largest and least dense, and the smallest, LDL-IV, is the most dense. Furthermore, LDL subspecies have been dichotomized into two distinct phenotypes, denoted A and B. Phenotype A is mainly characterized by large buoyant LDL particles and phenotype B is associated with a high proportion of small dense LDL particles.[291] The presence of an increased proportion of these small, dense LDL particles has been associated with elevated plasma TG, VLDL, and apo B concentrations along with reduced HDL-C, and apo A-I concentrations.[11] However, the pattern B phenotype can persist even when the concentrations of TG, VLDL, and HDL are normal.[292] It also appears that phenotype B is inherited as a single-gene trait with a dominant mode of inheritance.[11]

Low density lipoprotein subclass distribution has been shown to contribute valuable information in determining CHD risk that is independent of the concentrations of TC, as well as LDL-C. The clinical significance of small, dense LDL was examined in the Stanford Coronary Risk Intervention Project. Two hundred and thirteen male subjects, with angiographically documented CHD, were randomized to a usual care group or to a CHD risk reduction program. The CHD risk reduction program included exercise, diet, and other lifestyle modifications, including lipid-lowering medications. Subjects were followed for 4 years and underwent annual coronary angiograms. No changes in annual coronary angiograms between the two treatment groups were noted for subjects exhibiting large, buoyant LDL. Conversely, among subjects with small, dense LDL, those in the risk reduction group showed less progression of CHD based on minimum artery diameter, and marginally favorable differences in stenosis.[293] In one case-control study, the pattern B phenotype was associated with a threefold increased CHD risk.[294] In further support of these findings, a report from the Physician's Health Survey also noted a threefold increased CHD risk for subjects exhibiting the pattern B phenotype.[295]

Vakkilainen and coworkers[296] demonstrated that men with small LDL particles, mildly elevated TGs, low HDL-C, and normal LDL-C have impaired endothelium-dependent vasodilation compared with men of similar age, BMI, and LDL-C concentrations. Moreover, the degree of endothelial dysfunction was significantly correlated with LDL particle size as opposed to LDL-C, HDL-C, or TG concentrations.

Levels of small, dense LDL have also been found to be associated with the intima-media thickness of the common carotid artery.[297]

In addition to LDL size, the total number of LDL particles may also provide a better index for predicting future coronary events. Otvos et al.[298] examined LDL and HDL particle numbers and size at baseline and after 7 months of gemfibrozil therapy in a substudy of the Veterans Affairs High-Density Lipoprotein Intervention Trial. While LDL-C and HDL-C concentrations were not appreciably altered, gemfibrozil therapy resulted in an increased LDL particle size and a reduction in the number of LDL particles. These changes were associated with a reduced risk of CHD events.[298]

Generation of small, dense LDL

Insulin resistance or a fundamental defect in free fatty acid incorporation into adipocytes can lead to the increased mobilization of FFA to the liver, leading to increased TG formation, decreased LDL proteolysis, enhanced VLDL production and secretion. The enhanced secretion of VLDL from the liver is often accompanied by a subsequent series of events involving 2 key proteins in lipoprotein metabolism, CETP and HTGL. As the triglyceride-enriched VLDL is entering the plasma compartment at this accelerated rate, the TG in the VLDL are exchanged for the cholesterol ester in the core of LDL, producing a depleted, but TG-enriched LDL particle. The TG in the core of LDL is then hydrolyzed by HTGL thereby producing small dense LDL particles. The CE in the core of the HDL may also be exchanged by CETP for the TG in VLDL, producing a TG-enriched but CE depleted HDL particle. The TG–enriched HDL

appears to be catabolized more rapidly by the kidney, thus resulting in low HDL levels.[237, 239, 243, 244, 262]

Small, dense LDL particles may also be generated when excess TG on VLDL are exchanged for cholesterol esters on LDL by CETP, producing TG-rich LDL, which then undergoes lipolysis by HTGL to produce smaller and denser LDL particles.[299] In a cross-sectional investigation Zambon et al.[300] reported that high HTGLa is associated with an increase in small, dense LDL particles and a decrease in HDL_2-C. In the Familial Atherosclerosis Treatment Study, treatment with colestipol / lovastatin and colestipol / niacin significantly decreased HTGLa with a concomitant conversion of small, dense LDL to buoyant LDL, which was the strongest predictor of angiographic regression.[21]

Krauss[301] suggests that the metabolic pathway resulting in the formation of these atherogenic LDL subspecies originates with the production of a subset of large VLDL particles which undergo reduced clearance from the periphery and increased shunting through the plasma delipidation cascade, ultimately resulting in the increased transport of lipolytic remnants. Hypothetical TG enrichment of these remnant particles could lead to the formation of small, dense LDL, a process mediated by the action of HTGL.[301] Basically, the formation of small, dense LDL particles may arise through the exchange of cholesterol esters for TG, between LDL and these large VLDL. This action is mediated by CETP, which ultimately produces TG-rich LDL particles, which are then lipolyzed by HTGL.[297] Any therapeutic intervention that can reduce VLDL-TG will ultimately limit the availability of this substrate for exchange and is believed to be one of

the main mechanisms underlying the increases in the size of LDL particles and in HDL-C concentrations and particle diameter.[302]

Small LDL particles penetrate the endothelial barrier 1.7-fold more than large LDL particles; these electronegative small LDL particles interact with positively charged intimal proteoglycans.[11, 294] Furthermore, small, dense LDL particles bind less efficiently to the LDL receptor, thus prolonging their residence time in plasma.[303] This extended time allows them increased opportunities to infiltrate the arterial wall and exert atherogenic effects. The increased retention of small LDL particles in the vessel wall allows a longer time for reactive oxygen species modification of surface phospholipids and unesterified cholesterol. In addition, the small LDL phenotype is associated with a clustering of other risk factors, including elevated levels of triglycerides, VLDL-C, and IDL-C, reduced concentrations of HDL-C and HDL_2-C, and insulin resistance.[11]

It is important to continue research in this area as future clinical studies have the opportunity to enhance the ability of physicians to identify individuals at risk for CHD, and in addition to develop the most appropriate and individualized therapy for both primary and secondary CHD prevention.

CHD Prevention

Although age-adjusted CVD rates continue to fall, the rate of decline has diminished during the 1990s. CHD rates may also be leveling off, owing in part to a slowing in the rate of decline in risk factors such as smoking and increases in other risk factors such as obesity and physical inactivity. A risk factor can be defined as any characteristic of an individual that is present early in life and is associated with an

increased risk of developing future disease.[9] The concept for considering specific "cardiovascular risk factors" did not formally exist until the initial findings of the Framingham Heart Study began to appear in the early 1960's. Over the last several years, the concept of preventing CHD through risk factor reduction has gained widespread popularity. Both pharmacologic and non-pharmacologic strategies have been employed to aid in risk factor reduction and ultimate CHD prevention. Maintaining a physically active lifestyle has been associated with a more favorable lipid profile and a reduced risk of CHD.[41, 45] Given the prevalence of CHD, preventing even a small proportion of cases would save thousands of lives and billions of health care dollars. Compared to other more expensive modes of therapy (pharmacological), exercise is a relatively inexpensive treatment, and therefore economically appealing**.**

Role of Exercise in Prevention of CHD: Primary Prevention

Many of our jobs have become so physically undemanding that we can use computers and machines to do tasks for us while we become increasingly sedentary. The importance of physical activity and physical fitness to one's health has been continually promoted ever since Hippocrates advised that a lack of physical exercise was detrimental to health.[304] During the Industrial Revolution in England, King's College professor Dr. W.A. Guy contrasted mortality rates among sedentary and physically active workers. It was determined that the more active workers had a lower mortality rate compared to the sedentary workers.[305] Silversten and Dahlstrom[306] classified people from Minnesota according to contemporary occupational activity and discovered that death rates were lower at higher levels of physical activity, and that the average age of

death increased in a gradient fashion with jobs that were physically more demanding. After World War II, Morris and colleagues [45] began a series of investigations regarding the idea that the deaths related to CHD might be less common among men engaged in physically active work compared to those with a more sedentary occupation. These researchers found that active conductors from London seemed to have a protection against the development of CHD when compared to the sedentary drivers of double-decker buses. This finding was reproduced in a study involving active postmen compared to sedentary telephonists and other government workers.[45, 307] These findings led to the establishment of physical inactivity as one of the major modifiable risk factors for CHD.

Vigorous activity can be defined as expending more than 6 metabolic equivalents (METs) or a minimum of 7.5 kcals / min or working at a minimum of 70% of maximum heart rate or 70% of $\dot{V}O_{2peak}$.[137] The study of British Civil Servants conducted by Morris and colleagues[308] confirmed the benefits of vigorous physical activity in reducing the risk from CHD. A group of 17, 944 male British office workers between 45 and 65 years of age, free from CHD, volunteered for this prospective study. After 8.5 years of follow-up, the age-standardized cumulative incidence of CHD was 3.1% among men who reportedly took part in vigorous exercise, and 6.9% among those who did not.[308] The Harvard Alumni Study has also shown that vigorous activity reduces the risk of CHD.[309]

Recently, several investigations have reported the benefits of moderate intensity activity for cardiovascular health. Moderate intensity activity can be defined as

expending between 3 and 6 METs or approximately 5-7.5 kcals per minute or exercising at 60-70% of maximum heart rate or at 60% of $\dot{V}O_{2peak}$.[137] The British Regional Health Study was a large prospective study of cardiovascular disease which began in 1978 involving 7,735 men between the ages of 40 and 59. Men with and without pre-existing CHD were randomly chosen as potential subjects for this study. Participants completed a mailed questionnaire which included questions on leisure-time physical activities and other health habits. Results after an 8 year follow-up demonstrated that in men without pre-existing CHD those that participated in moderate or moderately vigorous activities had a 50% reduction in CHD risk, compared to those who were inactive. Furthermore, there was no threshold for benefit. Men with pre-existing CHD showed a similar inverse association up to moderate levels of activity. Interestingly, there was no additional benefit seen in those men participating in vigorous activity.[310]

Inadequate physical activity has been recognized as an independent risk factor for premature development of CHD. It is estimated that roughly 12% of all mortality in the United States is related to a lack of regular physical activity and that physical inactivity is associated with at least a twofold increase in the risk for coronary events.[311] Numerous investigations have shown that there is a strong inverse relationship between leisure time activity, energy expenditure, habitual exercise, and fitness and the risk of coronary disease and death.[312-315] A recent analysis suggested that 37% of deaths from CHD are attributable to physical inactivity; second only to high levels of blood cholesterol.[316]

Physical activity habits were analyzed in 10,269 Harvard Alumni (mean age 58 yrs) in a retrospective study conducted over a 12 year period. Those men who engaged in moderately vigorous sports activity (defined as total physical activity levels > 4200 kj / week or brisk walking, recreational cycling or swimming, home repair, and yard work for 30 min / day on most days) had a 23% lower risk of death than those who were less active. The improvement in survival with exercise was equivalent and additive to other lifestyle measures such as smoking cessation, control of hypertension, and avoidance of obesity. This reduction of risk was even seen in men with multiple coronary risk factors.[317, 318]

Regular walking also appears to be beneficial in reducing the risk for CHD in older individuals. This was illustrated in a report from the Honolulu Heart Program of 707 retired nonsmoking men (mean age 69 yrs) who were capable of participating in a low intensity activity on a daily basis. The distance walked was measured at baseline and mortality data then collected over a 12-year period. After adjustment for age, men who walked more than two miles per day (range 2 to 8 miles) had a significantly lower mortality rate than those who walked less than one mile per day (23.8% versus 40.5%, risk factor adjusted relative risk 1.8).[319] The type and intensity of exercise necessary for cardiovascular benefit were evaluated in a cohort of 44,452 men (age 40 to 75 yrs) enrolled in the Health Professional's Follow-up Study.[320] During 475,755 patient-years of follow-up, there were 1,700 new cases of CHD (first MIs or cardiovascular death). Several types of physical activity correlated with a significant reduction in CHD risk: running for 1 hour or more per week – relative risk 0.58; lifting weights (isometric

exercise) for 30 minutes or more per week – relative risk 0.77; rowing for one hour or more per week – relative risk 0.82; brisk walking for 30 minutes or more per day – relative risk 0.82.

In addition to the amount of exercise, the degree of cardiovascular fitness, as determined by the duration of exercise and maximal oxygen uptake on a treadmill, is also associated with a reduction in CHD risk and overall cardiovascular mortality.[312, 313, 315] A prospective study evaluated 9,777 men with two clinical examinations (mean age 43 yrs, mean interval between examinations, 4.9 yrs) to assess the association of change or lack of change in physical fitness with the risk of mortality during a mean 5.1 year follow-up after the second examination. The age-adjusted all cause death rate was approximately three times higher in men who were unfit at both examinations compared to those who were physically fit at both examinations (122 versus 40 per 10,000 man-years). An intermediate rate (68 per 10,000 man-years) was noted in men who improved from unfit to fit between the first and subsequent examinations.[313] In another report, 6,213 men referred for exercise testing (mean age 59 yrs) were followed for a mean of 6.2 years: 59% had an abnormal exercise test and / or a history of cardiovascular disease.[321] After adjustment for age, peak exercise capacity (measured in METS), was the strongest predictor of mortality among men with and without cardiovascular disease. One MET is defined as 3.5 mL O_2 uptake / kg per min, which is the resting oxygen uptake in a sitting position. For each 1 MET increase in exercise capacity there was a 12% improvement in survival.

Younger subjects have also been shown to benefit from improved cardiovascular fitness levels. A population-based study of over 5,000 men and women (18 to 30 yrs), demonstrated a relationship between fitness and the development of CHD risk factors at a 15 year follow-up.[315] During the follow-up, new onset diabetes, hypertension, and the metabolic syndrome developed at a rate of 0.3, 1.3, and 1.0 percent per year, respectively. Individuals with low fitness (< 20th percentile) were three to six fold more likely to develop diabetes, hypertension, and the metabolic syndrome than individuals with high fitness ($\geq$ 60th percentile). Furthermore, fitness levels were related to the development of hypercholesterolemia. Almost 2,500 subjects repeated the exercise test after seven years. Improved fitness was associated with reductions in the rate of developing diabetes and the metabolic syndrome. However, the significance of these changes was diminished after accounting for alterations in body weight.

Role of Exercise in Prevention of CHD: Secondary Prevention

There are also a number of studies that suggest that exercise and fitness are beneficial in patients who have pre-existing CHD.[321, 322] One investigation of 772 men (mean age 63 yrs) with documented CHD who were followed for up to five years found that the lowest incidence of all-cause and cardiovascular mortality was seen in those who engaged in light and moderate activity.[322] This activity included recreational (nonsporting) activity ($\geq$ 4 hours / week), regular walking (> 40 min / day), or moderate or heavy gardening (adjusted relative risk 0.42 and 0.47 compared to inactivity or occasional light activity). A recent meta-analysis[323] evaluated trials of cardiac rehabilitation (including exercise with or without risk factor education) among patients

with coronary disease (most post-MI). It was found that exercise rehabilitation alone produced a significant reduction in all-cause mortality (6.2 versus 9%, summary risk ratio 0.72) and an almost significant reduction in recurrent MI (summary risk ratio 0.76). A combined program of exercise rehabilitation and risk factor education produced an almost significant reduction in all-cause mortality (9.3% versus 10.8 %, summary risk ratio 0.88) and a significant reduction in recurrent MI (summary risk ratio 0.62). The overall mortality benefit from the cardiac rehabilitation program was present at two years (summary risk ratio 0.53), but not when evaluated after one year.[323]

Physical Activity, Exercise, and Lipid Metabolism

Cross-sectional Studies

Athletes and persons with a long history of endurance training tend to have lower blood TG and higher HDL-C concentrations than their sedentary counterparts.[48, 131] Furthermore, in most cross sectional studies endurance trained individuals exhibit higher concentrations of HDL-C, apo A-I, LPLa, and lower concentrations of LDL-C, apo B, TG, and HTGLa as compared with untrained individuals.[41, 46-51, 95, 129-131] However, it is important to note that the process of subject selection, differences in body weight, body fat (%), dietary, and behavioral habits of the subjects can all contribute to the differences in lipoprotein-lipids noted between the two groups.[41, 95, 129-131] Even so, cross-sectional investigations demonstrate that maintaining a physically active lifestyle is associated with a more favorable lipid profile and a reduced risk of developing CHD compared to people who continue to live a relatively sedentary lifestyle. A strong inverse relationship between the concentration of HDL-C and CHD events has been established.

It is estimated that for every 1 mg / dL increase in HDL-C, the risk for a CHD event is reduced by 2% in men and at least 3% in women.[75]

It has been reported that men engaging in vigorous muscular activity had a lower incidence of sudden cardiac death when compared to men who were less active.[87] Research from the late 1970's indicates that lumberjacks, who perform activities similar to resistance exercise, had higher concentrations of HDL-C and lower TG concentrations when compared to a group of less active electricians. However, TC, VLDL-C, and LDL-C were not different between the two groups. The investigators concluded that the physical work of the lumberjacks, which requires more energy than most other occupations, was responsible for the favorable lipid levels.[324]

In an additional study, Lehtonen and Vikari [88] examined lipoprotein-lipids in middle-aged or older men undergoing training compared to selected control groups and correlated them with the amount of physical activity. Runners (≥ 83 km / week) had significantly lower TG when compared to aged matched controls. The concentration of HDL-C was higher in the runners compared to all other groups. A positive correlation was found between the number of km run per week and the concentration of HDL-C. The researchers concluded that a running volume of at least 70 km / week was needed to increase HDL-C above normal levels.

The following year, Lehtonen et al.[325] examined the concentrations of apo A-I, apo A-II, and HDL-C in athletes compared to age matched sedentary controls. The athletes trained at least 4 times per week and ran an average of 25 km per week.

Athletes exhibited higher concentrations of apo A-I and HDL-C compared to the sedentary control group.

Castelli and coworkers[8] examined the relationship between the prevalence of CHD and fasting lipid levels in The Cooperative Lipoprotein Phenotyping Study. This investigation consisted of subject data from epidemiologic studies of five diverse populations. The investigators concluded that the mean concentrations of HDL-C in each major study group were lower in people with CHD than those without the disease.

Enger and coworkers[326] reported that 220 trained men, who participated in lipoprotein-lipid screenings the day before taking part in a cross-country ski race, had higher concentrations of HDL-C, as well as a higher HDL-C / TC ratio when compared to age-matched controls. The more favorable lipid profile of the trained men was attributed to the chronic effects of physical activity.

Herbert and coworkers[327] compared the HDL kinetics and lipoprotein enzyme activities of 5 trained runners with 5 sedentary men. The trained subjects had higher concentrations of HDL-C (65 mg / dL vs. 41 mg / dL) and apo A-I (167 mg / dL vs. 139 mg / dL) compared to the control group. The difference was mostly attributed to the HDL_2-C subfraction. The trained runners catabolized less HDL protein compared to controls. Furthermore, LPLa was 80% higher in the trained subjects, whereas HTGLa was 38% lower compared to sedentary controls. The researchers concluded that a reduced catabolism rather than enhanced HDL apolipoprotein synthesis distinguished the trained from the sedentary men.

In a similar study, Thompson et al.[48] compared HDL kinetics in 10 endurance trained athletes and 10 sedentary adults. The increased concentration of HDL-C (40%) compared to sedentary controls was attributed to elevated HDL_2-C. Moreover, the concentration of TG was 45% lower while apo A-I was 25% higher in trained subjects compared to sedentary controls. LPLa and HTGLa were not significantly different between the two groups, but the lower HTGLa (27%) in trained subjects approached statistical significance. The clearance rate of fat was 80% faster in trained subjects. The fractional catabolic rate of HDL and apo A-I, apo A-II was also 20-30% lower in the trained athletes compared to sedentary controls, a similar finding to that reported by Herbert et al.[327]

Sady and coworkers[47] evaluated the clearance rate of plasma TG following an intravenous infusion of a fat emulsion in 13 well-trained and 12 untrained men. The endurance trained athletes displayed higher concentrations of HDL-C, HDL_2-C, and apo A-I, and lower concentrations of TG while adjusting for body fat (%). However, there were no significant differences in LPLa between the 2 groups. It was determined that the trained men exhibited a more rapid fat clearance compared to the sedentary individuals.

Skoumas and colleagues[328] examined the effect of physical activity status on lipids in men and women without CHD. Subjects were part of the ATTICA study, a health and nutrition survey in the province of Attica. Physically active women had significantly lower TC, LDL-C, oxidized LDL, TG, apo B, and higher HDL-C and apo A-I compared to sedentary women. This finding remained after adjustment for age, BMI

and smoking habits. These results were similar in the men, except that they did not reach statistical significance. The researchers concluded that even moderate exercise (4-7 kcal / min; > 3 times per week) was enough to increase HDL-C in women.

Kokkinos and coworkers[67] examined the association between miles run per week and HDL-C concentrations. The male subjects were stratified into 6 groups based on the number of miles run each week. The concentration of HDL-C increased with increasing mileage in a dose response relationship. When compared to sedentary controls, HDL-C reached significance at distances of 7 or more miles per week.

Williams and colleagues[329] examined the dose response relationship between the reported distance run per week and risk factors for CHD from subjects in the National Runners Health Study. The concentration of HDL-C increased significantly in relation to longer weekly run distances. HDL-C was higher with each 16 km increment in weekly running distance up to 48 km per week and at or above 64 km per week.

Rotkis et al.[330] also explored the relationship between training volume and HDL-C concentrations. Researchers reported a stepwise increase in the concentrations of HDL-C in groups designated as non-runners, low-mileage (10 - 19 miles per week), intermediate (20 - 39 miles per week), and high-mileage (≥ 40 miles per week) runners. Furthermore, this relationship remained significant even after correcting for age, alcohol intake, and body fat (%).

Williams et al.,[331] using more sophisticated analytical techniques, compared the lipoprotein subfraction profiles and lipoprotein enzymes activities of 12 trained runners to 64 sedentary males. The trained runners had lower LDL-C (reduced cholesterol

concentrations of the smaller LDL particles), TG, TC, VLDL, HDL_3-C, and higher concentrations of HDL_2-C. The data was even adjusted for BMI. Runners also had significantly higher LPLa and lower HTGLa compared to sedentary controls.

Halle and coworkers[332] examined the LDL subfraction profile in hypercholesterolemic men with different leisure time physical activity and aerobic fitness levels. Results indicated that trained men with high TC had a more favorable lipoprotein profile (lower TG and increased concentrations of HDL_2-C) compared to the men who were less fit. The trained men also had significantly less small, dense LDL particles and a higher concentration of large LDL subfraction particles despite an equal total LDL particle number. Furthermore, the LDL particles of the trained men had a higher free cholesterol content compared to the LDL of the untrained men.

In a follow-up study, Halle and colleagues[333] ranked subjects according to fitness levels based on the results of a $\dot{V}O_{2peak}$ bike test. A significantly more favorable lipid profile was observed in regularly exercising men with good fitness ($\dot{V}O_{2peak}$ > 50 ml / kg / min). The men with a $\dot{V}O_{2peak}$ > 50 ml / kg / min had a 25% lower concentration of small, dense LDL-C and apo B compared to the other groups.

Kamigaki et al.[334] examined the relation of LDL subfraction phenotypes and LDL particle size with the incidence of MI in a sample of young women from the Women's Cardiovascular Health Study. The researchers reported that a predominance of small LDL particles was associated with a more than 3-fold increased risk of MI. MI cases had significantly higher concentrations of TC, LDL-C, TG, and lower HDL-C

compared to controls. Furthermore, mean LDL particle size was smaller for the MI cases compared to the controls.

Ziogas et al.[335] examined whether differences existed in postprandial TG levels and LDL subfraction distribution among groups of different fitness levels. Endurance trained subjects had significantly lower LDL_3-C and LDL_3-apo B100 (particle number) concentrations compared with the sedentary group even though baseline concentrations of TC and LDL-C were similar among the groups.

Lippi and colleagues[336] examined extensive lipid profiles obtained from 60 sedentary male controls and compared them to profiles from 142 athletes (skiers and cyclists). TC, TG, and LDL-C were lower and HDL-C higher in athletes compared to sedentary controls. However, Lp (a) was not different between the two groups.

Pischon et al.[337] examined the relationship between physical activity and the obesity-related inflammatory markers, IL-6, and hs-Crp. The researchers noted that there was a significant inverse association between physical activity and plasma levels of inflammatory markers. Subjects who ran 4 or more hours per week had 6% lower IL-6 and 49% lower hs-Crp levels compared to subjects who ran less than 0.5 hours per week. However, adjustments for BMI and leptin weakened the association of physical activity and hs-Crp by 62% and IL-6 by 14%, suggesting that body fat (%) may partially mediate some of these associations.

As part of the ATTICA study, Pitsavos and coworkers[122] reported that higher physical activity levels were associated with lower blood concentrations of various inflammatory markers (33% lower hs-Crp, 10% lower white blood cell count (WBC),

and 17% lower serum amyloid A levels). The activity levels were stratified into low (expended calories ≤ 4 kcal / min), moderate (expended calories 4 to 7 kcal / min), and high activity levels (expended calories ≥ 7 kcal / min). This study demonstrated that even light-to-moderate physical activity is associated with lower hs-Crp, WBC counts, and serum amyloid A levels.

Tomaszewski et al.[202] compared lipoprotein-lipid and inflammatory parameters in regular long distance runners with sedentary controls. Subjects were matched with regards to age, and BMI. The ultra-marathon runners had significantly lower concentrations of LDL-C and hs-Crp compared to the control group. Furthermore, the difference in LDL-C between the runners and controls remained significant even after adjusting for age and BMI.

Albert and coworkers[338] evaluated the relationship between hs-Crp and physical activity in men and women with and without CHD. Subjects were part of the Pravastatin Inflammation / CRP Evaluation (PRINCE) study, which evaluated the effects of pravastatin (40 mg / day) or placebo on hs-Crp levels over a 6 month period. It was determined that hs-Crp levels were significantly lower among men who self reported a higher level of physical activity compared to men who reported rare physical activity. There was also a progressive decline in hs-Crp levels with increasing physical activity levels. This relationship remained after adjusting for age, HDL-C, and BMI. The researchers noted that there were not any significant relationships with the female subjects and this may have been due to a lower level of physical activity reported for this group. Furthermore, the researchers speculated that by lowering BMI, through increased

endurance physical activity, subjects may realize a decrease in adipocyte production of IL-6, which happens to be a stimulator of hepatic hs-Crp production.

Colbert et al.[339] examined the association between physical activity and inflammatory markers in the elderly (73 yrs) while exploring any potential interactions with body fat (%) and antioxidant use. Three levels of physical activity were determined based on the results of an interview: 1) none; 2) 1 to 179 minutes per week; and 3) 180 minutes per week or more. The researchers observed that higher levels of exercise were associated with lower levels of hs-Crp, IL-6, and TNFα. When investigators looked within the group reporting no exercise, higher levels of other physical activity were related to lower levels of hs-Crp and IL-6.

Using data from the Cardiovascular Health Study (CHS), Geffkin and colleagues[340] evaluated the association of self reported physical activity with several markers of inflammation in the elderly. Higher physical activity levels were associated with significantly lower levels of hs-Crp, WBC count, and fibrinogen. Furthermore, these findings were independent of any known CHD risk factors.

Wannamethee et al.[341] examined the relationships between physical activity and inflammatory markers (hs-Crp and WBC) in a large population-based study of 4,000 British men. Subjects from the British Regional Heart Study were reexamined 20 years after their initial visit. Volunteers answered questions regarding their current level of physical activity and were then assigned to one of 6 different groups based on that activity level status. Physical activity was inversely associated with WBC, hs-Crp, and platelet count. This inverse relationship was similar in men with and without prevalent

CHD. The researchers reported that men, who were initially sedentary but adopted a physically active lifestyle later, had levels of WBC, hs-Crp, and platelets similar to men who had been continuously active all through the observation period. These findings further extend the association between higher levels of physical activity and reduced levels of inflammation and hemostatic markers.

Ford et al.[121] examined the association between physical activity and hs-Crp, fibrinogen, and WBC count in a national sample of the US population (NHANES III). Researchers concluded that leisure-time physical activity was inversely associated with hs-Crp, fibrinogen, and WBC count in a dose-response manner. Investigators also speculated that the favorable association may be attributable to the effects of exercise on BMI. Pro inflammatory cytokines are produced by adipocytes as body mass increases. If body mass is reduced through physical activity, the production of these cytokines (IL-6) may be attenuated and lead to a lower hs-Crp level. However, hs-Crp levels were still strongly associated with physical activity levels even after correcting for BMI and waist-to-hip ratio, suggesting that exercise favorably influences the inflammatory process through additional mechanisms. One other potential mechanism is that exercise exerts its beneficial effects through improvements in endothelial function. Endothelial cells can also secrete IL-6 and IL-1, which can induce an acute phase response. It is known that exercise can improve endothelial function, thus attenuating the secretion of these pro inflammatory cytokines. Thus, the end result is a lower level of hs-Crp.

King and coworkers[342] sought to characterize elevated levels of hs-Crp, fibrinogen, and WBC count for various forms of exercise in the adult U.S. population.

This was part of the NHANES III study. The main goal of this analysis was to determine whether exercise type was associated with markers of inflammation. Researchers noted that different types of activity had produced different associations with the various inflammatory markers. After controlling for age, BMI, and smoking, only people who regularly jogged, and took part in aerobics, had a significantly lower likelihood of having elevated inflammatory markers. No association was noted for activities such as cycling, swimming, or weight lifting (performed > 12 times per month).

Berg and coworkers[343] evaluated the lipid profiles of 293 healthy, well trained athletes with different types of training backgrounds: 1) endurance, 2) mixed, 3) power training, and 4) untrained controls. The endurance trained athletes had lower concentrations of LDL-C and VLDL-C compared to control subjects. Furthermore, the concentration of HDL-C was significantly lower in the power athletes compared to the control subjects as well as the other training groups. Researchers speculated that the results pertaining to the power athletes may have been influenced by anabolic steroid use. Similar findings were again reported by Berg et al.[344] They examined blood lipids in 44 power athletes compared to 52 sedentary control subjects. The concentration of HDL-C was significantly lower in the power athletes compared to the control group. This difference was unaffected by body weight. The investigators concluded that the difference in HDL-C may be due to type of training involved with the power athletes.

Clarkson and coworkers[345] evaluated the concentrations of TC and HDL-C in college aged weight trained athletes, sedentary control subjects, and long distance

runners. The lipid profile did not differ from the controls. The long distance runners had significantly higher HDL% and lower TC compared to the other groups. The weight lifters did have significantly higher body weights compared to the runners and control subjects. However, body weight did not correlate with the concentration of TC or HDL%.

Farrell et al.[346] compared blood lipids between three groups of male subjects with different physical training backgrounds. The groups consisted of 11 weight lifters, 11 speed skaters, and 11 sedentary control subjects. Training for speed skating involves both anaerobic and aerobic components. Body fat (%) was significantly higher in the sedentary subjects compared to the rest of the groups. Body weight was significantly lower in the speed skaters compared to the other groups. TC and TG were not different between the groups. However, HDL-C was significantly higher than both weight lifters and control subjects. Thus, subjects who are both anaerobically and aerobically trained demonstrated higher HDL-C compared to male weight lifters and male sedentary control subjects. These results were not correlated with maximal aerobic capacity or relative body fat (%). Similar results have also been reported. Mean concentrations of HDL-C have been shown to be higher in endurance runners compared with weight lifters and sedentary controls.[46, 347]

Hurley et al.[107] examined the relationship between lipoprotein-lipids and different types of weight training (bodybuilding vs. power lifting). Body builders train using moderate-resistance, high-repetition exercises with short rest intervals. In contrast, power lifters train using heavy-resistance exercises with few repetitions and longer rest

intervals between exercise bouts. Subjects were compared to runners of similar age and body fat (%) and had not used exogenous androgens during the previous 10 weeks. The researchers then evaluated the lipid profile in certain strength-trained athletes after self administration of various anabolic steroids. Blood samples were collected 24 h after the last training session. TC was not different between all 4 groups. TG concentrations of all the exercise trained men were significantly lower when compared to the control group. The power lifters had LDL-C concentrations comparable to the control group, but significantly higher than both body building and running groups. Furthermore, HDL-C was significantly lower in the power lifters when compared to all other groups. HDL_2-C followed the same pattern. The researchers concluded that strength-trained athletes using moderate-resistance, high-repetition exercises along with short rest intervals have lipid profiles that may protect them from the development of CHD. These results also suggest that in order to induce beneficial changes in the lipid profile, subjects need to perform weight lifting activities which are more aerobic in nature as well as promoting a higher caloric expenditure per exercise bout. After administration of anabolic steroids, the lipid profiles were unfavorably altered with decreased concentrations of both HDL-C and HDL_2-C and elevated LDL-C. Taggart et al.[348] have demonstrated that even administration of a low dose anabolic steroid (stanozolol; 6 mg / day for 4 weeks) lowered both HDL-C and HDL2-C concentrations by 50% and raised LDL-C by 21%.

Prospective Studies

Sesso et al.[349] examined the quantity, type, and intensity of physical activity and how it related to someone's risk for developing CHD. Subjects were part of the Harvard Alumni Study and responded to questionnaires from 1977 through 1993. A 20% reduction in CHD risk was noted for people expending greater than 4200 kJ / week with physical activity. A nonsignificant 10% reduction in CHD risk was noted in men expending 2100 - 4199 kJ / week. It was also reported that physical activity of a vigorous nature (> 6 METs) was associated with a reduced risk of CHD, whereas moderate or light activities (≤ 6 METs) had no clear association. The researchers concluded that physical activity can favorably affect CHD risk even in the presence of other CHD risk factors.

In addition to the previous work of Sesso et al.,[349] Lee and associates[350] further examined the association between the relative intensity of physical activity and risk of developing CHD in the Harvard Alumni Study. Men who expended 1000 - 2499 kcal / week experienced a 20% decrease in the CHD rate of those less active. It was also reported that greater energy expenditure was not associated with additional increased risk. However, men participating in vigorous activities (≥ 6 METs) experienced significantly lower CHD rates. Thus, the relative intensity of physical activity was a strong predictor of lower CHD rates among older men in this cohort.

Manson and coworkers[351] evaluated the comparative roles of walking and vigorous exercise in the prevention of CHD in women enrolled in the Nurse's Health Study. Both walking and vigorous exercise were associated with substantial reductions

in the incidence of coronary events. Furthermore, the magnitudes of risk reduction associated with brisk walking and vigorous exercise were similar when the total energy expenditures were similar.

Lee and associates[318] evaluated the effects of different exercise durations on the risk of developing CHD. Specifically, researchers examined whether the duration of an exercise episode predicted risk, after the total energy expended on physical activity was accounted for. Among men who expended similar total amounts of energy in physical activity, a longer duration per episode of activity did not further decrease CHD risk. It appears that the accumulation of shorter sessions of activity is associated with equivalent benefit compared with longer sessions, as long as the total amount of energy expended is the same.

To assess the amount, type, and intensity of physical activity in relation to risk of developing CHD, Tanasescu and colleagues[320] questioned male subjects participating in the Health Professionals follow-up study and classed their reported physical activity as either vigorous ($\geq$ 6 METs) or nonvigorous ($\leq$ 6 METs). Cycling and swimming were not associated with risk reduction whereas running for 1 or more hours per week was associated with a 42% risk reduction. Of interest, weight training for 30 minutes or more per week was associated with a 23% risk reduction. The researchers concluded that increased total physical activity was associated with a reduced risk of CHD in a dose dependent manner. Furthermore, the intensity of exercise was associated with an additional risk reduction.

St-Pierre and coworkers[289] examined the long-term risk of ischemic heart disease (IHD) associated with large LDL and small LDL using 13 year follow-up data in men from the Quebec Cardiovascular study. The data suggest that there isn't any evidence of increased CHD risk with increased cholesterol levels in the large LDL particles. Men with elevated cholesterol in the large LDL particles had a more favorable CHD risk profile compared with men with low levels of cholesterol in the large LDL particle and a 50% lower IHD risk over the first 7 years of follow-up. The researchers concluded that increased CHD risk was largely related to accumulation of small, dense LDL particles.

Williams et al.[352] examined the relationship of LDL and HDL subfractions to CHD progression rates, as determined by coronary arteriograms. Subjects were part of the Stanford Coronary Risk Intervention Project (SCRIP). LDL-IVb was the subfraction most strongly related to CHD progression. These results support other findings that indicate smaller peak LDL size is predictive of increased risk for MI and that angiographic progression of CHD is related to increased LDL density.[21]

In summary, both cross-sectional and prospective investigations overwhelmingly suggest that physically active individuals exhibit a less atherogenic blood lipid profile and more favorable non-traditional CHD risk marker levels compared to their sedentary counterparts. Furthermore, a dose-response relationship was noted for this relationship. However, it is important to note again that the process of subject selection, differences in body weight, body fat (%), dietary, behavioral habits of the subjects, and not eliminating the possible acute effects from the last training session, can all contribute to the differences in lipoprotein-lipids and non-traditional CHD risk markers noted between the

two groups.[41, 95, 129-131] Despite these potential limitations, these research studies have provided the framework for conducting longitudinal exercise training studies.

Lipid Metabolism in Response to Exercise Training

Endurance Training

Exercise may provide protection against the development of CHD partly through improvements in the lipoprotein-lipid profile.[2] Traditionally, research examining the effectiveness of physical activity on CHD risk reduction has been conducted using endurance exercise as the exercise intervention. In most cross-sectional studies endurance trained athletes exhibit higher concentrations of HDL-C, apo A-I, LPLa, and lower concentrations of LDL-C, apo B, TG, and HTGLa as compared with untrained individuals.[46-51] However, the results from longitudinal training studies have been inconsistent. A majority of the published research has reported that the concentrations of HDL-C and HDL_2-C may be increased while TG is lowered in response to exercise training.[55-57, 60, 68, 140-142, 148, 169, 175, 176, 178, 181-183, 194, 195, 199, 201, 203, 204, 349-354] Furthermore, while the concentrations of TC, VLDL-C, and LDL-C are rarely altered, reductions in response to training have been reported.[55, 56, 60, 169, 175, 178, 183, 193, 195, 199, 204, 350, 351, 353, 355] Other lipoprotein enzymes such as HTGL, CETP and other non-traditional CHD risk markers have been studied although the results have been inconclusive.[41, 56, 60, 125, 140, 142, 168, 169, 173, 174, 176-178, 181] Explanations for the conflicting findings have been attributed to differences in exercise volume (caloric expenditure), duration of training, type of exercise, baseline subject characteristics, dietary influences, baseline lipid concentrations, and timing of blood sampling after the last session of exercise.[58, 66-68] It

is also possible that subtle changes in lipoprotein metabolism may have gone undetected in a number of studies. For example, Crouse et al.[43] reported that 6 months of endurance training by men with elevated cholesterol resulted in a significant rise in HDL_2-C and fall in HDL_3-C, but no change in total HDL-C.

The baseline lipoprotein-lipid concentrations of research subjects have reportedly been identified as a potential predictor of the lipoprotein-lipid response to exercise training. In a meta-analysis on training studies, Tran et al.[353] identified the importance of baseline lipid levels in determining the magnitude and direction of change in lipid levels over the course of exercise training studies. It was observed that subjects with initially low HDL-C tended to respond more favorably to exercise training than subjects who completed the exercise training intervention with normal or high initial HDL-C levels. However, this is not always the case[164] and similar alterations to the lipoprotein-lipid profile have been reported in subjects demonstrating a variety of baseline lipoprotein-lipid levels.[129-131]

Zmuda et al.[164] compared the effects of 12 months of endurance exercise training, without weight loss, on HDL metabolism in sedentary men with initially low or normal HDL-C concentrations. The authors defined low HDL-C as < 40 mg / dL and normal as > 44 mg / dL. The exercise training sessions consisted of a 5 minute warm-up with stretching exercises followed by 50 minutes of walking, jogging, and stationary cycling ending with 5 minutes of cool-down activity. This was repeated 4 times a week with an intensity designed to elicit 60-80% of the subject's measured maximal heart rate. Subjects were seated during all phlebotomy procedures and had not eaten or exercised

during the preceding 12 h. Neither body weight nor relative body fat (%) decreased significantly in either group in response to the training. HDL-C rose by 5 mg / dL in the normal group, with most of the change attributed to a 3.8 mg / dL increase in HDL_2-C (significant). Conversely, HDL-C and HDL_3-C were not significantly altered in the low HDL-C group. The concentrations of TG and apo B were significantly lower (12% and 16%) in the normal group but not in low HDL-C group after training. Interestingly, apo A-I was significantly increased in both groups. The catabolic rates for HDL apolipoproteins decreased 7-14% and the biologic ½ lives increased 10-15% with training in the normal group, but did not change in the low group. The enzymatic data followed a similar pattern with significant elevations in LPLa (27%) in response to training and a 16% decrease in HTGLa in the normal group. However, neither enzyme activity was altered in the low HDL-C group. This study suggests that changes in HDL-C and HDL_2-C as well as the biologic ½ life of HDL apolipoproteins with exercise training are considerably greater in men with higher pre-training HDL-C levels. The researchers concluded that men with initially low HDL-C levels may have a limited ability to increase HDL-C with exercise training.

Raz et al.[354] evaluated the effects of a 9 week, moderate endurance exercise training program (45 min / day, at ~ 70 – 85% of max heart rate, 3 days per week) in young men with initially low HDL-C levels (≤ 40 mg / dL). The estimated maximal aerobic capacity was significantly elevated (15%) in the exercise group. Changes in body weight and body fat (skinfolds) were minimal and not different between the exercise and controls groups. Furthermore, there were no significant differences

between the groups with respect to TC, HDL-C, HDL2-C, HDL3-C, or LDL-C. TG was significantly lower (4%) after training only in the exercise group. The authors concluded that 9 weeks of moderate exercise in young men with initially low HDL-C did not favorably alter the lipid profile, in spite of improved fitness.

Williams et al.[165] examined the possibility that people with certain lipid profiles may be more readily persuaded to adopt active lifestyles. The investigators focused on the main issue of the relationship between running dose (miles / week) and physiological response over time in the setting of a 1 year randomized, controlled trial of previously sedentary men. Eighty one healthy sedentary men (30-55 yrs) were randomly assigned to a supervised running or sedentary control group. Subjects underwent follow-up after 12 months. The exercise program initially had subjects training 3 times a week with 5 minute warm-up, 20 minute walk / jog (70-85% of max heart rate), concluding with a 5 minute cool-down. After 2-3 weeks, 1 additional day of exercise was added. At 6 weeks, the exercise duration was increased to 45 minutes of running. After the 8^{th} week of training, another day was added to the weekly training volume. Blood samples were drawn after a 12-16 h fast and no physical activity. The subjects who were persuaded to run more miles had initially higher baseline HDL-C and lower TG concentrations compared to lower mileage runners. Baseline HDL-C was a significant predictor of miles subsequently run when included along with baseline body fat (%), $\dot{V}O_{2peak}$, alcohol intake, and smoking variables in a multiple regression equation. Increasing the number of miles run per week also produced increases in HDL-C and fitness levels while decreasing LDL-C, VLDL-C, and body fat (%). More importantly, HDL-C did not

increase unless an average exercise training volume of running 10 miles per week or more was achieved during the 1 year period.

Some researchers have reported that a subject's baseline body composition or perhaps changes in body composition as a result of exercise training are responsible for the favorable changes in the lipoprotein-lipid profile that follow exercise training regimens. In support of this, correlations between body weight and / or body fat (%) reductions in response to exercise training and changes in lipoprotein-lipids have been reported.[49, 56, 186, 354, 358] However, there are those who have reported an independent effect of exercise training on changes in lipoproteins.[14, 57, 140-142, 182, 201, 352] Increases in HDL-C,[57, 195, 349] and decreases in LDL-C,[166, 182] and TG[57] have been reported to occur following exercise training without changes in either body weight or body fat (%). Thus, the independent effect of exercise training on lipoprotein-lipid metabolism can't be completely ignored.

In addition to subject's baseline physiological characteristics such as body weight and body fat (%), correlations between changes in aerobic capacity ($\dot{V}O_{2peak}$) with exercise training and changes in lipoprotein-lipids have been reported.[355] However, this is not always the case.[43, 141, 147, 170, 197] Furthermore, lipoprotein-lipids do not always respond to exercise training.[354, 356] Thus, increases in aerobic capacity with training are not generally related to lipoprotein-lipid changes.[131]

Nicklas et al.[167] determined that plasma concentrations of HDL-C and HDL_2-C were significantly elevated with exercise training in lean and moderately obese middle-aged and older men, but were not significantly altered in obese men of the same age. In

support of this notion, Woods et al.[184] reported that fat reduction produced comparable changes in lipoproteins whether the loss was achieved through diet or exercise. Several other studies reported that the beneficial alterations to the lipid profile as a result of exercise training were attributed to large decreases in body weight after training.[49, 68, 191, 354]

Williams and colleagues[68] examined the effects of diet-induced weight loss or exercise-induced weight loss on lipid metabolism in overweight men with different baseline concentrations of HDL-C. The diet program was designed to reduce total body fat by 1/3 during the course of the 9 months. The training sessions consisted of 40-50 minutes of exercise (60-80% of max heart rate) 4 days each week. At the end of the year-long training program, HDL-C, HDL_2-C, and HDL_2 mass increased with exercise as well as a calorically restricted diet. The overweight men with the highest baseline concentrations of HDL-C ($\geq$ 48 mg / dL) and who took part in the exercise training regimen demonstrated the largest elevations in HDL-C and subfractions per unit of weight loss. However, the baseline concentrations of HDL-C in the diet group were not related to the subsequent alterations in HDL-C. Thus, weight loss, either diet induced, or as a result of exercise can produce alterations in HDL metabolism. Furthermore, the authors concluded that weight loss induced through exercise as opposed to caloric restriction affects HDL-C concentrations differently depending on the subject's initial HDL-C concentrations.

In a similar study Wood et al.[184] evaluated the effect of diet-induced weight loss or exercise-induced weight loss on lipid metabolism in 89 sedentary, obese men with

different baseline concentrations of HDL-C. The diet program was again designed to reduce total body fat by 1/3 during the course of the training. The training sessions consisted of 40-50 minutes of exercise (60-80% of max heart rate) 4 days each week. The decrease in relative body fat (%) was similar for both the exercise group and the diet group. However, lean body mass was preserved in the exercise group compared to the diet group. Increases in the concentrations of HDL-C and the subfractions were similar for both groups, even though physiologic changes were apparent (total body weight loss greater in diet group). The authors concluded that body fat loss, whether through diet or exercise training, induces similar alterations in lipid metabolism.

Leon et al.[163] reported on the observed variability in the plasma HDL-C response to 20 weeks of exercise training in the HERITAGE study, and tried to identify possible contributors to this variability. Sedentary members of 200 two-generation white and black families completed 20 weeks of supervised cycle ergometer exercise training. Blood lipid levels were compared before and after training. Exercise was performed 3 times a week, progressing from an initial duration of 30 minutes to 50 minutes per session during the last 6 weeks. Intensity was progressively increased from 55% to 75% $\dot{V}O_{2peak}$. The estimated energy expenditure for each session was 328 kcal or 984 kcals per week. Blood samples were obtained after a 12 h fast and 24 - 72 h after the last exercise session. Baseline concentration of HDL-C in women and men were 44.3 mg / dL and 37 mg / dL, respectively. The exercise training resulted in a significant increase in HDL-C with small decreases in TG and VLDL-TG. Mean increases in HDL-C for the entire cohort was 1.4 mg / dL, with no significant differences by gender or race.

However, there was noticeable variability in response to training, ranging from a mean 9.3% decrease in HDL-C in quartile 1 to a mean 18% increase in quartile 4. Significant increases in LPLa were noted for both men (18%) and women (6.6%). HTGLa was significantly reduced 6.9% in men and 5.1% in women following training. The authors stated that a possible heritable factor contributing to the HDL-C responsiveness to exercise training was the relative proportion of type 1 red skeletal muscle fibers, which are known to have higher LPLa. In contrast to the findings of Zmuda et al.[164] and Williams et al.[68], in HERITAGE, the percent change in HDL-C with training was inversely related to the baseline HDL-C concentrations, which is also consistent with the findings of a previous meta-analysis.[357]

Stefanick et al.[171] examined the effects of changes in diet and exercise, alone and together, on plasma lipids. The design was a 1-year randomized, controlled study of men and postmenopausal women with low HDL-C and elevated LDL-C. The subject groups were: 1) NCEP Step 2 diet; 2) aerobic exercise alone; 3) NCEP diet and exercise; and a control. Subjects took part in walking or jogging, 3 times a week for 60 minutes a session. Fasting Blood samples were collected at 2 morning visits and 12 h after the last session of vigorous physical activity. Significant changes in HDL-C were not observed for either sex, nor were changes in TG. TC and LDL-C were significantly reduced among both men and women in the diet + exercise group, as compared with the group assigned to exercise only. No significant reductions in TC and LDL-C were noted for either sex in the diet only group. Dietary intake of fat and cholesterol decreased during the 1 yr study as did body weight in women and men in either the diet group or the diet +

exercise group as compared to controls and the exercise group, in which dietary intake and body weight were unchanged. The NCEP Step 2 diet failed to lower LDL-C in men and women with high-risk lipoprotein levels who did not engage in aerobic exercise. When diet was combined with exercise, the reductions in LDL-C were significant, with no adverse effects on HDL-C. The researchers concluded that the combination of reduced dietary fat and increased use of energy from fat through exercise may have created a physiologic state that is beneficial to lipid metabolism even in the absence of weight loss.

Higuchi et al.[192] examined the effects of 4 weeks of treadmill running (50 min / day, 5 days per week) on lipoprotein-lipids in 5 young, active men. Body weight was maintained throughout the 4 weeks of training. While TC and TG did not change in response to training, the concentration of HDL-C increased (19 mg / dL). The authors concluded that exercise had an independent effect on lipid metabolism.

Schwartz and colleagues[191] examined the effects of intensive endurance training (45 min / day, 50-85% of heart rate reserve, 5 days per week) on lipid responses in older (68 yrs) and younger (28 yrs) men. Increases in $\dot{V}O_{2peak}$, and reductions in both body weight and body fat (%) were similar for both groups. It is important to point out that body weight, as well as body fat (%) did not significantly change in response to 6 months of training. The response of HDL-C to training was similar in the young men (14% increase) and the older men (15% increase). However, there was a significant increase in HDL_2-C (63%) and a 21% decrease in TG only in the older men. The

authors concluded that the changes in the lipoprotein-lipid profiles were not correlated to any changes in body weight or body fat (%).

Thompson and colleagues[160] examined HDL-C levels and HDL apoprotein survival before and after 1 year of endurance exercise training (50 min / day, 60 – 80% of max heart rate, 4 days per week) without weight loss in sedentary overweight men. Subjects were maintained on controlled diets for 18 days during each study of HDL metabolism. Maximal aerobic capacity increased 27% with training. TG was decreased (7%) with exercise training while HDL-C increased (10%). This increase was attributed to an increase (33%) in HDL_2-C. The concentration of apo A-I was significantly elevated (9%) while apo B was lowered (10%) in response to training. The metabolism studies indicated that the catabolic rate of HDL was decreased (5%) with training while the synthetic rate of apo A-I was significantly elevated (13%). The lipoprotein enzyme data indicated that LPLa was elevated (11%) but did not reach statistical significance, while HTGLa was significantly lower after the 12 month training program.

Brown et al.[358] examined the effects of a 3 month endurance exercise training program (50-60 min / day, 70-80% $\dot{V}O_{2peak}$, 4 days per week), without weight loss, on the lipid profiles of 7 overweight subjects. This amounted to a caloric expenditure of 2000 kcals per week. While body weight was maintained throughout the program, body fat (%) was significantly decreased (4%) after training. Maximal aerobic capacity was significantly elevated (11%) as a result of the training. HDL-C was significantly higher (15%) and LDL-C significantly lower (14.7%) after training. The authors did not report any correlations with changes in lipoprotein-lipids and alterations in body fat (%).

Nye and coworkers[182] examined alterations in lipid metabolism in response to a mild exercise program (30-45 min / day, 2 days per week, approximately 950 kcals per week). Seventeen sedentary, middle-aged men volunteered for this investigation. Training resulted in a significant decrease in LDL-C. The concentration of HDL-C was not significantly altered with training, which the authors attributed to an increase in HDL_2-C and a concomitant decrease in HDL_3-C. Conversely, Thompson et al.[57] reported that sedentary men taking part in a high-volume training program (32 weeks of cycling) increased HDL-C and lowered their LDL-C concentrations. Body weight and body fat were not significantly altered in response to this training program. The increase in HDL-C was attributed to nonsignificant increases in both HDL_2-C and HDL_3-C. Increased LPLa and decreased HTGLa were also reported after the 32 week training program.

The training intensity of exercise programs has also been reported to be an integral factor in inducing favorable changes in lipoprotein-lipids.[195, 359, 363] However, studies have reported changes in lipid metabolism with high[56, 148, 195, 197, 349] and low-moderate[43, 167, 182, 184, 350, 352, 363] training intensities. What seems to be more important in order for favorable alterations in lipids to occur is the volume of the exercise regimen. It is believed that lipoprotein-lipid changes most often occur when the exercise regimen is one that consists of a large volume of work (caloric expenditure).[41, 44, 130-132, 364]

In order to examine the effects of a moderate exercise training program (4 months at 3-4 days per week), on serum high-density lipoproteins, Huttunen et al.[359]

randomly assigned 100 sedentary middle-aged men to either exercise or control groups. HDL-C was significantly elevated and TG decreased in the exercise group.

Sunami et al.[360] examined the effects of low intensity endurance training (60 min / day, 50% of $\dot{V}O_{2peak}$, 2-4 days per week for 5 months) on lipoprotein-lipids in healthy older adults (67 yrs). While maximal aerobic capacity was significantly elevated (7%) with training, body weight and body fat (%) were not significantly altered. The exercise group significantly increased concentrations of HDL-C (9%), HDL_2-C (21.6%), while HDL_3-C was lower (12%) with training. The changes in $\dot{V}O_{2peak}$, body weight and body fat (%) were not correlated with any of the lipid parameters in the training group. Total exercise duration per week was correlated with the change in HDL_2-C. These results should be interpreted with caution, since the authors did not report the length of time between the last exercise session and blood sampling. Thus, the authors did not eliminate the possible acute effects from the last training session.

In contrast to the findings reported by Sunami[360], Branth and coworkers[361] examined the effect of high-volume low-intensity exercise training (120 min / day, 40% of $\dot{V}O_{2peak}$, 5 times per week for 6 weeks) on blood lipids in 8 untrained men. Diet and energy balance were tightly controlled with registered dieticians preparing all food consumed by the subjects. Body weight, body fat (%), and aerobic capacity did not change during the study. The training protocol did not substantially affect blood lipids. However, nonsignificant decreases in apo B and Lp (a) did occur after training. The researchers concluded that the training program's intensity was too low. However,

Crouse et al.[43] observed changes in blood lipids after only 8 weeks of exercise training at either 50% or 80% of $\dot{V}O_{2peak}$.

Stein and colleagues[166] examined the effects of a 12 week cycle ergometer exercise training program (30 min / day, 3 times per week,) on lipoprotein-lipids. 49 healthy men were divided into groups exercising at 65%, 75%, and 85% of maximal heart rate, with an additional sedentary control group. Body weight and body fat (%) did not change. Maximal aerobic capacity was significantly elevated in all training groups. The concentration of HDL-C was significantly elevated and LDL-C decreased only when the intensity was above 75% of maximal heart rate. However, the authors failed to report if they controlled for the last bout of exercise before post-training blood sampling and also did not control for training volume differences between groups, each of which can lead to inaccurate results.

Stubbe et al.[56] examined the effects of cycle ergometer exercise training of varying intensities and duration on lipid metabolism in 18 sedentary men. For 6 weeks, 12 men exercised for 50 minutes a day, 3 times per week at 85% of their maximal heart rate. A second group of 6 men exercised for 50 minutes a day, 3-5 times per week at 70% of their maximal heart rate. This group exercised for a total of 12 weeks. Blood samples were obtained 48 h to 72 h after the last training session. Body weight and body fat (%) were not significantly altered with training. $\dot{V}O_{2peak}$ was significantly increased (19%) in the high intensity group after 6 weeks of training compared to 10% in the moderate intensity group. However, the moderate intensity group further increased their

$\dot{V}O_{2peak}$ (18%) when they completed the 12 weeks of training. Training significantly increased HDL-C levels (14%) in the moderate group and 4% in the high intensity group, which did not reach statistical significance. The concentration of apo A-I was significantly elevated (7%) in both groups after training. LDL-C was significantly reduced (17%) after training in the moderate group and mildly lower (6%) in the high intensity group. Four subjects from the high intensity group had their lipid samples separated by zonal ultracentrifugation in order to characterize lipoprotein subclasses. While the concentration and composition of LDL remained constant, HDL_2-C was increased 36% after training. Post-heparin LPLa was increased in both groups after training, though not statistically significant. However, HTGLa was significantly reduced in both groups after 6 weeks of training. While the activity of skeletal muscle LPL was not altered after training in the high intensity group, adipose tissue LPLa was markedly elevated (50%) at the end of 6 weeks of training. While the authors concluded that alterations in the lipid profile were not influenced by the negligible loss of body weight, the reduction in body fat (%) might have contributed to the rise in HDL-C during the training program. Furthermore, the authors concluded that intensity of training may be responsible for their findings, since they noted a negative correlation between the change in HDL-C and training intensity.

Seals et al.[362] examined the effects of 6 months of low intensity aerobic training (45 minutes / day, 60% of maximal heart rate, 3 times per week) followed by 6 months of high intensity aerobic training (45 minutes / day, 80-90% of maximal heart rate, 3 times per week) on plasma lipid levels in older men and women (63 yrs). Blood samples

were obtained only 14 h after the last training session. Body weight was significantly lower only after the higher intensity training period. $\dot{V}O_{2peak}$ increased 12% after the low training and an additional 18% after completing the high intensity training. Plasma lipids did no change after the low training period, but a decrease in TG (21%) and an increase in HDL-C (14%) were reported after the high intensity training period. The authors concluded that the intensity of exercise must be high in order to favorably alter the lipid profile in sedentary men and women.

A recent study by O'Donovan et al.[363] sought to determine if similar improvements in fitness could be derived from moderate or high intensity exercise training of equal energy costs (3 times per week for 24 weeks, 400 kcal per day, 60% or 80% of $\dot{V}O_{2peak}$). Adjustments were made monthly to update the training program due to increases in subject fitness levels. The authors reported that the higher intensity training was better at improving maximal aerobic capacity compared to the lower intensity group. Furthermore, significant reductions in TC, LDL-C, and NONHDL-C were only observed in the high intensity group. It was also reported that changes in fitness and body fat were not related to changes in lipids. The authors concluded that high-intensity training is more effective in improving cardiorespiratory fitness than moderate intensity training of equal volume. Moreover, it appears as if changes in CHD risk factors are influenced by exercise intensity.

Woolf-May and colleagues[183] examined the effects of a moderate intensity exercise program performed in shorter bouts throughout the day compared to that of a program that consisted of one longer session of daily exercise of similar intensity and

total duration. The program lasted 18 weeks and both walking groups improved their fitness levels. However, no significant changes were noted for any of the lipid variables in either of the walking groups in spite of improved fitness.

Grandjean et al.[170] examined the influence of a progressive worksite aerobic training program (20-60 min / day, 60-80% $\dot{V}O_{2peak}$, 3 days per week for 24 weeks) on cardiovascular fitness and lipoprotein profiles in 37, previously untrained, female employees. $\dot{V}O_{2peak}$ increased 14.8% in the exercise group. Body weight and body fat (%) were significantly reduced (2 kg and 4%) with training. HDL-C increased (11.7%) in the exercise group, which approached, but did not reach statistical significance. In contrast, HDL-C decreased in the control group. No relationships between the change in body fat (%) and lipids were determined. There were nearly identical reductions in TC and LDL-C in the exercise and control groups, indicating that the exercise program probably was not responsible for these changes.

William's et al.[329] examined the dose response relation between the reported distance run per week and CHD risk factors in 1,837 female runners. The aim was to determine whether health benefits accrue in females at levels of exercise that exceed current minimal guidelines. The reported miles run per week were compared with medical data provided by physicians. The authors concluded that women who ran greater weekly distances tended to adopt certain types of behavior that reflected greater health consciousness. HDL-C concentrations were found to increase significantly in relation to longer weekly distances run. HDL-C was also significantly higher with each 16-km increment in the weekly running distance up to 48 km run per week and at or

above 64 km per week. HDL-C was increased with greater running distances in premenopausal women who were not using oral contraceptives and in postmenopausal women who were not taking estrogen and in postmenopausal women taking estrogen. Furthermore, these data contradict the idea that generally higher HDL levels in women limit the potential for these levels to increase with exercise (no ceiling effect).

Wilund and coworkers[364] examined the effect of a 6 month aerobic exercise training program (20-40 min / day, 50-70% of heart rate reserve, 3 days per week) on HDL containing only apo A-I (LpAI) and HDL containing both apo A-I and apo A-II (LpAI:AII). Maximal aerobic capacity increased 17% with training. Body weight and relative body fat (%) was significantly lower (1kg and 2.8%) after training in the exercise group. The concentrations of TC, TG, and LDL-C were not significantly altered with training. However, HDL particle size and HDL-C were both significantly increased with training. Furthermore, the concentration of apo A-I within LpAI increased significantly (12%) despite no change in total apo A-I or the concentration of apo A-I within LpAI-AII. The LpAI represents the HDL_2-C subfraction. Despite the significant increases in aerobic capacity and reductions in body weight and body fat (%), the magnitude of these changes was not correlated with the changes in lipoprotein-lipids.

Tokmakidis et al.[151] examined the adaptations of body composition, muscular strength, lipids, and apolipoproteins to a combination aerobic / resistance exercise training program. The researchers also instructed the subjects to detrain for 3 months. The exercise group participated in an eight month training program (60 min / day, 4 times per week; 2 aerobic and 2 resistance exercise, 60-85% of max heart rate and 60%

of 1RM). The circuit training sessions consisted of 3 sets (12 -15 repetitions per set) of eight exercises: bench press, seated row, leg extension, pull-down, "pec-deck", leg curl, curl-ups, and back extension. The rest period lasted less than 30 seconds, with a 5 minute rest between each set. $\dot{V}O_{2peak}$ was significantly elevated, while significant reductions in both body weight and body fat (%) occurred as a result of the training program. Furthermore, upper and lower body strength were significantly improved in response to training. The concentrations of TC and TG were significantly reduced and HDL-C and apo A-I were significantly elevated after training. However, Lp (a) did not change with training. Detraining resulted in a reverse action in all lipid variables.

Seip et al. [60] compared plasma CETP levels in sedentary men and women before and after 1 year of exercise training (45-60 min, 65-85% max heart rate, 3-5 times per week). Body weight was significantly reduced in both men and women after training. Maximal aerobic capacity was significantly increased 18% in women and 22% in men. Exercise training resulted in significant reductions in TG (20%), TC (4%), and LDL-C (4.6%) while HDL-C was significantly elevated (4.9%). Most of the increase in HDL-C was attributed to an increase in HDL_3-C. Lp (a) and apo A-I did not change after training. The concentration of apo B decreased (17%) while CETP was lower (13.5%) in response to the training program. Moreover, the concentration of CETP decreased in both subjects who lost weight and in those who remained weight stable. Thus, exercise training decreased plasma CETP independent of weight change. The researchers noted that plasma volume expansion may be partly responsible for the reported decrease in CETP and unfortunately this was not measured. The researchers also obtained the post-

training blood sample only 16 h after the last exercise session, which may have confounded their results.

Ring-Dimitriou et al.[355] examined whether 9 months of low-intensity running training (40-60 min / day, 64-73% of $\dot{V}O_{2peak}$, 3 times per week) can favorably alter cardiovascular fitness and blood lipoprotein-lipids in untrained adults. Subjects were randomly assigned to exercise or control groups and maintained a typical Austrian diet (45% carbohydrate, 37% fat, and 15% protein). Blood samples were obtained before and after the training program. However, the authors did not report if they controlled for the last bout of running before obtaining the post-training sample. The exercise training group significantly increased $\dot{V}O_{2peak}$ by 24%. Body weight and body fat (%) did not change with training. A significant decrease (20 mg / dL) in apo B was noted for the running group. However, this change in apo B was related to the change in aerobic fitness. Neither the training intervention nor the increase in fitness had a favorable influence on Lp (a).

Vasankari et al.[365] evaluated the effects of a 10 month exercise training program (3-5 hours per week, 65-80% $\dot{V}O_{2peak}$) on LDL oxidation in 114 sedentary men and women. Body weight and body fat (%) were significantly lower (2-3 kg and 2-3%) after training. $\dot{V}O_{2peak}$ was significantly higher (19%) after training. The concentrations of LDL-C were significantly lower (10%) and HDL-C higher (15%) after training. The oxidation of LDL was significantly decreased 23% in men and 26% in women. Furthermore, this decreased oxidation was not influenced by changes in bodyweight.

Hs-Crp Response to Endurance Training

General population studies report that there is an inverse association between serum hs-Crp levels and self-reported physical activity and physical fitness.[341] It is believed that regular exercise might favorably lower hs-Crp levels by an anti-inflammatory action. However, another explanation provided is that exercise lowers hs-Crp levels by reducing total or abdominal body fat. It is known that adipocytes synthesize cytokines that are involved in the production of hs-Crp. It has been proposed that adipose tissue-secreted IL-6 and TNF-alpha may contribute to elevated levels of hs-Crp observed in obese subjects.[366] Thus, exercise training may reduce hs-Crp levels by reducing adiposity. It is also known that interleukin release from adipose tissue is augmented by increased sympathetic stimulation, which is down regulated by physical activity.

Hammett et al.[367] examined the effects of 6 months of endurance exercise training (45 min / day, 80% of $\dot{V}O_{2peak}$, 4 times per week) on lipoprotein-lipids and hs-Crp levels in healthy elderly adults (60-85 yrs). Subjects were randomly assigned to either exercise or sedentary control groups. Fasting blood samples were obtained before and after training. However, the post-training blood sample was only taken 24 h after the last exercise session. Maximal aerobic capacity was significantly elevated (18%) after training. However, body weight, body fat (%), and blood lipids did not change in response to the training. Furthermore, hs-Crp levels did not change in either group. Thus, 6 months of endurance training in healthy elderly subjects did not favorably alter

blood lipids or hs-Crp despite a significant improvement in cardiovascular fitness with the training group.

More recently Hammett et al.[368] examined the effects of 6 and 12 weeks of endurance exercise training (45 min / day, 60-70% of max heart rate, 3 times per week) on inflammation markers in female smokers. 142 healthy females were randomized to either 12 weeks of training or health education. Fasting blood samples were obtained before, 6 weeks, and 12 weeks after training. All samples were collected at least 48 h after the last session of exercise. Subjects continued smoking for the first 6 weeks, and then stopped for the last 6 weeks of the training program. Maximal aerobic capacity was increased (17%) at the end of the 12weeks. Despite improved cardiovascular fitness, training did not decrease inflammatory markers (hs-Crp, circulating white blood cells, or fibrinogen) at either 6 or 12 weeks post-training. Thus, exercise had no effect on inflammatory marker levels either during the first 6 weeks of the program when smoking was maintained or the last 6 weeks when smoking was discontinued.

In a recent study Marcell et al.[369] examined the effects of 2 different exercise training intensity levels (30 min / day, 5 times per week for 16 weeks) on serum hs-Crp levels. The researchers also attempted to determine if exercise induced alterations in insulin sensitivity are in response to changes in certain inflammatory markers. The "moderate intensity" group exercised for 30 minutes per day with no heart rate guidelines (approximately 3.5 METS) while the "intense training group" followed the same protocol at an intensity equivalent to 80-90% of the subject's age predicted maximum heart rate. Body weight and body fat (%) were reduced after training while

significant improvements in aerobic capacity were only noted for the intense training group. Furthermore, only the higher intensity training group showed improvements (moderate) in insulin sensitivity. No significant group changes were noted in hs-Crp after training. The authors concluded that 4 months of regular exercise and improved cardiovascular fitness were not associated with decreased hs-Crp or adiponectin levels, even when subjects were stratified by their changes in fitness levels or obesity. The authors noted that exercise itself may be involved in the inflammatory response.[342] While, the time course for such a cytokine response to exercise is not completely known, circulating levels of IL-6 and hs-Crp may take up to 48 h to return to baseline levels after intense physical activity.[341] The blood samples in Marcell's study were collected 24-48 h after the last training session, thus any exercised induced inflammatory responses may not have completely resolved by that time.

Huffman and coworkers[370] evaluated hs-Crp levels in response to 6 months of exercise training in a population at risk for CHD (STRRIDE study). Subjects were middle-aged, overweight to mildly obese men and women and assigned to control, low amount-moderate intensity (40-55% of $\dot{V}O_{2peak}$), low amount-high intensity (65-80% of $\dot{V}O_{2peak}$), or high amount-high intensity (65-80% of $\dot{V}O_{2peak}$) exercise. Subjects were counseled to maintain their normal dietary intake throughout study. Significant improvements in body weight, body fat (%), and $\dot{V}O_{2peak}$ were noted after training. Despite improvements in cardiovascular fitness, hs-Crp levels did not change with exercise training, although the trend was for a decrease in the high amount high-intensity

group. Furthermore, the authors failed to detect a relationship between the change in aerobic capacity and change in hs-Crp levels.

Similar to the findings reported by Huffman,[370] Marcell,[369] and Hammett,[367, 368] Smith et al.[371] determined that hs-Crp levels were not significantly altered after 6 months of endurance exercise training (70 minutes / day, 2 days per week, moderate intensity) in people at risk for developing ischemic heart disease. Body weight was significantly reduced (2.7 kg) with training. Moderate exercise training reduced blood mononuclear cell production of cytokines with atherogenic properties by 58.3% (interleukin 1α, TNF-alpha, and interferon gamma). Both interleukin 1α and TNF-alpha, which have been identified in early and advanced atherosclerosis, were particularly attenuated in response to the exercise training. Furthermore, the production of cytokines with atheroprotective properties (interleukin 4, interleukin 10, and transforming growth factor beta 1) were elevated (35.9%). The levels of hs-Crp were lower after training, but this did not reach statistical significance. It is important to note that the previously mentioned changes were unrelated to aspirin ingestion, diet, weight loss, or smoking cessation during the study.

Despite the number of research studies reporting the inability of endurance exercise training to favorably alter hs-Crp levels,[147, 170-173] several investigations have reported findings to the contrary.[125, 185-189] Fallon et al.[185] examined the presence or absence of the acute phase response after a 9 month training program intended for court and field sports (Australian women's soccer and netball team). Soccer training consisted of running, cycling, and weight training, while netball training consisted of weight

training, court work, and practice games. Hs-Crp, which may increase by a factor of 100-1000 during the acute phase response, did not significantly change during each of the periods of netball training or in the heavy period of soccer training. Moreover, hs-Crp and WBC levels declined during the moderate soccer training period. However, the authors failed to report whether they controlled for the last session of exercise before obtaining blood samples.

Obisesan and coworkers[188] examined the possibility of hs-Crp gene variants affecting baseline and training induced changes in plasma hs-Crp levels. In this study, middle-aged to older (58 yrs) at risk men and women had blood samples analyzed for hs-Crp before and after 6 months of endurance training (20-40 min / day, 50-70% of $\dot{V}O_{2peak}$, 4 times a week). Fasting blood samples collected after training were drawn 24-36 h after the last exercise session. Subjects maintained the AHA Step 1 diet for the duration of the study. Body weight and body fat (%) were reduced and $\dot{V}O_{2peak}$ elevated after training. While exercise training resulted in a significant reduction (15%) in plasma hs-Crp levels, exercise training did not interact with any of the 4 hs-Crp genotypes to differentially alter hs-Crp levels.

Milani et al.[187] assessed the effects of 3 months of formal phase II cardiac rehab and exercise training (3 times per week) on hs-Crp levels in patients with established CHD. Body fat (%) was significantly lower while exercise capacity was significantly elevated in response to the training program compared to the control group. The concentration of TG was reduced (7%) and HDL-C increased (7%) after training. Furthermore, hs-Crp was significantly (36%) reduced in patients enrolled in cardiac

rehab and exercise training programs, which contrasted with the lack of change in hs-Crp in control subjects. 3 months of cardiac rehab and exercise training produced significant reductions of hs-Crp of similar or greater magnitude as therapy with statin drugs. Moreover, this benefit was independent of the effects of statin therapy as well as with changes in body weight, body fat (%), and exercise capacity.

Okita et al.[189] examined the effects of a 2 month aerobic exercise training program (110-140 minutes / day, 60-80% of max heart rate, 3 times per week) with weight reduction on obesity related inflammatory markers and conventional cardiovascular risk factors. Body weight was significantly reduced (3 kg) after training. The concentrations of TC (8.5%), TG (18%), and LDL-C (8.7%) were significantly lower after training. While the conventional variables were improved with training, hs-Crp, SAA protein, and WBC levels were all significantly lowered (35%, 24%, and 8%). Changes in hs-Crp and SAA were not associated with the extent of weight loss. One main limitation in this study is that they did not control for the last bout of exercise before collecting post-training blood samples.

Mattusch et al.[125] evaluated the hs-Crp levels in the blood of 12 moderately trained runners (34 yrs) preparing for a marathon. The training program (50 minutes / day, 75% of anaerobic threshold, 3-4 times per week) was maintained for 9 months and increased in intensity. In 10 of 12 runners the baseline hs-Crp levels were significantly reduced (31%) after training. No changes were noted in the non-exercising control group. These results suggest that endurance training may have a suppressive effect on certain inflammatory processes in the body. The authors hypothesized that after training

less interleukin-6 and other cytokines are produced in the exercising muscle as a result of an enhanced antioxidative protection.

Goldhammer and colleagues[186] examined the effects of 3 months of endurance exercise training (45 minutes / day, 70-80% of max heart rate, 3 times per week) on hs-Crp, IL-1, IL-6, IL-10, INF-γ activity in men and women with CHD. Fasting blood samples were collected at least 24 h after the last bout of exercise in order to avoid the immediate effects of exercise. Twelve weeks of exercise training did not alter body weight, BMI, or hemodynamic parameters. The concentration of LDL-C was significantly reduced (9.6%) after training. Plasma hs-Crp was also significantly lower (48%) after training and the change was independent of any changes in body weight or BMI. Thus, exercise training improved aerobic capacity in CHD patients and had reductions in IL-1, IL-6, INF-γ, and increased anti inflammatory IL-10 levels.

Lipoprotein Subfraction Response to Endurance Training

The value of including measurements of lipoprotein subfractions and subspecies is highlighted by the fact that small changes within specific size ranges for these lipoprotein particles are associated with important clinical differences in CVD risk. For a given level of LDL-C, individual risk differs depending on LDL particle number and then size. Increased risk is realized by having increased numbers of LDL particles and having increased smaller rather than larger LDL particles. Another benefit is that changes in subfractions as a result of an intervention can occur even when the standard lipid panel remains unchanged.[28, 198, 199]

Kraus and coworkers[14] examined the effects of the amount and intensity of exercise on risk factors for CHD in the STRRIDE study. Subjects were randomly assigned to a control group or one of three exercise groups: 1) high-amount-high intensity (caloric equivalent of jogging approximately 20 miles per week at 65-80% of $\dot{V}O_{2peak}$) 2) low-amount-high intensity (caloric equivalent of jogging approximately 12 miles per week at 65-80% of $\dot{V}O_{2peak}$) 3) low-amount moderate intensity (caloric equivalent of walking approximately 12 miles per week at 40-55% of $\dot{V}O_{2peak}$). The exercise training program lasted 8 months. Exercise at a caloric equivalent of 17-18 mi / week and an intensity equivalent to that of jogging at a moderate pace significantly decreased the concentration of small LDL and LDL particles while increasing the average size of LDL particles. These results occurred without changing the plasma LDL cholesterol concentration. While the two high intensity exercise groups had similar increases in $\dot{V}O_{2peak}$, only the high amount group had extensive improvements in the lipoprotein-lipid profile. Moreover, even though the low-amount high intensity and low-amount moderate intensity groups responded differently with regards to cardiovascular fitness levels, they both demonstrated similar lipoprotein-lipid responses to training. Thus, the authors concluded that the amount of exercise appears to make a greater difference than the intensity of exercise on changes to the lipoprotein-lipids.

Halverstadt et al.[190] examined the effects of 24 weeks of endurance exercise training (40 minutes / day, 50-70% of $\dot{V}O_{2peak}$, 3 times per week) on plasma lipoprotein-lipids in sedentary older adults. All blood samples were drawn 24 h to 36 h after a usual

exercise training session. All subjects followed the AHA diet throughout the study in an effort to remain weight stable. However, body weight and body fat (%) were significantly reduced and $\dot{V}O_{2peak}$ was significantly elevated (15%) after training. TC, TG, and LDL-C were significantly lower while HDL_2-C and HDL_3-C were significantly elevated after training. These changes were independent of baseline body fat (%) and body fat (%) changes with training. Total LDL particle concentration decreased significantly with training and this included significant reductions in medium and very small LDL particle concentrations. Conversely, large LDL particle concentration was significantly increased. Mean HDL particle size increased significantly with training while VLDL size decreased significantly. Mean LDL particle size increased, although this was not statistically significant. These results differ from that of Kraus et al.[14] (in regards to statistical significance) where it was reported that LDL particle size did significantly increase in exercise training groups compared to a control group.

Houmard et al.[372] examined the effects of 14 weeks of endurance exercise training (45 minutes / day, 70-85% of maximal heart rate, 3-4 times per week) on the chemical composition of plasma LDL in sedentary men. Fasting blood samples were obtained 48 h after the last training session. Maximal aerobic capacity was increased (20%) after training. Body weight and body fat (%) were significantly reduced (2 kg and 3 kg) after training. While the concentrations of TC and LDL-C remained unchanged, TG was significantly lower and HDL-C significantly higher after training. No significant changes in LDL diameter or density were noted. However, the ratio of total lipid to total protein was significantly increased with training. This favorable

alteration is in contrast to the LDL characteristics of individuals who are at risk for, or have CHD (cholesterol-poor, protein enriched LDL particles). Significant increases in both LDL free cholesterol and cholesterol ester were noted to have occurred. Increases in LDL molecular weight and particle diameter were associated with reductions in fat mass, and TG. No changes in LDL particle characteristics were related to changes in maximal aerobic capacity. The authors concluded that an important finding was that antiatherogenic alterations in LDL composition were noted with training despite no changes in calculated LDL-C. An underestimation of the cardioprotective effects of exercise training might have been reported if only absolute LDL mass had been examined.

Elosua and colleagues[126] assessed the effects of a 16 week endurance training program (50 minutes / day, 65-80% of $\dot{V}O_{2peak}$, 4-5 times per week) on antioxidant enzyme activity, oxidized LDL concentration, and LDL resistance to oxidation in young (19 yrs) sedentary men and women. Body weight and body fat (%) did not change while $\dot{V}O_{2peak}$ was significantly increased with training. No significant changes in TC, LDL-C, TG, and HDL-C were observed. However, the trend was towards an increase in HDL-C. The concentration of oxidized LDL was significantly lower after training. A significant increase in LDL resistance to oxidation was also observed. However, no statistically significant changes in LDL components, antioxidant content or LDL diameter were noted following the 16 week training program.

Halle and coworkers[333] assessed the influence of a 4 week intervention program including cycle ergometer exercise (30 minutes / day, 70% of maximal heart rate, 5

times per week) and changes in diet (1000 kcal diabetic diet) on body weight and lipoprotein metabolism in obese subjects with type 2 diabetes. A total energy expenditure of 2200 kcals per week occurred with the training program. Body weight was significantly lower (3 kg) after training. The concentrations of TC, TG, VLDL-C, LDL-C, and apo B were all significantly reduced after the intervention program. No significant changes were noted with regards to concentrations of HDL-C or HDL subfractions. LDL subfraction analysis demonstrated that small, dense LDL particles could be reduced by almost 50%. Furthermore, the cholesterol concentrations of LDL_5 and LDL_6 (density > 1.040 g / mL) were reduced, while the concentrations of medium, dense LDL particles (LDL_2 and LDL_3, density 1.031 to 1.037 g / mL) were elevated after training.

Altena et al.[373] compared fasting lipoprotein subfractions and postprandial lipemia before and after 4 weeks of either continuous exercise training or intermittent exercise training. Untrained, normolipidemic men and women were randomly assigned to complete continuous run training (30 min / day, 75% of maximal heart rate, 5 times per week) or interval run training (30 min / day, 75% of maximal heart rate, 5 times per week). Each exercise session was designed to expend approximately 245 kcals for a weekly total of 1200 kcals. The interval training sessions were performed in three 10 minute bouts separated by 20 minute rest periods. Blood samples were obtained 48 h after the last training session. Body weight did not change with this training study. No significant differences between the two groups were noted with regards to changes in lipoprotein-lipids. With groups combined (time main effect), TC, LDL-C, and IDL-C

were significantly lower (7.8%, 8.4%, and 6.7%) after training. HDL-C, HDL_2-C, and HDL_3-C increased 2.9, 2.0, and 0.5%, respectively after training. However, only the change in HDL_2-C reached statistical significance. LDL_1-C, LDL_2-C, and LDL_3-C decreased 4.1, 20.6, and 51.7% after training, although not statistically significant. Both types of training shifted the lipoprotein profile and LDL size from smaller to larger, less atherogenic subfractions. These results are consistent to the findings reported by Wolf-May et al.[183] and Halle et al.[333]

Shadid et al.[374] examined the effects of diet (500 kcal daily dietary deficit) and endurance exercise (45 minutes / day, 60-70% of heart rate reserve, 4 times per week) training compared to treatment with pioglitazone (insulin sensitizer, 30 mg daily) on lipid metabolism in non-diabetic, insulin resistant adults. The 19 week individualized exercise program was designed to eventually approximate a 1,500 kcal weekly energy expenditure. Fasting blood samples were obtained before and after training. Prior to blood sampling, subjects consumed an isocaloric diet for 1 week. Body weight was significantly reduced (11.4 kg) after training. The diet and exercise group demonstrated significant decreases in the concentrations of TC, TG, and LDL-C. Furthermore, LDL and HDL size (nm) was significantly increased after training. This finding was attributed to a decrease in the concentrations of small LDL while concomitantly increasing the concentrations of large LDL.

Kang et al.[375] evaluated whether high intensity physical training (250 kcal / day, 55-60% $\dot{V}O_{2peak}$: moderate group, 75-80% $\dot{V}O_{2peak}$: high group, 5 times per week for 8 months) would favorably affect components of the insulin resistance system in obese

adolescents. The high intensity group experienced greater improvement in cardiovascular fitness compared to the non-exercise control group. No significant differences were noted between the two different exercise intensity groups with respect to the dependent variables. However, the youths who improved the most in cardiovascular fitness and had greater reductions in body fat (%) had the greatest increase in LDL particle size (nm).

Varady et al.[376] examined the effect of a 24 week weight loss program (reduction of energy intake by 20% throughout the weight loss phase) that combined a low fat diet with moderate exercise training (40 minutes / day, moderate intensity, 3 times per week) on LDL particle size and distribution in obese hypercholesterolemic women. Subjects decreased their energy intake by 20% and increased energy expenditure by 10% during the program. Body weight was significantly lower (12 kg) after training. TC, TG, and LDL-C were significantly lower and HDL-C significantly higher after training. The estimated cholesterol concentrations in large- and medium-sized LDL particles were significantly lower by 15.3% and 5.9%, respectively, as a result of weight loss. Correlational analysis revealed a weak, albeit significant association between greater weight loss and an increase in peak LDL particle size. No changes were noted for estimated cholesterol concentrations in the small, LDL particles. The authors concluded that weight loss, resulting from a low-fat diet / exercise program, had only a minimal effect on LDL particle size and distribution. The estimated cholesterol concentrations of large and medium LDL decreased by 15% and 6% and this was explained by possibly replacing carbohydrates with fat in the low fat diets.

Seip and colleagues[181] examined the effects of apo E genotype on the response of lipoprotein subfraction concentrations to long term exercise (40 minutes / day, 60-85% of maximal heart rate, 3-4 times per week for 6 months) in healthy men and women. Fasting blood samples were obtained 24 h after the last training session. Body weight was significantly lower after training. $\dot{V}O_{2peak}$ increased (10%) with exercise. Besides a significant decrease in the concentration of TG after training, serum lipids were minimally altered in response to the training program. LDL particle subpopulations were changed significantly with training, with the changes being dependent on apo E genotype. However, the changes were poorly related to changes in body fat (%). Apo E 3 / 3 subjects decreased small LDL particle cholesterol and raised medium LDL particle cholesterol concentrations, whereas the opposite occurred in the apo E 2 / 3 and 4 / 3 subjects.

Resistance Training

Recently the American Heart Association and the Surgeon General have recommended resistance training as an integral part of a well-rounded physical activity program for health and disease prevention.[89, 90] With the increasing popularity of resistance exercise training, more people will likely adopt this type of activity, making it important to study the effects of this type of exercise on CHD risk factors.[89, 90] However, compared to the endurance exercise literature, there is a lack of information related to the effects of resistance exercise on circulating lipids and lipoproteins. Moreover, a review of the resistance training literature from the previous 22 years has produced contradictory results. In several studies, resistance training reduced blood

LDL-C concentrations and increased HDL-C concentrations.[93-100] However, contrasting findings have also been reported.[101-106] Interpreting the results from many of the resistance training studies is difficult, as they seem to suffer some of the same design problems present in many endurance training studies. Methodological differences, such as differences in training procedures, subject characteristics, dietary controls, and timing of blood sampling after exercise, may be responsible for some of the variability in the literature.[93-97, 100] For example, it has been suggested that resistance training using high repetitions and moderate resistance may promote favorable changes in the lipid profile, whereas resistance training consisting of low repetitions and heavy resistance does not.[107] Others have reported that neither low repetition nor high repetition resistance training effectively altered lipoprotein-lipids.[101] Although resistance exercise may be recommended to the general public for its proven skeletal muscle benefits, the beneficial influence of this mode of exercise on circulating lipids, lipid enzymes, apolipoproteins, and lipoprotein particle size remains to be established.

Blessing et al.[93] examined the effects of 12 weeks of resistance training or jogging on changes in body weight, body fat (%), strength, blood lipids, and hormones in untrained men. Thirty three men (44 yrs) were assigned to either resistance training (N = 9), jogging (N = 11), or sedentary control (N = 13) groups. Fasting blood samples were obtained at least 40 hours after the last exercise session before, 6 weeks, and again after 12 weeks of training. However, the authors did not state whether the lipid variables were adjusted for plasma volume changes which may have occurred in response to the last session of exercise. The resistance training (RT) program consisted of 6 large

muscle mass, multisegment exercises. All RT exercises were performed for 3 sets of 10 repetitions for the first 6 weeks and then 3 sets of 5 repetitions for the duration of the program. The total duration of each session was 45 minutes. The volume of training in this investigation was high, similar to that adopted by bodybuilders. The jogging program involved walking / jogging at 70-75% of each subject's predicted maximum heart rate for the first three weeks. The intensity was raised to 75-80% during the next 3 weeks and ultimately to 80-85% during the final 6 weeks of training. The duration was gradually increased to 30 minutes which was then held during the final 6 weeks. While body weight did not change, both training groups significantly decreased body fat (%) and increased lean body mass when compared to the control group. As expected, the RT group's strength gains were greater than both of the other groups. TC increased in the control group but was not altered in either training group. HDL-C was significantly increased (10.5%) in the RT group and jogging group (16%) compared to the control group. The researchers noted the greatest change in lipid levels occurred during the highest volumes of work. Moreover, the magnitude of change was the same in both training groups. Thus, the researchers concluded that both jogging and resistance training can favorably alter health and fitness levels.

More recently, Fahlman et al.[377] examined the effects of endurance (ET) and resistance exercise training (RT) on plasma lipids in active elderly women. These women were not formally exercising prior to the study. Subjects in the ET group (N = 15) completed 10 weeks of endurance training (50 minutes / day, 70% of heart rate reserve, 3 days per week). The RT group (N = 15) also completed 10 weeks of training

(3 days per week). Exercises consisted of 3 sets of 8 repetitions of leg extension, leg curl, plantar flexion, and dorsi flexion; two sets of hip flexion and hip extension; and one set of hip adduction and hip abduction. All sets were at 8 RM loads and a 2 minute rest interval was observed between sets. Every Friday the 3rd set was performed to volitional fatigue. A control group (N = 15) maintained their normal activities of daily living during the 10 weeks. Fasting blood samples were obtained 48 h after the last exercise session. Both RT and AT groups demonstrated favorable changes in plasma lipids after 10 weeks of exercise training. This occurred without concurrent changes in body weight or dietary habits. The RT group experienced an increase in HDL-C and a decrease in TG. The women in each training group increased their HDL-C concentration by at least 9 mg / dL, whereas the control group decreased their concentration of HDL-C by almost 5 mg / dL.

Boyden et al.[94] examined serum lipid changes in a group of healthy, premenopausal women (34 yrs) randomly assigned to either resistance training (RT) or sedentary control for 5 months. Training consisted of 12 exercises (3 sets of 8 repetitions) performed at 70% of the 1 RM. Subjects exercised for 60 minutes per day, 3 times a week. All subjects were asked to maintain their current dietary habits throughout the duration of the investigation. Fasting blood samples were obtained during the early follicular phase of the menstrual cycle, and 36 h - 48 h after the last exercise session. Body weight did not change in response to training. However, the RT group demonstrated a significant decreased in body fat (%) and increase in lean body mass when compared to the control group. The concentrations of TG and HDL-C were not

altered. However, concentrations of TC and LDL-C were significantly decreased (0.33 mmol / L and 0.36 mmol / L) compared to the control group. The changes in serum lipids were not related to the changes in body weight and / or body composition.

Fripp et al.[378] examined changes in body composition and lipoprotein-lipids in male adolescents (15 yrs) before and after a 9-week resistance training (RT) program. The researchers compared the changes in lipids with those in non-exercising controls. The RT group exercised 3 times a week for 60-80 min with 2-3 minute rest intervals. The subjects completed as many exercises as they could in the allotted time, but spent at least 10 min per exercise station. Exercises included bench press, lat pull down, military press, weighted dips (10, 8, 6, 4, and 2 repetitions per session for the previously mentioned exercises), leg extension, leg curl, neck extension, neck shrug, and lateral raises (3 sets of 10 repetitions for these exercises). Blood samples were obtained after an overnight fast. The researchers did not report if they controlled for the last bout of exercise. No attempt was made by the researchers to control dietary intake. Body weight and body fat (%) did not change in response to training. However, the control group demonstrated a significant increase in body weight over the 9-week training period. The RT group demonstrated a significant decrease in LDL-C and elevated HDL-C concentrations after training. TC and low density lipoprotein B did not change with training. No changes in lipoprotein-lipids were noted in the control group. Furthermore, the changes in lipoprotein-lipids (in the RT group) were independent of changes in BMI.

Goldberg and coworkers[95] used resistance training (RT) as a model of burst-activity resistance exercise to examine lipoprotein-lipids before and after 16 weeks of

resistance training in sedentary men and women. Fasting blood samples were obtained at the start and end of the 16-week training program and at least 36 h after the last exercise session. Subjects exercised on Universal gym equipment 3 times a week for 45-60 minutes. Resistance was roughly 84% of the 1 RM. Subjects completed 7 or 8 exercises for 3 sets of 8 repetitions with 2 minute rest intervals between sets. Body weight did not change in the women subjects (N = 8). They did demonstrate a 9.5% decrease in TC, 17.9% decrease in LDL-C, 28% decrease in TG and an insignificant increase (4.8%) in HDL-C concentrations. Similar to the women subjects, body weight was not significantly changed in the male subjects (N = 6). The male subjects demonstrated a 6.8% decrease in TC, 16% decrease in LDL-C, 15.8% increase in HDL-C, and an insignificant change in TG concentrations. Once the data for the men and women subjects was combined, the changes in HDL-C were no longer significant. However, TC and LDL-C were significantly lower (8% and 16.5%) after training compared to baseline values. Despite the absence of a sedentary control group, the researchers concluded that 16 weeks of resistance training produced favorable changes in the lipid profiles of sedentary man and women.

Hurley et al.[96] examined the effects of a Nautilus resistive training program on $\dot{V}O_{2peak}$, lipoprotein-lipids, glucose tolerance, insulin levels, and resting blood pressure in healthy men. Subjects trained on Nautilus exercise machines (3-4 days per week for 16 weeks). Subjects performed 1 set of 8-12 repetitions for upper body exercises and 1 set of 15-20 repetitions for the lower body exercises. Subjects completed 14 different exercises with less than 15 seconds of rest allotted between exercises. Fasting blood

samples were drawn approximately 24 h after the last exercise session. Body weight, body fat (%), and $\dot{V}O_{2peak}$ did not change as a result of the training program. TC and TG concentrations were not altered with training. LDL-C was lower (5 %) and HDL-C higher (10%) after training. The concentration of HDL_2-C was increased by 43% with training. The insulin response to a test meal was significantly lower after training in the exercise training group, but no change in fasting insulin levels were observed. A 50% increase in upper body strength (average of 5 upper body exercises) and a 33% increase in lower body strength (average of 3 lower body exercises) were noted for the training group. A significant decrease was noted in supine diastolic blood pressure after training (84 mm / Hg to 79 mm / Hg). The control groups post-training values were not different from their pre-training values for any of the measured dependent variables. The researchers concluded that a resistive training program can produce beneficial changes in blood lipids without altering body weight, body fat (%), or maximal aerobic capacity. However, the researchers admit that the changes in lipids may have been the result of the last exercise session, since blood samples were collected within 24 h of the last exercise session.

Johnson and colleagues[97] examined the effects of a 12 week resistance training (RT) program on body composition and serum lipids in sedentary middle-aged men. Subjects were assigned to either RT (N = 14), endurance training (ET; N = 10), or sedentary control (CG) groups (N = 10). The RT group trained three times per week for 45-60 minutes. The ET group was already exercising and was instructed to maintain their jogging program (10 km / week). Fasting blood samples were obtained before, 6

weeks, and 12 weeks after the start of the investigation. No effort was made to control for last exercise session. Body weight did not change, but a significant increase in lean body mass and decreased body fat (%) was reported in the RT group. The control group increased their body weight primarily through an increased body fat (%). No changes were noted in the ET group. TG concentrations were unaltered for all groups. Serum TC was significantly decreased in both exercise training groups after 12 weeks. HDL-C increased 15% and LDL-C decreased 39% in the RT group, both reaching significance. No changes in lipids were noted in the other groups.

Joseph et al.[98] examined the effects of a 12 week resistance training (RT) program on body composition and serum lipids in weight stable, moderately overweight older men and women (62 yrs). Subjects performed resistance training two times per week, which consisted of 5 exercises: 1) unilateral knee extension, 2) unilateral knee flexion for men and bilateral knee flexion for women, 3) double leg press, 4) seated chest press, and 5) seated arm pull. The first 2 sets consisted of 8 repetitions, with the 3rd set performed to failure or 12 repetitions. The resistance was set at 80% of the 1RM. Each subject's 1 RM was reassessed every 2 weeks in order to adjust training loads. Fasting serum samples were obtained 72 h after the last exercise session. TC, LDL-C, and TG did not change in response to the training program for either men or women. The male subjects significantly increased HDL-C (5.7%) while the women significantly decreased HDL (5.6%). Body fat was significantly lower (2%) and lean body mass significantly higher (2.2. kg) after the training program in the male subjects. No changes were noted in the women subjects. No significant correlations were noted for changes in

HDL-C and changes in body fat% and lean mass for either men or women. The researchers concluded that men and women responded differently in terms of changes in body composition and lipoprotein-lipid metabolism following a 12 week resistance training program. One limitation was that a control group was not used in this investigation.

Prabhakaran et al.[99] studied the effects of an intensive (85% of 1RM) 14 week resistance training (RT) program on the lipid profile and body fat (%) in healthy, sedentary premenopausal women (27 yrs). Subjects completed 8 exercises (2 sets of 8 repetitions and a 3rd set to failure), 3 times per week for a duration of 45-50 minutes. Rest intervals were set at 30-60 seconds. Fasting blood samples were taken 3 days after the last exercise session. Estimated 1 RM increased significantly in all eight exercises after training, while strength decreased in the control group. Body weight did not change as a result of training, but the RT group demonstrated a significant lower body fat (1.4%) after training. Significant decreases in TC (9%) and LDL-C (14%) were noted in the RT group. No differences were seen in the concentrations of TG and HDL-C. Furthermore, no changes were noted in any of the variables in the control group. The researchers concluded that an intense resistance training program can be an effective therapeutic modality for favorably altering lipid profiles in sedentary premenopausal women.

Ullrich et al.[100] examined the effects of 8 weeks of resistance training (9 exercises were completed 3 times per week on a universal gym apparatus) on lipoprotein-lipids in untrained males. Subjects were randomly assigned to 1 of 4 groups:

endurance lifting (N = 9), strength I (N = 7), strength II (N = 6), or explosive lifting (N = 3). The endurance group performed 2 sets of 15 repetitions (15-18 RM load). The strength I group performed 3 sets of 6 repetitions (6-8 RM load). The strength II group performed 1 set of 3 repetitions (3-5 RM load) once per week and 1 set of 10 repetitions (10-12 RM load) twice per week. The explosive group started at 1 set of 15 repetitions (40% of 1 RM load) and progressed to 1 set of 15 repetitions (15-18 RM load). Exercises consisted of leg extension, leg curls, seated leg press, calf raise, bench press, military press, latissimus pull, triceps extension, and biceps curl. Fasting blood samples were obtained 36 h after the last exercise session. No differences between the groups for any of the dependent variables were detected by ANOVA, so all the groups were combined. Body weight did not change in response to training. However, a significant increase in lean body mass and a significant decrease in body fat (%) did occur. $\dot{V}O_{2peak}$ was also higher after the 8 week training program. TG did not change in response to training. There was a significant decrease in TC (3%), LDL-C (8%) and a significant rise in HDL-C (14%). HDL-C was not related to $\dot{V}O_{2peak}$, muscle mass, body fat (%) or changes in these variables. The researchers admitted that limitations to this project included a lack of a suitable control group as well as a lack of dietary observations.

Weltman et al.[379] examined the effects of 14 weeks of circuit resistance training (45 min / day, 3 days per week) using hydraulic-resistance machines on serum lipids in prepubertal boys. The program was set up as a circuit (10 exercises) and completed 3 times. Thirty second rest intervals were used. Fasting blood samples were obtained within 24 h to 48 h after the final exercise session. No significant changes in body fat

(%) were noted in the training group (N = 16) or the control group (N = 10). However, both groups reported a significant increase in body weight. The major finding of this study was that the resistance training group demonstrated a significantly lower concentration of TC (15.7%) after 14 days of training. TG and HDL-C were not significantly altered in this investigation.

Bemben and Bemben[380] reported that a 16 week Dynaband resistance training program (45 min / day, three days per week) was associated with elevated HDL-C in 18 postmenopausal women (73 yrs). This finding was also not related to changes in body weight. Subjects performed exercises targeting 8 muscle groups: chest, back, shoulder, biceps, triceps, quadriceps, hamstrings, and gastrocnemius. Once subjects could complete 15 repetitions in an exercise, they were given a high strength band to use. There were no significant changes in body weight or body fat (%) during the training program. TC, TG, VLDL-C, LDL-C did not change in response to training. However, HDL-C was significantly higher (13%) after training compared to baseline. Furthermore, these improvements were not accounted for by body weight loss.

Tucker et al.[381] examined the effects of 12 weeks of resistance training (3 times per week) on blood lipids in sedentary women (43 yrs). Subjects completed 3 sets of 8-12 repetitions of the following 8 exercises: leg press, seated rowing, leg extension, leg curls, military press, latissimus pulls, arm curls, and bench press. Subjects performed a fourth set of each exercise during weeks 9 through 12. Resistance was set so that subjects could complete at least 8 repetitions but not more than 12 for each set. One to three minutes of rest was allowed between each exercise. Blood samples were obtained

12 h-18 h and 36 h-42 h after the last exercise session. The exercise group significantly increased lean body mass and muscular strength compared to the control group. Body fat (%) was lower after training in the exercise group, but this did not reach significance. The major finding was that there were no significant differences in LDL-C and HDL-C between exercise and control groups at the 12 h-18 h time point. However, LDL-C was significantly lower in the exercise group compared to controls at the 36 h-42 h time point.

Several studies have shown that training-induced alterations in the lipoprotein-lipid profile can be realized without changes in body fat (%), indicating an independent effect for resistance exercise.[95, 96, 367] Hurley et al.[96] and Goldberg et al.[95] both reported elevated HDL-C in young and middle-aged men after a resistance training program in which body weight and body fat (%) was not significantly altered. Thompson et al.[57, 160] demonstrated that elevations in HDL-C following endurance training is associated with a decrease in the fractional catabolic rate of HDL proteins and apo A-I and increases in the synthetic rate of apo A-I. Thus, the possibility that resistance training might also affect lipid metabolism independently of changes in body weight and body fat (%) can't be completely ruled out.

While there are numerous studies that support the beneficial effects of resistance training on the lipoprotein-lipid profile, they are not without opposition.[101-106, 370] Studies reporting the beneficial effects of resistance training on lipoprotein-lipids have been cited for lack of employing a suitable control group,[95, 100] using only one blood sample before and after training,[95-97, 100, 366, 367] used subjects who were not at risk for

CHD,[95, 96, 100, 366] not controlling for the effects of the last session of exercise,[95-97] or reporting significant changes in body weight and body fat (%).[97, 100]

Alén et al.[382] examined the effects of anabolic steroids and testosterone combined with resistance training on serum lipids in power athletes. Seven subjects used anabolic steroids and seven subjects served as control subjects. Subjects trained six times per week for 8 weeks. Both groups received a high calorie, low fat diet with additional protein supplements. Fasting blood samples were taken on 14 athletes before and after 8 weeks of resistance training. The group of athletes receiving steroids had significantly higher TG concentrations after training compared to the clean athletes. Furthermore, HDL-C was significantly decreased in the steroid group (54%) after training. A main limitation was that the researchers did not control for the acute effect of last session of exercise.

The type of resistance training has been thought to be a major determinant regarding the favorable effects on the lipoprotein-lipid profile. People who train using moderate resistance, high repetition exercise, similar to bodybuilders, are reported to have higher HDL-C and lower LDL-C compared to people who train like powerlifters, using primarily heavy resistance, low repetition exercises.[96] Kokkinos et al.[101] examined the effects of both low and high repetition RT on lipoprotein-lipids in healthy untrained males. Subjects were randomly assigned to one of three groups: low repetitions and heavy resistance (LR) group (4-6 RM), high repetitions and low resistance (HR) group (14-16 RM), or a sedentary control group. Subjects in the training groups performed 10 exercises, 3 times per week for 10 weeks. The LR group performed 3 sets with a rest

interval of 60-80 seconds. The HR group performed 1-2 sets of each exercise. The total amount of work (volume) between the 2 groups was identical. Fasting blood samples were obtained 24 h and 72 h after the last training session. Neither training program resulted in significant changes in body weight or body fat (%), but both training groups demonstrated significant increases in lean body mass. The concentrations of TC, HDL-C, HDL_2-C, and LDL-C did not change in response to the training. These results were the same for the blood samples obtained at both 24 and 72 h following the last session of exercise. The researchers concluded that low or high repetition resistive exercise training does not favorably alter the lipoprotein-lipid profile of young males with low initial TC levels.

Kokkinos et al.[102] evaluated the effects of 20 weeks of resistance training on lipoprotein-lipid profiles in people who were at risk for developing CHD. Subjects were untrained males with abnormal lipid profiles and at least 2 other risk factors for CHD. Subjects trained 3 times per week for the duration of the study using Nautilus equipment. The training program consisted of 2 sets of 12-15 repetitions using 11 different exercises and modified sit-ups. Rest intervals were strictly controlled at 90 seconds. Fasting blood samples were collected 1 day and 2 days after the last exercise session. Subjects demonstrated a 50% increase in upper body strength and a 37% increase in lower body strength. Body weight, body fat (%), and $\dot{V}O_{2peak}$ did not change in response to the training regimen. The concentrations of TC, TG, HDL-C, and LDL-C did not change with training at 1 day or 2 days following the last exercise session. Furthermore, the activities of LPL and HTGL were also unchanged following training. Thus, the

researchers concluded that 20 weeks of strength training did not alter plasma lipoprotein-lipid profiles or lipoprotein regulatory enzymes of TG and HDL-C in men at risk for CHD.

Stone and colleagues[383] examined the effects of a 12 week non-circuit weight training program (3 days per week) on body composition and blood lipids in 31 untrained men. Subjects were divided into control, weight training, or running groups. The weight training sessions consisted of 7 different exercises. Subjects completed 3-5 sets of 10 repetitions per exercise at light (60-65% of heavy load), moderate (75-85% of heavy load), and heavy loads (maximum amount of weight for the number of sets and repetitions). Body weight did not change. However, body fat (%) was significantly lower in the weight training group after the 12 weeks. The weight training group experienced a non-significant drop in TC and a non-significant increase in HDL-C. The changes in lipids were not associated with any changes in body weight or body fat (%).

Elliot et al.[384] examined the effects of 8 weeks of low intensity resistance training (3 sets of 8 repetitions at 80% of the 10 RM, 3 days per week) in healthy postmenopausal women. This protocol is equivalent to 60% of the 1 RM. A 2 minute rest period was allowed in-between sets. Blood samples were collected 48 h after the last training session. Body weight and body fat (%) did not change. Results indicated that this resistance training program did not have an effect on the blood lipid profile. Similar results were reported by Volek et al.[385] The determined that 12 weeks of heavy resistance training, with or without, creatine supplementation, had no significant effects on serum TC, HDL-C, LDL-C, and TG in healthy men.

Manning et al.[104] studied the effects of resistance training on time course changes in strength, lipids, and apolipoproteins in sedentary obese women. Subjects were randomly assigned to one of two groups: a resistance training group (N = 16) or a control group (N = 6). Fasting blood samples were obtained one two separate occasions to establish a pretraining baseline value. Post-training blood samples were collected approximately 3-4 days after the last exercise session. Three-day diet records were obtained on all subjects prior to and immediately at the end of the investigation. Subjects in the resistance training group trained 3 times per week for 12 weeks. The exercise program consisted of 8 exercises performed in the following sequence: bench press, knee extension, latissimus pull, sit-ups, triceps push down, knee flexion, shoulder press, and the biceps curl. Subjects performed 2 sets of 6-8 repetitions for the first week, adjusting to 3 sets of 8 repetitions for the remainder of the program. Resistance was set at 60-70% of the 1 RM. Rest intervals were set at 60 seconds. This 12 week resistance training program did not result in any significantly changes in body weight or BMI. The mean improvements from start to week 12 of the program for all strength measures were 58%. The concentrations of TC, TG, HDL-C, LDL-C, and apo B-100 did not change in response to the training program. Apo A-I demonstrated a significant increase at the end of the 12 weeks; however these changes were also paralleled by the control group. The researchers concluded that these negative results may be attributed to a lack of body weight loss, the lack of a negative caloric balance, and the low energy expenditure associated with this form of exercise.

Rhea and coworkers[105] examined the effects of resistance training, with and without weight loss, on lipoprotein-lipids in moderately obese, postmenopausal women. Subjects were randomly assigned to one of three groups: a resistance training + weight loss group (N = 8), resistance training only group (N = 7), or a control group (N = 19). Subjects who were assigned to the weight-loss group were placed on a calorie restricted diet designed to help them lose 0.5 kg per week. Subjects in the other training group were asked to maintain a heart healthy diet for the duration of the program. Fasting blood samples taken 24 h and 72 h after the last exercise session. Subjects in the heavy resistance training program trained three times per week for 16 weeks. Subjects performed 13 exercises (15 repetitions for upper body exercise and 20 repetitions for lower body exercises; 1 set of upper and 2 sets of lower body exercises) using the Keiser K-300 variable resistance exercise machines. Initial resistance was set at the subject's 5 RM. Significant decreases in body weight, BMI, and body fat (%) were observed only for the resistance training plus weight loss group. All training groups increased both upper and lower-body strength. None of the lipid variables were favorably altered 24 h after the last training session. However, there was a significant increase in TC in the resistance training only group at the 72 h post training time point. There were no significant correlations between changes in total body mass and changes in TC, HDL-C, and LDL-C. Thus, resistance training, with or without weight loss, does not significantly improve plasma lipids in previously inactive postmenopausal women.

Smutok et al.[106] compared the effectiveness of resistance training to endurance training for risk factor intervention in subjects who were at risk for CHD. Researchers

defined “at risk” by the presence of 2 or more major risk factors. Subjects were randomly assigned to one of three groups: a resistance training group (N = 14), an endurance training group (N = 13), or a sedentary control group (N = 10). Subjects in the resistance training group trained 3 times per week for 20 weeks using 11 different exercises. Subjects completed 2 sets of 12-15 repetitions for each exercise. Rest intervals were set at 90 seconds. The endurance group walked or jogged for 30 minutes / day, three times per week. Subjects started at an intensity of 50-60% of maximal heart rate reserve and gradually progressed to 85% of maximal heart rate reserve. Fasting blood samples were obtained 1 day and 2 days after the last exercise session. Body fat (%) was significantly reduced and $\dot{V}O_{2peak}$ increased (19%) in the endurance training group. No significant changes in any of the lipid variables, with either mode of training, were noted. Subjects in the resistance training program demonstrated a 50% increase in upper body strength and a 36% increase in lower body strength. However, both resistance and endurance training subjects reduced glucose and insulin responses to glucose ingestion during an oral glucose tolerance test (OGTT).

Elliot and colleagues[386] examined the effects of 8 weeks of low intensity strength training (3 days per week, 80% of 10 RM) on muscle strength and lipoprotein-lipids in sedentary, postmenopausal women. Subjects were randomly assigned to either resistance training (N = 8) or sedentary control (N = 7) groups. Subjects in the training group performed 5 different exercises for 3 sets of 8 repetitions, with a 2 minute rest period in-between sets. Fasting blood samples were obtained at least 48 h after the last training session. Body weight, body fat (%), and BMI did not change in response to the

training program. Furthermore, TC, TG, HDL-C, LDL-C, VLDL-C were unaffected by 8 weeks of low intensity resistance training. Thus, while this particular resistance training program produced significant increases in 10RM strength, it failed to induce any favorable changes in the blood lipid profile of postmenopausal women.

Volek et al.[385] demonstrated that 12 weeks of heavy resistance training, with or without creatine supplementation, did not produce any favorable alterations in serum TC, HDL-C, LDL-C, and TG in healthy men. Body fat (%) and fat mass were not significantly altered in response to this 12 week resistance training program. This study is limited by the fact that the post-training blood samples were obtained only 24 h after the last exercise session. These results are similar to those reported by Staron and coworkers.[387] It was reported that 8 weeks of high-intensity resistance training had little or no effect on lipoprotein-lipid concentrations in both young men and women. Body fat (%) was significantly lower after the 8 week resistance training program. However, fasting blood samples were obtained within 36 h - 48 h of the last exercise session, a similar design flaw found in the study from Volek et al.[385]

Combination Resistance / Endurance Exercise Training

Boardley and coworkers[134] examined the effects of different exercise modes (resistance training, endurance training, and a combination of resistance and endurance training) on lipids in sedentary older adults (74 yrs). The exercise program lasted 16 weeks (50 minutes / day, intensity equal to a rating of 11 – 16 on the Borg Rating of Perceived Exertion scale, 3 times per week). The resistance training group performed 1-2 sets of 10-12 repetitions of 13 different exercises using Thera-bands. The combination

group walked for 20 minutes and performed 1 set of 10 repetitions of each of the 13 exercises. While the modes of exercise were different, the duration of exercise remained similar with all three groups. Body weight did not change with training. While the exercise training resulted in significant improvements in strength and aerobic capacity, blood lipids were not affected. In fact, all groups (even sedentary control) experienced similar decreases in TC, TGT, LDL-C, and HDL-C over time. Therefore, the authors concluded that these results are probably due to a seasonal effect on blood lipids.

LeMura et al.[103] evaluated the effects of various modes of exercise training on changes in lipoprotein-lipids, cardiovascular fitness, and body composition after 16 weeks of training and 6 weeks of detraining in young (20 yrs), untrained women. Subjects were randomly assigned to either resistance only (RT), aerobic only (AT), or combination resistance and aerobic exercise training (CT). Subjects in the RT group performed 11 different exercises on Nautilus machines three times per week for 16 weeks. Subjects in the AT group also trained three times per week for 16 weeks while the CT group trained two times per week. The exercise protocol for the RT group consisted of 2 sets of 8-10 repetitions at 60-70% of the subject's 1 RM during the first 2 weeks. A third set was added for the last 14 weeks of the training program. The rest intervals were set at 60 seconds. The AT group's program consisted of an initial 10 minute warm-up, 30 minute exercise session, followed by a 10 minute cool-down. The intensity was set at 70-75% of the subject's maximum heart rate. Eventually, the duration was increased to 45 minutes, the frequency to 4 days per week, and the intensity to 85% of the subject's maximum heart rate. The CT group performed both RT and AT

2 times per week for the 16 week program. Fasting blood samples were collected 1 and 2 days after the last training session. Body fat (%) was significantly lower after training in the AT group only. Upper body strength was increased 29% and lower body strength 38% in the RT group. The CT group experienced an increase of 19% in upper body strength and 25% in lower body strength. No significant changes in any of the lipid variables were noted for either the RT or CT groups. However, HDL-C was significantly higher (28%) and TG significantly lower in the AT group after training. The authors concluded that the lack of changes in lipoprotein-lipids in the RT and CT groups was most likely attributable to the type and intensity of the training programs in those groups.

The previous review of the endurance and resistance exercise training literature has consistently demonstrated that favorable alterations in lipoprotein-lipids and non-traditional CHD risk markers can occur and these changes are independent of any changes in body composition and cardiovascular fitness.[14, 43, 57, 94-96, 98, 100, 140-142, 147, 170, 182, 197, 201, 352, 365, 366, 368] In addition, these studies have reported changes in lipid metabolism with high[56, 148, 195, 197, 349] and low-moderate[43, 167, 182, 184, 350, 352, 363] training intensities. The commonality seems to be the volume of the exercise regimen. It is believed that lipoprotein-lipid changes most often occur when the exercise regimen is consists of a large volume of work (caloric expenditure).[41, 44, 130-132, 364] Lastly, the research clearly demonstrates that subjects with differing baseline lipoprotein-lipid profiles can improve upon this with a sound exercise training regimen.[129-131, 134, 142]

Lipid Metabolism in Response to a Single Session of Exercise

Endurance Exercise

Many of the lipoprotein-lipid changes that occur after chronic exercise training are similar to those reported after a single exercise session. Moreover, some of the lipoprotein-lipid modifications attributed to chronic exercise training may actually be stimulated by a single exercise session (acute effect). Endurance exercise has an acute effect on circulating lipids lasting at least 48 hours. When blood concentrations are corrected for changes in plasma volume, HDL-C concentrations are generally increased, while TG concentrations are reduced 24 h to 48 h after a single session of exercise, even in those with elevated cholesterol.[42, 44] Therefore, if the timing of blood sampling is not controlled and occurs $\leq$ 48 h after the last session of exercise, researchers may mistakenly attribute changes in the lipid profile and non-traditional CHD risk markers to the effects of chronic exercise training when in fact the lipid alterations were induced by recent exercise. Failure to control for this effect may have confounded the results of many published endurance training studies.

This effect was reported by Holloszy and colleagues[388] during a six month endurance training study conducted in 1964. These investigators were examining the effects of a six month endurance exercise program on both TC and TG levels. Twenty seven sedentary men were randomly assigned into either a supervised (n = 15) or unsupervised (n = 12) exercise group. The training protocol consisted of endurance calisthenics and running, approximately three times per week (2 to 4 miles / session). A sedentary control group of five men were used to check seasonal variations in the lipid

profiles. The exercise training program resulted in increased aerobic capacity. However, body weight remained unchanged for the two groups. After training, serum TG levels were significantly lower than pretraining values while TC levels remained unchanged. The blood sampling protocol employed in this study allowed the researchers the opportunity to examine the daily variation in lipids before and after the exercise program. In addition, monthly blood samples were also taken during the program. This blood sampling design revealed that TG levels were decreased in some subjects after two days of exercise while the next month's TG levels remained unchanged when the blood sample was taken after three days of inactivity. Furthermore, the investigators observed a relationship between body weight and changes in lipid levels. It was noted that when the body weight of a few subjects decreased, so did their TC levels. After their body weights stabilized, their TC levels returned to baseline values. Thus, the results from this investigation provide evidence that it may be the effects of an acute session of aerobic exercise and not chronic exercise training that favorably alter TG levels.

Short-term alterations in lipoprotein-lipid metabolism in response to single, prolonged endurance events (2.5 -13 hours) have been examined.[72, 76-79, 85, 207, 376-382] Kuusi and colleagues[389] measured the acute effects of marathon running on serum lipoprotein-lipid levels in 20 moderately trained men. VLDL-TG and VLDL-C levels were significantly lowered while HDL-C and HDL_2-C levels were significantly elevated within 15 minutes after completing the 26.2 mile race. No other lipid changes were noted after the marathon.

In addition to Kuusi et al.,[389] Thompson et al.[78] also investigated the effects of a marathon run on the lipid profile of 12 well-trained runners. These researchers measured serum lipoprotein-lipids before and up to 66 h after completion of the 26.2 miles. It was reported that plasma volume adjusted TC, LDL-C, and TG levels were decreased at the 4 h and 18 h post-race time-points, and remained depressed throughout the 66 h time point. An increase in HDL-C occurred at the 18 h time-point; however this increase did not remain at the additional time-points. Another research group also reported on the lipoprotein-lipid response of well-trained subjects completing the 1982 Ocean State Marathon.[76] Serum TG levels were lower 18 h after the race and this reduction remained throughout the 42 h time-point. TC and LDL-C levels were reduced at the 18 h time-point but were no longer significant at the 42 h time-point. In contrast to Thompson's group,[78] plasma volume adjusted HDL-C was significantly elevated both 18 h and 42 h after the marathon. The increase in HDL-C at the 42 h time-point was attributed to a significant increase in the HDL_2-C subfraction. The difference in the HDL-C response between the two studies may be partially explained by the subject's fitness levels, as they completed the marathon in a much shorter time compared to the subject's in the study from Thompson et al.[78]

Kaikkonen and colleagues[390] evaluated the effects of completing the 1996 Helsinki City Marathon on the resistance of serum lipids to oxidation and the oxidative susceptibility of atherogenic lipoproteins VLDL and LDL. A beneficial effect of the marathon run was indicated by the increased HDL-C concentrations immediately after the run. This exercise effect also decreased the oxidation susceptibility of serum lipids

by 24% as well as increasing the plasma antioxidant capacity by almost 15%. However, the oxidative susceptibility of the VLDL + LDL fractions increased by 11%.

Nieman and coworkers[197] examined the influence of carbohydrate intake, age, and gender on cytokine changes of runners after 2 marathons. Ninety-eight trained male and female runners volunteered as subjects. Blood samples were taken before and 1.5 h after finishing the races. Researchers noted that the plasma levels of 4 cytokines, IL-6 (pro-inflammatory), IL-10 (anti-inflammatory), IL-1ra (anti-inflammatory), and IL-8 rose strongly in response to the marathon.

The lipoprotein-lipid changes associated with a bicycle marathon (230 km) were examined in 8 well-trained men by Foger and colleagues.[218] Fasting blood samples were taken 2 days before, then up to 8 days after the race. No pre-race exercise restriction was noted, but researchers did prohibit any exercise during the 8 days following the race. Diet and fluid intake was not monitored during the recovery blood sampling period. Plasma volume adjusted TC and TG concentrations were significantly decreased (32% and 63%) 24 h after the exhaustive exercise and remained lower up to 48 later. The HDL-C concentration increased significantly by day two, resulting from equal increases in both HDL_2-C and HDL_3-C. However, the concentration of HDL_2-C continued to increase and peaked 72 h after exercise while the concentration of HDL_3-C decreased towards baseline values. LDL-C concentrations were significantly depressed (37%) 24 h after exercise and remained depressed 72 h later. Apo B was significantly reduced 24 h after exercise while apo A-I significantly increased 48 h (20%), peaking 72 h after exertion. An interesting finding in this study was that CETP mass and CETPa was

significantly reduced (44% and 33%) 24 h after exertion; which may help explain the increases in HDL_2-C.

In 1986, Dufaux and coworkers[72] investigated the lipoprotein-lipid changes after a 3-hour running test (77% of anaerobic threshold). These changes were examined in 14 moderately trained young male subjects. One day after the test, TC and TG were lower compared to pre-exercise concentrations. Furthermore, HDL-C rose significantly above the pre-exercise value, and this was associated with an elevation of the HDL_3-C subfraction. On the following day (48 h) a significant increase in HDL_2-C was noted, while TC and TG remained depressed. The apolipoproteins A-I, A-II, and B, did not change during the first hours and the first two days after the race. On the second post-exercise day, Lp (a) concentrations rose significantly above pre-exercise values. Compared with pre-exercise measurements, the LCAT activity was significantly elevated three hours after the race. However, this increased activity was significantly decreased when blood samples were taken two days later.

Annuzzi et al.[79] reported reduced concentrations of TC, TG, VLDL-C, LDL-C, 24 h after a 3 hour exercise session consisting of alternating running and cycling at 70-85% max heart rate. All lipids were adjusted for plasma volume shifts that occurred as a result of the prolonged exercise session. Similar to the study from Thompson's group,[78] the TC and TG concentrations remained depressed up to 72 h after exertion. HDL-C was not measured in this investigation.

Lamon-Fava and coworkers[85] examined the effects of an endurance triathlon on plasma lipoprotein-lipids. Thirty-four men completed the grueling 2.4 mile swim, 112

mile bicycle ride, and 26.2 mile run, in succession. Plasma lipoprotein-lipids were measured 16 h before the start of the triathlon and within 10 minutes of completing the race. Plasma volume adjusted TG levels were reportedly decreased by 67%, while HDL-C levels increased by 18%. No changes were noted for TC and LDL-C concentrations. However, apo A-I significantly increased by 7% while apo B was reduced nearly 9%, while also reaching significance. One interesting addition to this study was the fact that the researchers measured LDL particle size using nondenaturing gradient gel electrophoresis. LDL particle size increased significantly in seven males participating in the study. An increase in LDL size is believed to confer a decreased CHD risk.

Baumstark and colleagues[206] used preparative density gradient ultracentrifugation to examine the effects of a 30 km cross-country run on serum lipoprotein-lipid concentrations and on the composition of lipoprotein subfractions in 13 trained men. Fasting blood samples were obtained before, 1 h, and 20 h after the run. TC was reportedly decreased (7%) 20 h after the run. Serum TG concentration was significantly reduced (36%) as a consequence of a reduction in the number of VLDL particles (31%). It was reported that the prolonged exercise did not induce significant changes in the average concentration of the LDL subfractions. Similar to the work of Lamon-Fava,[85] a reduction in dense LDL occurred in subjects who experienced large reductions in serum TG. Immediately after the run (1 h) the TG content was significantly reduced in all LDL subfractions. It is generally accepted that beneficial changes in the lipid profile which occur after exercise are the result of increased LPLa producing an increase in the

peripheral clearance of TG-rich lipoproteins. This enables the body to replenish intramuscular TG stores which may have been used as a source of fuel during the actual exercise session. If increased lipolysis were the only factor leading to the decreased TG levels after exercise one would not expect a reduction in VLDL number but a reduced lipid content of the VLDL particle. In this study, Baumstark and coworkers have shown that the secretion of VLDL may be reduced after a prolonged exercise session. These findings were reiterated by Borsheim and colleagues[391] after they determined VLDL and VLDL related particles were decreased after 90 minutes of cycle ergometer exercise (58% of $\dot{V}O_{2peak}$) in active young men.[391]

Zhang and coworkers[195] examined the time course changes in LPLa and RCT variables after an acute bout (60 minutes) of treadmill exercise (60% $\dot{V}O_{2peak}$) in 16 sedentary men with normal and abnormal lipid profiles. Fasting blood samples were obtained before, 4 h, 8 h, 12 h, and 24 h after the exercise session. It was noted that LPLa was significantly elevated 24 h after the 60 minute exercise session in these sedentary subjects. Furthermore, HTGLa was significantly elevated at 8 h, 12 h, and 24 h post-exercise compared with the 4 h time-point. The activities of LCAT and CETP did not change over the 24 h time period. The exercise session also did not alter HDL-C or HDL_2-C concentrations during the 24 h post-exercise period.

A number of injury / inflammation markers were evaluated in 18 trained male endurance athletes competing in a 160 km triathlon.[200] Blood sampling took place before, 30 min, 24 h, and 48 h after the race. The WBC count was significantly elevated immediately after the race (100%) and at the 30 min post race time point (158%).

Cortisol levels followed a similar time change, with the concentrations of both variables returning to baseline levels at 24 h and 48 h. Hs-Crp was not significantly elevated above baseline until 24 h after the race (266%). The concentration of hs-Crp returned to baseline by 48 h.

Berger et al.[392] investigated the effects of a moderate exercise session (approximately 70% of max predicted heart rate) on blood lipids in a group of 12 moderately fit men (8 trained & 4 sedentary). The same subjects completed a control session of quiet sitting for comparison purposes. Blood samples were collected before and after the 5.5 km run. TC and LDL-C were not significantly altered after exercise. The concentrations of HDL-C and HDL_3-C were significantly elevated (3.6% and 6.3%) 2 h after the exercise. LCATa was not significantly altered in response to the exercise session; however a small elevation was noted.

Ginsburg et al.[393] examined the effects of a single bout of ultra endurance exercise (1994 Hawaii Ironman Triathlon) on lipoprotein-lipid levels and oxidative susceptibility of lipids in 39 highly trained athletes. Blood samples were obtained 2 days before and immediately after finishing the competition. Significant decreases in plasma volume adjusted TC (9%), TG (39%), LDL-C (11%), and apo B (10%) were reported. Conversely, non-significant increases in HDL-C and apo A-I occurred. The susceptibility of lipids to peroxidation was reduced by exercise, and this appeared to be independent of any antioxidant supplementation use by the subjects and may be mediated by inducing endogenous antioxidants. One year later, Yu et al.[205] analyzed acute changes in serum lipoprotein-lipids, using NMR spectroscopy, in 28 elite athletes

completing the same event. Similar to the work of Ginsburg,[393] significant decreases in TC (7%) and TG (22%) occurred with LDL-C (3%) approaching significance. The concentrations of VLDL-C (51%), apo B (12%), Lp (a) (18%), and HDL_3-C (16%) were also significantly reduced after the race. The concentration of HDL-C was significantly elevated (30%), primarily due to increases in the HDL_2-C subfraction (11%). It is noteworthy that small, dense LDL particles significantly decreased (62%) while HDL size significantly increased by almost 3%.

Contrary to the findings reported by Ginsburg et al.,[393] Wetzstein and coworkers[394] examined the effect of an acute bout of 30 minutes of treadmill walking on the susceptibility of LDL to in vitro oxidation. Eleven trained and 12 untrained subjects each exercised at 70% and 55% of $\dot{V}O_{2peak}$, respectively. They determined that their exercise session was sufficient to increase the susceptibility of LDL to oxidation. This difference was not statistically significant for the individual groups, but was significant for the combined groups.

Savard and colleagues[395] examined the acute effects of a 90 minute cycling session (88% of max heart rate) on adipose tissue LPLa. Twenty-seven healthy, but untrained, young men volunteered to be subjects in this study. Tissue sampling occurred before and after the exercise session. Mean adipose tissue LPLa increased by 28% when expressed per gram of tissue. The authors also point out that LPLa showed interindividual variations as the responses ranged from a 131% increase to a 30% decrease. Subjects were also allowed to eat a small (560 kcal) meal before the exercise session. However, the authors felt that this small meal did not influence the results.

A majority of the previously mentioned research investigations used subjects who were trained or who participated regularly in strenuous physical activity. Among other methodological differences, an individual's training status may influence how lipoprotein-lipids are altered after prolonged exercise. In an effort to compare and contrast the lipoprotein-lipid responses to prolonged exercise in trained and sedentary subjects, changes in lipid metabolism were examined in trained (N = 11) and sedentary (N = 10) men before and after cycle ergometry exercise (80% of max heart rate) lasting 1 and 2 hours, respectively.[69] Plasma volume adjusted LDL-C was significantly lower in both trained and untrained men immediately after exertion, returning towards baseline afterwards. After adjusting for plasma volume changes, LPLa was significantly elevated 24 h after exercise in both exercise groups while HTGLa was no significantly altered. Furthermore, HDL-C concentrations were significantly elevated 48 h after the cycling in both groups. However, the increase in HDL-C concentrations after prolonged endurance exercise was due to elevated HDL_2-C concentrations in endurance trained subjects, but to elevated HDL_3-C in untrained subjects. The authors suggest that the different responses may be related to baseline HDL-C concentrations. The trained subjects had higher HDL-C compared to the untrained subjects. Furthermore, the caloric expenditure of the cycling session was unequal between the groups; the trained group exercised twice as long and would naturally expend more calories compared to the untrained subjects.

In an effort to determine if the lipid response to acute exercise is similar in both sedentary and trained men, Cullinane and colleagues[145] measured serum lipoprotein-lipids in 8 young sedentary males before and 66 h after 30 minutes of cycle ergometer

exercise (75% of max heart rate). The only significant finding was a small decrease (10 mg / dL) in LDL-C 66 h after exertion. One year later Cullinane and coworkers[80] set out to examine the effects of varying durations of exercise on the lipoprotein-lipid levels of exercise trained and untrained subjects. Their main purpose was to determine if a particular threshold exists for acute changes in lipids and whether this effect is limited to trained subjects. Specifically, the researchers had 9 well-trained and 10 untrained men complete a single cycle ergometry exercise session for 1 h, with trained subjects repeating another session, for 2 h at their anaerobic threshold. At the 24 h post-exercise time-point, TG was decreased in both the trained (17%) and untrained (22%) men after the 1 h session and in the trained men (33%) after the 2 h session. However, this change was only significant in the trained men following the 2 h exercise session. In contrast to the findings reported by Kantor and colleagues,[69] no other lipid changes were noted. The greater decrease in TG in the untrained men after the 1 h session of exercise may be due, in part, to the higher baseline TG levels noted in this group.

In order to determine how many repeated bouts of exercise where necessary to increase HDL-C and the HDL subfractions, Angelopoulos et al.[396] had 9 untrained men complete 30 minutes of treadmill exercise (65% $\dot{V}O_{2peak}$). Blood samples were drawn and lipids analyzed before, 24 h, and 48 h, after exercise. One week later, subjects returned and performed two, 30 minute treadmill exercise sessions, 48 h apart. Following this series, subjects returned for the last time to complete three, 30 minute treadmill sessions, again separated by 48 h. No significant interactions were detected. HDL-C was significantly elevated in all series at the 24 h post-exercise time-point,

returning to baseline levels thereafter. However, there was a significant decrease in HDL_2-C 48 h after exercise while HDL_3-C increased during the same time period. The authors determined that three repeated exercise sessions produced a prolonged and clinically significant (4 mg / dL) elevation in HDL-C.

Preβ_1-HDL is considered as the initial acceptor of cellular cholesterol during RCT. Sviridov and coworkers [397] examined the formation of Preβ_1-HDL in the leg muscles of diabetics and controls after an acute bout of cycle ergometer exercise. Nine type 2 diabetics and 7 healthy controls completed the acute exercise session, which consisted of 25 minutes of cycling at 60% of their $\dot{V}O_{2peak}$. Blood samples were obtained before and 25 minutes after the exercise session. There was no difference between nondiabetic and diabetic subjects in the ability to generate preβ_1-HDL. Furthermore, the exercise session was sufficient to significantly increase plasma concentrations of preβ1-HDL (20%). Unfortunately, it was not reported if the researchers controlled for the last bout of exercise or if plasma volume shifts were taken into consideration. In a follow-up to this study, Jafari et al.[398] evaluated the effects of a single session of jogging on plasma preβ_1-HDL levels in 19 healthy men and women subjects. Blood sampling occurred before and immediately after the 4 km run (approx 300-350 kcal). TC, TG, and LDL-C were all decreased immediately after exercise, while HDL-C was elevated. However, none of the changes reached significance. The exercise was sufficient to increase preβ_1-HDL (25%) and decrease HDL-TG (46%). These investigations support the contention that a single session of exercise can induce alterations in lipid metabolism of sedentary individuals.

Similar to the exercise training literature, the influence of exercise intensity on lipoprotein-lipid responses to acute exercise has been reported in both trained and untrained subjects.[66, 71, 82, 86, 392, 393] Davis and coworkers[175] evaluated alterations in lipid metabolism in 10 well-trained men after isocaloric bouts (950 kcals) of treadmill running at both 50% and 75% $\dot{V}O_{2peak}$. Blood samples were obtained 24 h before, immediately, 24 h, 48 h, and 72 h after exercise. No significant alterations to any of the lipoprotein-lipids measured were reported for either exercise intensity. The authors determined that the exercise protocol used in their investigation was not sufficient to alter lipid metabolism in these trained subjects.

Contrary to the findings reported by Davis, Hicks et al.[399] examined the effects of varying exercise intensity on the acute response of blood lipids. Twelve trained men completed a 12 km run on two separate occasions (60% and 90% $\dot{V}O_{2peak}$). Fasting blood samples were obtained before, immediately, and 20 minutes after exercise. The concentrations of TC, HDL-C, and apo A-I were significantly elevated after exercise at both intensities, but larger increases were noted with the higher intensity. TG was decreased, although not significantly, after both intensities. However, researchers only checked hematocrit levels in order to determine plasma volume shifts, which is not as reliable as using both hematocrit and Hb.

Using a randomized, crossover design, Gordon and coworkers[71] evaluated the effects of two isocaloric (800 kcals) sessions of treadmill running at 60% or 75% $\dot{V}O_{2peak}$ in 12 recreational runners. Subject diets were replicated during each blood sampling

period, which occurred before, immediately, 1 h, 6 h, and 24 h after exercise. The only lipids alteration was a significant time by intensity interaction for HDL-C. The plasma volume adjusted concentration of HDL-C was significantly elevated (5 mg / dL) 24 h after exercise only with the higher intensity (75%). The increase in HDL-C was attributed to an increase in HDL_3-C, with no change in HDL_2-C. When trials were combined, lipoprotein enzyme analysis revealed a significant increase in LPLa (15%) 24 h after exercise with a concomitant decrease in HTGLa (12.5%). These results suggest that alterations in HDL metabolism following an acute session of aerobic exercise may be influenced by the intensity of exercise session.

Gordon et al. [176] demonstrated increases in plasma volume adjusted HDL-C and HDL_3-C in 12 moderately trained men after a prolonged running session on a treadmill. Subjects exercised at 75% of their $\dot{V}O_{2peak}$ for a duration that allowed them to expend 800 kcals. However, the concentrations of TC, TG, and LDL-C were not significantly altered. Analysis of lipoprotein enzyme data reveal that LPLa was elevated and HTGLa depressed 24 h after the exercise session, although neither reached significance.

Park et al.[400] examined the acute effects of exercise at lactate threshold (LT) and 70% of lactate threshold on the metabolism of HDL and HDL subfractions. 18 healthy men completed 2 isocaloric (350 kcals) sessions of treadmill running at their LT and again at 70% of their LT. Fasting blood samples were collected before, 15 minutes, and 24 h after exercise. No significant intensity by time interaction was found. However, significant time effects were detected for the plasma volume adjusted concentrations of HDL-C, VLDL-TG, and TG only for the LT intensity. HDL-C was elevated (6%) at 24

h post-exercise and this increase was due to elevations in both HDL_2-C (6.5%) and HDL_3-C (6.6%). TG was decreased (13%) after exercise at LT. The authors concluded that a single session of isocaloric exercise at a higher intensity produces a more favorable lipoprotein-lipid response in healthy young men.

Pay and colleagues[86] examined the acute effects of a low intensity, prolonged walking (2 hours at 30% $\dot{V}O_{2peak}$) session on lipoprotein-lipids in 11 trained and 11 untrained men and women. Blood samples were obtained before and every 30 minutes during the 2 h exercise session, with the last sample taken immediately after the exercise. The pre-exercise HDL-C concentration was 17% higher in the trained group compared to the untrained group. The response of plasma volume adjusted HDL-C to the exercise session was not significantly different between untrained and trained subjects. However, trained subjects demonstrated a modest rise in HDL-C during the first hour of exercise followed by a further increase. This represented an overall 20% increase in HDL-C compared to baseline values. In contrast, the concentration of HDL-C increased markedly during the first hour of exercise (midpoint) in the untrained subjects followed by a decline thereafter, approaching baseline values. These results demonstrate that an acute prolonged session of low-intensity exercise can modify lipid metabolism in both trained and untrained subjects.

In an effort to evaluate temporal changes in blood lipids, Durstine et al.[73] examined the effects of an acute prolonged session of low-intensity (45% of $\dot{V}O_{2peak}$) exercise in 10 trained men. Subjects exercised till exhaustion (3-4.4 mph & 2-4% grade) on a treadmill while blood samples were obtained before, during, and 30 minutes after

the exercise. TC was significantly elevated at the time of exhaustion and this elevation continued 30 minutes after the exercise. Furthermore, the concentration of HDL-C was significantly elevated 2 h into the exercise session (5.6%) and continued until exhaustion, approximately 2.5 h later (10.8%). The concentrations of TG, VLDL-C and LDL-C were not significantly altered in response to the exercise stimulus. These results should be interpreted with caution since changes in plasma volume were not taken into consideration.

In an effort to evaluate the effect of different volumes (kcals) of exercise on lipoprotein metabolism, Visich and coworkers[133] examined the lipoprotein-lipid response in 12 trained men after treadmill exercise (75% $\dot{V}O_{2peak}$) of varying energy expenditures (expending ~ 400, 600, and 800 kcals). Blood samples were obtained before, immediately, 1 h, 6 h, and 24 h after exercise. No exercise volume by time interactions were significant for any of the dependent variables. When the data were collapsed across exercise volumes, an increase in plasma volume adjusted HDL-C (5.8%) and HDL_3-C (11.7%) was noted 24 h after exercise. The concentration of TG was also significantly depressed (13%) 24 h after exercise. With respect to lipoprotein enzyme activities, LPLa was significantly elevated (19%) while HTGLa was alternately depressed (14%) 24 h after exercise. The authors were not able to determine an exercise threshold necessary to significantly alter HDL-C.

Visich and coworkers[401] evaluated the effects of a single session (600 kcals) of treadmill running (75% $\dot{V}O_{2peak}$) on blood lipids in 12 trained men. Blood samples were obtained before, 6 h, and 24 h after exercise. No significant time changes were noted for

any of the plasma volume adjusted lipoprotein-lipids. However, LPLa was significantly elevated (27.5%) 24 h after exercise. Researchers determined that a caloric volume of 600 kcals was insufficient to promote beneficial alterations in lipid metabolism despite an increase in LPLa.

One year later, Visich et al.[402] examined the effects of normal (1000 kcal) and above normal (1500 kcal) sessions of cycle ergometry exercise (70% $\dot{V}O_{2peak}$) on lipid metabolism in 12 trained cyclists. Blood samples were collected before, 24 h, 48 h, and 72 h after exercise. All lipid variables were corrected for plasma volume changes. No significant changes were observed of TC, HDL-C, or HDL subfractions. However, a significant decrease in TG (20.3%) occurred 24 h after exercise. The authors concluded that no additional increases in HDL-C occurred after completing an above normal session of cycle ergometer exercise.

In an effort to determine the energy expenditure necessary to favorably alter lipoprotein-lipids, Ferguson and coworkers[132] examined the lipid response in 11 well-trained men after completing 4 different exercise sessions of varying energy expenditures (expending ~ 800, 1100, 1300, 1500 kcals). Exercise sessions were spaced 2 weeks apart at 70% of the subject's $\dot{V}O_{2peak}$. Blood samples were obtained before, immediately, 24 h, and 48 h after exercise. A transient decrease in TG (26%) was noted to occur 24 h after the 800 kcal exercise session. Plasma concentrations of HDL-C were only significantly elevated in exercise sessions that consisted of energy expenditures of 1100 kcal or more. The authors concluded that energy thresholds for trained men do indeed exist. Energy expenditures of 1100 kcal were required in order to elevate plasma

HDL-C, while 1300 kcal expenditure was necessary to decrease LDL-C. LPLa was significantly elevated 24 h after exercise in the 1100, 1300, and 1500 kcal sessions, and continued to remain elevated 48 h after exercise in the 1500 kcal session. A significant decrease in HTGLa was noted to occur 24 h after exercise in the 1300 kcal session.

Magkos et al.[403] examined alterations in lipid metabolism after a single, prolonged session (2 h) of cycle ergometer exercise (60% of $\dot{V}O_{2peak}$). Fasting blood samples were obtained before and 24 h after exercise. Exercise did not affect the VLDL-TG secretion rate. However, exercise did significantly reduce the number of VLDL particles while small LDL particles were reduced (7.8%), which approached, but did not reach statistical significance. Lipoprotein enzyme data revealed that while muscle LPLa was not altered, plasma LPLa was significantly elevated (20%) after exercise. Both HTGLa and LCATa were not affected by the exercise session, whereas CETP concentration was decreased (10%) after exercise. While the authors did control for the last bout of exercise before obtaining the baseline blood sample, it was not reported whether the variables were corrected for plasma volume changes.

Ferguson et al.[209] examined the effects of acute, moderate intensity exercise (70% $\dot{V}O_{2peak}$; 1500 kcal) on plasma lipids. Blood was obtained during the exercise session drawn after 1000, 1100, 1200, 1300, and 1400 kcals. A minimum energy expenditure of 1100 kcals was required in order to induce reductions in TC and LDL-C. Exercise induced increases in HDL-C and HDL_2-C were reported immediately after the exercise session was completed. The authors again report that their data support the

contention that a threshold of exercise may be necessary in order to induce alterations to the lipid profile during exercise.

Campbell et al.[404] examined the differences in the lipid response to an isocaloric session (expending ~ 450 kcals) of treadmill running (65% of $\dot{V}O_{2peak}$) in 1 continuous session or 2 intermittent and 3 intermittent sessions, each separated by 4 hours. Subjects (16 healthy men) had blood samples taken before, immediately, 24 h, and 48 h after each exercise trial. No significant alterations were noted for plasma volume adjusted TC, TG, HDL-C, LDL-C, LDL particle size, and CETPa. The concentration of HDL_2-C was significantly elevated 48 h after exercise in the continuous (15%), 2 intermittent (13%), and 3 intermittent (24%) exercise sessions. Furthermore, LCATa was significantly elevated 48 h after exercise in the continuous (12%), and 3 intermittent (12%) exercise sessions. The authors concluded that treadmill exercise, whether continuous or accumulated, can favorably alter HDL_2-C concentrations, which were augmented by an elevated LCATa.

Mestek and colleagues[178] compared the lipid response to accumulated sessions of exercise in one day to one continuous exercise session of equal caloric expenditure. Nine moderately fit men completed one continuous session of treadmill exercise (70% of $\dot{V}O_{2peak}$; 500 kcals) and then repeated the protocol one week later except in 3 separate bouts of 167 kcal (separated by 4 h intervals). Blood samples were obtained before, 24 h, and 48 h after the exercise. TG and LDL-C were unaltered by exercise. The concentration of HDL-C was elevated 7mg / dL over baseline 48 h after exercise with 3 accumulated sessions versus 2 mg / dL with 1 continuous exercise session of equal

caloric expenditure. The authors concluded that exercise accumulated in smaller bouts in 1 day was more effective in raising HDL-C than 1 continuous bout of exercise of similar caloric expenditure.

In an effort to determine the effects of acute endurance exercise on changes in the concentration of Lp (a), Gruden et al.[405] had 10 healthy men and women exercise on a cycle ergometer for 20 minutes at a constant workload of 600 kpm / min. Fasting blood samples were taken before, 30 minutes, and 60 minutes after exercise. The authors reported that Lp (a) was not significantly altered at either of the post-exercise time-points. Gruden's findings were reiterated one year later by Hubinger and coworkers[203] who evaluated the acute response of Lp (a) and hs-Crp to level treadmill running (60 minutes at 90% of max heart rate) and downhill treadmill running (40 minutes at 75-80% of max heart rate) in 14 untrained men and women. The concentrations of both Lp (a) and hs-Crp were not altered in response to either 1 h of high intensity level treadmill running or to 40 minutes of moderately high downhill treadmill running.

Plaisance and coworkers[204] examined the inflammatory response to a single endurance exercise session (500 kcals; 70% $\dot{V}O_{2peak}$) between individuals of high and moderate fitness levels. 10 highly fit men and 11 moderately fit men completed the single session of treadmill exercise. Fasting blood sampling occurred before, 24 h, 72 h, and 120 h after exercise. The subjects in the high fit group were significantly leaner compared to the moderately fit group. Hs-Crp levels were 76% lower at baseline in the high fit group compared to moderately fit group. However, hs-Crp, fibrinogen, and

WBC count remained unaltered in the days after exercise. The authors concluded that the exercise volume used may have required lower mechanical forces, resulting in less tissue damage and glycogen depletion that reported in other investigations. A study by Thomas et al.[406] supports this theory. Researchers studied the inflammatory response after running compared with weight training (high mechanical forces) and reported that weight training exercise produced sporadically higher levels of hs-Crp compared to no changes in hs-Crp after running.

Resistance Exercise

The effects of an acute session of resistance exercise on parameters of lipoprotein-lipid metabolism have not been thoroughly studied. Jürimäe et al.[144] examined the blood lipid response to an intensive single-circuit weight training session in untrained males (N =15). Subjects performed 10 exercises in the circuit. 3 circuits were performed using a work to rest ratio of 30 seconds:30 seconds at 70% of their 1 RM. The whole program lasted 30 minutes. Blood samples were obtained 30 minutes before exercise, immediately, 1 h, 6 h, and 24 h after the exercise session. The researchers reported that concentrations of HDL-C and TG were not significantly altered in untrained subjects 5 min after completion of the 30 minute single-circuit weight-training session. However, a measured elevation in HDL-C did reach significance 1 h after the single session of resistance exercise (+ 0.21mmol / L). Caution must be taken with interpretation of these results, as the researchers do not mention controlling for the last bout of exercise with regards to the blood-sampling period.

Recently, Wallace et al.[108] examined the blood lipid responses of 10 healthy, trained men before and after 90 min of either low volume or high volume resistance exercise. The high volume session used 8-12 RM loads performed to exhaustion with 60 seconds of rest while the low volume session used 1-5 RM loads with 3 minute rest intervals. Fasting blood samples were drawn before and after exercise as well as 24 h, 48 h, and 72 h after the exercise session. It was reported that the concentrations of HDL-C and TG were not significantly altered 5 minutes after a single session of both low and high volume resistance exercise. However, increases in the concentrations of HDL-C (11%) and HDL_3-C (12%) reached significance 24 h after the single, high volume, resistance exercise session (800 kcal), but not after the low volume exercise session (200 kcal). The estimated total energy expenditure for the volume of resistance exercise in the low volume group was around 210 kcals, similar to that estimated for the subjects in Jürimäe et al.[144] The exercise stimulus employed by Jürimäe and colleagues consisted of low volume circuit weight training. Wallace and coworkers employed both a low and high volume non-circuit approach. Future studies are needed to expand upon the limited body of knowledge in this area.

Hill and coworkers[143] evaluated the short term changes in blood lipids in response to a constant volume of resistance exercise of varying intensities. Six young (21 yrs), untrained males performed three different protocols: control (no exercise), high intensity resistance exercise, and low intensity resistance exercise. Each protocol was completed after a one week washout period. The eight exercises utilized by both protocols were the bench press, leg extension, shoulder press, incline sit-ups, seated

rowing, lateral pull-downs, barbell bicep curls, and leg presses. The high intensity session consisted of completing 8 different exercises at each subject's 10 RM. Subjects completed 3 sets of 10 repetitions with a 1 minute rest period in-between sets. The low intensity protocol was similar to the high protocol except that subjects performed the lifts at 50% of their respective 10 RM and each set consisted of 20 repetitions. Thus, the total work was the same for both protocols. Fasting blood samples were collected before, immediately, and 15 minutes after each trial. Moreover, blood sampling occurred 48 h after the last training session. The researchers reported that HDL-C was significantly elevated (42%) immediately after the high intensity exercise session. HDL-C increased 42% in the low intensity trial, but this did not reach statistical significance. Thus, the researchers concluded that an intensity threshold must exist for resistance exercise. However, while the researchers did measure plasma volume, the low number of subjects was a major limitation. The researchers reported that this might have reached significance if more subjects were included in the study.

Past and present research indicates that lipoprotein-lipid changes following a single session of prolonged exercise will often, but not always, include lower concentrations of TG,[69, 72, 77-82, 84, 85, 207, 376, 377, 398, 399] TC,[72, 78, 79, 81, 84-86, 207, 377, 382] VLDL-C,[79, 81, 83, 379, 382] and LDL-C.[69, 76, 78, 79, 81, 377, 388] Furthermore, transient increases in HDL-C[72, 76-78, 82, 84-86, 108, 376-379, 382, 385, 389, 390, 393-395, 401, 403] and the $HDL_{2\&3}$-C subfractions[69, 71, 72, 76, 77, 379, 385, 389, 394, 401, 402] have also been shown to occur. These alterations have been shown to occur during, immediately, and up to several days (72 h) after the acute exercise stimulus. However, it must be pointed out that similar to the

exercise training literature, the acute response is dependent on several factors. These include baseline physiological characteristics, initial lipoprotein-lipid profiles, training status and dietary habits of subjects, mode and intensity of the exercise stimulus, timing of blood sampling, and whether or not investigators eliminated the possible acute effects of previous exercise.

The Effect of Exercise on Lipoprotein-Lipid Metabolism: Possible Mechanisms

Lipoprotein Lipases

The role of exercise in reducing one's risk for developing CHD may be partly due to favorable alterations on the blood lipid profile.[41] Research supports the fact that health benefits, including an improved lipid profile, may result from a single session of exercise.[42-44] The biological mechanisms by which these improvements occur with exercise are not fully understood, but it is apparent that the activities of some lipid-regulating enzymes are enhanced with exercise. These enzymes and transfer proteins include lipoprotein lipase (LPL), hepatic triglyceride lipase (HTGL), lecithin:cholesterol acyltransferase (LCAT), and cholesterol ester transfer protein (CETP).

Endothelial-bound Lipoprotein Lipase

Energy for endurance exercise, a dynamic activity involving large muscle groups contracting rhythmically at low relative intensities, is provided primarily by oxidation of fats.[114] The energy demands associated with endurance exercise can eventually deplete intramuscular TG concentrations. It has been suggested that this depletion of intramuscular TG might stimulate secretion or synthesis of LPL in muscle capillaries.[115, 407] The main physiological function of LPL is to hydrolyze TG in chylomicrons and

VLDL to provide free fatty acids as an energy source in muscle tissue, to replenish intramuscular TG stores which may have been depleted during prolonged exercise, and for re-esterification and storage in adipose tissue. Furthermore, LPL-induced lipolysis of TG in muscle may be a major contributor to the generation of HDL-C.[211-214] Thus, greater LPLa is associated with increased TG clearance and HDL-C concentrations, changes indicative of decreased CHD risk.[115, 407] A decrease in LPLa is associated with high plasma concentrations of VLDL-TG, delayed and elevated postprandial lipids, and low HDL-C concentrations, leading to an increased risk for the development of CAD.[211-214]

Resistance exercise results in a different metabolic stress in muscle compared to endurance exercise. It is possible that resistance exercise, a high-intensity intermittent exercise involving small muscle groups, may produce unique changes in lipid metabolism compared to endurance exercise. A substantial portion of the energy requirement for resistance exercise is provided by stored phosphocreatine, blood glucose, and muscle glycogen. Pascoe and colleagues[109] have reported that strenuous resistance exercise has the potential to deplete muscle glycogen stores. It is believed that during recovery from resistance exercise lipids may be utilized as a primary source of energy (i.e., increased oxidation of fats) thus sparing carbohydrate to be used for the resynthesis of glycogen stores.[110, 111] Increases in fat oxidation may also be attributed to elevated levels of catecholamines, resulting in increased rates of lipolysis.[112] Catecholamine levels have also been shown to be distinctly increased during heavy resistance exercise compared with cycling or running exercise of similar volumes.[113]

There are data which suggest that both resistance and endurance training act through similar mechanisms to produce beneficial effects on circulating lipids. For example, induction of LPL has been reported after intense local contractile activity in muscles of both rats [116] and humans, [117] suggesting that local contractile activity may be necessary for increased LPL expression during exercise training.[116] Furthermore, Kiens et al.[52] reported that 8 weeks of one-legged dynamic knee exercise resulted in an increase in muscle LPL and the concentration of HDL_2-C in the trained legged, but not in the untrained muscle. Since muscle is an important site of TG removal in humans, LPL induction and lipolysis in muscle may be essential for increasing HDL-C concentrations.[117] Given that strenuous muscle contraction accompanies both resistance and endurance exercise, both modes of exercise could, in theory, be capable of inducing an LPL response in skeletal muscle.

Regulation of LPL: Diet & Weight Loss

It has been shown that 8 h of normal eating in humans will increase adipose tissue (AT) LPLa by 46%, and decrease skeletal muscle (SM) LPLa by 32%.[53] Weight loss can also have a profound effect on SM LPLa. Both acute caloric deficits and substantial weight loss maintained via isocaloric feeding produced a decrease in SM LPLa. In a 3 month supervised weight-loss study, 11 obese women were studied after 2 days of isocaloric feeding. Before the study, SM LPLa was 13% lower when compared to normal weight controls. After the study, and an average weight loss of 12 kg, an additional 70% decline in fasting SM LPLa was noted.[408]

Elevated insulin levels, which accompany carbohydrate ingestion, may lower SM LPLa. It appears that SM LPLa is responsive to insulin, but the response is impaired in insulin resistance. Insulin is predominantly responsible for the effects of fasting and feeding on AT LPLa. Insulin resistance in adipose tissue has been suggested to be the cause of hypertriglyceridemia in obese people with noninsulin dependent diabetes.[268]

Regulation of LPL: Hormones

Data in both rats and humans show that catecholamines increase SM LPLa and decrease AT LPLa. Plasma norepinephrine was positively related to SM LPLa during a 2-hour saline infusion. Also, isoproterenol (beta agonist) significantly increased muscle LPLa. Pedersen et al.[409] reported the effects of exogenous epinephrine on SM LPLa and total-body lipid oxidation in 8 healthy male volunteers. Subjects reported to the lab having refrained from physical activity during the preceding 24 h. Muscle biopsies were obtained before, during, and after 2 h of epinephrine infusion. Somatostatin was also infused in order to suppress endogenous insulin production. Epinephrine stimulated SM LPLa by 21.8% above baseline levels, increased FFA 270%, and increased lipid oxidation by 45%.

SM LPLa is usually elevated in hyperthyroidism and depressed in hypothyroidism. SM LPLa has been shown to be 46% higher in thyrotoxic patients.[271] Active LPL anchored to the capillary wall might be displaced by elevated local arterial concentrations of circulating fatty acids. It is speculated that fatty acids may inhibit the translocation of LPL from its site of synthesis to its functional site at the capillary endothelium.[410] Thus, the effect of LPLa on lipid metabolism has been shown to depend

on the intensity of the exercise stimulus, the hormonal response to the exercise intervention, the training status of the subject, and the nutritional composition of the individual's diet.[49, 57, 214]

Regulation of LPL and Hepatic Triglyceride Lipase: Exercise

LPL mRNA has been shown to increase when skeletal muscle has been biopsied shortly after exercise. The greatest rise in LPL mRNA occurs between 0 and 8 h post-exercise. Elevated muscle LPLa may explain the rise in post-heparin plasma LPLa that occurs 24 h following acute exercise.[76] Insulin levels are decreased in response to acute exercise, remain attenuated after the exercise session, and are depressed following chronic exercise training. Furthermore, SM LPLa is elevated in these same scenarios suggesting an inverse relationship between insulin and muscle LPL. It has been shown that catecholamines can also increase resting SM LPLa.[408] Cycle ergometry exercise of approximately 40-70% $\dot{V}O_{2peak}$ has demonstrated increases in catecholamine levels.[411] In young healthy adults, the maximal rate of lipid oxidation occurs during work intensities around 65% $\dot{V}O_{2peak}$, and at this intensity, utilization of intramuscular triglyceride is maximal as well. When work intensities reach 80-90% $\dot{V}O_{2peak}$, lipid substrate utilization is decreased and CHO becomes the primary fuel.[412] Cross-country skiing, lasting 8 h, depleted the intramuscular TG content of slow twitch fibers by 65% and fast twitch fibers by 35%.[53] When endurance exercise (55-70% of $\dot{V}O_{2peak}$) was performed for several hours, intramuscular TG content decreased by 30-41%, demonstrating that high volume exercise can indeed deplete intramuscular lipid stores.[53]

Skeletal muscle contributes about half of the metabolic activity in our bodies during the resting state and makes up about 40% of our total body weight.[272] There is an apparent interindividual variation in the muscle fiber distribution. There may be as much as a 10-90% variation of the percentage of ST fibers within the population. People with a high ST fiber % tend to have higher LPLa in their SM, thus being able to utilize more fatty acids liberated from TG-rich lipoproteins than people with a lower percentage of ST fibers.[272, 413] Wade et al.[414] reported an inverse relationship between the proportion of ST fibers and levels of fatness. Using data obtained from the respiratory exchange ratio during exercise, it was revealed that lean men with a higher % of ST fibers consumed more fat during the exercise session than obese men with a lower ST fiber %. Tikkanen et al.[413] also reported finding a relationship between an individual's muscle fiber distribution and their lipoprotein-lipid levels. Groups of sedentary men, active joggers, and CHD patients all demonstrated different serum lipid levels as well as the percentages of ST fibers in the lateral portion of the quadriceps femoris muscle. A positive association was found between the HDL-C concentration and the ST % while a negative association was reported between the serum TG concentration and percentage of ST fibers. The authors attributed the results to increased capillaries around the ST muscle fiber which would result in higher LPLa within the muscle.

In general, the highest amounts of LPL are detected in slow-twitch red fibers, followed by fast-twitch red fibers. Fast twitch white fibers have very low LPL activity. Tikkanen et al.[272] demonstrated an association between muscle LPL of various fiber types and plasma HDL levels. They determined that slow-twitch fibers with a high

capacity for oxidative energy metabolism are especially important for high plasma HDL levels.

Kiens and Lithell [52] evaluated the effects of both acute exercise and exercise training on lipoprotein-lipid and skeletal muscle tissue metabolism. Six healthy male subjects underwent 8 weeks of single-leg knee extensor exercise training (1-2 h / day, 65% of $\dot{V}O_{2peak}$, 3-4 days per week). Lipoprotein-lipid and lipoprotein enzyme activity in the trained knee extensors was compared to the non-exercising leg at rest. Muscle biopsies were performed to examine LPLa. Arteriovenous (A-V) differences across the muscle bed were taken from both legs of the subjects. A significant increase in capillary density was observed in the trained muscle after the 8 week exercise training program. Furthermore, there was a significantly greater A-V VLDL-TG difference over the trained thigh, compared to the contralateral thigh. A higher production of HDL-C and HDL_2-C was also observed in the trained leg. Moreover, muscle LPLa in the trained leg was 70% higher compared to the non-trained leg, and this increase correlated with the increased capillary density. Thus, 8 weeks of exercise training induced an increase in TG uptake as well as HDL-C production.

A subsequent study from the previous investigation examined the lipoprotein enzyme response, in the trained leg, to 2 h of knee extension exercise at 65% $\dot{V}O_{2peak}$. The post-exercise muscle LPLa was elevated after the acute bout of knee extension exercise, but this did not reach statistical significance. Furthermore, when compared with resting values, the venous HDL_2-C concentrations were greater during exercise.

The researchers concluded that the increases in HDL-C production were related to the degradation of VLDL-TG during the exercise session.

Seip and coworkers[117] assessed the effects of 5-13 consecutive days of exercise ($\geq$ 60 minutes / day, 60-75% of $\dot{V}O_{2peak}$) on the tissue expression of LPL in 32 untrained, weight stable adults. Blood and biopsy samples were obtained 14 h -18 h after the last exercise session. Significant decreases in plasma TG (26%), TC (3.9%), and VLDL-C (27%) were noted after exercise. Furthermore, the concentrations of HDL-C and HDL_2-C were significantly elevated after the exercise. In skeletal muscle, short-term exercise training increased the mean LPL mRNA level by 117%, LPL protein mass by 53%, and the total LPLa by 35%. In contrast, no changes in adipose tissue LPL metabolism were observed.

Baumstark and colleagues[206] examined the effects of a 30 km cross-country run on serum lipoprotein-lipid concentrations and on the composition of lipoprotein subfractions in 13 trained men. Fasting blood samples were obtained before, 1 h, and 20 h after the run. Serum TG concentrations were significantly reduced (36%) as a consequence of a reduction in the number of VLDL particles (31%). It was reported that the prolonged exercise did not induce significant changes in the average concentration of the LDL subfractions. Similar to the work of Lamon-Fava,[85] a reduction in dense LDL occurred in subjects who experienced large reductions in serum TG. Immediately after the run (1 h) the TG content was significantly reduced in all LDL subfractions. As previously mentioned, it is generally accepted that beneficial changes in the lipid profile which occur after exercise are the result of increased LPLa producing an increase in the

peripheral clearance of TG-rich lipoproteins. This enables the body to replenish intramuscular TG stores which may have been used as a source of fuel during the actual exercise session. If increased lipolysis were the only factor leading to the decreased TG levels after exercise one would not expect a reduction in VLDL number but a reduced lipid content of the VLDL particle. In this study, Baumstark and coworkers have shown that the secretion of VLDL may be reduced after a prolonged exercise session. These findings were reiterated by Borsheim and colleagues[391] after they determined VLDL and VLDL related particles were decreased after 90 minutes of cycle ergometer exercise (58% of $\dot{V}O_{2peak}$) in active young men.[391]

Magkos et al.[403] examined alterations in lipid metabolism after a single, prolonged session (2 h) of cycle ergometer exercise (60% of $\dot{V}O_{2peak}$). Fasting blood samples were obtained before and 24 h after exercise. Skeletal muscle LPLa was not altered but plasma LPLa was significantly elevated (20%) after exercise. Both HTGLa and LCATa were not affected by the exercise session, whereas CETP concentration was decreased (10%) after exercise.

Zhang and coworkers[195] examined the time course changes in LPLa and RCT variables after an acute bout (60 minutes) of treadmill exercise (60% $\dot{V}O_{2peak}$) in 16 sedentary men with normal and abnormal lipid profiles. Fasting blood samples were obtained before, 4 h, 8 h, 12 h, and 24 h after the exercise session. It was noted that LPLa was significantly elevated 24 h after the exercise session. Furthermore, HTGLa

was significantly elevated at 8 h, 12 h, and 24 h post-exercise compared with the 4 h time-point. The activities of LCAT and CETP did not change over the 24 h time period.

In an effort to evaluate the effect of different volumes (kcals) of exercise on LPLa, Visich and coworkers[133] examined the lipoprotein-lipid response in 12 trained men after treadmill exercise (75% $\dot{V}O_{2peak}$) of varying energy expenditures (expending ~ 400, 600, and 800 kcals). Blood samples were obtained before, immediately, 1 h, 6 h, and 24 h after exercise. No exercise volume by time interactions were significant for any of the dependent variables. Data collapsed across exercise volumes revealed an increase in plasma volume adjusted HDL-C (5.8%) and HDL_3-C (11.7%) 24 h after exercise. The concentration of TG was also significantly depressed (13%) 24 h after exercise. LPLa was significantly elevated (19%) while HTGLa was alternately depressed (14%) 24 h after exercise. The authors were not able to determine an exercise threshold necessary to significantly alter HDL-C.

Subsequently, Visich and coworkers[401] evaluated the effects of a single session (600 kcals) of treadmill running (75% $\dot{V}O_{2peak}$) on LPLa in 12 trained men. Blood samples were obtained before, 6 h, and 24 h after exercise. No significant time changes were noted for any of the plasma volume adjusted lipoprotein-lipids. However, LPLa was significantly elevated (27.5%) 24 h after exercise. Researchers determined that a caloric volume of 600 kcals was insufficient to promote beneficial alterations in lipid metabolism despite an increase in LPLa.

Increased LPLa has also been observed in exercise training studies. In addition, exercise training has also been shown to increase intramuscular TG stores as well as

oxidative enzymes, which will ultimately aide skeletal muscle in taking up and metabolizing fat for energy production.[53, 215] Increases in muscle capillary density have also been reported in addition to increased gene expression, production, and secretion of skeletal muscle LPL.[57, 117, 215]

Svedenhag et al.[415] investigated the effects of 8 weeks of cycle ergometer training on thigh muscle LPLa and capillary density in healthy young men. In addition, they blocked the sympatho-adrenal influence on the LPLa response to training by treating a subgroup of volunteers with propranolol (beta blocker). The training sessions were held four times per week and each session lasted 40 minutes. Training intensities started at 60% of $\dot{V}O_{2peak}$ during the first week, eventually progressing to 75% $\dot{V}O_{2peak}$ during weeks 5-8. $\dot{V}O_{2peak}$ increased 8% by the end of the program. Muscle LPLa increased 47% in the placebo group and 31% in the subgroup receiving propranolol. Capillary density increased 19% in the placebo group and 17% in the subgroup receiving propranolol.

Duncan and coworkers[416] reported that LPLa was significantly higher after 6 months of endurance exercise training, (30 minutes / day, 45-75% of heart rate reserve, 3-7 days per week) without weight loss, in previously sedentary adults.

Stubbe and coworkers[56] evaluated lipoprotein enzyme activity after 6 weeks of endurance training in 18 healthy sedentary men. A 50% increase in AT LPLa was noted after the training program. Likewise, Peltonen and colleagues[55] observed increases in both plasma (33%) and AT (56%) LPLa, respectively, after a 15 week endurance training program in 20 middle-aged men.

An investigation by Hamilton and colleagues[116] provided evidence that local contractile activity can be a major determinant of LPL regulation in skeletal muscle. Rats that had access to voluntary running wheels and were estimated to have run about 3 hours a day demonstrated significant increases in LPL mRNA, protein concentration, total LPL enzyme activity, and heparin-releasable activity in skeletal muscles with a large increase in contractile activity (recruited for running). The high activity of LPL mRNA, mass, and activity in the soleus muscle decreased significantly after the hind limbs of a group of rats were immobilized for 7 days. This suggests that the activation of postural muscles (local contractile activity) primarily caused the increased LPL levels. Furthermore, expression of LPL mRNA, protein, and activity was significantly greater in the tibialis anterior muscle after electrical stimulation for 4 hours a day compared to the inactive tibialis anterior muscle in the contralateral leg.

There are two schools of thought on how muscle senses "exercise signals" to induce LPL expression. One category of stimuli is "systemic signals" related to plasma hormones and the other category is "local signals" related to contractile activity. Results from Hamilton et al.[116] clearly support the latter category. Moreover, support for the humoral hypothesis might be indicated if LPLa was induced in a non-contracting muscle. However, there were no increases in LPL mRNA, mass, total activity, or heparin-releasable activity in the masseter muscle (jaw muscle), which was not recruited during voluntary cage running. Overall, these studies have demonstrated that local contractile activity is a major determinant of LPL regulation in skeletal muscle.

Hepatic triglyceride lipase (HTGL) activity (HTGLa) has also been shown to be altered in response to a single prolonged exercise session as well as with exercise training. HTGL also plays a role in the regulation of plasma HDL levels. HTGL has been shown to participate in the conversion of HDL_2-C particles into the smaller and denser HDL_3-C. This occurs through the hydrolysis of TG and phospholipids from the HDL_2-C substrate and the subsequent transfer of cholesterol esters to other lipoproteins.[273] It has been reported that concentration of HDL-C is inversely correlated to postheparin plasma HTGL activity (HTGLa).[262, 269] Thus, a decrease in HTGLa should result in an increase in HDL_2-C due to a slower catabolism thereby promoting a favorable lipid profile, changes indicative of decreased CHD risk.[115] In contrast, an increase in HTGLa is associated with the lowering of plasma HDL_2-C.[262]

Gordon and coworkers[71] evaluated the effects of two isocaloric (800 kcals) sessions of treadmill running at 60% or 75% $\dot{V}O_{2peak}$ in 12 recreational runners. The plasma volume adjusted concentration of HDL-C was significantly elevated (5 mg / dL) 24 h after exercise only with the higher intensity (75%). The increase in HDL-C was attributed to an increase in HDL_3-C, with no change in HDL_2-C. When trials were combined, lipoprotein enzyme analysis revealed a significant increase in LPLa (15%) 24 h after exercise with a concomitant decrease in HTGLa (12.5%). These results suggest that alterations in HDL metabolism following an acute session of endurance exercise may be influenced by the intensity of exercise session.

Gordon et al. [176] demonstrated increases in plasma volume adjusted HDL-C and HDL_3-C in 12 moderately trained men after a prolonged running session on a treadmill.

Subjects exercised at 75% of their $\dot{V}O_{2peak}$ for a duration that allowed them to expend 800 kcals. Analysis of lipoprotein enzyme data reveal that LPLa was elevated and HTGLa depressed 24 h after the exercise session, although neither reached significance.

In an effort to determine the energy expenditure necessary to favorably alter lipoprotein-lipids, Ferguson and coworkers[132] examined the lipid response in 11 well-trained men after completing 4 different exercise sessions of varying energy expenditures (expending ~ 800, 1100, 1300, 1500 kcals). Exercise sessions were spaced 2 weeks apart at 70% of the subject's $\dot{V}O_{2peak}$. Blood samples were obtained before, immediately, 24 h, and 48 h after exercise. A transient decrease in TG (26%) was noted to occur 24 h after the 800 kcal exercise session. Plasma concentrations of HDL-C were only significantly elevated in exercise sessions that consisted of energy expenditures of 1100 kcal or more. The authors concluded that energy thresholds for trained men do indeed exist. Energy expenditures of 1100 kcal were required in order to elevate plasma HDL-C, while 1300 kcal expenditure was necessary to decrease LDL-C. LPLa was significantly elevated 24 h after exercise in the 1100, 1300, and 1500 kcal sessions, and continued to remain elevated 48 h after exercise in the 1500 kcal session. A significant decrease in HTGLa was noted to occur 24 h after exercise in the 1300 kcal session. While there are studies supporting a reduced HTGLa with prolonged exercise,[71, 394, 396, 399] others have demonstrated that HTGLa was not altered prolonged exercise.[76, 77]

Inconsistent responses of HTGLa with exercise training have also been reported. Stubbe et al.[56] reported a reduction in HTGLa (6%), in addition to the increase in AT LPLa previously reported. Thompson and coworkers[57] also reported a lowered HTGLa

several weeks of stationary cycle training. Leon et al.[163] reported significant increases in LPLa for both men (18%) and women (6.6%). HTGLa was significantly reduced 6.9% in men and 5.1% in women following 20 weeks of supervised bicycle training. The authors stated that a possible heritable factor contributing to the HDL-C responsiveness to exercise training was the relative proportion of type 1 red skeletal muscle fibers in their subjects, which are known to have higher LPLa. Conversely, Grandjean et al.[162] reported that HTGLa did not change in response to exercise training in pre- and postmenopausal women.

Lecithin: Cholesterol Acyltransferase

LCAT catalyzes a transesterification reaction in which an acyl group from the 2-position of phosphatidylcholine (PC) is transferred to the 3-hydroxyl group of cholesterol, converting PC to lyso-PC and cholesterol to cholesterol ester.[237, 239] The optimal substrate for LCAT is discoidal HDL. The activity of LCAT decreases as CE accumulates in the core of the spherical molecule. With the increase in the uptake of CE, HDL will increase in size to form the HDL_3 particle. A continual transfer of cholesterol esters into the hydrophobic core eventually yields the larger HDL_2 particle.[241, 246, 256] In addition, exercise may increase the concentration of LCAT's cofactor, apo A-I.[42, 56, 85, 131, 140, 169, 390, 393] It is generally accepted that high cholesterol esterification rates promote efflux of cholesterol from peripheral tissues, and that elevated LCAT activity presumably protects against atherosclerosis.

Cross-sectional investigations have reported elevated LCAT activity in physically fit subjects when compared to sedentary controls.[59] Marniemi et al.[417] and

Tsopanakis et al.[418] both reported elevated LCAT activity in endurance trained men. Furthermore, Gupta and colleagues[59] reported increased LCAT activity in athletes when compared to sedentary control subjects.

Alterations in LCAT activity in response to prolonged exercise have been inconsistent. Magkos et al.[403] examined alterations in lipid metabolism after a single, prolonged session (2 h) of cycle ergometer exercise (60% of $\dot{V}O_{2peak}$). LCAT activity was not affected by the exercise session. Zhang and coworkers[195] examined the time course changes in reverse cholesterol transport variables after an acute bout (60 minutes) of treadmill exercise (60% $\dot{V}O_{2peak}$) in 16 sedentary men with normal and abnormal lipid profiles. The activity of LCAT did not change over a 24 h time period. Grandjean et al.[138] did not observe any changes in LCAT activity in normo- and hypercholesterolemic men after a single session of treadmill walking. Berger et al.[392] investigated the effects of a moderate exercise session on LCAT activity in a group of 12 moderately fit men. Blood samples were collected before and after the 5.5 km run. LCAT activity was not significantly altered in response to the exercise session; however a small elevation was noted.

In contrast, Dufaux et al.[72] noted a significant increase in LCAT activity in 14 active men after completing a 3 h treadmill run. Campbell et al.[404] examined the differences in the lipid response to an isocaloric session (expending ~ 450 kcals) of treadmill running (65% of $\dot{V}O_{2peak}$) in 1 continuous session or 2 intermittent and 3 intermittent sessions, each separated by 4 hours. LCAT activity was significantly

elevated 48 h after exercise in the continuous (12%), and 3 intermittent (12%) exercise sessions.

There are few exercise training studies that have examined LCAT changes. Thomas et al.[419] observed no change in LCAT activity or HDL-C concentrations in college students after 11 weeks of interval or continuous exercise training. In addition, Grandjean et al.[162]found that LCAT activity was unaltered after 12 weeks of exercise training in pre- and postmenopausal women. In contrast, Sutherland and coworkers[420] reported increases in the fractional rate of cholesterol esterification (indices for LCAT activity) in both normo and hypercholesterolemic subjects completing a 16 week exercise training program. It appears that both a single session of exercise and exercise training can induce alterations in LCAT activity. However, the reported results are inconsistent.

Cholesterol Ester Transfer Protein

CETP is not considered an enzyme, but a protein that has an affinity for non-polar lipid transfer.[237] CETP mediates the transfer of CE (produced from the LCAT reaction) from HDL to VLDL or LDL and of TG from VLDL and LDL to HDL. The CETP mediated transfer of these non-polar lipids is reversible; however, this net transfer is driven by preexisting concentration gradients. The rate and direction of the net lipid transfer is established by gradients maintained by LPL and LCAT.[237]

The CETP reaction increases the capacity of the plasma to clear CE, by reusing VLDL, IDL, and LDL molecules to transfer the CE back to the liver for catabolism. Thus, the CETP-mediated transfer of neutral lipids is a process that works in concert

with the LCAT reaction. Furthermore, the utilization of HDL to transfer TG back to the liver provides an additional pathway involving HTGL.[237]

The atherogenicity of CETP activity has been consistently debated. It has been suggested that CETP can potentially inhibit atherogenesis by enhancing the rate of reverse cholesterol transport. CETP mediated transfers from HDL to VLDL and LDL provide a potential indirect pathway by which HDL CE's can be delivered to the liver for catabolism.[242, 243] Prolonged exercise, which commonly results in reduced TG concentrations after lipolysis, might decrease the rate of CETP activity. This would allow HDL-C to remain elevated in the circulation. Human subjects with a homozygous CETP deficiency have elevated concentrations of HDL cholesterol, apo A-I, apo A-II, and apo E. The increased HDL concentration is primarily due to a reduction in the rate of catabolism, with a markedly delayed catabolism of apo A-I and apo A-II. However, if elevated HDL_2-C levels occur due to a CETP deficiency a reduced capacity for cholesterol efflux occurs.[274] The HDL_2-C from CETP-deficient patients has a reduced ability for cholesterol efflux compared to normal HDL_2. Conversely, species with high or moderate levels of CETP activity are susceptible to atherosclerosis, and do not develop prominent HDL-C. Enhanced CETP activity may promote increased cholesterol-rich IDL particles and cholesterol-poor HDL particles, which may lead to promoting premature atherosclerosis.[276]

Serrat-Serrat et al.[61] reported that CETP activity was lower in marathon runners compared to sedentary control subjects. The runners also had lower TG, VLDL-C, and higher HDL-C concentrations than the control group. A positive correlation between

CETP activity and TC and LDL-C was noted, while apo A-I was negatively associated with CETP activity in the marathon runners. In contrast, Gupta et al.[59] examined lipid metabolism and reverse cholesterol transport in athletes and sedentary control subjects. The athletes were reported to have higher CETP activity compared to their sedentary counterparts.

Seip et al. [60] compared plasma CETP concentrations in sedentary men and women before and after 1 year of exercise training. HDL-C significantly rose (4.9%) in response to exercise training, with most of the increase attributed to an increase in HDL_3-C. The concentrations of CETP was lower (13.5%) in response to the training program. It has previously been demonstrated that concentrations of CETP have been positively correlated with CETP activity.[421] Moreover, the concentration of CETP decreased in both subjects who lost weight and in those who remained weight stable. Thus, exercise training decreased plasma CETP independent of weight change.

Takanami and colleagues[422] reported that CETP concentrations were significantly lower, while HDL-C was elevated, in 32 male athletes 24 h after completing an endurance triathlon. Magkos et al.[403] reported that CETP concentrations were lower (10%) after a single, prolonged session (2 h) of cycle ergometer exercise (60% of $\dot{V}O_{2peak}$). This result approached, but did not reach statistical significance. Foger and colleagues[218] examined lipoprotein-lipid changes associated with a bicycle marathon (230 km) in 8 well-trained men. Blood samples were taken 2 days before, then up to 8 days after the race. The HDL-C concentration increased significantly by day two, resulting from equal increases in both HDL_2-C and HDL_3-C. CETP mass and

CETP activity were significantly reduced (44% and 33%) 24 h after exertion; which may help explain the increases in HDL_2-C.

In contrast, Zhang and coworkers[195] examined the time course changes in reverse cholesterol transport variables after an acute bout (60 minutes) of treadmill exercise (60% $\dot{V}O_{2peak}$) in 16 sedentary men with normal and abnormal lipid profiles. The CETP activity did not change over the 24 h time period. Furthermore, Campbell and coworkers[404] determined that CETP activity was unaltered after subjects completed an isocaloric session (expending ~ 450 kcals) of treadmill running (65% of $\dot{V}O_{2peak}$) in 1 continuous session or 2 intermittent and 3 intermittent sessions. Grandjean and coworkers[138] reported similar results in sedentary normo- and hypercholesterolemic men after a single session of treadmill walking (70% $\dot{V}O_{2peak}$, 500 kcals expended).

The concentration of CETP and / or CETP activity can be altered in response to exercise training or a single prolonged exercise session.[59-61, 376, 400] Similar to the literature regarding LCAT, consistent data is lacking. Additional research is warranted before definite mechanisms in response to exercise can be established.

Non-Traditional Risk Markers

Hs-Crp

Numerous research studies have reported a significant association between elevated serum or plasma concentrations of hs-Crp and the prevalence of underlying atherosclerosis and the incidence of first cardiovascular events among individuals at risk for atherosclerosis.[120] Furthermore, hs-Crp levels > 6 mg / l were associated with a 75%

higher risk of restenosis compared to subjects with values < 1 mg / l during a 5-year follow-up study in patients with CVD.[282] Among patients with stable angina and established CHD, levels of hs-Crp have consistently demonstrated an association with the recurrent risk of cardiovascular events.[282]

General population studies report that there is an inverse association between serum hs-Crp levels and self-reported physical activity and physical fitness.[341] It is believed that regular exercise might favorably lower hs-Crp levels by an anti-inflammatory action. Mattusch et al.[125] evaluated the hs-Crp levels in the blood of 12 moderately trained runners (34 yrs) preparing for a marathon. In 10 of 12 runners the baseline hs-Crp levels were significantly reduced (31%) after training. No changes were noted in the non-exercising control group, suggesting that endurance training may have a suppressive effect on certain inflammatory processes in the body. The authors hypothesized that after training less interleukin-6 and other cytokines are produced in the exercising muscle as a result of an enhanced antioxidative protection.

However, another explanation provided is that exercise lowers hs-Crp levels by reducing total or abdominal body fat. It is known that adipocytes synthesize cytokines that are involved in the production of hs-Crp. It has been proposed that adipose tissue-secreted IL-6 and TNF-alpha may contribute to elevated levels of hs-Crp observed in obese subjects.[366] Thus, exercise training may reduce hs-Crp levels by reducing adiposity. It is also known that interleukin release from adipose tissue is augmented by increased sympathetic stimulation, which is down regulated by physical activity.

Research also suggests that exercise favorably influences the inflammatory process through additional mechanisms. One other potential mechanism is that exercise exerts its beneficial effects through improvements in endothelial function. Endothelial cells can also secrete IL-6 and IL-1, which can induce an acute phase response. It is known that exercise can improve endothelial function, thus attenuating the secretion of these pro inflammatory cytokines.[276, 277] Thus, the end result is a lower level of hs-Crp.

LDL Subfractions

Increasing evidence suggests that several subfractions of LDL, which are characterized by variations in size, flotation rate, density, and chemical composition of LDL particles, have important clinical significance in relation to CHD risk reduction. Given a certain level of LDL-C, the risk for developing CHD can differ depending primarily on the LDL particle number as well as the size of the lipoprotein particle.[286, 287] One's risk for developing CHD is increased if they have larger numbers of LDL particles and smaller rather than larger LDL diameters.[289]

Production of these small dense, atherogenic LDL particles have been mentioned previously. Enhanced VLDL secretion from the liver is often accompanied by a subsequent series of events involving 2 key proteins in lipoprotein metabolism, CETP and HTGL. As TG-enriched VLDL enters the plasma at an accelerated rate, the TG in the VLDL are exchanged for the cholesterol ester in the core of LDL, producing a depleted, but TG-enriched LDL particle. The TG in the core of LDL is then hydrolyzed by HTGL producing small dense LDL particles. The CE in the core of the HDL may also be exchanged by CETP for the TG in VLDL, producing a TG-enriched but CE

depleted HDL particle. The TG–enriched HDL appears to be catabolized more rapidly by the kidney, thus resulting in low HDL levels.[213, 216, 241, 245, 246]

Theoretically, decreased activities of both HTGL and CETP would prohibit these conversions from occurring. A lower CETP activity would diminish the exchange of TG from VLDL to LDL, thus preventing the eventual hydrolysis of the TG-enriched LDL particle and production of a small dense LDL particle. Furthermore, a lower HTGL activity would limit the hydrolysis of both TG-enriched LDL and HDL particles, changes indicative of decreased CHD risk.[115]

Small, dense LDL particles may also be generated when excess TG on VLDL are exchanged for cholesterol esters on LDL by CETP, producing TG-rich LDL, which then undergoes lipolysis by HTGL to produce smaller and denser LDL particles.[299] In a cross-sectional investigation Zambon et al.[300] reported that high HTGLa is associated with an increase in small, dense LDL particles and a decrease in HDL_2-C. As previously mentioned, a single prolonged exercise session and exercise training have both been reported to lower the activities of CETP.[59-61, 376, 400] While there are studies supporting a reduced HTGLa with exercise training[56, 57, 181] and prolonged exercise,[71, 394, 396, 399] others have demonstrated that HTGLa was not altered prolonged exercise.[76, 77]

Resistance Exercise and Excess Post Exercise Oxygen Consumption (EPOC)

Energy expenditure associated with exercise consists of both the energy expended during the actual exercise session as well as the energy expended during the post exercise recovery period. The elevation in energy expenditure above resting levels during the post exercise period is often referred to as excess post exercise oxygen

consumption or EPOC.[423] Researchers have found that high intensity intermittent exercise may favor increased lipid oxidation during recovery when compared with steady state exercise.[424] Since resistance training is considered to be intermittent in nature; thus, it may induce a prolonged EPOC and a greater use of fat during recovery. Some indicate that the greater the exercise perturbation, the greater the magnitude of EPOC. Such metabolic perturbations may include elevated blood lactate levels, resynthesis of glycogen from lactate, elevated body temperature, phosphagen resynthesis, elevated catecholamines, and residual hormonal effects.[425]

As the intensity of exercise increases, the contribution of fat as a fuel source decreases, resulting in a greater reliance of carbohydrate utilization during exercise. Performing strenuous resistance exercise depends on the anaerobic metabolism of phosphocreatine and glycogen for energy leading to a depletion of glycogen stores. During recovery from exercises that deplete glycogen stores, lipid becomes the predominate fuel. This indicates a shift towards elevated fat oxidation while sparing CHO to be used for glycogen resynthesis.[426] Vigorous, glycogen depleting, anaerobic exercise may contribute to a possible lipid deficit, which may lead to greater lipid oxidation in the post exercise state and an overall change in energy balance. However, it is important to note that the amount of fat oxidized is very small and may be physiologically insignificant in terms of any meaningful change in body fat or body weight reduction.

Another possibility for differences in recovery energy relates to changes in homeostasis resulting from the physiological response to exercise. Factors affecting post

exercise recovery include elevated body temp, additional cardio respiratory work, phosphagen resynthesis, resynthesis of glycogen from lactate, resaturation of tissue water, tissue repair, and residual effects of hormones. Hormonal perturbations for catecholamines, cortisol, and growth hormone can be substantial if the repetitions per set of resistance exercise are high and the rest periods between the sets are less than 1 minute. Tissue damage and stimulus for tissue hypertrophy resulting from resistance training may be sufficient to contribute to the increased total energy required to recover.[427]

The magnitude and duration of EPOC appears to be influenced more by intensity than duration of exercise. Gore and Withers[428] suggest that there is no sustained elevation of metabolic rate after exercise of intensities less than 55% $\dot{V}O_{2peak}$ and 3 h duration. Thus, the low to moderate intensity exercise capable of being performed by the general public produces little excess energy expenditure during recovery and would appear to have little impact on weight control.

Binzen et al.[429] examined the acute effects of 45 minutes of resistance exercise on EPOC and substrate oxidation in 10 moderately trained women (premenopausal). Subjects participated in 2 energy expenditure (EE) trials on separate days. EE measures consisted of 3 time periods: pre-trial (20 min of baseline), trial (45 min of resistance exercise or controlled sitting), and post-trial (120 min of recovery to assess EPOC). The exercise session consisted of 3 sets of the following 9 exercises: chest press, shoulder press, leg squat, leg extension, leg press, seated row, latissimus dorsi pull down, bicep curl, and triceps extension (10 reps per set at 70% of 1RM). Rest intervals were

controlled at 1 minute between sets. Measurements were made during the follicular phase, 48 h after the last exercise session and 4-5 h postprandially. The exercise session burned 155 kcals compared to 50 kcals for the control trial. Estimates of substrate utilization were made during last 30 minutes of recovery when blood lactate levels returned to steady state conditions. Fat oxidation was significantly elevated for the final 30 minutes of recovery after resistance exercise vs. the control trial. Although the total EE was not different for the last 30 minutes, 79% more fat was used after the exercise bout than controlled sitting. The major finding was that after 45 minutes of resistance exercise, total EE remained significantly elevated above resting levels for at least 1 h and that fuel utilization favored lipid oxidation in the post-exercise period. The RER was lower after exercise demonstrating greater utilization of fats vs. controlled sitting.

Burleson et al.[430] determined that more energy can be required for recovery from weight training than typical steady-state exercise when the exercise sessions are matched for duration and oxygen consumption. EPOC was higher during the first 30 minutes of recovery but not at 60 or 90 minutes, after completion of a circuit of resistance exercises compared with EPOC measured after steady state endurance exercise.

Melby et al.[110] determined that the metabolic rate remained elevated above baseline levels during the post-exercise period for > 2 h and probably longer after a bout of resistive exercise. Subjects performed 6 sets (8-12 repetitions) of 10 different exercises at 70% 1 RM. Rest intervals were controlled at 3 minute turnovers. The total exercise duration was 90 minutes. Exercises used in the protocol were: bench press, bent-over row, leg extension, leg curl, military press, sit-ups, biceps curl, triceps

extensions, half-squats, and lateral raises. The authors reported that a strenuous bout of high-volume resistive exercise produced an elevation of post-exercise metabolic rate during a 2 h measured recovery period and a significantly higher resting metabolic rate (RMR) when measured 15 h after the exercise session. The RER was significantly lower the morning after, reflecting greater fat oxidation.

Melby and coworkers[431] determined the magnitude of EPOC during 60 minutes of continuous measurement following a single 42 minutes session of moderate intensity resistance exercise. Oxygen consumption was measured under resting conditions for 30 minutes before and 60 minutes after the exercise session. This procedure was repeated, for control purposes, on a separate day of quiet sitting. Each subject performed 3 consecutive sets of 10 repetitions of 4 upper and 3 lower body lifts at a weight equal to a 12 RM. Exercises used in the protocol were: bench press, bicep curl, triceps extension, leg extension, leg flexion, military press, and squats. A 2 minute turnover was used for the rest periods. Oxygen consumption was significantly higher during the 60 minutes of recovery following resistance exercise vs. pre-exercise and post-sitting values. The RER fell below 0.70. However, the authors noted that this result was most likely due to the conservation of CO_2 in response to the loss of excessive amounts of CO_2 during and shortly after the exercise session which was needed to buffer the lowered blood pH due to lactate accumulation. The EPOC was elevated for at least 60 minutes following the exercise session. However, the elevated metabolic rate only accounted for an expenditure of approximately 20 additional kcals.

Elliot et al.[384] measured the EPOC generated by: heavy-resistance, priority lifting; low-resistance, circuit-style weight training; and cycling endurance exercise. It was reported that both cycling and circuit training used significantly greater calories than did heavy lifting. However, heavy lifting and circuit training produced a significantly greater EPOC than cycling.

Osterberg et al.[432] examined the effects of strenuous resistance exercise on oxygen consumption in healthy, resistance trained women during the 3 h immediately following the exercise session. Furthermore, the RMR was measured 16 h following the exercise session. The exercise protocol (5 sets of 10-15 repetitions) consisted of the following exercises: bench press / bent-over row, leg extension / curl, military press /sit ups, bicep curl / triceps extension, and lunges followed by lateral raises. Resistance was set at 70% of the 1 RM. Rest periods were controlled at 2 minute intervals with the total exercise duration set at 100 minutes. During the final 30 minutes of the 3 h recovery, oxygen consumption was 13% higher than the pre-exercise baseline values. The RER measured during the 3 h recovery period was significantly lower compared to the pre-exercise baseline RER values. A mean increase of 4.2% in RMR from day 1 to day 2 was also noted. There was a 62% increase in resting fat oxidation at the time the RMR was measured on day 2 following resistance exercise compared to when measured on day 1 prior to the exercise session.

Melanson et al.[433] examined the effect of endurance and resistance exercises on post- exercise and 24 h energy expenditure and substrate oxidation. The researchers speculated that fat oxidation, post-exercise, and 24 h energy expenditures would be

greater on a day in which resistance exercise was performed. It was determined that the resistance exercise had a similar effect on 24 h energy expenditure and macronutrient oxidation as a comparable bout of endurance exercise. The increase in 24 h EE on the exercise days was primarily the result of an increase in the amount of CHO oxidized, with no difference in 24 h fat oxidation across exercise conditions.

Researchers have found that high intensity intermittent exercise favors increased lipid oxidation during recovery.[424] Resistance exercise is believed to induce a prolonged EPOC and a greater use of fat during recovery. This may occur in order to spare CHO to be used for glycogen resynthesis.[426] Vigorous, glycogen depleting, anaerobic exercise may contribute to a possible lipid deficit, which may lead to greater lipid oxidation in the post exercise state and an overall change in energy balance. Thus, this type of exercise may induce favorable alterations in the lipid profile. However, as mentioned previously, it is important to remember that the amount of fat oxidized is very small and may be physiologically insignificant in terms of any meaningful change in body fat or body weight reduction.

Conclusions

As mentioned previously, CHD is the single largest killer of American males and females.[2] Evidence indicates that CHD is associated with high blood concentrations of TC, LDL-C, TG, and with low concentrations of HDL-C. The risk for development of CHD may be reduced by increasing HDL-C, the less dense subfraction HDL_2-C, and by decreasing both LDL-C and TG concentrations.[4-10] Thus, an atherogenic lipid profile may be described as consisting of elevated TC, LDL-C, and TG and decreased

concentrations of HDL-C.[2, 11] However, most coronary events occur in people with normal LDL-C and HDL-C concentrations.[35] Thus, the traditional lipid panel may fail to detect almost 50% of people who are at an increased risk for CHD, possibly due to an inability to measure additional highly atherogenic biomarkers, such as Lp (a), IDL-C, NONHDL-C, LDL subfractions, and hs-Crp.[36] A more comprehensive lipid profile, including all lipoprotein classes as well as subclasses might lead to a more effective preventive treatment strategy for CHD.

The role of chronic exercise training in reducing one's risk for developing CHD may be partly due to favorable alterations on the blood lipid profile.[41] However, the biological mechanisms by which these improvements occur with exercise are not fully understood. It is apparent, though, that the activities of some lipid-regulating enzymes (e.g. lipoprotein lipase) are altered with exercise. While adhering to a physically active lifestyle has been associated with a more favorable lipid profile and a reduced risk of CHD,[41, 45] information regarding the optimal training modality (endurance, resistance, or combination endurance/resistance exercise) and volume (caloric expenditure) of exercise that will provide the most benefit has not been well defined.

Research supports the fact that health benefits, including an improved lipid profile, may result from a single session of exercise.[42-44] A single session of exercise may acutely alter lipoprotein-lipid concentrations for at least 48 hours after exercise. Therefore, depending on the timing of blood sampling in certain research studies, researchers may mistakenly attribute changes in the lipid profile to the effects of chronic exercise training when in fact the lipid alterations were induced by recent exercise.

In summary, published literature regarding the interrelationships between non-traditional lipid variables, hs-Crp levels, LDL subclass, and other behavioral risk factors, such as exercise, are limited and urgently require verification by additional research.[120] If exercise therapy is going to be effectively utilized as an intervention for CHD risk reduction, it is important to clearly define the role of each of these components (mode, volume) in order to provide physicians and exercise professionals with guidelines for developing and implementing safe and effective exercise prescriptions for their patients.

APPENDIX B

METHODS AND PROCEDURES

In this section a description of subjects, testing procedures, and exercise interventions will be provided. Testing procedures included physical measurements such as body composition, maximal strength testing, and maximal oxygen uptake. Blood sampling is described as well as blood sample analysis. Discussion of data in terms of statistical analysis will also be included.

Subjects

Recruitment

Subject recruitment began after the investigation was approved by the Texas A&M University Review Board for Human Subjects in Research and was limited to Bryan / College Station, Texas. Potential volunteers responded to flyers which were posted in a majority of the buildings on the Texas A&M University main campus.

Subject Selection

Thirty-six untrained male volunteers were initially recruited for this investigation from Texas A&M University and the surrounding community. To be eligible for this study, the volunteers had to be below the age of 40 and above the age of 18. Subjects were considered untrained if they have not participated regularly in endurance or resistance training (less than 2 exercise sessions / week and $\leq$ 20 minutes per exercise session) for at least the last three months. A verbal verification as to each volunteer's training status was obtained by the primary investigator prior to inclusion in the research study. All volunteers were asked to sign an informed consent approved by the Texas

A&M Institutional Review Board for Research with Humans (Appendix D) and completed a Health History Questionnaire. Volunteers were screened to exclude those who exhibited evidence of medical contraindications to exercise and heparin, were taking drugs known to affect lipid / lipoproteins or blood clotting, used tobacco products, or consumed more than two ounces of alcohol per day. A total of four subjects did not complete the study due to various injuries obtained from the exercise training program and one subject dropped out for unknown reasons. Therefore, the final subject selection included a total of 31 subjects. A copy of the Health History Questionnaire is found in Appendix E.

Experimental Protocol

Following an orientation meeting (week 1), the subjects were randomly placed into three groups (endurance, resistance, combination endurance / resistance) of twelve. The following week, all subjects, regardless of group assignment, were asked to report to the Applied Exercise Science Laboratory at Texas A&M University on two days for baseline physiological and performance measurements (week 2). During this week, body height / weight, daily physical activity, lung volumes, body composition, and waist-to-hip ratio was measured. Maximal exercise testing for both endurance and resistance exercise was also performed during this week. After the week of pre-testing, all subjects completed a series of blood draw procedures on three consecutive days, termed the pre-training, acute exercise period (week 3). Dietary data was also collected during all blood draw procedures. The subjects assigned to the exercise groups completed endurance, resistance, or combination exercise (see below acute exercise) at

an intensity of 70% maximal capacity. Blood was drawn the day before (baseline), and 24 hours (24 h) after exercise for assessment of dependent variables. All pre-training testing procedures were repeated at the end of the training period (post-training, acute exercise period). Thus, a series of 2 blood samples and dietary data were collected on two separate occasions in all subjects; pre-training acute, and post-training acute exercise periods. Maximal exercise testing and assessment of physical activity were performed on all subjects on three separate occasions; prior to training, after 6 weeks of training, and after 12 weeks of training. There was a total of 4 blood samples of about 16 ml (3 teaspoons) each taken from each subject. A generalization of the experimental protocol is presented in Figure B-1.

Diet and Physical Activity Records

Self-reported dietary records were used to assess the nutritional composition and caloric intake in each subject's diet over each of the two blood sampling periods. Subject's recorded their diet over a 7 day period (4 days prior and 3 days during the blood sampling protocol). The dietary intake logs prompted each subject to record the date, time, type, portion size, and preparation methods for anything that was consumed during the period of interest. In addition, subjects were given verbal instruction on the proper techniques for completing the dietary intake log. Also, each dietary intake log was accompanied by a written example of proper form completion and a summary of portion size estimation methods. Subjects were asked to maintain a similar diet during the post-training blood sampling protocol as they did during the pre-training blood

sampling series. All daily diet records were analyzed for caloric consumption and nutrient intake using the Food Processor SQL (Version 9.3, Copyright 2004) program.

A seven – day physical activity questionnaire (PAQ) was used to assess routine daily activity over the same period in which the dietary intake logs were kept. The questionnaire was adapted from the seven – day recall interview developed by Blair et al.[142] Subjects recorded the time they spent in certain activities that they rated as moderate, hard, or very hard. Subjects were also asked to record total sleep time for each day. The time each subject spent in a certain activity was multiplied by the rate of energy expenditure (kcal / kg / hr) in METS for that particular activity (sleep = 1 MET; light activity = 1.5 METs; moderate activity = 4 METs; hard activity = 6 METs; very hard activity = 10 METs). The daily relative kcal expenditure (kcal / kg / day) was calculated by summing the relative kcal expenditure from each particular activity (kcal / kg). Individual daily energy expenditure (kcal / day) was determined by multiplying the daily relative kcal expenditure by the subject's body weight (kg). Copies of the dietary intake log and physical activity questionnaire are found in Appendices F and G.

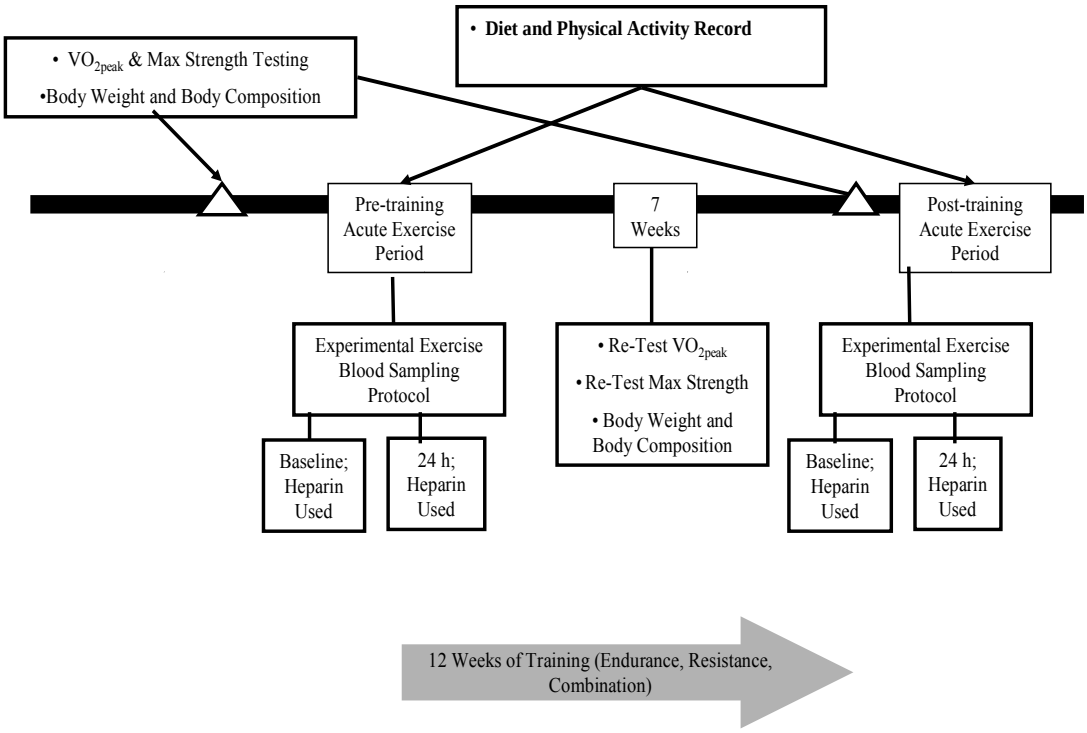

Figure B-1. Experimental Design. Baseline represents blood obtained 24 h before the acute exercise; 24 h represents blood obtained 24 hours after the acute exercise, respectively.

Physiologic Testing

Physiological testing was completed one week (week 2, visits 2 and 3) prior to the start of the blood sampling protocol (week 3). After reporting to the laboratory, each subject was measured for: 1) height and body weight (Weight); 2) waist girth (Waist) and hip girth (Hip); 3) relative body fat (% Fat); 4) lung volumes 5) peak oxygen consumption ($\dot{V}O_{2peak}$), and; 6) one-repetition maximum strength assessments (1RM).

Waist / Hip Girth and Relative Body Fat

Waist and hip girth measurements were recorded while the subjects were standing in an upright, but relaxed position. The waist measurement was recorded at the narrowest part of the torso, above the umbilicus and below the xiphoid process. The hip measurement was recorded at the maximal circumference of the hips or buttocks region, above the gluteal fold.[137] All measurements were recorded by the same trained exercise physiologist. The measurements were determined as the average of duplicate measurements within a range of 0.25 inches. The waist to hip ratio (W / H ratio) was calculated by dividing the average waist measurement by the average hip measurement.

Percent fat and lean body mass were calculated from body density measured hydrostatically at residual volume (RV).[434] Subjects were hydrostatically weighed while sitting on a PVC-pipe chair suspended from a Chatillon autopsy scale (John Chatillon & Sons, Inc., Model 1315 HDD – capacity 15 kg, Kew Gardens, NY) in a rapid-drain water tank. The weight of the subject was recorded after they completely submerged themselves underwater and exhaled 100% of their vital capacity. The hydrostatic weighing procedure was performed by the same trained exercise physiologist. The

procedure was performed until 3 consecutive underwater weight (UWW) measurements, within a range of 0.25 kg, were obtained. The average of these 3 UWW was then used to determine body volume (BV).

Body volume was determined as the difference between the subject's weight on land and their net weight under water at RV.[135] The net underwater weight (UWW minus the chair weight underwater) was corrected for residual volume, which is air trapped in the lungs after a maximal exhalation, the estimated volume of air in the gastrointestinal tract, and water density determined from water temperature.[135] Body volume was then calculated as:

$$BV = \frac{\text{Weight (kg)} - (\text{net UWW} + RV + GV)}{dW.}$$

Where: BV = body volume

WT = body weight

Net UWW = net underwater weight (under water weight minus the chair weight underwater)

RV = residual volume (estimated from gender and height) [435]

GV = gastrointestinal volume

dW = water density

Body density was then calculated as:

$$BD = \frac{WT}{BV}$$

Where: BD = body density
WT = body weight
BV = body volume

Relative body fat, expressed as a percentage of body weight, was estimated according to the formula of Brozek et al.:[434]

$$\% \text{ Fat} = [(4.570 / BD) - 4.142] \times 100$$

Where: % Fat = relative body fat

BD = body density

Exercise Testing for the Determination of $\dot{V}O_{2peak}$ and Maximal Strength

All subjects completed a standardized maximal graded exercise test (GXT) on a motor driven treadmill (Quinton Model # Q-65, Quinton Instrument Co., Seattle, WA) under the supervision of trained laboratory personnel.[136] Resting and maximum-exercise heart rate measurements were taken during the $\dot{V}O_{2peak}$ testing through the use of Polar® heart rate monitors. Blood pressure was determined manually, and ratings of perceived exertion were obtained during the last 30 seconds of every stage of the protocol.

Respiratory gas exchange (V_e, $\dot{V}O_2$, and $\dot{V}CO_2$) was measured continuously via open-circuit spirometry utilizing an automated metabolic cart (CPX / D Exercise Stress Testing System, Medical Graphics Corp., Minneapolis, MN) calibrated with gas mixtures of known composition (reference gas: O_2 = 20.85 %, CO_2 = 0.00 %; calibration gas: O_2 = 12.00 %, CO_2 = 5.00 %) before and after each test. The $\dot{V}O_{2peak}$ test was considered valid if at least two of the following criteria were met: 1) the maximum age-predicted maximum heart rate was achieved or; 2) the respiratory exchange ratio was greater than 1.1 or; 3) $\dot{V}O_2$ failed to rise with increasing workload.

All subjects were tested for strength by determining the maximum weight that can be successfully lifted one time with proper technique (1RM) after completion of a standardized warm-up. The warm-up consisted of 5 minutes of cycling, 5 minutes of stretching, and sets of light sets of 8, 5, 3, and 2 repetitions for each exercise. Subjects were required to perform a 1RM test in all of the exercises that were incorporated into the resistance-training program (leg press, leg curl, standing calf raise, barbell bench press, lat pull-down, dumbbell military press, barbell curl, and an abdominal crunch). Recovery time between sets and exercises were strictly controlled with two-minute turnovers.

Experimental Exercise Session Calculations

Using exercise data collected from the GXT tests, $\dot{V}O_2$ (L / min), heart rate (HR), respiratory exchange ratio (RER), and workrate at 70 % of $\dot{V}O_{2peak}$ were used in the individual exercise prescriptions for the experimental exercise sessions. This process is briefly described as follows: 1) $\dot{V}O_{2peak}$ was multiplied by 0.70; 2) the actual $\dot{V}O_2$ (L / min) from the GXT that corresponded closest to the value obtained in step 1 was obtained; 3) all GXT variables corresponding to the actual $\dot{V}O_2$ (L / min), identified in step 2, were used in creating the exercise prescription. These data were also used in the estimation of the exercise session duration needed to elicit an energy expenditure of 350 kcals. The kcal equivalent (kcals expended / L O_2) was determined from the RER at 70 % $\dot{V}O_{2peak}$.[423] Secondly, the rate of energy expenditure (kcal / min) was calculated by

multiplying the kcal equivalent by the respective absolute $\dot{V}O_2$ (L / min). Exercise duration (min) was estimated by dividing the target energy expenditure (350 kcals) by the rate of energy expenditure (kcals / min).

Pre-Training Acute Exercise Testing

After abstaining from any physical exercise for at least 72 hours, each subject reported to the laboratory (12-hour fast, water allowed *ad libitum*) for pre-exercise blood sampling (baseline). The following day subjects returned to the laboratory to complete the submaximal, experimental exercise session and additional blood sampling. Specifically, for the acute bout of endurance exercise, subjects were asked to walk or jog on a motor-driven treadmill at 70% of their $\dot{V}O_{2peak}$ for the duration required to expend 350 kcals of energy. Prior to the exercise session, subjects completed a 3 minute warm-up, walking on the treadmill at 3 mph with a 2% grade in elevation. After this warm-up, a stopwatch was started and the speed and grade were adjusted to a workrate determined to elicit 70 % of $\dot{V}O_{2peak}$. Exercise intensity and rate of energy expenditure were verified by respiratory gas exchange data, measured by open-circuit spirometry, at the start of exercise and at 10 minute intervals throughout the exercise session.

The total energy expended and the remaining exercise time was calculated from the respiratory gas exchange data at each interval. The rate of energy expenditure (kcals / min) was calculated as described previously. Secondly, the current energy expended (kcals) was calculated by multiplying the rate of energy expenditure by the length of time (min) the subject exercised at this intensity. The current energy expended was

added to the previous energy expenditure to obtain the total energy expended. Finally, the remaining exercise time was determined at each interval by subtracting the total energy spent from the target energy expenditure (350 kcals) and dividing this number by the current energy expenditure rate. When needed, adjustments were made in either speed or grade to maintain the prescribed intensity. All experimental exercise sessions were supervised by two trained laboratory technicians. A copy of the endurance experimental exercise data sheet is found in Appendix H.

Due to the low caloric cost of resistance exercise, the estimated time required to expend 350 kcal required a duration that most subjects would not be able to complete. Thus, subjects in the resistance exercise group completed the first workout of their training program (duration = 58 min). Weights used for each exercise were calculated as approximately 70% of the 1RM, and chosen so that the subject would be challenged, but yet able to complete all repetitions in each exercise set, and continue exercise until completion of the session. Heart rate was monitored continuously and expired gases were measured during 16 minutes of exercise with a portable metabolic system (Medical Graphics CPX / D) to determine the caloric expenditure of the training session. A copy of the resistance experimental exercise data sheet is found in Appendix I.

For those in the combination group, subjects were asked to either walk or jog at an intensity equal to 70% of their maximal effort recorded on their earlier exercise test ($\dot{V}O_{2peak}$) for a length of time needed to burn 175 kcals of energy. After they are finished with this activity, they performed several resistance exercises at the number of sets, repetitions, and duration required to expend 175 kcal of energy. Weights used for

each exercise were calculated as approximately 70% of the 1RM, and chosen so that the subject would be challenged, but yet able to complete all repetitions in each exercise set, and continue exercise until 175 kcal of energy was expended. Heart rate was monitored continuously and expired gases were measured every 10 minutes of exercise with a portable metabolic system (Medical Graphics CPX / D) to determine the duration required to expend 175 kcal of energy. Subsequently, a fasting blood sample was obtained 24 hours (24 h) later, time of day controlled, and no exercise allowed in the intervening days. Diet records were kept by each subject throughout each blood-sampling period.

Post-Training Acute Exercise Testing

These acute exercise procedures were completed again after 12 weeks of training. In order to ensure that the volume of the post-training acute endurance exercise session will sufficiently provide an appropriate stimulus for the newly "trained" subjects, the caloric expenditure of the post-training acute endurance exercise sessions was increased from 350 to 500 kcals. The combination group expended 250 kcal of energy for both the single endurance and resistance exercise sessions.

Exercise Training Program

Upon completion of the pre-training testing described above, all subjects initiated their training programs. The exercise training varied for each of the three groups. Members of each group took part in a training program that lasted twelve weeks, allowing for one week of mid-training re-testing during week seven. The resistance-training group participated in a basic resistance-training program conforming to the

guidelines by the American College of Sports Medicine.[137] Every odd number week this group trained two times per week, and every even number week this group trained three times per week. This training schedule was adopted in order to accommodate the schedules of all the subjects as well as the availability of the fitness trainers and equipment. The resistance-training program entailed a total body workout consisting of 4 sets of 6-10 repetitions on 8 exercises that trained all the major muscle groups. The exercises included leg press, leg curl, standing calf raise, barbell bench press, lat pull-down, dumbbell military press, barbell curl, and abdominal crunches. A percentage of each subject's 1RM was used to determine the intensity for each week. Recovery time between sets was determined by two-minute turnovers. The intensity and number of repetitions performed for each exercise changed bi-weekly. A more detailed description of the progression of the resistance-training program can be seen in Table B-1. The endurance group's training consisted of walking / jogging on a motor-driven treadmill or outdoors 2-3 times per week. This group followed the same pattern of the resistance-training group by training twice on odd number weeks and three times on even number weeks. The running intensity was determined using a percentage of the heart rate reserve.[153] Resting and exercise maximum heart rate measurements were taken during $\dot{V}O_{2peak}$ testing through the use of Polar® heart rate monitors.[153] The duration of the training sessions lasted between 20-40 minutes. The intensity and duration of each session increased bi-weekly as the training progressed. A more detailed description of the progression of the endurance-training program can be seen in Table B-2. The CT group trained five times per week. Every odd number week this group performed the

resistance program three times and the endurance program twice. Every even number week the combination group performed the endurance program three times and the resistance program twice. During training all subjects were asked to avoid making any dietary changes and maintain their habitual diet. Compliance was assessed through the use of dietary records during the first and last week of training. Ninety percent subject compliance (27 out of 30 workouts for the RT and ET subjects and 54 out of 60 for CT subjects) was required for a subject's data to be included in the final statistical analysis. All exercise protocols complied with the 7th edition of the American College of Sports Medicine's "Guidelines for Exercise Testing and Prescription."[137]

Table B-1. Resistance Training Program Progression.

Week #	1 & 2	3 & 4	5 & 6	8 & 9	10 & 11	12 & 13
Intensity	1 warm-up set of 10 reps @ 50% 1RM 3 sets @ 10RM	1 warm-up set of 10 reps @ 50% 1RM 3 sets @ 8RM	1 warm-up set of 10 reps @ 50% 1RM 3 sets @ 6RM	1 warm-up set of 10 reps @ 50% 1RM 3 sets @ 10RM	1 warm-up set of 10 reps @ 50% 1RM 3 sets @ 8RM	1 warm-up set of 10 reps @ 50% 1RM 3 sets @ 6RM

Table B-2. Endurance Training Program Progression.

Week #	1 & 2	3 & 4	5 & 6	8 & 9	10 & 11	12 & 13
Intensity	20 minutes @ 65% of HRR	25 minutes @ 70% of HRR	30 minutes @ 70% of HRR	35 minutes @ 75% of HRR	40 minutes @ 75% of HRR	40 minutes @ 80% of HRR

Mid- and Post-Testing

Percent body fat, $\dot{V}O_{2peak}$, and 1RM tests were re-tested during week seven of the study. All testing was conducted using the same methods and procedures that were used during the pre-testing. This re-testing allowed the 1RM to be adjusted for the remaining weeks of the resistance-training program. Resting (RHR) and exercise maximum heart rates were also reassessed in order to adjust the intensity of the endurance-training program for the remainder of the program. The week following the completion of the training program, all variables tested during pre-testing were tested for the final time. This post-training testing followed the same methods and procedures as the pre-training testing.

Blood Sampling

A series of 2 blood samples: pre-exercise (baseline) and 24 hours (24 h) after the experimental exercise session were obtained on two different occasions; pre-training acute exercise period and post-training acute exercise period (Figure 3). For each blood draw series, the following blood collection procedures were completed. Each subject reported to the laboratory at approximately the same time each morning after a 12-hour fast in which water was allowed *ad libitum*. Prior to each blood draw, the subjects completed a form reporting their physical activity and dietary adherence over the last 24 hours and the time of their last meal. A blood sample (termed pre-heparin) was drawn into 2 (10 mL) vacutainer "purple top" tubes containing 10.5 mg Na-EDTA (no. 310547, Sherwood Medical Co., St. Louis, MO) and 2 vacutainer "tiger top" tubes containing a serum clotting factor (Becton Dickinson and Company, Rutherford, NJ) through a small

teflon catheter (no. 3828781 Angiocath, Becton Dickinson, Franklin Lakes, NJ) inserted into the antecubital vein of each subject. All blood sampling was performed using sterile technique with the subjects in a seated position. A small sample of blood was extracted from one of the "purple top" vacutainer tubes to determine plasma volume changes (description to follow). All "purple top" tubes were then replaced on crushed ice prior to centrifugation. The "tiger top" vacutainer tubes were allowed to clot at room temperature for 20 minutes and then placed on ice. Immediately after these first blood samples were obtained, a small, sub-therapeutic dose of heparin (75 IU / kg body weight; 1000 IU / ml, Elkins-Sinn, Inc., St. Louis, MO) was introduced through the catheter in order to release endothelial-bound lipoprotein lipase from the vessel walls into the circulation.[140] After the heparin was allowed to circulate for ten minutes, a second blood sample (10 ml, termed post-heparin) was drawn through the catheter into a heparinized "green top" vacutainer tube (no. 320751, Sherwood Medical Co., St. Louis, MO) containing 143 USP Na-heparin. The dose of heparin administered in the present investigation has been used frequently in previous studies and is considered optimal for assaying postheparin plasma lipolytic activity. Furthermore, it has been reported that daily injections of this dose for three consecutive days had little effect on serum lipids or lipase activities.[140] Since we proposed to treat with heparin only twice in each series, and not on consecutive days, we anticipated no effect on any of our dependent measures. Both serum and plasma from pre- and post- heparin blood was isolated by centrifugation at 1500 x g for 20 minutes at 4°C. Aliquots of pre- and post-heparin plasma were then sealed separately in 2 mL cryovials (no. 66008-284, VWR Scientific Inc., Westchester,

PA) and stored at -80°C for later analysis. All lipid and lipoprotein concentrations were adjusted for plasma volume shifts that occurred as a result of acute exercise using hematocrit and hemoglobin measurements from each sample.[139]

Biochemical Analysis of Plasma and Serum Samples

Plasma Volume Changes

Relative plasma volume shifts (% changes) that resulted from the experimental exercise session were calculated from hematocrit (Hct) and hemoglobin (Hb) measurements at each of the 2 blood sampling time-points. Immediately following collection of blood into the vacutainer tubes, three capillary tubes were filled with blood and sealed with Critoseal® (Oxford Labware, St. Louis, MO, #8889-215003) in order to measure Hct levels. These tubes were centrifuged for 5 minutes at 1500 x g (Adams-Readacrit microhematocrit centrifuge, Clay Adams, Parsippany, NJ). Measurements of packed cell volume and plasma volume were obtained by use of a ruler and measuring to the nearest 0.25 mm. The ratio of packed red cell volume to the total sample volume contained in the tube was calculated for each tube and multiplied by 0.96 (a correction for approximately 4 % of the plasma trapped in the red cell mass). Hct at each time-point was taken as the average of the corrected ratios obtained from the three capillary tubes.

The preparation to measure hemoglobin consisted of 20 microliters of whole blood pipetted into 5 ml of Drabkin's Solution (Sigma cat, no. 525-2, Sigma 430AG-6). After ensuring complete evacuation of the pipette tip by rinsing it 5 times, the solution was mixed by inversion and allowed to incubate at room temperature for 20 minutes and

stored in the dark. Hemoglobin assays were performed within 6 hours of blood collection. Drabkin's solution destroys the red blood cell and oxidizes hemoglobin to methemoglobin which eventually reacts with potassium cyanide to form cyanmethemoglobin. Cyanmethemoglobin has a maximum absorbance at 540 nm and the color intensity measured on a spectrophotometer (Model 1001, Milton-Roy, Rochester, NY) would be directly proportional to the hemoglobin concentration. Hemoglobin standards (Sigma cat. no. 525-18) were used to create calibration curves and subsequently calculate hemoglobin concentration. The Hb concentration for each time point was calculated by introducing the average of the triplicate absorbances into the regression equation.

It is well known that the experimental exercise sessions used in this investigation would stimulate transient changes in plasma volume. This change in volume has the potential to interfere with the interpretation of lipoprotein-lipid concentrations measured during the study. Therefore, plasma volumes were estimated by the method described by Dill and Costill[139] using the hematocrit and hemoglobin measures taken on the blood sample at each time point. These plasma volume estimations were used to correct lipoprotein-lipid measurements to baseline plasma volume levels. This allows comparison of changes without the influence of plasma volume shift. The plasma volume shift at the blood sampling time point after exercise, relative to the baseline blood sample ($\Delta PV\%$) was calculated using the equation derived from those published by Dill and Costill[139] and is as follows (Subscript $_B$ represents before and $_A$ represents any time point after the exercise session, respectively):

$$\Delta PV\% = [(PV_A / PV_B) - 1] \times 100$$

Where: $PV_A = (Hb_B / Hb_A) \times (1 - Hct_A)$

$$PV_B = (1 - Hct_B)$$

Plasma concentrations of the measured lipid variables were adjusted according to the magnitude of the plasma volume shift at each time point. Lipoprotein enzyme activities and hs-Crp were also adjusted for the plasma volume shifts.

Lipoprotein-Lipid Profiles

Frozen aliquots of serum were sent to Atherotech, Inc (Birmingham, AL) for complete lipoprotein-lipid analyses (TC, TG, HDL-C, $HDL_{2\&3}$-C, LDL-C, IDL-C, VLDL-C, NONHDL-C, Lipoprotein (a), low density lipoprotein subfraction $_{1\text{-}4}$ ($LDL_{1\text{-}4}$) cholesterol ($LDL_{1\text{-}4}$-C), and hs-Crp). A complete "VAP" lipoprotein-lipid profile was provided by Atherotech, Inc using the VAP procedure (Vertical Auto Profile, Atherotech Inc., Birmingham AL). Atherotech is a fully certified and licensed clinical Laboratory. Atherotech is part of the "Cholesterol Reference Method Laboratory Network". Atherotech also participates in 3 highly recognized "Proficiency Testing Programs". These are *Northwest Lipid Research Laboratories (NWLRL),* one of five "CDC-NHLBI" cholesterol reference labs; *New York State Department of Health*, a "CLIA" approved program; and *"Accutest"*, a "CLIA" approved program. The VAP is an inverted, rate zonal, single vertical spin, density gradient ultracentrifugation technique that simultaneously measures the cholesterol concentrations of all five lipoprotein classes (HDL, LDL-Real, VLDL, IDL, and Lp(a) and their subclasses (HDL_2, HDL_3, LDL_1, LDL_2, LDL_3, and LDL_4).[36] Briefly, serum samples were placed in an ultracentrifuge

tube and adjusted to a high density; a lower density solution was layered on top of serum samples, and the tubes were placed into a vertical ultracentrifuge rotor. The lipoproteins are eventually separated across the shorter, horizontal axis of the centrifuge tube. During centrifugation, the two density layers blend to form a continuous density gradient, and the lipoproteins present in the serum sample float toward the top of the tube and stop at their characteristic density. Thus, VLDL will float to the top of the tube, LDL will form a band in the middle, and HDL will remain near the bottom of the tube. Following separation, the tubes were placed in a fractionator assembly and punctured through the bottom with a needle. The material in the tube was drained from the bottom and was slowly mixed with a flowing enzymatic reagent, specific for cholesterol, into a heated Teflon tube. The enzymatic reagent reacted with the cholesterol in the sample to form a colored product which was then detected and measured photometrically at 505 nm. The accuracy of the VAP test was routinely determined by comparing its results with those obtained using a beta-quantification reference method performed at CDC-designated lipoprotein reference laboratories.[36]

Lipoprotein Density

Frozen aliquots of serum were also sent to SpectraCell Laboratories, Inc (Houston, TX) for complete LDL density analyses. A complete "Lipoprotein Particle Profile™" test was provided by SpectraCell Laboratories, Inc using analytical ultracentrifugation with two enhancements. First, a continuous gradient (density of 1.000 to 1.300) was generated through four hour spin at 600,000g's using a non-ionic gradient. This allowed for an accurate separation of lipoprotein subgroups for VLDL,

LDL, and HDL. Following this spin, lipoprotein particles were stained with a phospholipid analog that fluoresces when the hydrophobic end of the phospholipid dye embeds into the hydrophobic environment of the lipoprotein. The particle numbers were measured by extracting the contents of the centrifuge tube and processing it through a fluorescence detector. Integration of the fluorescence signal at the precise position for each lipoprotein subgroup provided the particle numbers by subgroup.

Apolipoprotein A-I and Apolipoprotein B Analysis

Apolipoprotein (apo) A-I and apo B were determined using a solid phase capture sandwich enzyme linked immunoassay (ELISA) procedure (ELISA kits no. A70101 and no. A70102, ALerCHEK, Inc., Portland, Maine).[436, 437] Using the solid phase capture sandwich ELISA assay (using a microwell format, SpectroMax 110 Microplate Reader), a polystyrene, 96 well microplate, was coated with affinity-purified antibodies prepared against the apolipoprotein being measured (apo A-I or apo B). All residual binding sites on the microplate had been previously blocked with albumin. To start the assay, 100 µL of diluted plasma samples and control standards were introduced to the microplate wells and allowed to incubate with the immobilized antibody for 2 hours at room temperature. Following the incubation, the microplate was decanted on a stack of paper towels and washed extensively with the wash buffer. Following the extensive washing, the antibody-antigen complex in the wells of the plate was incubated with 100 µL of HRP conjugated goat anti-apo A-I (a second detecting antibody which is enzyme labeled) for another 2 hours at room temperature. Another extensive decanting and well-washing was performed. Next, 100 µL of TMB / peroxide substrate (color developer) was

introduced to the wells and incubated for 30 minutes at room temperature. The reaction was quickly terminated with the addition of 100 µL of 0.18 N sulfuric acid.

The amount of bound conjugated antibody is a direct measure of the antigen concentration. After the microplate reader was zeroed at 450 nm using the specimen diluent zero control well, the optical density (O.D.) of the remaining wells was determined. A standard curve was established with a known standard using serial dilutions. The curve was created using a polynomial regression, to the 4^{th} degree. Samples of known apo A-I concentration were analyzed and served both as a calibrator and quality control. The technique and calculation for apo B analysis was mechanistically similar to the apo A-I procedure.

High Sensitivity C-reactive protein Analysis

Additional aliquots of serum were sent to Atherotech, Inc (Birmingham, AL) for the quantitative determination of C-reactive protein (Crp) using an immunoturbidity assay. Briefly, the Crp in the serum sample binds to a specific anti-Crp antibody. This antibody has been previously adsorbed to latex particles and eventually agglutinates. This process is detected as a change in absorbance when read on an automated clinical chemistry analyzer at 570 nm. The magnitude of the change is proportional to the quantity of Crp in the serum sample. The actual concentration of Crp is then determined by interpolation from a calibration curve prepared from calibrators of known concentrations.

Post-heparin Lipase Activity

Total plasma lipase activity (TLa) and hepatic triglyceride lipase activity (HTGLa) were determined from post-heparin plasma using the methods described by Thompson et al.[140] and Belfrage and Vaughn.[141] Briefly, post-heparin plasma samples were mixed with a prepared substrate emulsion which consisted of radioactive-labeled triglyceride along with a cofactor (apolipoprotein C-II). In the presence of the labeled substrate and supplied apo C-II (as the cofactor), the rate of hydrolysis of the labeled substrate was measured in a timed assay at physiologic temperature. TLa was determined in a low sodium buffer, while HTGLa was determined using a high sodium buffer. The reaction was stopped by denaturing the plasma lipase proteins and the labeled free fatty acids were partitioned from the mono-, di-, and triglycerides. The radioactivities of the labeled free fatty acids were then measured in a liquid scintillation (beta) counter. Thus, the activity of endothelial-bound lipase (LPLa) was calculated as the difference between the TLa and that of HTGLa.

The radio-labeled substrate mixture was prepared according to the methods described by Thompson.[140] The substrate mixture consisted of the following: 206 µL triolein (T7140, Sigma Chemical Co., St. Louis, MO), 8 µL L-α Lecithin from egg yolk (P2772, Sigma Chemical Co., St. Louis, MO), and 125 µL ^{3}H-triolein in toluene (glycerol tri [9,10(n)-3H] oleate in a toluene solution, TRA-191, 1 mL = 5 µCi, Amersham, Arlington Heights, Ill.). Following this preparation, the substrate was placed under N2 gas in order to evaporate off the toluene contained in the mixture. Next, 600 µL of a 1 % solution of Triton X-100 (X-100, Sigma Chemical Co., St. Louis, MO) was

added to the emulsion. This mixture was then combined with 10 mL of an albumin buffer, containing the plasma Apolipoprotein C-II source (0.6 g FA-free albumin, A6003, Sigma Chemical Co., St. Louis, MO; 10 mL 0.194 Tris-HCl buffer, 0.15 NaCl, pH 8.6; 1 mL plasma, heat-deactivated at 56°C for 10 minutes). The final substrate solution was sonicated, at level 7 setting, for 1 minute (Heat Systems-Ultrasonics Inc. Cell Disrupter, Model W185, Plainview, NY). The solution was sonicated for an additional minute after a 30 second rest period. Following the final sonication, the mixture was placed on ice until the start of the procedure.

15 mL Falcon tubes (no. 2096 Falcon, Becton Dickinson, Franklin Lakes, NJ) were prepared in triplicate with the addition of 80 µL of either a low sodium buffer (0.194 Tris-HCl, 0.19 M NaCl, pH 8.6), or a high sodium buffer (0.194 Tris-HCl, 2.31 M NaCl, pH 8.6). These two buffers were used in determining either TLa or HTGLa. Subject samples and control tubes were prepared by adding 20 µL of plasma, which was diluted (1:3, v / v) with an albumin buffer (FA-free albumin, A6003, Sigma Chemical Co., St. Louis, MO; 10 mL 0.194 Tris-HCl buffer, 0.15 NaCl, pH 8.6), into the 15 mL Falcon tubes. Blanks for TLa and HTGLa were also prepared in triplicate using 20 µL of distilled water instead of the diluted plasma samples. All tubes were vortexed and placed on ice prior to starting the assay. Using 30 second intervals, 100 µL of the labeled substrate was pipetted into each tube, vortexed, and placed in a water bath, with shaker, at 37°C for 45 minutes.

Following the 45 minute incubation period, the tubes were removed in 30 second intervals from the shaking water bath. Next, 3.25 mL of MeOH: $CHCl_3$: C_7H_{14} (18:15:3,

v /v / v) was added to the removed tube, followed by 1.05 mL of a K_2CO_3 buffer (0.1 M $K_2CO_3 – H_3BO_3$ buffer, pH 10.5).[141] After all tubes had been removed and processed, they were centrifuged at 2500 x g for 25 minutes at 4°C. This centrifugation process allowed free fatty acids to be partitioned from the mono, di, and triglycerides in an upper, aqueous phase.[141] Following this centrifugation, 1 mL of the top phase was carefully removed and added to a 20 mL scintillation vial (R2555, Kimble Glass Co., Vineland, NJ), containing 10 mL of scintillation cocktail (ECONO2 – SX21-5, Fisher Scientific, Fairlawn, NJ). In order to determine the total radioactivity of the substrate, 10 μL of substrate was also added, in triplicate, to the scintillation vials containing the scintillation fluid. All scintillation vials were vortexed and placed in a dark cupboard overnight. The radioactivity (cpm) of each scintillation vial was counted for 10 minutes in a liquid scintillation counter (Beckman LS 3801, Fullerton, CA). The sample, control, and blank cpm were averaged and the TLa and HTGLa (μmol FFA / mL / hr) were calculated using the following equation:

μmol FFA / mL / hr = [(sample cpm / total cpm) x 132.4275] x 3

132.425 is a correction factor representing the procedure time and the total radioactivity relative to the actual substrate mixture volume. The product of this part of the equation is then multiplied by 3 in order to account for the radioactivity of the reaction product (^{3}H-FFA) relative to the substrate (^{3}H-triolein). The activity of endothelial-bound lipase (LPLa) was calculated as the difference between the TLa and that of HTGLa.

Reliability

The order in which subject samples were chosen for data analysis was randomly determined prior to each specific biochemical / enzymatic procedure. Inter-assay variation for each lipid variable was eliminated by measuring all time points of each subject's blood in the same analytical run. Within each run, standard controls were analyzed at regular intervals throughout each assay run in order to evaluate intra-assay variation. The coefficients of variation (CV) were calculated from the control absorbances and used in determining intra and interassay reliability according to the following equation:

CV = (standard deviation of the absorbances / mean of the absorbances) x 100

Triplicate measurements of radioactivity within a range of 10 % were accepted for the enzyme assay. When differences between triplicate cpm were greater than 10 %, all samples for that subject were re-analyzed. Control samples were included at regular intervals throughout each assay run. CVs were determined from the control cpm as described in the previous equation.

Statistical Analysis

The Effect of Resistance, Endurance, and Combination Exercise Training on Lipid Metabolism and Non-Traditional Cardiovascular Disease Risk Markers in Previously Untrained Males

Initial Group Differences

A statistical test for normality was performed on all pre-training dependent variables prior to hypothesis testing. Following this procedure, baseline differences

between the subjects assigned to the different exercise training groups were determined for physiological, diet, physical activity, lipid, lipoprotein enzyme, and non-traditional CHD risk marker variables using one-way analysis of variance (ANOVA). Furthermore, relationships between the physiological and pre-training serum lipid, non-traditional CHD risk markers, and lipoprotein enzyme values were determined using Pearson product-moment correlation coefficients.

Dietary Analysis and Physical Activity

Total daily caloric intake, nutrient composition of the subject's diet, and daily physical activity were analyzed using a 3 (GROUP) x 2 (TRAINING PERIOD) analysis of variance (ANOVA) with repeated measures on the second factor. Duncan's New Multiple Range Test was employed for post hoc analyses, where appropriate. Due to the exploratory nature of this study, the comparisonwise α level was set at 0.05 for all statistical tests of significance.

The Responses of Serum Lipids, Non-Traditional CHD Risk Markers, and Lipoprotein Enzyme Activities to Exercise Training

A statistical power test was performed to estimate that approximately 12 subjects in each group, would be required to ensure an 80% chance of detecting a: 1) 5 mg / dL change in HDL-C; and 2) 20 mg / dL change in TG.[438] The dependent variables of interest in this study were the physiological variables: body weight (Weight), lean body mass (LBM), Fat Mass (FMass), body mass index (BMI), waist girth (Waist), hip girth (Hip), waist girth / hip girth (W / H ratio), % Fat, resting heart rate (RHR), resting systolic blood pressure (RSBP), resting diastolic blood pressure (RDBP), $\dot{V}O_{2peak}$,

maximal duration (minutes) for the GXT test (TDMTM), maximal lower body strength as determined by a 1RM on the leg press (LPMAX), and maximal upper body strength as determined by a 1RM on the bench press (BPMAX); the diet / physical activity variables: total daily caloric intake (KCAL), total daily grams of carbohydrate (CHO), fat (FAT), protein (PROT), saturated fat (SFAT), polyunsaturated fat (PSAT), total daily milligrams of cholesterol (CHOL), the ratio of polyunsaturated to saturated fat (P / S ratio) and the average daily energy expenditure in kcal (DAYEXP); the lipid concentrations: blood TC, TG, HDL-C, $HDL_{2\&3}$-C, LDL-C, IDL-C, VLDL-C, NONHDL-C, Lp (a), apo A-I, apo B, LDL_1-C, LDL_2-C, LDL_3-C, LDL_4-C, LDL density, the enzyme activities (LPLa and HTGLa), and the inflammatory marker (hs-Crp). Furthermore, the following ratio variables were determined: TC / HDL-C, LDL-C / HDL-C, HDL_2 / HDL_3-C, and apo B / apo A-I.

The two independent variables in this study were exercise training GROUP and TRAINING PERIOD. GROUP had three levels: 1) Endurance, 2) Resistance, and 3) Combination Training. TRAINING PERIOD had two levels: 1) Pre-training and 2) Post-training. In order to determine the chronic effects of twelve weeks of resistance, endurance, and combination exercise training on the dependent variables, a 3 (GROUP) x 2 (TRAINING PERIOD) ANOVA (repeated for TRAINING PERIOD) was employed as a global test for significance. Significant interactions were additionally explored using simple main effects analysis. In addition, mean separation procedures were carried out using Duncan's New Multiple Range Test when appropriate.

Change scores for the dependent variables were calculated as: post-training time-point minus pre-training time-point. Simple relationships among the change variables were determined using Pearson product-moment correlation coefficients.

Due to the exploratory nature of this study, the comparisonwise α level was set at 0.05 for all statistical tests of significance. Each test for significance was performed independently and it is known that the experimentwise error rate may actually be somewhat higher than $p < 0.05$. All data was analyzed using the Statistical Analysis System (SAS, version 9.13, Cary, NC).

The Effect of a Single Session of Resistance, Endurance, and Combination Exercise on Lipid Metabolism and Non-Traditional Cardiovascular Disease Risk Markers in Previously Untrained Males

Initial Exercise Group Differences

A statistical test for normality was performed on all pre-exercise dependent variables prior to hypothesis testing. Following this procedure, baseline differences between the subjects assigned to the different exercise groups were determined for physiological, diet, physical activity, lipid, non-traditional CHD risk markers, and enzyme variables using one-way analysis of variance (ANOVA). Furthermore, relationships between the physiological and pre-exercise serum lipid, non-traditional CHD risk markers, and enzyme values were determined using Pearson product-moment correlation coefficients.

Dietary Analysis and Physical Activity

Total daily caloric intake, nutrient composition of the subject's diet, and daily physical activity were analyzed using one-way analysis of variance (ANOVA). Duncan's New Multiple Range Test was employed for post hoc analyses, where appropriate. Due to the exploratory nature of this study, the comparisonwise α level was set at 0.05 for all statistical tests of significance.

The Responses of Serum Lipids, Non-Traditional CHD Risk Markers, and Lipoprotein Enzyme Activities to Acute Exercise in Previously Untrained Males

The dependent variables of interest for this investigation were the lipid concentrations: blood TC, TG, HDL-C, $HDL_{2\&3}$-C, LDL-C, IDL-C, VLDL-C, NONHDL-C, Lp (a), apo A-I, apo B, LDL_1-C, LDL_2-C, LDL_3-C, LDL_4-C, LDL density, the enzyme activities (LPLa and HTGLa), and the inflammatory marker (hs-Crp). Furthermore, the following ratio variables were determined: TC / HDL-C, LDL-C / HDL-C, HDL_2 / HDL_3-C, and apo B / apo A-I.

The two independent variables for this portion of the study were exercise GROUP and TIME. GROUP had three levels: 1) Endurance, 2) Resistance, and 3) Combination Exercise. TIME had two levels: 1) Baseline (24 hours before exercise) and 2) 24 h (24 hours after exercise). A global test for significance was performed using a 3 (GROUP) X 2 (TIME) ANOVA with repeats across TIME. Significant interactions were additionally explored using simple main effects analysis. In addition, mean separation procedures were carried out using Duncan's New Multiple Range Test when appropriate.

Due to the exploratory nature of this study, the comparisonwise α level was set at 0.05 for all statistical tests of significance. Each test for significance was performed independently and it is known that the experimentwise error rate may actually be somewhat higher than $p < 0.05$. All data was analyzed using the Statistical Analysis System (SAS, version 9.13, Cary, NC).

The Effect of a Single Session of Resistance, Endurance, and Combination Exercise on Lipid Metabolism and Non-Traditional Cardiovascular Disease Risk Markers in Trained Men

Initial Exercise Group Differences

A statistical test for normality was performed on all pre-exercise dependent variables prior to hypothesis testing. Following this procedure, baseline differences between the subjects assigned to the different exercise groups were determined for physiological, diet, physical activity, lipid, non-traditional CHD risk markers, and enzyme variables using one-way analysis of variance (ANOVA). Furthermore, relationships between the physiological and pre-exercise serum lipid, non-traditional CHD risk markers, and enzyme values were determined using Pearson product-moment correlation coefficients.

Dietary Analysis and Physical Activity

Total daily caloric intake, nutrient composition of the subject's diet, and daily physical activity were analyzed using one-way analysis of variance (ANOVA). Duncan's New Multiple Range Test was employed for post hoc analyses, where

appropriate. Due to the exploratory nature of this study, the comparisonwise α level was set at 0.05 for all statistical tests of significance.

The Responses of Serum Lipids, Non-Traditional CHD Risk Markers, and Lipoprotein Enzyme Activities to Acute Exercise in Trained Males

The dependent variables of interest were the lipid concentrations: blood TC, TG, HDL-C, $HDL_{2\&3}$-C, LDL-C, IDL-C, VLDL-C, NONHDL-C, Lp (a), apo A-I, apo B, LDL_1-C, LDL_2-C, LDL_3-C, LDL_4-C, LDL density, the enzyme activities (LPLa and HTGLa), and the inflammatory marker (hs-Crp). Furthermore, the following ratio variables were determined: TC / HDL-C, LDL-C / HDL-C, HDL_2 / HDL_3-C, and apo B / apo A-I.

The two independent variables were GROUP and TIME. GROUP had three levels: 1) Endurance, 2) Resistance, and 3) Combination Exercise. TIME had two levels: 1) Baseline (24 hours before exercise) and 2) 24 h (24 hours after exercise). A global test for significance was performed using a 3 (GROUP) X 2 (TIME) ANOVA with repeats across TIME. Significant interactions were additionally explored using simple main effects analysis. In addition, mean separation procedures were carried out using Duncan's New Multiple Range Test when appropriate.

Due to the exploratory nature of this study, the comparisonwise α level was set at 0.05 for all statistical tests of significance. Each test for significance was performed independently and it is known that the experimentwise error rate may actually be somewhat higher than $p < 0.05$. All data was analyzed using the Statistical Analysis System (SAS, version 9.13, Cary, NC).

APPENDIX C

RESULTS

The primary purpose of this investigation was to characterize the effects of both acute and chronic resistance, endurance, and combination exercise on circulating lipids, apolipoproteins, non-traditional CHD risk markers, and lipoprotein enzymes in previously untrained males. In this investigation, acute and chronic changes in all dependent variables were compared between subjects randomly assigned to complete a single session of endurance (ET), resistance (RT), and combination endurance / resistance (CT) exercise. This acute exercise protocol was completed on two different occasions corresponding to 0 and 12 weeks of training. The results are presented in the following order: **A) The Effect of Resistance, Endurance, and Combination Exercise Training on Lipid Metabolism and Non-Traditional Cardiovascular Disease Risk Markers in Previously Untrained Males:** 1) baseline physiological / dietary characteristics, lipid profiles, non-traditional CHD risk markers, and lipoprotein enzyme activities; 2) dietary and physiological variable analyses; 3) the responses of serum lipids, non-traditional CHD risk markers, and lipoprotein enzyme activities to chronic exercise training, and; 4) the reliability of the biochemical analyses; **B) The Effect of Resistance, Endurance, and Combination Exercise on Lipid Metabolism and Non-Traditional Cardiovascular Disease Risk Markers in Previously Untrained Males:** 1) baseline physiological / dietary characteristics, lipid profiles, non-traditional CHD risk markers, and lipoprotein enzyme activities; 2) the responses of serum lipids, non-traditional CHD risk markers, and lipoprotein enzyme activities to acute exercise, and;

3) the reliability of the biochemical analyses; **C) The Effect of Resistance, Endurance, and Combination Exercise on Lipid Metabolism and Non-Traditional Cardiovascular Disease Risk Markers in Trained Males:** 1) baseline physiological / dietary characteristics, lipid profiles, non-traditional CHD risk markers, and lipoprotein enzyme activities; 2) the responses of serum lipids, non-traditional CHD risk markers, and lipoprotein enzyme activities to acute exercise, and; 3) the reliability of the biochemical analyses.

Exercise Training

The Effect of Resistance, Endurance, and Combination Exercise Training on Lipid Metabolism and Non-Traditional Cardiovascular Disease Risk Markers in Previously Untrained Males

Baseline Physiological / Dietary Characteristics, Lipid profiles, Non-Traditional CHD Risk Markers, and Lipoprotein Enzyme Activities

While every effort was taken to ensure that subjects randomly assigned to the three different exercise groups were similar with respect to age, body weight, and relative body fat, baseline analysis of the physiological data did indicate that significant differences ($p < 0.05$) did occur. Body weight and waist circumference were all lower in the RT group compared to the CT group. Baseline descriptive physiological characteristics are presented in Table C-1.

Dietary intake logs were analyzed (see Appendix F) for: 1) total daily caloric intake (KCAL); 2) total daily grams of carbohydrate (CHO), fat (FAT), protein (PROT), saturated fat (SFAT), polyunsaturated fat (PSAT), and total daily milligrams of

Table C-1. Baseline Physiological Variables.

Variable	RT	ET	CT	Range
Age (yrs)	22 ± 1 [a]	24 ± 1 [a]	22 ± 1 [a]	18 - 34
Height (in)	68.9 ± 0.66 [a]	69.7 ± 0.91 [ab]	71.7 ± 0.54 [b]	65 - 75
Weight (kg)	73.8 ± 4 [a]	85.6 ± 5 [ab]	95.9 ± 4.7 [b]	56 - 117
BMI (kg/m^2)	23.98 ± 1.04 [a]	27.4 ± 1.78 [a]	29.05 ± 1.64 [a]	19 - 37
% Fat	15 ± 1 [a]	19 ± 3 [a]	20 ± 3 [a]	7 - 36
Waist (in)	32 ± 1.2 [a]	36 ± 1.6 [ab]	38 ± 1.4 [b]	25 - 46
Hip (in)	38.6 ± 1 [a]	41.6 ± 1 [ab]	43.3 ± 1 [b]	34 - 49
RSBP (mmHg)	122 ± 2.9 [ab]	118 ± 5.1 [a]	133 ± 3.7 [b]	90 - 158
RDBP (mmHg)	72 ± 2.7 [a]	77 ± 2.9 [ab]	82 ± 2.1 [b]	60 - 94
$\dot{V}O_{2peak}$ (mL/kg/min)	43.6 ± 1.6[a]	41.8 ± 2.7[a]	42.7 ± 2.2[a]	27.4 - 55.5

All data are presented as the mean ± SEM. % Fat = body fat relative to body weight; BMI = body mass index; W / H ratio = waist girth / hip girth; RSBP = resting systolic blood pressure; RDBP = resting diastolic blood pressure; $\dot{V}O_{2peak}$ = peak oxygen consumption as measured during a standardized graded exercise test. Exercise group means within each row with same letters are not different ($p < 0.05$).

Table C-2. Baseline Dietary Variables.

	Exercise Group			
Variable	RT	ET	CT	Range
KCAL	2513 ± 99 [a]	2375 ± 244 [a]	2233 ± 175 [a]	1247 - 3343
CHO	302 ± 17 [a]	310 ± 30 [a]	329 ± 32 [a]	140 - 461
FAT	98 ± 6 [a]	81 ± 9 [a]	69 ± 7 [a]	27 - 121
PROT	103 ± 8 [a]	88 ± 8 [ab]	71 ± 3 [b]	53 - 140
SFAT	34 ± 3 [a]	27 ± 3 [ab]	21 ± 2 [b]	6 - 46
CHOL	375 ± 64 [a]	240 ± 36 [b]	182 ± 25 [b]	52 - 668
PSFAT	7.6 ± 0.81 [a]	6 ± 0.97 [a]	4.7 ± 1.2 [a]	0.96 - 11
P / S ratio	0.23 ± 0.02 [a]	0.25 ± 0.04 [a]	0.22 ± 0.05 [a]	0.04 – 0.48

All data are presented as the mean ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n =10; CT = combination exercise group, n = 12. Dietary means are daily averages calculated from seven day dietary intake logs. Daily energy expenditure means are daily averages calculated from seven day physical activity records. CHO, FAT, PROT, SFAT, PSFAT are nutrients expressed as grams / day. CHOL is expressed as milligrams / day. Exercise group means within each row with same letters are not different ($p < 0.05$).

cholesterol (CHOL); 3) and the ratio of polyunsaturated to saturated fat (P / S ratio). Seven day physical activity records were analyzed (see Appendix G) for average daily energy expenditure (DAYEXP). It was determined that the average daily intake of PROT and SFAT were lower in the CT group compared to the RT group, while CHOL was higher in the RT group compared to the other two groups.

Baseline differences in dietary variables are presented in Table C-2. Baseline lipid and lipid ratios are displayed in Table C-3. With respect to the non-traditional CHD risk markers, significant differences were determined between exercise groups for LDL density and apo B concentration ($p < 0.0176$). The density of LDL was significantly higher ($p < 0.0053$) in the ET group compared to the CT group. The apo B concentration was greater in the ET group compared to the RT and CT exercise groups. Initial differences between exercise groups were also found for the apo B / apo A-I ratio ($p < 0.0046$). These baseline variables are displayed in Table C-4.

Significant correlations between selected baseline lipid, non-traditional CHD risk markers, and enzyme activities are summarized in Tables C-5 to C-6. Significant correlations between 12-week changes in selected physiological, lipid, non-traditional CHD risk markers, and enzyme activities are summarized in Tables C-7 to C-8.

Table C-3. Baseline Lipids and Lipid Ratios.

	Exercise Group			
Lipids	RT	ET	CT	Range
TC	165 ± 11 [a]	163 ± 7 [a]	163 ± 8 [a]	118 – 226
LDL-C	98 ± 10 [a]	103 ± 8 [a]	99 ± 9 [a]	62 - 164
HDL-C	48 ± 3 [a]	42 ± 2 [a]	48 ± 2 [a]	31 - 60
HDL_2-C	10 ± 1 [a]	8 ± 0.4 [a]	10 ± 1 [a]	6 - 14
HDL_3-C	38 ± 2 [a]	34 ± 2 [a]	38 ± 2 [a]	25 - 46
TG	94 ± 13 [a]	123 ± 16 [a]	85 ± 10 [a]	30 - 167
Lipid Ratios				
TC / HDL-C	3.47 ± 0.26 [a]	3.95 ± 0.26 [a]	3.53 ± 0.32 [a]	2.4 - 5.8
LDL-C / HDL-C	2.09 ± 0.23 [a]	2.5 ± 0.24 [a]	2.18 ± 0.3 [a]	1.1 - 4.2
HDL_2-C / HDL_3-C	0.26 ± 0.01 [a]	0.24 ± 0.01 [a]	0.26 ± 0.01 [a]	0.19 - 0.31

All data are presented as the mean ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n =10; CT = combination exercise group, n = 12; Lipid values are in mg / dL; Exercise group means within each row with same letters are not different ($p < 0.05$).

Table C-4. Baseline Non-Traditional CHD Risk Markers and Enzyme Activities.

	Exercise Group			
Variable	RT	ET	CT	Range
hs-Crp	2.1 ± 1 [a]	0.88 ± 0.17 [a]	1.17 ± 0.26 [a]	0.2 – 6.9
Lipids[#]				
LDL_1-C	16 ± 2 [a]	17 ± 1 [a]	18 ± 3 [a]	5 - 41
LDL_2-C	35 ± 4 [a]	33 ± 4 [a]	40 ± 4 [a]	18 - 70
LDL_3-C	30 ± 4 [a]	35 ± 5 [a]	27 ± 4 [a]	14 - 60
LDL_4-C	4 ± 1 [a]	4 ± 1 [a]	3 ± 0.5 [a]	1 - 13
LDL density	1.0314 ± 0.0002 [ab]	1.0319 ± 0.0002 [a]	1.0308 ± 0.0002 [b]	1.0291 – 1.0326
apo A-I	118 ± 3 [a]	111 ± 9 [a]	128 ± 8 [a]	79 - 168
apo B	86 ± 7 [b]	121 ± 9 [a]	92 ± 9 [b]	49 - 163
apo B /apo A-I	0.73 ± 0.05 [b]	1.15 ± 0.12 [a]	0.73 ± 0.08 [b]	0.32 - 2.05
VLDL-C	18 ± 2 [a]	19 ± 1 [a]	16 ± 1 [a]	12 - 29
IDL-C	7 ± 2 [a]	9 ± 2 [a]	6 ± 2 [a]	0 - 20
NONHDL-C	116 ± 11 [a]	121 ± 7 [a]	115 ± 9 [a]	74 - 187
Lp (a)	6 ± 1 [a]	5 ± 0.5 [a]	6 ± 0.5 [a]	3 - 10
Enzyme Activities[Π]				
LPLa	6.13 ± 0.69 [a]	5.22 ± 0.32 [a]	5.92 ± 0.38 [a]	4 - 10
HTGLa	12.0 ± 1.4 [a]	12.22 ± 1.8 [a]	11.25 ± 1 [a]	6 - 21

All data are presented as the mean ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n =10; CT = combination exercise group, n = 12; hs-Crp expressed in mg / L. [#] Lipid values are in mg / dL, LDL density expressed in g / cm^2; [Π]LPLa and HTGLa values are in μmol FFA / mL / hr. Exercise group means within each row with same letters are not different ($p < 0.05$).

Table C-5. Pearson Product – Moment Correlations for Selected Lipid, Non-Traditional CHD Risk Markers, and Enzyme Variables at Baseline.

Variable	TC	HDL-C	HDL_2-C	HDL_3-C	TG	LDL-C	Lp (a)	apo A-I
VLDL-C	0.516			-0.360	0.484	0.482		-0.510
IDL-C	0.757	-0.376		-0.380	0.437	0.762		
LDL-C	0.967							
LDL density	0.453				0.460		-0.382	
LDL_1-C	0.776					0.791		
LDL_2-C	0.631					0.641	0.370	
LDL_3-C	0.590	-0.436	-0.550	-0.369	0.467	0.648		
HDL-C			0.887	0.984	-0.547	-0.356		
HDL_2-C				0.794	-0.504	-0.361		
HDL_3-C			0.794		-0.533			
TG			-0.504	-0.533				-0.554
apo B	0.365	-0.382		-0.373		0.469		
LPLa			0.380					
Lp (a)					-0.462			0.414
NONHDL-C	0.969	-0.369	-0.366			0.994		

Relationships were determined after combining data from all exercise groups. All relationships shown are statistically significant ($p < 0.05$).

Table C-6. Pearson Product – Moment Correlations for Selected Physiological, Lipid, Non-Traditional CHD Risk Markers, and Enzyme Variables at Baseline.

Variable	Weight (kg)	RSBP	LPMAX	BPMAX	$\dot{V}O_{2peak}$ (mL/kg/min)
LDL_2-C		0.465			
LDL_4-C	-0.362				
apo A-I			0.431		
Weight (kg)			0.532	0.514	-0.543
LBM				0.716	

Relationships were determined after combining data from all exercise groups. All relationships shown are statistically significant ($p < 0.05$).

Table C-7. Pearson Product – Moment Correlations for 12-Week Changes in Selected Lipid, Non-Traditional CHD Risk Markers, and Enzyme Variables.

Variable	TC	HDL-C	HDL_2-C	HDL_3-C	LDL-C	VLDL-C	apo A-I
VLDL-C	0.376						
IDL-C	0.605				0.593	0.675	
LDL density	0.966	0.534		0.584			
LDL-C	0.966	0.534		0.584			
LDL_1-C	0.658				0.705	0.360	
LDL_3-C	0.611				0.641		
HDL-C	0.714						
HDL_2-C	0.541	0.910		0.833			
HDL_3-C	0.747	0.987					0.374

Relationships were determined after combining data from all exercise groups. All relationships shown are statistically significant ($p < 0.05$).

Table C-8. Pearson Product – Moment Correlations for 12-Week Changes in Selected Physiological, Lipid, Non-Traditional CHD Risk Markers, and Enzyme Variables.

Variable	Weight (kg)	% Fat	Waist	LPMAX	BPMAX	$\dot{V}O_{2peak}$ (mL/kg/min)
LDL_2-C				-0.383		
LDL_3-C						-0.365
VLDL-C				0.501		
apo B						-0.408
Lp (a)				-0.448		
LPLa		0.374				
HTGLa	0.501	0.431	0.577			
Waist		0.405			0.376	-0.462
% Fat						-0.598
Weight (kg)		0.516	0.712		0.461	-0.546
LBM (kg)				0.361	0.628	
FMass (kg)		0.916				-0.637

Relationships were determined after combining data from all exercise groups. All relationships shown are statistically significant ($p < 0.05$).

The Effects of Exercise Training on Diet and Physiological Variables

Significant GROUP x TRAINING PERIOD interactions were noted for CHOL ($p < 0.0063$), LBM ($p < 0.0001$), LPMAX ($p < 0.0001$), and BPMAX ($p < 0.0001$). There was a significant difference in CHOL between the exercise groups only at the pre-training time point. Dietary cholesterol was greater in the RT group compared to both ET and CT exercise groups. There was also a significant difference in CHOL, with respect to 12 weeks of training, in the CT and RT exercise groups. Dietary cholesterol was significantly higher post-training compared to pre-training in subjects of the CT exercise group. Furthermore, dietary cholesterol was significantly lower post-training compared to pre-training with subjects in the RT exercise group.

There was a significant difference in LBM between the training groups at both pre-training and post-training time-points. LBM was significantly higher in the CT group compared to both ET and RT groups at the pre-training time-point. Furthermore, the increase in LBM following 12 weeks of training was significant for the CT and RT groups compared to the ET group. In addition, LBM was significantly higher in the CT group compared to the ET and RT groups at the post-training time-point.

There was a significant difference in LPMAX between the exercise groups only at the post-training time-point. The maximum weight lifted on the leg press was significantly higher in the CT group compared to the ET and RT exercise groups. There was also a significant difference in LPMAX, with respect to training, in all the exercise groups. The maximum weight lifted on the leg press was significantly higher post-training compared to the pre-training values in all exercise groups. There was a

significant difference in BPMAX, with respect to training, in the CT and RT exercise groups. The maximum weight lifted on the bench press was significantly higher post-training compared to pre-training in both exercise groups.

GROUP main effects were determined for Weight ($p < 0.0080$), Waist ($p < 0.0217$), and Hip ($p < 0.0124$). Each of these variables were greater in the CT exercise group when compared to the RT exercise group. The GROUP main effects for Weight, Waist, and Hip are reported in Table C-9.

Table C-9. GROUP Main Effects for Weight, Waist, and Hip.

	Exercise Group		
Variable	RT	ET	CT
Waist (in)	32 ± 1^{b}	36 ± 1^{ab}	37.7 ± 1^{a}
Weight (kg)	74.7 ± 3^{b}	85.2 ± 3^{ab}	96.4 ± 3^{a}
Hip (in)	38 ± 1^{b}	41 ± 1^{ab}	43 ± 1^{a}

Values are the exercise mode means ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n =10; CT = combination exercise group, n = 12; Values are collapsed across training periods (pre-training and post-training). Exercise group means within each row with the same letters are not different ($p < 0.05$).

TRAINING PERIOD main effects were determined for Waist ($p < 0.0144$), Hip ($p < 0.0001$), W / H ratio ($p < 0.0210$), % Fat ($p < 0.0002$), FMass ($p < 0.05$), RHR ($p < 0.0003$), $\dot{V}O_{2peak}$ ($p < 0.0003$), and TDMTM ($p < 0.0002$). Each of the values for Waist, Hip, % Fat, FMass, and RHR were significantly lower after 12 weeks of training when compared to pre-training values. The values for W / H ratio, $\dot{V}O_{2peak}$, and TDMTM were all significantly higher after 12 weeks of training when compared to pre-training values. The TRAINING PERIOD main effects for Waist, Hip, W / H ratio, % Fat, FMass, RHR, $\dot{V}O_{2peak}$, and TDMTM are reported in Table C-10.

The Responses of Serum Lipids, Non-Traditional CHD Risk Markers, and Enzyme Activities to Exercise Training

Lipoprotein Lipids, Non-Traditional CHD Risk Markers, and Lipid Ratios

There were no GROUP x TRAINING PERIOD interactions determined from the 3 x 2 ANOVAs on any of the lipid variables or lipid ratios.

Table C-10. TRAINING PERIOD Main Effects for Waist, Hip, W / H ratio, % Fat, FMass, RHR, $\dot{V}O_{2peak}$, and TDMTM.

	Training Periods	
Variable	Pre-Training	Post-Training
Waist (in)	36 ± 1	35 ± 1*
Hip (in)	41 ± 1	40 ± 1*
W / H ratio	0.86 ± 0.01	0.87 ± 0.01*
% Fat	18.1 ± 1	16.7 ± 1*
FMass (kg)	16.5 ± 1.8	15.4 ± 1.7
RHR	66 ± 2	60 ± 2*
$\dot{V}O_{2peak}$ (mL/kg/min)	42.7 ± 1.3	44.5 ± 1.1*
TDMTM	11.8 ± 0.28	12.5 ± 0.27*

Values are the training means ± SEM. Values are collapsed across exercise groups (RT, ET, and CT). * Significant differences between training periods ($p < 0.05$).

Thus, the exercise group differences (GROUP main effects) and the influence of 12 weeks of exercise training on lipid concentrations, non-traditional CHD risk markers, and lipid ratios (TRAINING PERIOD main effects) are reported.

GROUP main effects were determined for apo B ($p < 0.0185$) and the apo B / apo A-I ratio ($p < 0.0082$). Each of these lipid variables were greater in the ET exercise group compared to the CT and RT exercise groups. A GROUP main effect was also determined for LDL density ($p < 0.0002$). LDL density was higher in the ET and RT

groups compared to the CT group. No other GROUP main effects were determined for the remaining lipid and lipid ratio variables.

A TRAINING PERIOD main effect was observed for LDL_2-C ($p < 0.0096$) and apo A-I ($p < 0.0011$). Each of these lipid variables were significantly lower after 12 weeks of exercise training compared to pre-training values. The training effect on LDL_2-C and apo A-I is illustrated in Figure C-1.

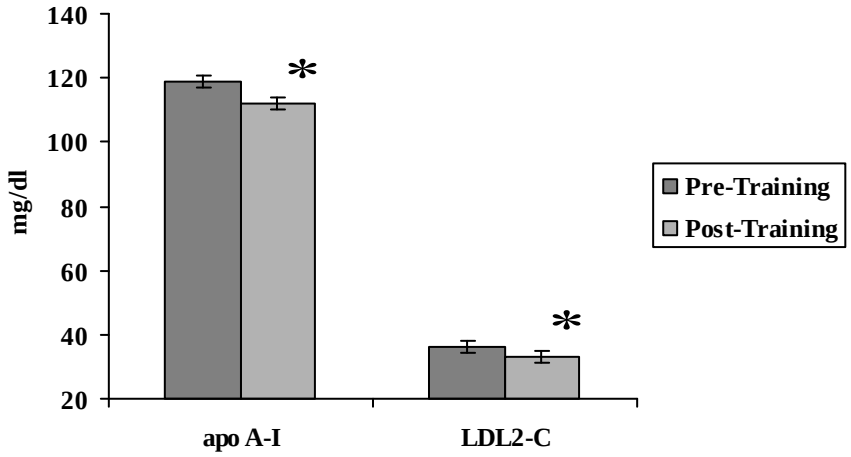

Figure C-1. TRAINING PERIOD main effect for LDL_2-C and apo A-I. LDL_2-C concentrations at each of the training periods were: Pre-Training = 36 ± 2; Post-Training = 33 ± 2. Apo A-I concentrations at each of the training periods were: Pre-Training = 119 ± 4; Post-Training = 112 ± 4. Values are means (mg / dL) ± SEM. * Significant differences between training periods ($p < 0.05$).

No TRAINING PERIOD main effects were noted for TC, HDL-C, HDL_3-C, HDL_2-C, TG, LDL-C, VLDL-C, IDL-C, LDL_1-C, LDL_3-C, LDL_4-C, LDL density, hs-Crp, and Lp (a). These results are presented in Table C-11.

Table C-11. Non-Significant Variable Results across TRAINING PERIOD.

	Training Period	
Variable	Pre-Training	Post-Training
TC	163.4 ± 4.9	159.8 ± 5.4
HDL-C	46.1 ± 1.3	43.7 ± 1.4
HDL_3-C	36.8 ± 1	34.8 ± 1.1
HDL_2-C	9.2 ± 0.4	8.9 ± 0.4
TG	99 ± 7.6	94 ± 6.9
VLDL-C	17.5 ± 0.6	17.1 ± 0.54
IDL-C	6.8 ± 1	6.9 ± 0.8
LDL-C	99.9 ± 4.9	98.6 ± 4.9
LDL_1-C	17 ± 1.3	16.3 ± 1.3
LDL_3-C	30.3 ± 2.5	32.6 ± 2.6
LDL_4-C	3.5 ± 0.5	3.6 ± 0.6
LDL density	1.0313 ± 0.0001	1.0313 ± 0.0001
Lp (a)	5.7 ± 0.3	5.3 ± 0.3
hs-Crp	1.3 ± 0.3	1.7 ± 0.3

Values are the means ± SEM. Hs-Crp expressed in mg / L, LDL density expressed in g / cm^2 while all other lipid values are in mg / dL. Values are collapsed across exercise groups (RT, ET, and CT).

Lipoprotein Enzyme Activities

No GROUP x TRAINING PERIOD interactions, GROUP main effects, or TRAINING PERIOD main effects were determined for any of the plasma volume

adjusted lipoprotein enzyme activities. The responses of LPLa and HTGLa are presented in Table C-12.

Table C-12. The Lipoprotein Enzyme Response to Chronic Exercise Training.

	Training Period	
Enzyme Activity	Pre-Training	Post-Training
LPLa	5.76 ± 0.27	5.66 ± 0.19
HTGLa	11.72 ± 0.78	11.72 ± 0.71

Values are means (μmol FFA / mL / hr) ± SEM. No significant differences were found between training periods for any of the lipoprotein enzyme activities listed.

Reliability of Biochemical Analyses

The interassay coefficients of variation determined from control serum measured with each assay run were total plasma lipase activity, 10.4%; HTGLa, 10.6%; apo B, 5%; apo A-I, 8%.

Intraassay coefficients of variation, determined from control serum measured multiple times within each assay run were: total plasma lipase activity, 7%; HTGLa, 3%; apo B, 10%; apo A-I, 3%.

Pre-Training Acute Exercise

The Effect of a Single Session of Resistance, Endurance, and Combination Exercise on Lipid Metabolism and Non-Traditional Cardiovascular Disease Risk Markers in Previously Untrained Males

Baseline Physiological / Dietary Characteristics, Lipid Profiles, Non-Traditional CHD Risk Markers, and Lipoprotein Enzyme Activities

While every effort was taken to ensure that subjects randomly assigned to the three exercise groups were similar with respect to age, weight, and relative body fat, baseline analysis of the physiological data indicated that significant differences ($p < 0.05$) did occur. Body weight and waist circumference were all lower in the RT group compared to the CT group. Baseline descriptive physiological characteristics are presented in Table C-13.

Dietary intake logs were analyzed (see Appendix F) for: 1) total daily caloric intake (KCAL); 2) total daily grams of carbohydrate (CHO), fat (FAT), protein (PROT), saturated fat (SFAT), polyunsaturated fat (PSAT), and total daily milligrams of cholesterol (CHOL); 3) and the ratio of polyunsaturated to saturated fat (P / S ratio). Seven day physical activity records were analyzed (see Appendix G) for average daily energy expenditure (DAYEXP). It was determined that PROT and SFAT were lower in the CT group compared to the RT group, while CHOL was higher in the RT group compared to the other two groups. Baseline differences in dietary variables are presented in Table C-14.

Table C-13. Pre-Training Acute Baseline Physiological Variables.

	Exercise Group			
Variable	RT	ET	CT	Range
Age (yrs)	22 ± 1 [a]	24 ± 1 [a]	22 ± 1 [a]	18 – 34
Height (in)	68.9 ± 0.66 [a]	69.7 ± 0.91 [ab]	71.7 ± 0.54 [b]	65 – 75
Weight (kg)	73.8 ± 4 [a]	85.6 ± 5 [ab]	95.9 ± 4.7 [b]	56 – 117
BMI (kg/m^2)	23.98 ± 1.04 [a]	27.4 ± 1.78 [a]	29.05 ± 1.64 [a]	19 – 37
% Fat	15 ± 1 [a]	19 ± 3 [a]	20 ± 3 [a]	7 – 36
Waist (in)	32 ± 1.2 [a]	36 ± 1.6 [ab]	38 ± 1.4 [b]	25 – 46
Hip (in)	38.6 ± 1 [a]	41.6 ± 1 [ab]	43.3 ± 1 [b]	34 – 49
W / H ratio	0.83 ± 0.02 [a]	0.87 ± 0.02 [a]	0.88 ± 0.02 [a]	0.75 – 1
RSBP (mmHg)	122 ± 2.9 [ab]	118 ± 5.1 [a]	133 ± 3.7 [b]	90 – 158
RDBP (mmHg)	72 ± 2.7 [a]	77 ± 2.9 [ab]	82 ± 2.1 [b]	60 – 94
$\dot{V}O_{2peak}$ (mL/kg/min)	43.6 ± 1.6 [a]	41.8 ± 2.7 [a]	42.7 ± 2.2 [a]	27.4 – 55.5
EXKCAL	232 ± 22 [a]	355 ± 5 [b]	353 ± 1.2 [b]	113 – 399
EXDUR	57 ± 2 [a]	30 ± 2 [b]	43 ± 1 [c]	24 – 78

All data are presented as the mean ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n =10; CT = combination exercise group, n = 12; % Fat = body fat relative to body weight; BMI = body mass index; W / H ratio = waist girth / hip girth; RSBP = resting systolic blood pressure; RDBP = resting diastolic blood pressure; $\dot{V}O_{2peak}$ = peak oxygen consumption as measured during a standardized graded exercise test; EXKCAL = caloric expenditure of acute exercise session; EXDUR = duration (minutes) of acute exercise session. Exercise group means within each row with same letters are not different ($p < 0.05$).

Table C-14. Pre-Training Acute Baseline Dietary Variables.

	Exercise Group			
Variable	RT	ET	CT	Range
KCAL	2513 ± 99 [a]	2375 ± 244 [a]	2233 ± 175 [a]	1247 – 3343
CHO	302 ± 17 [a]	310 ± 30 [a]	329 ± 32 [a]	140 – 461
FAT	98 ± 6 [a]	81 ± 9 [a]	69 ± 7 [a]	27 – 121
PROT	103 ± 8 [a]	88 ± 8 [ab]	71 ± 3 [b]	53 – 140
SFAT	34 ± 3 [a]	27 ± 3 [ab]	21 ± 2 [b]	6 – 46
CHOL	375 ± 64 [a]	240 ± 36 [b]	182 ± 25 [b]	52 – 668
PSFAT	7.6 ± 0.81 [a]	6.0 ± 0.97 [a]	4.7 ± 1.2 [a]	0.96 – 11
P / S ratio	0.23 ± 0.02 [a]	0.25 ± 0.04 [a]	0.22 ± 0.05 [a]	0.04 – 0.48

All data are presented as the mean ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n =10; CT = combination exercise group, n = 12. Dietary means are daily average calculated from seven day dietary intake logs. Daily energy expenditure means are daily average calculated from seven day physical activity records. CHO, FAT, PROT, SFAT, PSFAT are nutrients expressed as grams / day. CHOL is expressed as milligrams / day. Exercise group means within each row with same letters are not different ($p < 0.05$).

Baseline lipid and lipid ratios are displayed in Table C-15. With respect to the non-traditional CHD risk markers, significant differences were determined between exercise groups for LDL density and apo B ($p < 0.0176$). The density of LDL was significantly higher ($p < 0.0053$) in the ET group compared to the CT group. Apo B concentration was greater in the ET group compared to the RT and CT exercise groups. Baseline differences in the apo B / apo A-I ratio ($p < 0.0046$) were also determined.

Baseline differences in non-traditional CHD risk markers and lipoprotein enzyme activities are displayed in Table C-16. Significant correlations between selected baseline lipid, non-traditional CHD risk markers, and enzyme activities are summarized in Tables C-17 and C-18.

Table C-15. Pre-Training Acute Baseline Lipids and Lipid Ratios.

	Exercise Group			
Lipids[#]	RT	ET	CT	Range
TC	165 ± 11 [a]	163 ± 7 [a]	163 ± 8 [a]	118 – 226
LDL-C	98 ± 10 [a]	103 ± 8 [a]	99 ± 9 [a]	62 – 164
HDL-C	48 ± 3 [a]	42 ± 2 [a]	48 ± 2 [a]	31 – 60
HDL_2-C	10 ± 1 [a]	8 ± 0.4 [a]	10 ± 1 [a]	6 – 14
HDL_3-C	38 ± 2 [a]	34 ± 2 [a]	38 ± 2 [a]	25 – 46
TG	103 ± 13 [a]	129 ± 15 [a]	90 ± 10 [a]	30 – 172
Lipid Ratios				
TC / HDL-C	3.47 ± 0.26 [a]	3.95 ± 0.26 [a]	3.53 ± 0.32 [a]	2.4 – 5.8
LDL-C / HDL-C	2.09 ± 0.23 [a]	2.5 ± 0.24 [a]	2.18 ± 0.3 [a]	1.1 – 4.2
HDL_2-C / HDL_3-C	0.26 ± 0.01 [a]	0.24 ± 0.01 [a]	0.26 ± 0.01 [a]	0.19 – 0.31

All data are presented as the mean ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n =10; CT = combination exercise group, n = 12; [#] Lipid values are in mg / dL; Exercise group means within each row with same letters are not different ($p < 0.05$).

Table C-16. Pre-Training Acute Baseline Non-Traditional CHD Risk Markers and Enzyme Activities.

	Exercise Group			
Variable	RT	ET	CT	Range
hs-Crp	2.1 ± 1 [a]	0.88 ± 0.17 [a]	1.17 ± 0.26 [a]	0.2 – 6.9
Lipids[#]				
LDL_1-C	16 ± 2 [a]	17 ± 1 [a]	18 ± 3 [a]	5 – 41
LDL_2-C	35 ± 4 [a]	33 ± 4 [a]	40 ± 4 [a]	18 – 70
LDL_3-C	30 ± 4 [a]	35 ± 5 [a]	27 ± 4 [a]	14 – 60
LDL_4-C	4 ± 1 [a]	4 ± 1 [a]	3 ± 0.5 [a]	1 – 13
LDL density	1.0314 ± 0.0002 [ab]	1.0319 ± 0.0002 [a]	1.0308 ± 0.0002 [b]	1.0291 – 1.0326
apo A-I	118 ± 3 [a]	111 ± 9 [a]	128 ± 8 [a]	79 – 168
apo B	86 ± 7 [b]	121 ± 9 [a]	92 ± 9 [b]	49 – 163
apo B / apo A-I	0.73 ± 0.05 [b]	1.15 ± 0.12 [a]	0.73 ± 0.08 [b]	0.32 – 2.05
VLDL-C	18 ± 2 [a]	19 ± 1 [a]	16 ± 1 [a]	12 – 29
IDL-C	7 ± 2 [a]	9 ± 2 [a]	6 ± 2 [a]	0 – 20
NONHDL-C	116 ± 11 [a]	121 ± 7 [a]	115 ± 9 [a]	74 – 187
Lp (a)	6 ± 1 [a]	5 ± 0.5 [a]	6 ± 0.5 [a]	3 – 10
Enzyme Activities[Π]				
LPLa	6.13 ± 0.69 [a]	5.22 ± 0.32 [a]	5.92 ± 0.38 [a]	4 – 10
HTGLa	12.0 ± 1.4 [a]	12.22 ± 1.8 [a]	11.25 ± 1 [a]	6 – 21

All data are presented as the mean ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n =10; CT = combination exercise group, n = 12; Hs-Crp expressed in mg / L, LDL density expressed in g / cm^2. [#] Lipid values are in mg / dL; [Π]LPLa and HTGLa are in μmol FFA / mL / hr. Exercise group means within each row with same letters are not different ($p < 0.05$).

Table C-17. Pre-Training Acute Pearson Product – Moment Correlations for Selected Lipid, Non-Traditional CHD Risk Markers, and Enzyme Variables at Baseline.

Variable	TC	HDL-C	HDL_2-C	HDL_3-C	TG	LDL-C	Lp (a)	apo A-I
VLDL-C	0.516			-0.360	0.484	0.482		-0.510
IDL-C	0.757	-0.376		-0.380	0.437	0.762		
LDL-C	0.967							
LDL density	0.453				0.461		-0.382	
LDL_1-C	0.776					0.791		
LDL_2-C	0.631					0.641	0.370	
LDL_3-C	0.590	-0.436	-0.550	-0.369	0.467	0.648		
HDL-C			0.887	0.984	-0.547	-0.356		
HDL_2-C				0.794	-0.504	-0.361		
HDL_3-C			0.794		-0.533			
TG		-0.547	-0.504	-0.533				-0.554
apo B	0.365	-0.382		-0.373		0.469		
LPLa			0.380					
Lp (a)					-0.438			0.414
NONHDL-C	0.969	-0.369	-0.366			0.994		

Relationships were determined after combining data from all exercise groups. All relationships shown are statistically significant ($p < 0.05$).

Table C-18. Pre-Training Acute Pearson Product – Moment Correlations for Selected Physiological, Lipid, Non-Traditional CHD Risk Markers, and Enzyme Variables at Baseline.

Variable	Weight (kg)	RSBP	LPMAX	BPMAX	$\dot{V}O_{2peak}$ (mL/kg/min)
LDL_2-C		0.465			
LDL_4-C	-0.362				
apo A-I			0.431		
Weight (kg)			0.532	0.514	-0.543
LBM (kg)				0.716	

Relationships were determined after combining data from all exercise groups. All relationships shown are statistically significant ($p < 0.05$).

The Responses of Serum Lipids, Non-Traditional CHD Risk Markers, and Enzyme Activities to Acute Exercise in Untrained Men

The Exercise Session

The exercise sessions were developed to elicit a 350 kcal energy expenditure at 70% of the subject's measured $\dot{V}O_{2peak}$. Specifically, for the acute bout of endurance exercise, subjects were asked to walk or jog on a motor-driven treadmill at 70% of their $\dot{V}O_{2peak}$ for the duration required to expend 350 kcals of energy. Exercise intensity and rate of energy expenditure were verified by respiratory gas exchange data, measured by open-circuit spirometry, at the start of exercise and at 10 minute intervals throughout the exercise session.

Due to the low caloric cost of resistance exercise, the estimated time required to expend 350 kcal required a duration that most subjects would not be able to complete. Pilot data collected from our laboratory (unpublished observations) indicated that subjects would be required to complete roughly 80 minutes of resistance exercise to expend 350 kcal. However, during the acute resistance exercise session, all subjects were unable to continue after completing the standard 56 minute resistance training session. Thus, subjects in the RT exercise group completed the standard resistance exercise workout. Weights used for each exercise were calculated as approximately 70% of the 1RM, and chosen so that the subject would be challenged, but yet able to complete all repetitions in each exercise set, and continue exercise until completion of the session. Heart rate was monitored continuously and expired gases were measured during 16 minutes of exercise with a portable metabolic system (Medical Graphics CPX/D) to determine the caloric expenditure of the training session.

For those in the CT group, subjects were asked to either walk or jog at an intensity equal to 70% of their maximal effort recorded on their earlier exercise test ($\dot{V}O_{2peak}$) for a length of time needed to burn 175 kcals of energy. After they finished with this activity, they performed several resistance exercises at the number of sets, repetitions, and duration required to expend 175 kcal of energy. Weights used for each exercise were calculated as approximately 70% of the 1 RM, and chosen so that the subject would be challenged, but yet able to complete all repetitions in each exercise set, and continue exercise until 175 kcal of energy is expended. Heart rate was monitored continuously and expired gases were measured every 10 minutes of exercise with a

portable metabolic system (Medical Graphics CPX/D) to determine the duration required to expend 175 kcal of energy.

The average energy expenditure for the RT, ET, and CT exercise groups were 232 ± 22, 355 ± 5, and 353 ± 1.2 kcals respectively. The average exercise duration for the RT, ET, and CT exercise groups were 56 .67 ± 3.2, 30.45 ± 2.5, and 43.18 ± 1.5 minutes respectively. Thus, significant differences occurred with regards to both the caloric expenditure ($p < 0.0001$) and the duration ($p < 0.0001$) of the exercise sessions. The caloric expenditure was lower in the RT group compared to both the ET and CT exercise groups. The exercise duration was greater in the RT group compared to both the ET and CT exercise group.

Plasma Volume Changes

A single session of prolonged exercise can lead to alterations in plasma volume which, in turn, may have a significant effect on lipoprotein-lipid concentrations. Thus, all lipid, non-traditional CHD risk markers, and lipoprotein enzyme activities were adjusted for the plasma volume percent change that resulted from the prolonged exercise sessions.

No GROUP x TIME interaction, TIME main effect, or GROUP main effect was determined for the exercise-induced plasma volume shifts. However, plasma volume was expanded 2.6 % ± 2 above baseline values by the 24 h time-point.

Lipoprotein Lipids, Non-Traditional CHD Risk Markers, and Lipid Ratios

Significant GROUP x TIME interactions, as determined from the 3 x 2 ANOVAs, were noted for TC ($p < 0.0198$), HDL-C ($p < 0.0028$), HDL_3-C ($p < 0.0110$),

HDL_2-C ($p < 0.0075$), NONHDL-C ($p < 0.0445$), LDL-C ($p < 0.0224$), and LDL_1-C ($p < 0.0278$). There was a significant difference in TC, with respect to time, only in the RT exercise group. The TC concentration was significantly decreased 24 h after the exercise session compared to the baseline time-point.

There was a significant difference in HDL-C between the exercise groups only at the 24 h post exercise time-point. The HDL-C concentration was higher in the CT group compared to both ET and RT exercise groups. There was also a significant difference in HDL-C, with respect to time, in the RT exercise group. The HDL-C concentration was significantly lower 24 h after the exercise session compared to the baseline time-point.

There was a significant difference in HDL_3-C between the exercise groups only at the 24 h post exercise time-point. The HDL_3-C concentration was higher in the CT group compared to both ET and RT exercise groups. There was also a significant difference in HDL_3-C, with respect to time, in the RT exercise group. The HDL_3-C concentration was significantly lower 24 h after the exercise session compared to the baseline time-point.

There was a significant difference in HDL_2-C, with respect to time, in all exercise groups. The HDL_2-C concentration was significantly elevated 24 h after the exercise session compared to the baseline time-point in the CT and ET exercise groups. Conversely, the HDL_2-C concentration was significantly lower 24 h after the exercise session compared to the baseline time-point in the RT exercise group.

There was a significant difference in LDL_1-C, with respect to time, only in the ET exercise group. The LDL_1-C concentration was significantly elevated 24 h after the

exercise session compared to the baseline time-point. The calculations for simple main effects did not reach significance for the lipid variables NONHDL-C and LDL-C. No other GROUP x TIME interactions were noted for the remaining lipoprotein lipid, non-traditional CHD risk markers, or lipid ratios.

GROUP main effects were determined for apo B ($p < 0.0085$) and the apo B / apo A-I ratio ($p < 0.0038$). Each of these variables were greater in the ET group compared to the RT and CT exercise groups. A GROUP main effect was also determined for LDL density ($p < 0.0010$). LDL density was higher in the ET and RT groups compared to the CT group. The GROUP main effects for apo B, and apo A-I, and LDL density are reported in Table C-19.

Table C-19. GROUP Main Effects for apo B, apo B / apo A-I, and LDL Density.

	Exercise Group		
Variable	RT	ET	CT
apo B	82 ± 4.6 [a]	120 ± 6.5 [b]	93 ± 6.5 [a]
apo B / apo A-I	0.70 ± 0.03 [a]	1.17 ± 0.1 [b]	0.74 ± 0.06 [a]
LDL density	1.0316 ± 0.0002 [a]	1.0319 ± 0.0002 [a]	1.0308 ± 0.0001 [b]

Values are the exercise group means ± SEM, collapsed across time-points (baseline and 24 h post-exercise). Exercise group means within each row with same letters are not different ($p < 0.05$).

A TIME main effect was observed for TG ($p < 0.0329$) and LDL_2-C ($p < 0.0341$). A decrease in plasma volume adjusted TG and LDL_2-C concentrations occurred at the 24 h post-exercise blood draw time period. LDL_4-C concentrations followed a similar trend. However, none of the changes in LDL_4-C concentrations were statistically significant ($p > 0.05$). The exercise-induced effects on TG, LDL_2-C, and LDL_4-C are displayed in Figure C-2.

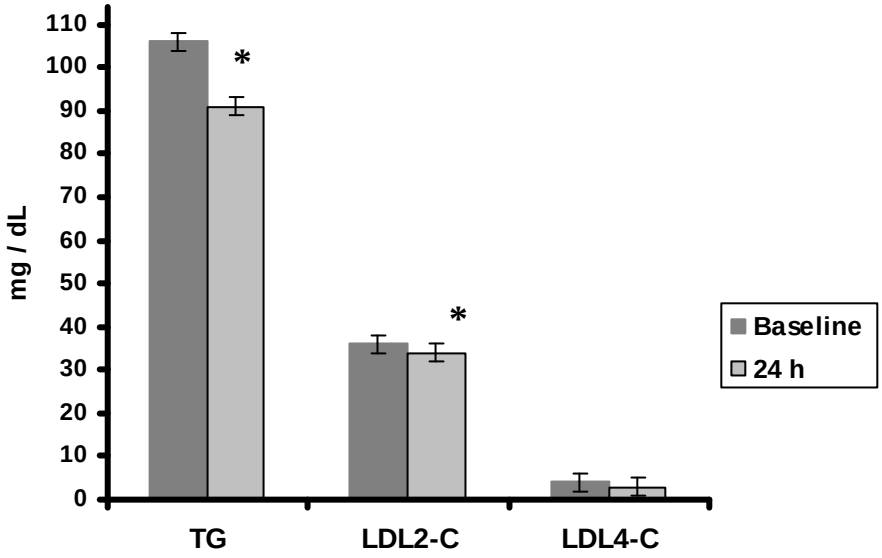

Figure C-2. TIME main effects for TG, LDL_2-C, and LDL_4-C. Values are means (mg / dL) ± SEM. TG concentrations at each of the time-points were: Baseline = 106 ± 8; 24 h = 91 ± 7. LDL_2-C concentrations at each of the time-points were: Baseline = 36 ± 2; 24 h = 34 ± 2. LDL_4-C concentrations at each of the time-points were: Baseline = 4 ± 1; 24 h = 3 ± 1. * Significant differences between time-points ($p < 0.05$).

A TIME main effect was found for LDL_3-C ($p < 0.0215$). An increase in plasma volume adjusted LDL_3-C concentration occurred at the 24 h post-exercise blood draw time-period. This exercise-induced effect on LDL_3-C is displayed in Figure C-3.

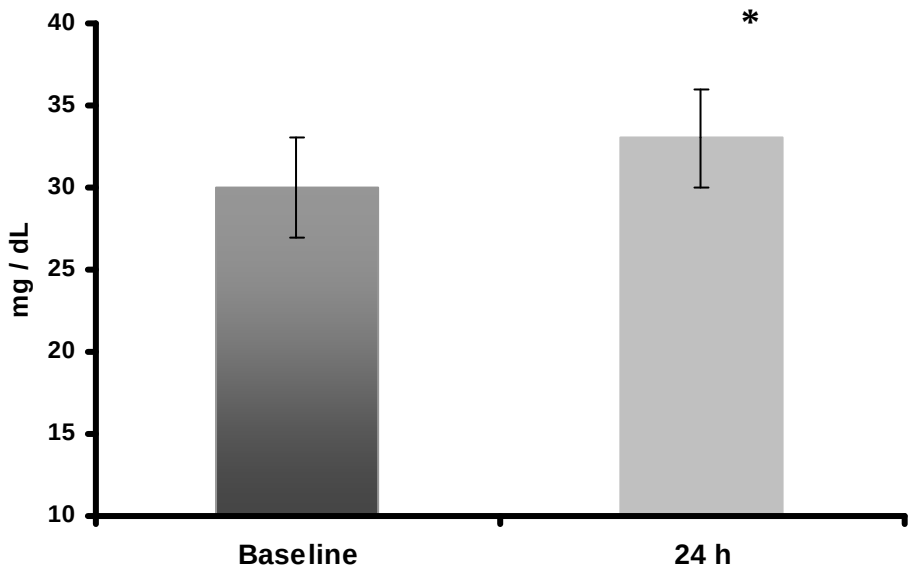

Figure C-3. TIME main effect for LDL_3-C. Values are means (mg / dL) ± SEM. LDL_3-C concentrations at each of the time-points were: Baseline = 30 ± 3; 24 h = 33 ± 3. * Significant differences between time-points ($p < 0.05$).

A TIME main effect was also noted for the TC / HLD-C ratio ($p < 0.0300$). The TC / HDL-C ratio was significantly elevated at the 24 h post-exercise time point. Both the LDL-C / HDL-C and HDL_2-C / HDL_3-C ratios remained essentially unchanged after exercise. The exercise induced effect on the TC / HDL-C ratio is illustrated in Table C-20.

Table C-20. TIME Main Effects for Lipid Ratios.

	Time	
Ratio	Baseline	24 h
TC / HDL-C	3.65 ± 0.17	3.71 ± 0.17*
HDL_2-C / HDL_3-C	0.25 ± 0.01	0.26 ± 0.01
LDL-C / HDL-C	2.26 ± 0.15	2.31 ± 0.15
apo B / apo A-I	0.88 ± 0.06	0.88 ± 0.08

Values are means ± SEM. * Significant differences between time-points ($p < 0.05$).

Lipoprotein Enzyme Activities

No GROUP x TIME interactions, GROUP main effects, or TIME main effects were determined for any of the plasma volume adjusted enzyme activities. However, LPLa demonstrated a non-significant increase at the 24 h post-exercise blood draw time period. The responses of LPLa and HTGLa are presented in Table C-21.

Table C-21. The Lipoprotein Enzyme Response to Acute Exercise.

	Time	
Enzyme Activity	Baseline	24 h
LPLa	5.76 ± 0.27	6.17 ± 0.36
HTGLa	11.72 ± 0.78	12.03 ± 0.85

Values are means (μmol FFA / mL / hr) ± SEM. No significant differences were found between time-points for any of the lipoprotein enzyme activities listed.

No TIME main effects were noted for apo B, apo A-I, hs-Crp, Lp (a), VLDL-C, IDL-C, LDL_4-C, or LDL density. These results are presented in Table C-22.

Table C-22. Non-Significant Variable Results across TIME.

	Time	
Variables[#]	Baseline	24 h
apo B	99.9 ± 5.6	97.8 ± 5.8
apo A-I	119 ± 4.2	116.3 ± 4.6
VLDL-C	17.5 ± 0.6	18.2 ± 0.7
IDL-C	7.2 ± 1	8.5 ± 1.3
Lp (a)	5.7 ± 0.3	5.4 ± 0.4
hs-Crp[*]	1.34 ± 0.3	1.29 ± 0.1
LDL density[γ]	1.0313 ± 0.0001	1.0314 ± 0.0002

All data are presented as means ± SEM. [#] Values are in mg / dL; [*]hs-Crp expressed in mg / L; [γ]LDL density expressed in g / cm^2.

Reliability of Biochemical Analyses

The interassay coefficients of variation determined from control serum measured with each assay run were total plasma lipase activity, 10.4%; HTGLa, 10.6%; apo B, 5%; apo A-I, 8%.

Intraassay coefficients of variation, determined from control serum measured multiple times within each assay run were: total plasma lipase activity, 7%; HTGLa, 3%; apo B, 10%; apo A-I, 3%.

Post-Training Acute Exercise

The Effect of a Single Session of Resistance, Endurance, and Combination Exercise on Lipid Metabolism and Non-Traditional Cardiovascular Disease Risk Markers in Trained Males

Baseline Physiological / Dietary Characteristics, Lipid Profiles, Non-Traditional CHD Risk Markers, and Lipoprotein Enzyme Activities

While every effort was taken to ensure that subjects randomly assigned to the three exercise groups were similar with respect to age, weight, and relative body fat, baseline analysis of the physiological data did indicate that significant differences ($p < 0.05$) did occur. Body weight and waist girth were lower in the RT group compared to the CT group. In addition, $\dot{V}O_{2peak}$ was lower in the CT group compared to both ET and RT groups. Baseline physiological characteristics are presented in Table C-23.

Table C-23. Post-Training Acute Baseline Physiological Variables.

	Exercise Group			
Variable	RT	ET	CT	Range
Age (yrs)	22 ± 1[a]	23 ± 1[a]	22 ± 1[a]	18 - 27
Height (in)	68.9 ± 0.66[a]	70.2 ± 0.84[a]	71.3 ± 0.61[a]	66 - 74
Weight (kg)	75.7 ± 4[a]	87.7 ± 4[ab]	99.7 ± 5[b]	60 - 117
BMI (kg/m^2)	24.62 ± 1.0[a]	27.7 ± 1.6[ab]	30.55 ± 1.8[b]	20 - 37
% Fat	14 ± 1[a]	17 ± 3[a]	21 ± 3[a]	5 - 35
Waist (in)	32 ± 1[a]	36 ± 1.5[ab]	39 ± 1.5[b]	27.5 - 44
Hip (in)	37.6 ± 1[a]	40.3 ± 1[ab]	43.2 ± 1[b]	34 - 47.5
W / H ratio	0.85 ± 0.01[a]	0.88 ± 0.02[a]	0.89 ± 0.02[a]	0.81 - 0.97
RSBP (mmHg)	123 ± 3.5[a]	124 ± 3.2[a]	130 ± 5.5[a]	108 - 160
RDBP (mmHg)	77 ± 3.6[a]	78 ± 1.9[a]	80 ± 3.6[a]	56 - 104
$\dot{V}O_{2peak}$ (mL/kg/min)	45.7 ± 1.2[a]	46.1 ± 2.2[a]	40.1 ± 1.5[b]	34.6 - 54
EXKCAL	254 ± 18[a]	500 ± 0.2[b]	500 ± 0.00[b]	117 – 501
EXDUR	58 ± 0.0[a]	35.35 ± 0.6[b]	63.56 ± 1.8[c]	33 – 71

All data are presented as the mean ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n = 9; CT = combination exercise group, n = 9; % Fat = body fat relative to body weight; BMI = body mass index; W / H ratio = waist girth / hip girth; RSBP = resting systolic blood pressure; RDBP = resting diastolic blood pressure; $\dot{V}O_{2peak}$ = peak oxygen consumption as measured during a standardized graded exercise test; EXKCAL = kcal expended during acute exercise; EXDUR = duration (minutes) of acute exercise session. Exercise group means within each row with same letters are not different ($p < 0.05$).

Dietary intake logs were analyzed (see Appendix F) for: 1) total daily caloric intake (KCAL); 2) total daily grams of carbohydrate (CHO), fat (FAT), protein (PROT), saturated fat (SFAT), polyunsaturated fat (PSAT), and total daily milligrams of

cholesterol (CHOL); 3) and the ratio of polyunsaturated to saturated fat (P / S ratio). Seven day physical activity records were analyzed (see Appendix G) for average daily energy expenditure (DAYEXP). Baseline differences in dietary variables are presented in Table C-24.

Table C-24. Post-Training Acute Baseline Dietary and Physical Activity Variables.

	Exercise Group			
Variable	RT	ET	CT	Range
KCAL	2467 ± 77 [a]	2256 ± 213 [a]	2277 ± 205 [a]	1071 - 3145
CHO	289 ± 34 [a]	300 ± 26 [a]	314 ± 33 [a]	61 - 443
FAT	91 ± 5 [a]	80 ± 11 [a]	81 ± 11 [a]	26 - 123
PROT	89 ± 5 [a]	80 ± 7 [a]	78 ± 5 [a]	43 - 116
SFAT	30 ± 3 [a]	27 ± 4 [a]	26 ± 4 [a]	7 - 50
CHOL	276 ± 62 [a]	213 ± 35 [a]	266 ± 56 [a]	51 - 668
PSFAT	7.9 ± 1.38 [a]	4.9 ± 0.76 [a]	7.9 ± 1.9 [a]	0.66 - 17
P / S ratio	0.30 ± 0.08 [a]	0.20 ± 0.04 [a]	0.30 ± 0.06 [a]	0.05 – 0.81

All data are presented as the mean ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n = 9; CT = combination exercise group, n = 9. Dietary means are daily average calculated from seven day dietary intake logs. Daily energy expenditure means are daily average calculated from seven day physical activity records. CHO, FAT, PROT, SFAT, PSFAT are nutrients expressed as grams / day. CHOL is expressed as milligrams / day. Exercise group means within each row with same letters are not different ($p < 0.05$).

Baseline analyses of lipoprotein-lipid, non-traditional CHD risk markers, and lipoprotein enzyme activity data revealed that LDL density was the only variable that

was significantly different between the three exercise groups ($p < 0.003$). The density of LDL was lower in the CT group compared to the other two exercise groups. Baseline lipid and lipid ratio data are displayed in Table C-25. Baseline non-traditional CHD risk markers and lipoprotein enzyme activities are represented in Table C-26. Significant correlations between selected baseline lipid, non-traditional CHD risk markers, and enzyme activities are summarized in Tables C-27 and C-28.

Table C-25. Post-Training Acute Baseline Lipids and Lipid Ratios.

	Exercise Group			
Lipids[#]	RT	ET	CT	Range
TC	164 ± 10 [a]	158 ± 9 [a]	166 ± 13 [a]	106 – 228
TG	83 ± 12 [a]	93 ± 10 [a]	94 ± 8 [a]	53 - 143
LDL-C	101 ± 9 [a]	98 ± 8 [a]	104 ± 11 [a]	50 - 161
HDL-C	45 ± 2 [a]	42 ± 2 [a]	45 ± 4 [a]	33 - 64
HDL_2-C	9 ± 1 [a]	9 ± 1 [a]	9 ± 1 [a]	5 - 14
HDL_3-C	36 ± 2 [a]	33 ± 2 [a]	36 ± 3 [a]	26 - 50
Lipid Ratios				
TC / HDL-C	3.65 ± 0.26 [a]	3.83 ± 0.26 [a]	3.83 ± 0.36 [a]	2.47 - 5.25
LDL-C / HDL-C	2.26 ± 0.23 [a]	2.39 ± 0.24 [a]	2.43 ± 0.33 [a]	1.16 - 3.72
HDL_2-C / HDL_3-C	0.25 ± 0.01 [a]	0.26 ± 0.01 [a]	0.26 ± 0.01 [a]	0.16 - 0.32

All data are presented as the mean ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n = 9; CT = combination exercise group, n = 9; [#] Lipid values are in mg / dL; Exercise group means within each row with same letters are not different ($p < 0.05$).

Table C-26. Post-Training Acute Baseline Non-Traditional CHD Risk Markers and Lipoprotein Enzyme Activities.

	Exercise Group			
Variable	RT	ET	CT	Range
hs-Crp	2.43 ± 1 [a]	1.67 ± 1 [a]	1.44 ± 0.4 [a]	0.3 - 9.2
Lipids[#]				
LDL density	1.0316 ± 0.003 [a]	1.0318 ± 0.002 [a]	1.0307 ± 0.002 [b]	1.0295 - 1.0328
LDL_1-C	15 ± 1 [a]	17 ± 2 [a]	18 ± 3 [a]	7 - 39
LDL_2-C	31 ± 4 [a]	34 ± 4 [a]	36 ± 5 [a]	15 - 67
LDL_3-C	35 ± 5 [a]	32 ± 4 [a]	33 ± 6 [a]	11 - 62
LDL_4-C	5 ± 2 [a]	2 ± 0.5 [a]	3 ± 0.6 [a]	1 - 17
apo A-I	111 ± 3 [a]	110 ± 8 [a]	120 ± 11 [a]	80 - 166
apo B	85 ± 8 [a]	108 ± 10 [a]	86 ± 10 [a]	45 - 158
apo B / apo A-I	0.77 ± 0.08 [a]	1.03 ± 0.13 [a]	0.73 ± 0.09 [a]	0.48 - 1.86
VLDL-C	17 ± 1 [a]	17 ± 1 [a]	17 ± 1 [a]	13 - 27
IDL-C	6 ± 2 [a]	7 ± 1 [a]	9 ± 2 [a]	0 - 21
NONHDL-C	118 ± 10 [a]	115 ± 9 [a]	121 ± 12 [a]	63 - 184
Lp (a)	5 ± 0.4 [a]	5 ± 0.6 [a]	5 ± 0.6 [a]	3 - 9
Enzyme Activities[Π]				
LPLa	6.00 ± 0.50 [a]	5.22 ± 0.22 [a]	5.78 ± 0.28 [a]	5 - 9
HTGLa	12.0 ± 1.1 [a]	12.11 ± 1.6 [a]	10.33 ± 1.2 [a]	5 - 19

All data are presented as the mean ± SEM. RT = resistance exercise group, n = 9; ET = endurance exercise group, n = 9; CT = combination exercise group, n = 9; Hs-Crp expressed in mg / L, LDL density expressed in g / cm^2. [#] Lipid values are in mg / dL; [Π]LPLa and HTGLa are in μmol FFA / mL / hr. Exercise group means within each row with same letters are not different ($p < 0.05$).

Table C-27. Post-Training Acute Pearson Product – Moment Correlations for Selected Lipid, Non-Traditional CHD Risk Markers, and Enzyme Variables at Baseline.

Variable	TC	HDL_2-C	HDL_3-C	TG	LDL-C	VLDL-C
VLDL-C	0.497			0.496	0.493	
IDL-C	0.714				0.712	
LDL-C	0.963					
LDL density	-0.450				-0.412	
LDL_1-C	0.786				0.781	0.479
LDL_2-C	0.688				0.684	
LDL_3-C	0.594				0.659	
LDL_4-C						0.461
HDL-C		0.900	0.987			
HDL_3-C		0.819				
apo B					0.403	
Lp (a)				-0.484	0.379	

Relationships were determined after combining data from all exercise groups. All relationships shown are statistically significant ($p < 0.05$).

Table C-28. Post-Training Acute Pearson Product – Moment Correlations for Selected Physiological, Lipid, Non-Traditional CHD Risk Markers, and Enzyme Variables at Baseline.

Variable	RSBP	LPMAX	BPMAX	$\dot{V}O_{2peak}$ (mL/kg/min)	W / H ratio
apo A-I					0.414
Weight (kg)	0.582	0.504	0.382	-0.842	

Relationships were determined after combining data from all exercise groups. All relationships shown are statistically significant ($p < 0.05$).

The Responses of Serum Lipids, Non-traditional CHD Risk Markers, and Enzyme Activities to Acute Exercise in Trained Men

The Exercise Session

The exercise sessions were developed to elicit a 500 kcal energy expenditure at 70% of the subject's measured $\dot{V}O_{2peak}$. Specifically, for the acute bout of endurance exercise, subjects were asked to walk or jog on a motor-driven treadmill at 70% of their $\dot{V}O_{2peak}$ for the duration required to expend 500 kcals of energy. Exercise intensity and rate of energy expenditure were verified by respiratory gas exchange data, measured by open-circuit spirometry, at the start of exercise and at 10 minute intervals throughout the exercise session.

Due to the low caloric cost of resistance exercise, the estimated time required to expend 500 kcal required a duration that most subjects would not be able to complete. Pilot data collected from our laboratory (unpublished observations) indicated that

subjects would be required to complete roughly 80 minutes of resistance exercise to expend just 350 kcal. Thus, subjects in the RT exercise group were only required to complete a standard resistance exercise workout. Weights used for each exercise were calculated as approximately 70% of the 1RM, and chosen so that the subject would be challenged, but yet able to complete all repetitions in each exercise set, and continue exercise until completion of the session. Heart rate was monitored continuously and expired gases were measured during 16 minutes of exercise with a portable metabolic system (Medical Graphics CPX/D) to determine the caloric expenditure of the training session.

For those in the CT group, subjects were asked to either walk or jog at an intensity equal to 70% of their maximal effort recorded on their earlier exercise test ($\dot{V}O_{2peak}$) for a length of time needed to burn 250 kcals of energy. After they finished with this activity, they performed several resistance exercises at the number of sets, repetitions, and duration required to expend 250 kcal of energy. Weights used for each exercise were calculated as approximately 70% of the 1RM, and chosen so that the subject would be challenged, but yet able to complete all repetitions in each exercise set, and continue exercise until 250 kcal of energy was expended. Heart rate was monitored continuously and expired gases were measured every 10 minutes of exercise with a portable metabolic system (Medical Graphics CPX/D) to determine the duration required to expend 250 kcal of energy.

The average energy expenditure for the RT, ET, and CT exercise groups were 254 ± 18, 500 ± 0.2, and 500 ± 0.2 kcals respectively. The average exercise duration for

the RT, ET, and CT exercise groups were 58 ± 0.0, 35.35 ± 0.58, and 63.56 ± 1.8 minutes respectively. The range was 33 – 71 minutes for all exercise modes combined. Thus, significant differences occurred with regards to both the caloric expenditure ($p < 0.0001$) and the duration ($p < 0.0001$) of the exercise sessions (See Table C-23).

Plasma Volume Changes

A single session of prolonged exercise can lead to alterations in plasma volume that, in turn, may have a significant effect on lipoprotein-lipid concentrations. Thus, all lipid, non-traditional CHD risk markers, and lipoprotein enzyme activities were adjusted for the plasma volume percent change that resulted from the acute exercise sessions.

No GROUP x TIME interaction or GROUP main effects were determined for Hb, Hct, or the exercise-induced plasma volume shifts. However, a TIME main effect ($p < 0.0024$) was determined indicating that a significant plasma volume shift occurred over the blood sampling period. Plasma volume was expanded 4.8 % ± 1 above baseline values by the 24 h time-point.

Lipoprotein Lipids, Non-Traditional CHD Risk Markers, and Lipid Ratios

There were no GROUP x TIME interactions determined from the 3 x 2 ANOVAs on any of the plasma volume adjusted dependent variables. Therefore, the group differences (GROUP main effect) and the influence of acute exercise on lipoprotein-lipids, non-traditional CHD risk markers, and lipoprotein enzymes (TIME main effect) are reported.

With regards to the non-traditional CHD risk markers, a GROUP main effect was noted for LDL density ($p < 0.01$). The density of LDL was significantly lower in the CT group compared to the other two groups. No other group differences in any of the other dependent variables were detected.

TIME main effects were determined for TC ($p < 0.0063$), LDL-C ($p < 0.0210$), NONHDL-C ($p < 0.0051$), VLDL-C ($p < 0.001$), IDL-C ($p < 0.0020$), HDL-C ($p < 0.0181$), HDL_2-C ($p < 0.0080$), LDL_3-C ($p < 0.0260$), and LDL density ($p < 0.040$). Each of these variables were significantly higher 24 h after the exercise session when compared to baseline values. The exercise-induced effects on these variables are displayed in Figures C-4 through C-8.

HDL_3-C concentrations were elevated from 35.2 ± 1.2 to 36.7 ± 1 mg / dL 24 h after the exercise session. However, this change in plasma volume adjusted HDL_3-C did not reach statistical significance ($p > 0.05$).

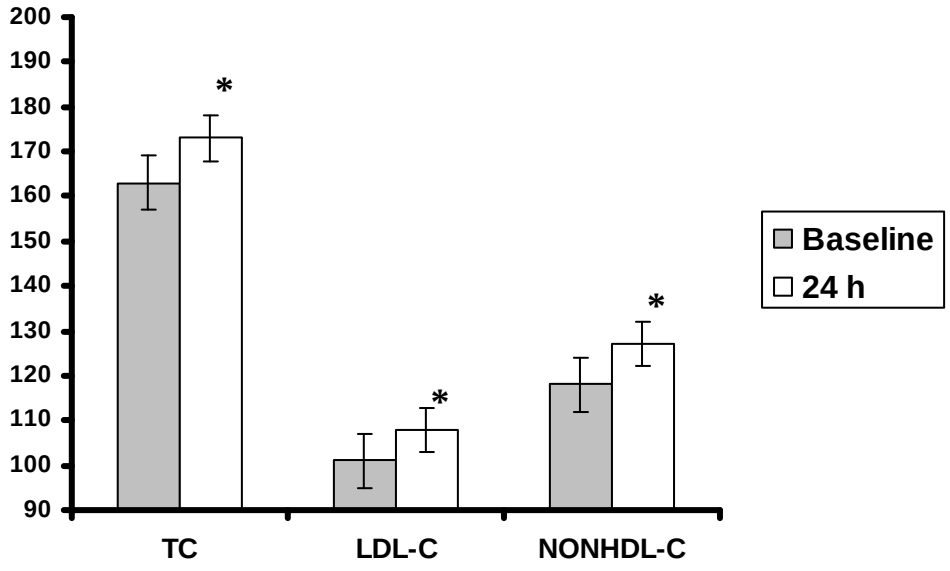

Figure C-4. TIME main effects for TC, LDL-C, and NONHDL-C. Values are means (mg / dL) ± SEM. TC concentrations at each of the time-points were: Baseline = 163 ± 6; 24 h = 173 ± 6. LDL-C concentrations at each of the time-points were: Baseline = 101 ± 5; 24 h = 108 ± 5. NONHDL-C concentrations at each of the time-points were: Baseline = 118 ± 6; 24 h = 127 ± 6. * Significant differences between time-points ($p < 0.05$).

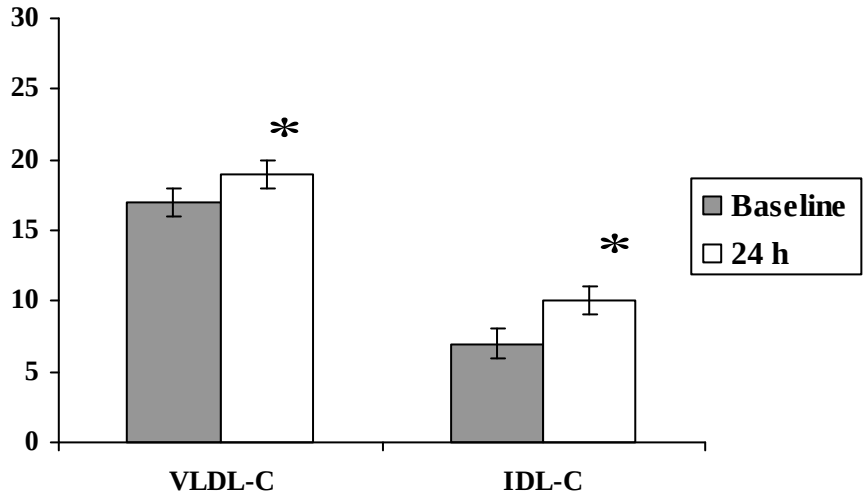

Figure C-5. TIME main effects for VLDL-C and IDL-C. VLDL-C concentrations at each of the time-points were: Baseline = 17 ± 1; 24 h = 19 ± 1. IDL-C concentrations at each of the time-points were: Baseline = 7 ± 1; 24 h = 10 ± 1. Values are means (mg / dL) ± SEM. * Significant differences between time-points ($p < 0.05$).

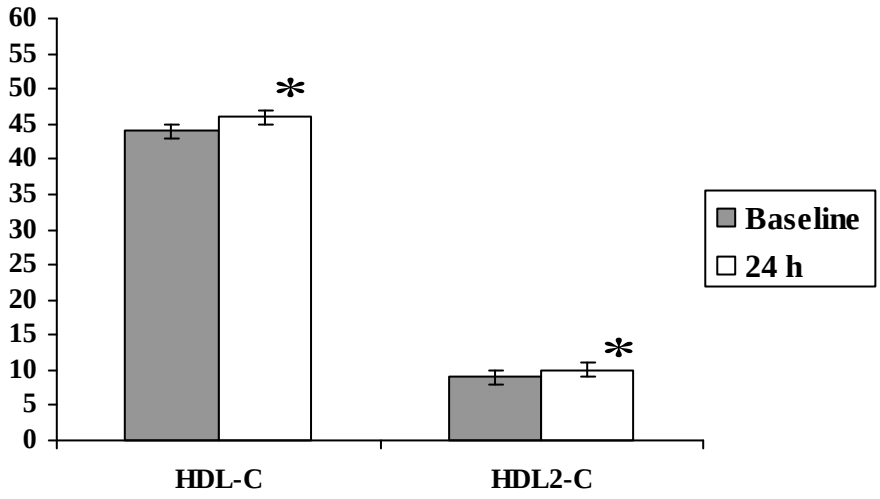

Figure C-6. TIME main effects for HDL-C and HDL_2-C. HDL-C concentrations at each of the time-points were: Baseline = 44 ± 1.5; 24 h = 46 ± 1.4. HDL_2-C concentrations at each of the time-points were: Baseline = 9 ± 0.4; 24 h = 10 ± 0.5. Values are means (mg / dL) ± SEM. * Significant differences between time-points ($p < 0.05$).

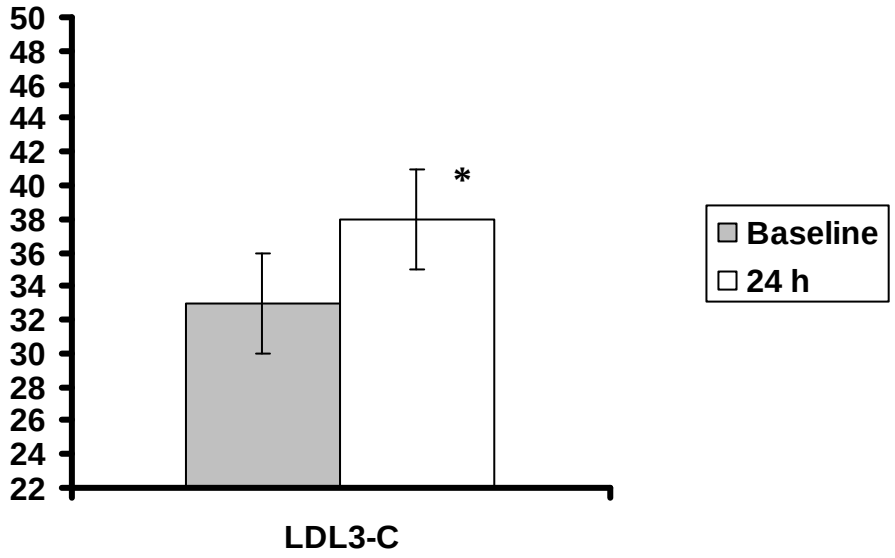

Figure C-7. Post-Training TIME main effect for LDL_3-C. Values are means (mg / dL) ± SEM. LDL_3-C concentrations at each of the time-points were: Baseline = 33 ± 3; 24 h = 38 ± 3. * Significant differences between time-points ($p < 0.05$).

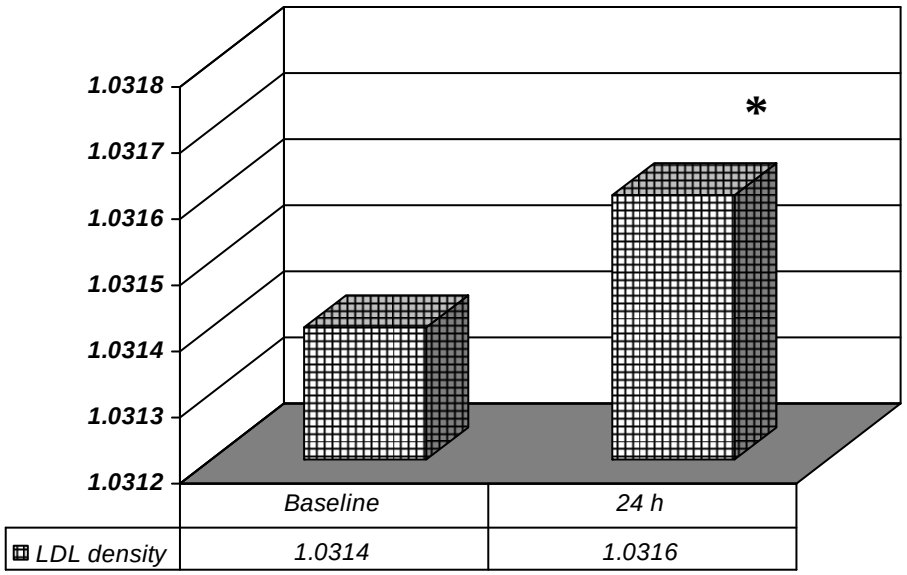

Figure C-8. TIME main effect for LDL density. Values are means (g / cm^2) ± SEM. The density of LDL at each of the time-points was: Baseline = 1.0314 ± 0.0001; 24 h = 1.0316 ± 0.0002. * Significant differences between time-points ($p < 0.05$).

Lipoprotein Enzyme Activities

No GROUP x TIME interactions or GROUP main effects were determined from the 3 x 2 ANOVAs on any of the plasma volume adjusted lipoprotein enzyme activities. Thus, the influence of acute exercise on lipoprotein enzymes (TIME main effect) are reported.

A TIME main effect was found only for LPLa ($p < 0.0493$). LPLa was elevated at the 24 h post-exercise blood draw time-period. The LPLa response to exercise is illustrated in Figure C-9.

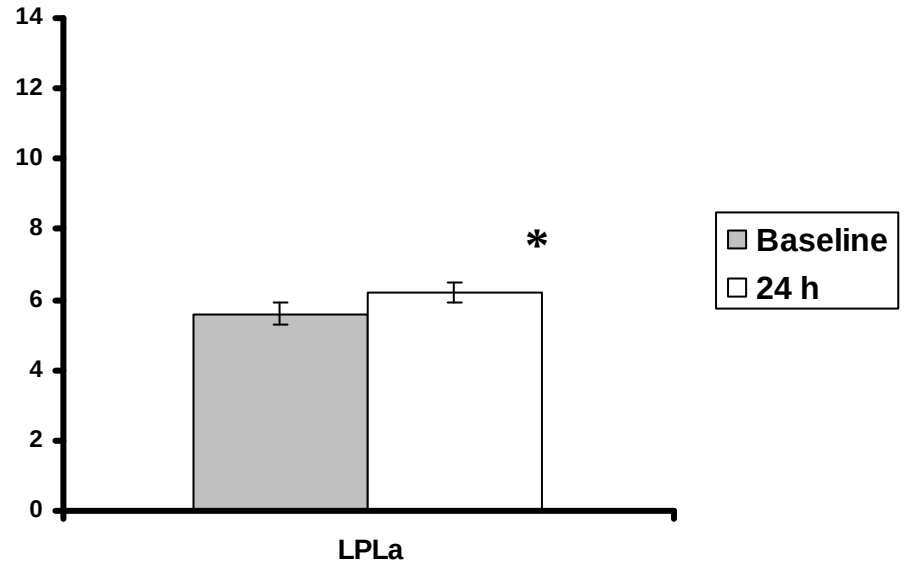

Figure C-9. TIME main effect for LPLa. Values are means (μmol FFA / mL / hr) ± SEM. LPLa at each of the time-points were as follows: Baseline = 5.6 ± 0.2; 24 h = 6.2 ± 0.3. * Significant differences between time-points ($p < 0.05$).

No TIME main effects were noted for TG, apo B, apo A-I, TC / HDL ratio, LDL-C / HDL-C ratio, HDL_2-C / HDL_3-C ratio, apo B / apo A-I ratio, HTGLa, hs-Crp, Lp (a), LDL_1-C, LDL_2-C, or LDL_4-C. These results are presented in Table C-29.

Table C-29. Post-Training Acute Non-Significant Variable Results Across TIME.

	Time	
Variables[#]	Baseline	24 h
TG	90 ± 5.9	96 ± 7.4
apo B	93.7 ± 5.7	98.6 ± 6.3
apo A-I	113.1 ± 4.3	114.3 ± 4.4
LDL_1-C	16.7 ± 1.4	18.1 ± 1.2
LDL_2-C	33.9 ± 2.3	33.8 ± 2.3
LDL_4-C	3.6 ± 0.6	3.3 ± 0.6
Lp (a)	5.3 ± 0.3	5.2 ± 0.2
hs-Crp[*]	1.85 ± 0.5	1.27 ± 0.2
Lipid Ratios		
TC / HDL-C	3.77 ± 0.17	3.81 ± 0.16
LDL-C / HDL-C	2.36 ± 0.15	2.39 ± 0.14
HDL_2-C / HDL_3-C	0.25 ± 0.01	0.26 ± 0.01
apo B / apo A- I	0.86 ± 0.06	0.85 ± 0.06
Enzyme Activities[Π]		
HTGLa	11.5 ± 0.77	11.7 ± 0.81

All data are presented as means ± SEM. [#] Values are in mg / dL; [*]hs-Crp expressed in mg / L; [Π]HTGLa expressed in μmol FFA / mL / hr.

Reliability of Biochemical Analyses

The interassay coefficients of variation determined from control serum measured with each assay run were total plasma lipase activity, 10.4%; HTGLa, 10.6%; apo B, 5%; apo A-I, 8%.

Intraassay coefficients of variation, determined from control serum measured multiple times within each assay run were: total plasma lipase activity, 7%; HTGLa, 3%; apo B, 10%; apo A-I, 3%.

APPENDIX D

INFORMED CONSENT

Title of the Study: The Effect of Resistance, Endurance, and Combination Exercise on Lipid Metabolism and Lipoprotein Particle Size in Previously Untrained Males.

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Address of Steven E. Martin or Dr. Stephen F. Crouse, Principal Investigators:

Applied Exercise Science Laboratory
Department of Health and Kinesiology
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I,_____, have been informed by the investigators that I have been selected to participate in a study entitled: *The Effect of Resistance, Endurance, and Combination Exercise on Lipid Metabolism and Lipoprotein Particle Size in Previously Untrained Males*.

I understand this study will be conducted between January 1, 2003 and December 31, 2004 at the Applied Exercise Science Laboratory located in the Steed building at Texas A&M University, College Station, Texas. Sixty males from the Texas A&M University and Bryan - College Station, Texas community will be recruited for this study. To be considered as a subject for this study, I must: 1) be an untrained male between the ages of 18 and 40 years; 2) be generally healthy without any known medical or physical problems which would keep me from performing endurance, resistance exercise, or combined endurance and resistance exercise; 3) have less than 35% of my total body weight as fat; 4) **not** have any medical disorder which may alter my blood fats, cholesterol, or my blood clotting ability; 5) **not** use drugs known to alter blood fats or cholesterol, including tobacco products and excessive consumption of alcohol (> 2 oz. per day); and **not** use drugs which might affect the ability of my blood to clot.

GENERAL INFORMATION CONCERNING MY RIGHTS AS A STUDY PARTICIPANT

I have been invited to participate in a research study about exercise and cholesterol. I have been informed that persons who participate in research are entitled to certain rights. These rights include but are not limited to my right to:

1. Be informed of the nature and goal of the research.

The general goals of this research project are to: 1) evaluate the acute and chronic effects of endurance, resistance, and combined exercise on the blood fat and cholesterol profiles in sedentary men; 2) compare the effects of resistance exercise versus endurance exercise versus combined exercise on blood fat and cholesterol changes in sedentary men; 3) relate the changes in blood fats and cholesterol that may occur following the exercise bout to changes in cardiovascular disease risk status.

To fulfill these general goals, this project has been designed to answer the following questions. (NOTE: the term "lipid risk factors" refers to those blood fats and cholesterol called lipids and lipoproteins that are thought to be related to heart disease.)

1. Are the changes in blood lipids and lipoproteins that occur after resistance exercise in sedentary men different than those found in sedentary men performing endurance or combination exercise?

2. Are the changes in blood lipids and lipoproteins that occur after an acute bout of endurance, resistance, and/or combination exercise any different between trained and untrained individuals?

<u>Procedures to be Followed:</u>

After I volunteer and give my informed consent to be a subject in this study, I understand I will be given a health history questionnaire to answer. I will be encouraged to answer these questionnaires to the best of my knowledge so that the investigators can make an accurate decision about the safety of the study for me. Following review of the questionnaire, the investigators will make a decision about allowing me to continue in the study. If I am selected to continue, I will be given instructions about dietary and physical activity requirements of the study. I will be asked to record my dietary habits over a three-day period, and my physical activity over a seven-day period. I will also be randomly assigned to one of four groups (endurance-exercise only, resistance-exercise only, combination resistance and endurance exercise, or a sedentary control group). After I am randomly assigned to one of the four groups, I will take part in the pre-training testing one week prior to the start of the training program.

On my next visit to the laboratory the investigators will record my height and weight, measure my lung function and volumes, assess my body composition, and

maximal oxygen consumption ($\dot{V}O_{2peak}$). To measure my lung function and volumes, they will ask me to breathe in and out as hard as I can through a mouthpiece attached to a machine that measures the amount of air I breathe in and out. I will also be asked to breathe pure oxygen from this machine while the machine calculates the amount of air I breathe in and out. This procedure enables the researchers to test my lungs. Next, they will have me put on a swimming suit. They will then use a pair of calipers to measure thicknesses of "pinches" of skin from several sites on my arms, legs, back, hips, stomach, and chest. They will use these skinfold measurements to estimate the amount of body fat I have. They will also use a tape measure to measure the circumference of my hips and waist. Next I will be asked to enter a large bathtub-like tank filled with warm water, and, with my head above water, sit on a chair attached to a scale. While seated on the chair, I will be asked to submerge myself and exhale all the air I can from my lungs. While I am under water for about five seconds, a technician will record my underwater weight from the scale. This procedure will be repeated several times. From this underwater weight the investigators will be able to determine the percentage of my total body weight which is composed of fat and non-fat tissue, like muscle and bone. In order to assess my maximal oxygen consumption ($\dot{V}O_{2peak}$), I will be asked to exercise on a motor-driven treadmill. For this test, ten electrodes will be placed on my skin for recording the activity of my heart at rest and during exercise. This heart recording is called an electrocardiogram (ECG). After resting ECG and blood pressure (BP) measurements have been made, I will be asked to complete a maximal graded exercise stress test (GXT). I have been informed that a standard Bruce Protocol will be used for the GXT. This type of test is used to determine my fitness level and is sometimes called a VO_{2max} test. It is performed hundreds of times each year in the laboratory without any problems. Strict protocols will be followed, and an exercise physiologist will be present throughout the test to insure my safety. For the treadmill test I will be asked to walk at a certain speed. The speed and incline I encounter while walking on the treadmill will increase every third minute until I can no longer continue walking or running. I will be in complete control to stop exercise when I decide I am too exhausted to continue. During the course of the test, I will breathe through a mouthpiece, which is connected to a computer so that exercise variables like my oxygen uptake and carbon dioxide production can be measured. Also, throughout the test, the technicians will monitor my ECG and blood pressure. The investigators will also ask me to return the three-day diet record and the physical activity record given to me previously. The investigators will determine the caloric intake and nutritional composition of my diet. I will continue to maintain my normal dietary habits throughout the length of the study. I will inform the investigators of any major changes in my diet during the study. I will also be asked to complete another three-day diet record at the end of the study.

One day later I will return to the laboratory so that investigators can measure my maximal torque production at two different speeds. As a subject I will also read as well as be verbally explained the methods and procedures that will be used to determine each of the above variables. Maximal torque production will be tested using a Biodex

isokinetic knee extension device at speeds of 90 and 240 degrees per second. Here the subjects will exert a maximal force at a velocity of 90 and 240 degrees per second while maximal torque and power are recorded.

About 2 days later, I will return to the laboratory so that investigators can measure my maximum strength during several different weight lifting exercises (i.e. one repetition maximum). My one repetition maximum will be determined for the following upper body exercises: the barbell bench press, lat pull-down, dumbbell military press, and barbell curl. Lower body exercises will include: the leg press and leg curl, and standing calf raise. The investigators will have me perform a light warm-up of 5-10 repetitions (for each exercise) at 40% of what they perceive as the most weight I could lift. After a 1-minute rest, I will perform 3-5 repetitions at 60%-80% of my perceived maximum. They will then add a small amount of weight to the exercise and I will attempt to complete the lift. I will rest for 3 to 5 minutes if I can complete the lift. They will then add another small amount of weight to the exercise. This process will continue until I fail to complete the lift with proper form. My one repetition maximum will be considered the weight of my last successfully completed lift. The investigators will also measure my vertical jump, and 40 yard dash time.

After about 3 days I will be asked to return to the laboratory on four consecutive for my pretraining, acute exercise testing blood draws. The blood sampling procedures for my first and third day will proceed as follows. Following a 12 hour fast, I will be asked to return to the laboratory to have my blood drawn. I will be asked to refrain from any moderate or strenuous physical activity for 72 hours (3 days) prior to the blood sampling. A blood sample, equal to about 3 to 4 teaspoons (15-20 ml), will be obtained by inserting a small plastic tube (catheter) into a vein in my arm. This catheter will remain in my arm for about 12 minutes until all blood samples have been obtained. This is much like an I.V. I might have in a hospital. This way, I will not need to receive more than one needle stick. While the catheter is in my arm, it does not usually cause pain. The blood collected will be analyzed for blood hemoglobin, hematocrit, and lipid risk factors. After this blood sample is obtained, I will receive an injection of a small amount of a substance called heparin through the catheter in my arm. I might recognize the name heparin as a “blood thinner” that some people with cardiovascular disease might take. This substance is indeed often used for this purpose. However, for the researcher’s purposes I will be receiving a much lower dose than is required to produce the “blood thinning” effect. The amount I receive will be based on my weight and may range from 1 to 1.5 teaspoons (4 to 8 ml). At the lower dosage level that the researchers will be using, this heparin will cause the release of certain proteins, called enzymes, from my blood vessels. The researchers are interested in measuring these enzymes since they affect the different kinds and amounts of lipid risk factors in the blood. After ten minutes, another 2 teaspoon (10 ml) blood sample will be drawn through the same catheter, and then the catheter will be removed and direct pressure will be held over the puncture site to prevent bleeding. The blood collected will be analyzed for blood hemoglobin, hematocrit, and lipid risk factors.

I have been informed that the blood sampling procedure for my second and fourth visit will be slightly different. For my second visit I will arrive at the laboratory following a 12 hour fast to complete a submaximal, experimental exercise session (day 2). If I am assigned to the control group, I will report to the lab for all blood sampling procedures, but will not perform any exercise. Specifically, if I am assigned to the endurance-only group, I will be asked to either walk or jog at an intensity equal to 70% of my maximal effort recorded on my earlier exercise test ($\dot{V}O_{2peak}$) for a length of time needed to burn 350 kcals of energy. This will involve exercising for about 30 to 60 minutes. If I am assigned to the resistance-training only group, I will perform each one of the assigned exercises for a total of 3 sets of 10 repetitions. The amount of weight used for this exercise session will be based on my one-repetition maximums, and designed so that I am challenged, but still able to complete all repetitions for each set and for a length of time needed to burn 350 kcals of energy. This exercise session should last about 60 – 70 minutes. If I am assigned to the combination exercise group I will be asked to either walk or jog at an intensity equal to 70% of my maximal effort recorded on my earlier exercise test ($\dot{V}O_{2peak}$) for a length of time needed to burn 175 kcals of energy. This will involve exercising for about 20 to 25 minutes. After I am finished with this activity, I will perform each one of the assigned resistance exercises for a total of 2 sets of 10 repetitions. The amount of weight used for this exercise session will be based on my one-repetition maximums, and designed so that I am challenged, but still able to complete all repetitions for each set and for a length of time needed to burn 175 kcals of energy. This exercise session should last about 30 to 40 minutes. The submaximal exercise bout will be personalized so that I will exercise at a level that is comfortable for me, and I will be allowed to take rest stops if I need to. My exercise session will be supervised by trained exercise technicians, and will be conducted in the Applied Exercise Science Lab at Texas A&M. The technicians will collect a blood sample immediately following the exercise session, and again 48 hours later (day 4). The blood sampling procedures for these days are as follows: A blood sample, equal to about 3 to 4 teaspoons (15-20 ml), will be obtained by inserting a small needle attached to a plastic tube (vacutainer) into a vein in my arm. The blood collected will be analyzed for blood hemoglobin, hematocrit, and lipid risk factors. (A total of four blood samples will be taken.) Over the four days the blood samples will be collected, the investigators will ask me to record my diet intake and refrain from any physical exercise and alcohol consumption.

As a subject I understand that upon completion of the pre-training testing described above I will begin the training program. I am aware that training will vary depending on which group I am placed in. If I am assigned to the control group, I will not perform any exercise, except for normal activities of daily living, over the duration of the study. I understand that each exercise group will take part in a training program that will last twelve weeks, allowing for one week of mid-training re-testing. The resistance-training group will train by participating in a basic resistance-training program. Every odd number week this group will train two times per week, and every even number week this group will train three times per week. The resistance-training

program will be a total body workout consisting of 2-4 sets of 6-12 repetitions on 8 exercises that train all the major muscle groups. The exercises will include leg press, leg curl, standing calf raise, barbell bench press, lat pull-down, dumbbell military press, barbell curl, and an abdominal crunch. A percentage of each subject's one-repetition maximums will be used to determine the intensity the subjects will work at each week. The intensity and number of repetitions performed for each exercise will change bi-weekly. The endurance only group will train by walking/running on a treadmill 2-3 times per week. This group will follow the same pattern of the resistance-training group by training twice on odd number weeks and three times on even number weeks. The running intensity will be determined by a percentage of the subject's maximum heart rate. Sessions will last between 20-45 minutes. The intensity and duration of each session will increase bi-weekly as training progresses. The combination training group will train five times per week. Every odd number week this group will perform the resistance program three times and the endurance program twice. Every even number week the combination group will perform the endurance program three times and the resistance program twice. I understand that the maximal oxygen uptake and one repetition maximum tests will be repeated during week seven of the study. I am aware that all testing will be conducted using the same methods and procedures that were used during the pre-testing. It has been explained to me that this re-testing will allow one-repetition maximums to be adjusted for weeks 8 – 13 of the resistance-training program. The week following completion of the training program I understand that all the variables tested during pre-testing will be tested for the final time, and that this post-training testing will follow the same methods and procedures as the pre-training testing.

After I have completed 12 weeks of exercise training sessions, I will be asked to return to the laboratory on four consecutive days for my posttraining, acute exercise testing blood draws. I am aware that these procedures will be the same as my pretraining, acute exercise testing blood draws. If I am assigned to the control group I will arrive at the lab along with the other subject groups for the blood sampling procedures, but will not exercise. I also realize that there will be a total of eight blood samples taken from me during the course of the study.

Discomforts or Risks to be Reasonably Expected:

I understand that the following few paragraphs give me information about the potential risks and discomforts that I may experience as a result of participating in this study. Additionally, the investigators have invited me to voice questions and concerns at any time during the course of the study so they may address these as they arise.

The body composition test requires that I be seated on a chair attached to scale in a tank of warm water. I will be asked to exhale all the air in my lungs and submerge myself completely. This procedure, though somewhat uncomfortable, is completed under the supervision of a trained technician and presents no more risks than swimming in an open pool under the supervision of a lifeguard.

The vertical jump test requires that I jump to my maximal ability. I understand that there is a possibility that I may injury myself upon landing but that this risk is minimal. This test will be administered on a level Astroturf surface to decrease the risk

of injury. The 40-yard dash test requires that I run as fast as I can for 40 yards in a straight line on Astroturf surface. I understand that during such a test, it is possible to suffer a muscle injury. This risk is minimal.

The assessment of lung function and residual volume simply requires that I place a clamp on my nose, and take several breaths into a tube connected to an open-loop spirometer supplied with pure oxygen. The analyzer will measure the concentration of nitrogen following completion of the test. The primary risk of this procedure is contamination of the mouthpiece and tubing between myself and the previous subject. This risk will be minimized by using disposable mouthpieces and by thoroughly washing the tubing between each subject use.

For the ECG, 10 electrodes are put on my skin to measure electrical activity of the heart. The 10 electrode sites will be prepped by cleaning the skin with alcohol and rubbing it lightly with an abrasive material like sandpaper. These procedures may cause some irritation and a mild stinging sensation. In addition, a slight possibility exists that I may be allergic to the gel used in the electrodes. This may cause some itching and redness of the area that might last for a day or two. The equipment used to record my ECG has been specifically designed to measure the electrical activity of my heart, and meets all safety specifications to minimize any risk of electrical shock.

I understand that the risks to me associated with the graded exercise treadmill test ($\dot{V}O_{2peak}$) are comparable to those I face whenever I perform hard exercise that causes me to sweat and breathe heavily. These include occasional abnormal blood pressure responses, the possibility of fainting, potentially abnormal heartbeats, heavy and difficult breathing, and, in rare instance, a heart attack. I am aware that I could also suffer orthopedic injuries, such as ankle, knee, hip or muscle strains and sprains, or, rarely, fractures of bones. I have been informed that studies have shown that my risk for death during this type of test is about 0.5 in 10,000, and my risk for harmful affects is about 5 to 8 in 10,000. The investigators have assured me that they will make every effort to minimize these risks by carefully reviewing my health and medical history questionnaire and evaluating my risk factors for disease. All these procedures will be done before I am allowed to exercise. If they find some physical problems that, in their judgment, make exercise risky, for my own protection they will not allow me to exercise in this study. In addition to these pretest procedures, trained exercise technicians and exercise physiologists will be in charge of conducting the test and observing my ECG and blood pressure during exercise. They are trained to recognize problems in my heart or in other bodily responses to the exercise test which could be dangerous, and to stop the test if necessary. The 6th edition of the American College of Sports Medicine's "Guidelines for Exercise Testing and Prescription" will be closely observed. One repetition maximum:

I understand that the risks associated with the one repetition maximum test are comparable to those I face whenever I perform hard exercise that causes me to sweat and breathe heavily. These include the risk of occasional abnormal blood pressure responses, injury to joints or muscles, such as ankle, knee, or hip sprains or, rarely, fractures, muscle strains/soreness, syncope, heart dysrhythmia, severe dyspnea, and, in rare instances, heart attack. I have been informed that studies have shown my risk for death

during this type of test is about 0.5 in 10,000, and my risk for harmful affects is about 5 to 8 in 10,000. The investigators have assured me that they will make every effort to minimize these risks by carefully reviewing my health and medical history questionnaire and evaluating my risk factors for disease. All these procedures will be done before I am allowed to exercise. If they find some physical problems that, in their judgment, make exercise risky, for my own protection they will not allow me to exercise in this study. In addition to these pretest procedures, trained exercise technicians and exercise physiologists will be in charge of conducting the test and observing my ECG and blood pressure during exercise. They are trained to recognize problems in my heart or in other bodily responses to the exercise test that could be dangerous, and to stop the test if necessary. Throughout all testing procedures, the 6th edition of the American College of Sports Medicine's "Guidelines for Exercise Testing and Prescription" will be closely observed.

I also understand that the risks associated with the resistance, endurance, or combination training sessions are comparable to those I face whenever I perform hard exercise that causes me to sweat and breathe heavily. These include the risk of occasional abnormal blood pressure responses, injury to joints or muscles, such as ankle, knee, or hip sprains or, rarely, fractures, muscle strains/soreness, syncope, heart dysrhythmia, severe dyspnea, and, in rare instances, heart attack. The investigators have assured me that they will make every effort to minimize these risks by carefully reviewing my health and medical history questionnaire and evaluating my risk factors for disease. All these procedures will be done before I am allowed to exercise. If they find some physical problems that, in their judgment, make exercise risky, for my own protection they will not allow me to exercise in this study. In addition, trained exercise technicians and exercise physiologists will be in charge of conducting the exercise training sessions and observing my heart rate and blood pressure during exercise. They are trained to recognize problems in my heart or in other bodily responses to the exercise test that could be dangerous, and to stop the exercise session if necessary. Throughout all exercise training sessions, the 6th edition of the American College of Sports Medicine's "Guidelines for Exercise Testing and Prescription" will be closely observed. I understand that obtaining the blood sample by using a catheter inserted into a vein in my arm is a routine procedure in this laboratory and in many clinical settings with rare adverse affects, although the puncture of the skin is accompanied by minor discomfort and may result in the development of a minor bruise next to the puncture site. However, as with any similar procedure disrupting the skin barrier, there is a risk of contracting an infection. The risk to me (and to the technician) will be minimized through the use of accepted sterile procedures which include: (1) use of surgical rubber gloves by the technician; (2) antiseptic cleansing (70% alcohol) of the involved site prior to puncture; (3) use of sterile equipment and instruments for each sample; and (4) proper dressing of the wound with antiseptic and bandaid following sample collection.

There is a small risk associated with the injection of heparin. Heparin is a drug that is used clinically to reduce blood clotting. The researchers will be using a very small dose (between 1/4 and 1/2 a teaspoon) to cause small amounts of fat-regulating enzymes

to be released from my blood vessels. There is a chance that this small dose of heparin may affect my blood clotting time and could, therefore, cause me to bleed more than I normally would if I were to suffer an injury soon after injection or had a medical condition, such as an ulcer, which can cause bleeding internally. In most people, however, blood clotting time is not measurably affected by a dose of heparin as low as the researchers will be using in this study. However, I will be asked not to consume anticoagulants such as aspirin, nonsteroidal anti-inflammatory medications, or Coumadin within 10 days prior to the administration of heparin. Furthermore, any effect caused by such a small dose will not last long, usually less than a few hours. Despite the minimal risk associated with the small amount of heparin used in healthy people, it would be particularly risky for me to receive heparin if I have any of the following conditions: known hypersensitivity or allergy to heparin, severe high blood pressure, hemophilia, thrombocytopenia, vascular purpuras, ulcers of the stomach or small intestine, liver disease with impaired hemostasis. If I am taking oral blood-thinning medication (Warfarin/Coumadin), I will not participate in this study, unless, on approval of my physician, I can discontinue use of these drugs prior to heparin treatment. However, I may also choose to participate without receiving the heparin treatments. This decision will be made by the investigators. I MUST make the researchers aware of any of these conditions before they draw my blood by truthfully informing them verbally and by answering the questions on the health and medical history questionnaire. The use of heparin will also increase the likelihood that I will have a bruise under my skin at the sight of the needle puncture for blood sampling. Finally, some people report local irritation or hypersensitivity to heparin with chills, fever, nausea, and vomiting.

Benefits of participation and alternative procedures:

I understand that the health/medical history and the exercise stress test will provide me with valuable information about the health of my heart, my risk of developing cardiovascular disease (CVD), and the safety of hard exercise. Furthermore, as part of the research procedures, blood pressure and ECG will be monitored during a maximal exercise test as well as during all experimental exercise sessions; this will provide me with important information related to the functional status of my cardiovascular system during maximal exertion and will be used diagnostically by the cardiologist to detect the presence or absence of abnormal heart beats and coronary heart disease. The blood tests for cholesterol, lipoproteins, and other blood fats will provide me with further information about my risk of developing heart disease.

I have been informed that the body composition assessment will provide me with information about the total amount of body fat I have, and what my ideal body weight should be. This will enable me to make educated decisions about how much weight I need to lose to achieve my ideal body weight.

Compensation:

As a subject in this study, I understand I will receive the previously outlined evaluations and tests at no cost to me. I will be given my individual results for; all screening procedures, the exercise test (GXT), and lipid response to the single exercise session. These results will be made available to me upon completion of all data analysis.

The investigators have informed me that they will make reasonable and proper efforts to prevent physical injury to me and to insure my safety throughout all phases of this research project. However, I am well aware that, as noted above, my participation in this study is not without risk. I understand that compensation for physical injuries or adverse effects incurred as a result of participating in this research is NOT available. **In the event of any emergency the investigators will call 911, however, Texas A&M University or the principle investigator will not cover any resulting medical bills or expenses.** The investigators have informed me that they are prepared to advise me about medical treatment in case I experience adverse consequences of any of the study procedures. However, I understand that it is my responsibility to report any injuries or ill effects to one of the investigators or study supervisors as soon as possible. The investigators have also provided me with Student Health Services Dial A Nurse number (979-845-2822) and the Health Center number (979-845-1511). I can access this system in case I have additional questions about my medical treatment. Phone numbers where the investigators may be reached are listed in the heading of this form.

Questions concerning the research and the procedures involved:

I understand that should I volunteer for this study, the procedures will be discussed with me in detail by one of the investigators. If I have any questions about the research or about my rights as a subject, the investigators have invited me to ask them. I am aware that if I have any questions later, I am invited to contact one of the investigators listed in the heading of this form.

Be instructed that consent to participate in the research may be withdrawn at any time, and that I may discontinue participation without prejudice.

Participation in this research is entirely voluntary. Refusal to participate will involve no penalty of any kind. If I decide to participate, I am free to withdraw my consent and discontinue participation at any time and for any reason. This will be without prejudice and any results which were obtained up to the time of my withdrawal will still be reported to me.

Be informed of the conditions under which my participation may be terminated by the investigator without regard to my consent.

I understand that falsification of any information provided by me to the investigators, whether verbal or written, will be grounds for termination of my participation without my consent. Furthermore, failure to comply with dietary recommendations prior to blood sampling, failure to report as scheduled for all blood sampling specified in the methods, or to follow instructions with regards to data collection and/or the submaximal exercise bout may result in termination of my participation in this study without my consent.

I have the opportunity to decide to consent or not to consent to participate in research without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on my decision.

My right to privacy.

I understand that I have the right to privacy. All information that is obtained in this study that can be identified with me will remain confidential, and will be stored in the laboratory of the principal investigator. All information that can be identified with me will be known only to the investigators and to those who will be responsible for statistical analysis of the data. It may be released to another physician of my choice upon my written request. The results of this study may be published in scientific journals without identifying me by name.

I have been given and have read an explanation of the procedures to be followed in this study, including an identification of those which are experimental.

I have been given and have read a description of the attendant risks and discomforts which may be associated with the experimental procedures used in this study, including those associated with blood sampling, exercise testing and training, assessment of body composition, and evaluation of lung function and volume.

I have been given and have read a description of the benefits that I may expect from participating in this study.

I have been offered an answer to any inquiries concerning the procedures.

I have been assured that steps will be taken to insure the confidentiality of my results, which will be housed in the Applied Exercise Science Laboratory. Neither my name nor any other descriptor that can identify me will be associated with the publication of the results of this study.

I understand that in the event of physical injury resulting from the research procedures described to me, there will be no financial compensation or free medical treatment offered to me.

I have not been requested to waive or release the institution, its agents or sponsors from liability for the negligence of its agents or employees. I have read and understand the explanations provided to me and voluntarily agree to participate in this study. I understand that I will be given a copy of the entire informed consent document to keep for my own records.

Date _____ Signature of Subject: _____
Address: _____
_____
Phone: _____
Signature of Principal Investigator: _____

This research has been reviewed and approved by the Institutional Review Board - Human Subjects in Research, Texas A&M University. For research related problems or questions regarding your rights, the Institutional Review Board may be contacted through Dr. Michael W. Buckley, Director, Research Compliance and Administration, Office of the Vice President for Research and Associate Provost for Graduate Studies, (979) 845-8585.
I understand that, in case of any further questions, I may contact one of the following individuals:

Mr. Steven Martin, M.S. or Dr. Stephen F. Crouse, Ph.D.
Applied Exercise Science Laboratory
(979) 845-9418 or 845-3997

APPENDIX E

HEALTH HISTORY QUESTIONNAIRE

Please complete this form as accurately and completely as possible. The information you provide will be used to evaluate your health by the physician or exercise physiologist who will see you in our laboratory. All information will be treated as privileged and confidential.

IDENTIFICATION AND GENERAL INFORMATION

1. Name _____ 2. Soc. Sec.#_____ 3. Today's Date _____
Last First M.I. mo/da/yr

4. Age _____ yrs 5. Date of Birth _____ 6. Sex ____Male ____Female

7.Home Address_____
Street City State Zip

8. Office Address or Department _____

9. Home Phone #_____ 10. Office Phone #_____ 11. Occupation _____
12.Personal Physician_____
Name Street City State Zip

ILLNESSES AND MEDICAL PROBLEMS Check all the conditions or diseases for which you have been diagnosed and/or treated. Also give the date of occurrence or diagnosis. If you suspect that you may suffer from one of the conditions, please indicate this in the right margin after the date.

Condition Diagnosed	Yes	Date (mo/yr)
13. AIDS	__	_____
14. Alcoholism	_	_____
15. Anemia	_	_____
16. Arthritis	_	_____
17. Asthma	_	_____
18. Bronchitis (chronic)	_	_____
19. Cancer:		
20. Breast	_	_____
21. Cervix	_	_____
22. Colon	_	_____
23. Lung	_	_____
24. Uterus	_	_____
25. Other_____	_	_____
26. Cirrhosis (liver)	_	_____
27. Colitis (ulcerative)	_	_____
28. Depression	_	_____
29. Diabetes	_	_____
30. Emphysema	_	_____
31. Epilepsy	_	_____
32. Frequent Bleeding	_	_____
33. Hepatitis B	_	_____
34. Pneumonia	_	_____

	Yes	Date (mo/yr)
35. Tuberculosis	_	_____
36. Renal/Kidney Problems	_	_____
37. Other_____	_	_____

Cardiovascular Problems Diagnosed

	Yes	Date (mo/yr)
38. Stroke	_	_____
39. Heart Attack	_	_____
40. Coronary Disease	_	_____
41. Rheumatic Fever	_	_____
42. Rheumatic Heart Disease	_	_____
43. Heart Valve Problem	_	_____
44. Heart Murmur	_	_____
45. Enlarged Heart	_	_____
46. Heart Rhythm Problem	_	_____
47. Other Heart Problems	_	_____
48. High Blood Pressure (controlled)	_	_____
49. High Blood Pressure (uncontrolled)	_	_____
50. High Blood Cholesterol	_	_____
51. Diseases of the Arteries	_	_____
52. Phlebitis	_	_____
53. Systemic or Pulmonary Embolus	_	_____
54. Other _____	_	_____
55. Other _____	_	_____

Do You Now Have or Have You Recently Had:

	Yes	Most Recent Occurrence (mo/yr)
56. Seizures	_	_____
57. Chest pain on exertion relieved by rest	_	_____
58. Chest pain not always associated with exertion?	_	_____
59. Shortness of breath lying down, relieved by sitting up?	_	_____
60. Unexpected weight loss (more than 10 lbs)?	_	_____
61. Unexpected rectal bleeding	_	_____
62. Leg Pain after walking short distances?	_	_____

Women Only (Men May Skip to Number 64)
Please Answer the Following:

	Yes	Date (mo/yr)
63. Was your last pelvic exam or Pap smear abnormal?	___	_____
64. Do you have menstrual period problems?	___	_____
65. List number of menstrual periods in last year		
66. When was your last menstrual period? (1st day) month_____day_____ yr		
67. Please give number of: pregnancies_____ living children_____		

Men And Women Answer the Following:

Have you ever had:	Yes	Date (mo/yr)
68. A chest x-ray?	__	_____
69. An abnormal chest x-ray?	__	_____
70. An ECG (electrocardiogram)?	__	_____
71. An abnormal ECG?	__	_____
72. An exercise stress test?	__	_____
73. An abnormal exercise stress test?	__	_____

MEDICATIONS Check those medications which you are currently taking on a regular basis. If your medication is not listed, please list it in blanks marked "other".

74. ___None
75. ___Aldomet
76. ___Allergy Medication
77. ___Aminophylline
78. ___Antacids
79. ___Aspirin
80. ___Asthma Inhaler
81. ___Birth control pills
82. ___Blocardren (Timolol)
83. ___Bumex
84. ___Butazolidin
85. ___Catapres
86. ___Cardizem (Diltiazem)
87. ___Corgard (Nadolol)
88. ___Coumadin
89. ___Crystodigin
90. ___Diabinese
91. ___Digitalis
92. ___Digitoxin
93. ___Digoxin (Lanoxin)
94. ___Dilantin
95. ___Dyazide
96. ___Dymelor
97. ___Feldane
98. ___Hydrodiuril
99. ___Hydropres
100. ___Hygroton
101. ___Inderal (Propranolol)
102. ___Insulin
103. ___Iron
104. ___Isoptin (Verapamil)
105. ___Isordil
106. ___Lanoxin
107. ___Lasix
108. ___Librium
109. ___Lopressor
110. ___Maxizide
111. ___Minipress
112. ___Motrin
113. ___Muscle Relaxant
114. ___Naprosyn
115. ___Nitro-bid
116. ___Nitroglycerin
117. ___Norpace
118. ___Norvasc
119. ___Oral hypoglycemic agents
120. ___Orinase
121. ___Penicillin
122. ___Persantine
123. ___Potassium
124. ___Pravachol
125. ___Prednisone
126. ___Pro-banthine
127. ___Procardia (Nifedipine)
128. ___Procan SR
129. ___Pronestyl
130. ___Quinaglut
131. ___Quinidine
132. ___Reglan
133. ___Reserpine
134. ___Ser-Ap-Es
135. ___Sleeping pills
136. ___Tagamet
137. ___Tenormin (Atenolol)
138. ___Thiazides
139. ___Thyroid
140. ___Trandate (Labetalol)
141. ___Valium
142. ___Visken (Pindolol)
143. ___Vitamins
144. ___Zantac
145. ___Zyloprim
146. ___Others
147. ___Others
148. ___Others
149. ___Others
150. ___Others
151. ___Others

SURGICAL HISTORY Check the surgical procedures you have had and give the date of the surgery.

	Yes	Date (mo/yr)
152. Appendectomy	__	_____
153. Knee Surgery or ankle surgery	__	_____
154. Arm or shoulder surgery	__	_____
155. Back surgery	__	_____

	Yes	Date (mo/yr)
156. Hysterectomy (women only)	__	_____
157. Vasectomy (men only)	__	_____

	Yes	Date (mo/yr)
Cancer related surgery		
158. Breast	__	_____
159. Cervix	__	_____
160. Colon	__	_____
161. Lung	__	_____
162. Uterus	__	_____
163. Liver	__	_____
164. Kidney	__	_____
165. Other (Specify)_____	__	_____

	Yes	Date (mo/yr)
Heart surgery		
166. Heart catheterization	__	_____
167. Angioplasty (PTCA)	__	_____
168. Coronary bypass (CABG)	__	_____
169. Valve repair/replacement	__	_____
170. Other	__	_____

ORTHOPEDIC PROBLEMS Place a check in the blank to indicate any of the following orthopedic problems you may have.

		Yes	Most Recent Occurrence (mo/yr)
171.	Low back pain	__	_____
172.	Shoulder pain	__	_____
173.	Elbow pain	__	_____
174.	Wrist or hand pain	__	_____
175.	Hip problems	__	_____
176.	Knee problems	__	_____
177.	Ankle or foot problems	__	_____
178.	Work or exercise limited by orthopedic problem?	__	_____
179.	Other _____	__	_____

FAMILY HISTORY Please identify blood relatives who have been diagnosed as having the following diseases and give their age at time of diagnosis.

	Yes	Age at Diagnosis
Heart Disease		
180. Father	__	_____
181. Mother	__	_____
182. Sibling	__	_____
183. Paternal grandparent	__	_____
184. Maternal grandparent	__	_____

	Yes	Age at Diagnosis
High Blood Pressure		
185. Father	__	_____
186. Mother	__	_____
187. Sibling	__	_____
188. Paternal grandparent	__	_____
189. Maternal grandparent	__	_____

Stroke		
190. Father	__	_____
191. Mother	__	_____
192. Sibling	__	_____
193. Paternal grandparent	__	_____
194. Maternal grandparent	__	_____

Have any of your blood relatives noted above had any of the following?

	Yes	Age Diagnosed
195. Heart attack under age 50	__	_____
196. Heart operations	__	_____
197. Stroke under age 50	__	_____
198. Elevated cholesterol	__	_____
199. High blood pressure under age 40	__	_____
200. Diabetes	__	_____
201. Obesity	__	_____
202. Cancer under age 60	__	_____

HISTORY OF TOBACCO USE

	Yes	No
203. Have you ever used tobacco products including smokeless?	___	___
204. Do you presently use tobacco products?	___	___

If you did or do use tobacco, please indicate the average amount used per day and the age you started.

	Amount	Age Started
205. Cigarettes (number cig. per day)	___	___
206. Cigars (number per day)	___	___
207. Pipe (number pipefuls per day)	___	___
208. Smokeless (fraction of packs/tins/day)	___	___

209. If you have quit using tobacco, when was it? (mo/yr)
210. How old were you when you quit using tobacco?

SMOKING/STRESS/TENSION

Smoking - My smoking history is:
Never____[0] Not for last 10 years____[2] Not for last 5 years____[3]
Recently quit____[4] Still smoke____[5]

Stress / Tension
Rate how closely you agree with each of the following statements by filling in the blank preceding each statement with a number from 1 to 10.

Strongly Disagree			Agree Somewhat				Strongly Agree		
1	2	3	4	5	6	7	8	9	10

_____1. I can't honestly say what I really think or get things off my chest at work, school, or home.
_____2. I seem to have lots of responsibilities but little authority.
_____3. I seldom receive adequate acknowledgment or appreciation when I do a good job.
_____4. I have the impression that I am repeatedly picked on or discriminated against.
_____5. I feel I am unable to use my talents effectively or to their full potential.
_____6. I tend to argue frequently with co-workers, customers, teachers, or other people.
_____7. I don't have enough time for family and social obligation or personal needs.
_____8. Most of the time I have little control over my life at work, school or home.
_____9. I rarely have enough time to do a good job or accomplish what I want to.
_____10. In general, I'm not particularly proud of or satisfied with what I do.

ALCOHOL CONSUMPTION

211. Do you drink alcoholic beverages? __Yes __No

If **YES,** please indicate the type and amount you consume per week.

	Amount
212. Glasses of beer per week (12 oz.)	_____
213. Glasses of wine per week (8 oz.)	_____
214. Ounces of liquor (cordials=1 oz)	_____
215. Ounces of hard liquor (shot=1 oz)	_____

SPORT ACTIVITIES Check those activities in which you regularly participate or in which you have participated over the past year. Also indicate the approximate number of months in the last year you engaged in these activities, the number of times per month, the number of minutes per session, and the intensity of your participation. **Note:** Rate your intensity on a scale of **1** to **10** with **1** being very low and **10** being very high intensity.

	# of months per year	# times per month	Min/session	Intensity (1=low;10=high)
216. Basketball	__	__	__	___
217. Volleyball	__	__	__	___
218. Softball	__	__	__	__
219. Baseball	__	__	__	___
220. Jogging	__	__	__	___
221. Running	__	__	__	___
222. Swimming	__	__	__	___
223. Bicycling	__	__	__	__
224. Golf	__	__	__	___
225. Tennis	__	__	__	___
226. Badminton	__	__	__	___
227. Racquetball	__	__	__	___
228. Handball	__	__	__	___
229. Table Tennis	__	__	__	___
230. Sailing	__	__	__	___
231. Water Skiing	__	__	__	___
232. Horseback Riding	__	__	__	___
233. Bowling	__	__	__	___
234. Calisthenics	__	__	__	___
235. Walking	__	__	__	___
236. Canoeing/Rowing	__	__	__	___
237. Fishing	__	__	__	___
238. Hunting	__	__	__	___
239. Dancing	__	__	__	___
240. Skating	__	__	__	___
241. Soccer	__	__	__	___
242. Lawnwork/Yard Care	__	__	__	___
243. Gardening	__	__	__	___
244. Housework	__	__	__	___
Other_____	__	__	__	__
Other_____	__	__	__	__
Other_____	__	__	__	__

In addition to the above information that you have listed, are you aware of any other conditions, symptoms, or special circumstances that might be related to our overall health and well being? _____If so, please give a detailed explanation below.

_____
_____
_____

APPENDIX F

COPY OF THE DAILY DIETARY RECORD

NAME: _____

DATE: _____

Please list all the food items that you have eaten during the day. Include the approximate portion size and the method of preparation (ie. fried, baked, etc).

TIME	FOOD	PORTION SIZE	PREPARATION

APPENDIX G

COPY OF SEVEN-DAY PHYSICAL ACTIVITY RECORD

Name:_____Age:_____Ht:_____ Wt:_____

Address:_____Phone:_____(W)_____(H)_____
Occupation:_____

DIRECTIONS: This Seven Day Physical Activity Record is designed to measure your habitual physical activities over the course of one week. You are asked to record your sleep habits as well as the physical activities you participated in over the course of the past seven days; include both occupational and leisure-time physical activities.

1. **BEFORE READING ANY FURTHER, PLEASE REVIEW ATTACHMENT 1 FOR EXAMPLES OF LIGHT, MODERATE, HARD, AND VERY HARD PHYSICAL ACTIVITIES!**

2. **DO NOT RECORD LIGHT ACTIVITIES.** See Attachment 1 for examples of LIGHT ACTIVITIES. Most of you will spend the majority of your waking hours in light activity. For example, a laboratory worker may be on their feet all day and may feel "fatigued", but the energy cost is in the "light" category.

3. For all other physical activities, which may be classified as moderate, hard, or very hard, **DOCUMENT ONLY THE TIME ACTUALLY SPENT PERFORMING THE ACTIVITY**: Include both occupational and leisure-time activities. For example, the laboratory worker in the illustration given above may spend a number of hours stocking shelves with supplies, which would likely be moderate exercise. It is unlikely, however, that they would spend an 8 hour day performing this task, and time should be subtracted for lunch, breaks, etc. Similarly, being at the pool for 2 hours but swimming for 15 minutes should be recorded as 15 minutes, not 2 hours.

4. For this record to be representative of your normal physical activity habits, it is critical that the week's activities be "normal" for you. For example, a week in which you take a holiday or a few days vacation would clearly NOT be a "normal" week for you. **IF THE UPCOMING WEEK'S ACTIVITIES WILL NOT REPRESENT YOUR NORMAL ACTIVITY PATTERNS, THEN PLEASE DO NOT COMPLETE THIS FORM - WAIT FOR A WEEK THAT WILL REFLECT YOUR NORMAL PHYSICAL ACTIVITY PATTERNS.** Note that a week is not necessarily Sunday through Saturday, but may be any consecutive 7 day period.

5. Use the record forms beginning on the next page to record; (1) the physical activity, (2) the total hours/minutes spent performing the activity, (3) and rate how hard you worked at the particular physical activity. Use the following scale to rate how hard you worked.

SCALE TO RATE HOW HARD YOU WORK

1 - Barely breaking a sweat; breathing just slightly elevated.
2 - Moderate sweating; breathing significantly above normal, but could talk normally.
3 - Heavy sweating; breathing very heavy to nearly winded, could NOT talk normally.

DAY ONE

Date:_____ Day of Week:_____

ACTIVITY	**TOTAL TIME (Hours / Minutes)**	**HOW HARD (1,2,3)**
Sleeping (include naps)		

CONCLUDING QUESTIONS

DIRECTIONS: At the end of the week, please answer the following questions.

1. Would you say that during the past week you were (check one):
   - _____ less active than usual
   - _____ about as active as usual
   - _____ more active than usual

2. Which statement most nearly describes your attitude toward leisure-time physical activity?
   - _____ I absolutely detest physical activity and exertion of any type.
   - _____ I do not enjoy physical activity or exertion of any type.
   - _____ I do not like activities which make me sweat, but I do like some types of light activities.
   - _____ I enjoy light physical activity of many types, and occasionally like hard physical activity.
   - _____ I thoroughly enjoy all types of physical activities, even those which are hard and very hard.

3. When you have time off from work (weekends/vacations) or during work breaks (lunch, etc), how often do you participate in physical activities, including recreational sports, which would be considered moderate to very hard?
   - _____ Never
   - _____ Seldom
   - _____ Sometimes/Irregularly
   - _____ Frequently/Regularly
   - _____ Almost Always

THANK YOU VERY MUCH FOR YOUR TIME AND ACCURACY IN COMPLETING THIS QUESTIONNAIRE. THIS INFORMATION IS INDISPENSABLE FOR OUR STUDY, AND WE THANK YOU FOR YOUR WILLINGNESS TO COOPERATE IN COMPLETING THIS FORM.

ATTACHMENT 1 - CLASSIFICATION OF PHYSICAL ACTIVITY

LIGHT ACTIVITIES

Household/Occupational		Sports/Recreational
Bakery, general	Painting, inside	Billiards
Bookbinding	Printing	Canoeing (leisure)
Carpet sweeping	Shoe repair, general	Card playing
Cooking	Sitting quietly	Drawing (standing)
Eating (sitting)	Standing quietly	Horse racing (walking)
Farming	Tailoring	Music Playing
driving harvester	cutting	accordion (sitting)
driving tractor	hand-sewing	cello (sitting)
milking by machine	machine-sewing	conducting
Ironing	Typing (electric and manual)	flute (sitting)
Knitting, sewing	Wallpapering	horn (sitting)
Lying at ease	Watch repairing	piano (sitting)
Machine-tooling	Writing (sitting)	trumpet (standing)
machining		violin (sitting)
working sheet metal		woodwind (sitting)

MODERATE ACTIVITIES

Household/Occupational		Sports/Recreational
Carpentry (general)	Locksmith	Archery
Cleaning	Machine-tooling	Croquet
Electrical work	operating lathe	Cycling, leisure 5.5 mph
Farming	tapping and drilling	Dancing (ballroom)
feeding animals	welding	Gymnastics
milking by hand	Mopping floor	Music playing
Food shopping	Painting (outside)	drums (sitting)
Gardening	Planting seedlings	organ (sitting)
weeding	Plastering	Table tennis
hedging	Scraping paint	Treading water, normal
raking	Stock clerking	Volleyball
Sawing	Pressing (tailoring)	Walking, normal pace
Woodworking	Window cleaning	Shopping/Walking

HARD ACTIVITIES

Household/Occupational		Sports/Recreational
Coal Mining	Scrubbing floors	Badminton
drilling coal, rock	Steel mill, working in	Canoeing (racing)
erecting supports	fettling	Circuit training
shoveling coal	forging	Universal
Farming	tipping molds	Nautilus
feeding cattle	Pushmowing yard	free weights
shoveling grain	Cricket	Forestry
ax chopping, slow	Dancing (medium aerobic)	
hoeing	Golf (without cart)	planting by hand

VERY HARD ACTIVITIES

Household/Occupational

Farming
forking straw bales
Forestry
hand rolling
barking trees
carrying logs
felling trees
sawing by hand
Digging
Marching, rapid
Steel mill, working in
ax chopping, fast
merchant mill rolling
removing slag
tending furnace
Horse grooming

Sports/Recreational

Basketball
Circuit training
Hydra-Fitness
aerobic (intense)
Cycling (racing)
Dancing
"twist" and "wiggle"
snowshoeing, soft snow
Squash
Football
Horse racing (galloping)
Jumping rope (70-145 per min)
Racquetball
Running (5 min.-11 min. mile)
Skiing, hard snow
Skindiving
Field hockey

APENDIX H

EXERCISE SESSION DATA SHEET

Date:					**Warm-up:**					
Time:		**Target Calories:**	**350**							
Subject:					**Choice 1:**					
Weight:										
rest BP:					**Choice 2:**					
rest HR:										
total	**Pre-dicted**	**Time:**		**Actual Exercise Time =**						
Speed	**Grade**	**Running Total Time**	**Interval Time**	**HR**	**VO2 (L/min)**	**RER**	**KCAL /L O2**	**KCAL / min**	**Total Calories Burned**	**Time Left**
Warm Up Data										
Exercise Data										

APPENDIX I

RESISTANCE EXERCISE SESSION DATA SHEET

Strength Week # 1 Workout

Name: _____	Leg Press	Leg Curl	Calf	Bench	Lat. PD	DB. Military	Curl
Weight: _____	380	75	540	80	105	27.5	55

Session # 1 Date: _____

	Set # 1		Set # 2		Set # 3		Set # 4	
Leg Press	190	x 10	266	x 10	266	x 10	266	x 10
Leg Curl	37.5	x 10	52.5	x 10	52.5	x 10	52.5	x 10
Calf Raise	270	x 10	378	x 10	378	x 10	378	x 10
Bench Press	40	x 10	56	x 10	56	x 10	56	x 10
Lat. Pull Down	52.5	x 10	73.5	x 10	73.5	x 10	73.5	x 10
DB. Military	13.75	x 10	19.25	x 10	19.25	x 10	19.25	x 10
Barbell Curl	27.5	x 10	38.5	x 10	38.5	x 10	38.5	x 10
Abs:								

	Leg Press	Leg Curl	Calf	Bench	Lat. PD	DB. Military	Curl
	380	*75*	*540*	*80*	*105*	*27.5*	*55*

Session # 2 Date: _____

	Set # 1		Set # 2		Set # 3		Set # 4	
Leg Press	190	x 10	285	x 10	285	x 10	285	x 10
Leg Curl	37.5	x 10	56.25	x 10	56.25	x 10	56.25	x 10
Calf Raise	270	x 10	405	x 10	405	x 10	405	x 10
Bench Press	40	x 10	60	x 10	60	x 10	60	x 10
Lat. Pull Down	52.5	x 10	78.75	x 10	78.75	x 10	78.75	x 10
DB. Military	13.75	x 10	20.625	x 10	20.625	x 10	20.625	x 10
Barbell Curl	27.5	x 10	41.25	x 10	41.25	x 10	41.25	x 10
Abs:								

APPENDIX J

VARIABLE KEY

Exercise Group, Training Period, and Acute Response Classifications

ET = endurance subjects; **RT** = resistance subjects; **CT** = combination subjects;
Pre-Training = untrained; **Post-Training** = after 12 weeks of training;
Baseline = 24 hours before exercise; **24 h** = measurement 24 hours after exercise

Physiological variables

Height = height in inches
Weight = body weight in pounds
Waist = waist girth in inches
Hip = hip girth in inches
W / H ratio = ratio of waist girth / hip girth
SFPCFT = body fat, from 7 site skinfolds
% Fat = body fat, from hydrostatic weighing
LBM = lean body mass in kg, determined from hydrostatic weighing
FMass = fat mass in kg, determined from hydrostatic weighing
RHR = resting heart rate in beats per minute
RSBP = resting systolic blood pressure in millimeters of mercury
RDBP = resting diastolic blood pressure in millimeters of mercury

$\dot{V}O_{2peak}$ = maximal oxygen uptake (mL/kg/min)
TDMTM = maximum time on treadmill in minutes
LPMAX = maximum weight lifted on the leg press machine in pounds (1RM)
BPMAX = maximum weight lifted on bench press in pounds (1RM)

Exercise variables

EX_INTEN = % of $\dot{V}O_{2peak}$ the subjects walked/jogged at during acute exercise session
% of the one-repetition maximum that the subjects lifted for their resistance exercises
EXKCAL = number of calories expended during acute exercise session
EXDUR = duration of the acute exercise session in minutes
DAYEXP = average daily energy expenditure

Dietary variables

KCAL = total daily caloric intake in kcals
CHO = total daily grams of carbohydrate
FAT = total daily grams of fat
PROT = total daily grams of protein
SFAT = total daily grams of saturated fat
PSFAT = total daily grams of polyunsaturated fat
CHOL = total daily milligrams of cholesterol
P/S ratio = polyunsaturated to saturated fat ratio

Lipid Variables

TC = total cholesterol (mg/dL)
HDL-C = high density lipoprotein cholesterol (mg/dL)
HDL_3-C = high density 3 lipoprotein cholesterol (mg/dL)
HDL_2-C = high density 2 lipoprotein cholesterol (mg/dL)
TG = triglyceride (mg/dL)
LDL-C = low density lipoprotein cholesterol (mg/dL)
apo B = apolipoprotein B (mg/dL)
apo A-I = apolipoprotein A-I (mg/dL)
apo B / apo A-I = apolipoprotein B to apolipoprotein A-I ratio
TC / HDL-C = total cholesterol to high density lipoprotein cholesterol ratio
HDL_2-C / HDL_3-C = high density 2 lipoprotein cholesterol to high density 3 lipoprotein cholesterol ratio
LDL-C / HDL-C = low density lipoprotein cholesterol to high density lipoprotein cholesterol ratio

Non-Traditional CHD Risk Marker Variables

LDL_1-C = low density lipoprotein subfraction 1 cholesterol (mg/dL)
LDL_2-C = low density lipoprotein subfraction 2 cholesterol (mg/dL)
LDL_3-C = low density lipoprotein subfraction 3 cholesterol (mg/dL)
LDL_4-C = low density lipoprotein subfraction 4 cholesterol (mg/dL)
LDL density = the density of the LDL particle (g / cm^2)
VLDL-C = very low density lipoprotein cholesterol (mg/dL)
IDL-C = intermediate density lipoprotein cholesterol (mg/dL)
NONHDL-C = non-high density lipoprotein cholesterol (mg/dL)
Lp (a) = lipoprotein (a) cholesterol (mg/dL)
hs-Crp = high sensitivity C-reactive protein (mg/L)

Enzyme activity variables

LPLa = lipoprotein lipase activity (μmol FFA/mL/hr)
HTGLa = hepatic triglyceride lipase activity (μmol FFA/mL/hr)

APPENDIX K

DELIMITATIONS

This investigation was delimited to the following:

1. Apparently healthy, untrained males who have not participated regularly in either endurance or resistance training for at least the last three months.

2. Men between 18 and 40 years of age.

3. Non-smoking subjects who are not currently taking any medications or substances known to alter lipid metabolism.

4. Two exercise sessions in which subjects walked/jogged on a motor driven treadmill at 70% of their $\dot{V}O_{2peak}$ expending 350 and 500 kcals of energy.

5. Two resistance exercise sessions in which subjects in the resistance exercise group completed the first workout of their training program (duration = 58 min). Weights used for each exercise will be calculated as approximately 70% of the one-repetition maximum, and chosen so that the subject will be challenged, but yet able to complete all repetitions in each exercise set, and continue exercise until completion of the session. This will be performed again at the completion of 12 weeks of training.

6. Two combination exercise sessions in which subjects in the combination group walked or jogged at an intensity equal to 70% of their maximal effort recorded on their earlier exercise test ($\dot{V}O_{2peak}$) for a length of time needed to burn 175 kcals of energy. After they are finished with this activity, they will perform several resistance exercises at the number of sets, repetitions, and duration required to expend 175 kcal of energy. Weights used for each exercise will be calculated as approximately 70% of the one-repetition maximum, and chosen so that the subject will be challenged, but yet able to complete all repetitions in each exercise set, and continue exercise until 175 kcal of energy is expended. This will be performed again at the completion of 12 weeks of training with the kcals increased to 250 for walking/jogging and 250 for resistance exercise.

7. Two fasting blood samples associated with each of the two acute exercise tasks (pre-training & post-training):
    1) 24 hours before the exercise and 2) 24 hours after the exercise.

8. Blood lipid concentrations corrected for estimated plasma volume shifts that occur as a result of the exercise sessions.

10. The measurement of serum TC, TG, HDL-C, HDL_3-C, HDL_2-C, VLDL-C, IDL-C, NONHDL-C, LDL-C, hs-Crp, Lipoprotein (a), Apolipoprotein A-I, and Apolipoprotein B.

11. The *in vitro* measurement of total lipase activity (TLA) and HTGLA; and LPLA as a calculated variable.

12. The measurement of serum LDL_1-C, LDL_2-C, LDL_3-C, LDL_4-C, and LDL density.

APPENDIX L

LIMITATIONS

This investigation was limited by the following:

1. All subjects resided in the same geographical area.

2. Self reported dietary information was used for dietary analysis.

3. Self reported daily activity was used to determine extraneous physical activity.

4. Normal daily variation in individual lipid profiles was not evaluated.

5. Findings are specific to apparently healthy, untrained males.

6. Self reported exercise abstinence during the blood sampling periods.

7. Subject compliance.

APPENDIX M

GLOSSARY

1. Atherosclerosis – a process where the diameter of affected arteries are decreased due to plaque/lipid build-up in the intima, or inner lining, of the vessel. This gradual occlusion will limit blood flow to that particular tissue the vessel is serving. The process can be broken down into 3 stages; fatty streak development, fibrous plaque/atheroma formation, and last and most detrimental is the complicated lesion with its fibrous cap and encroachment of the lumen.

2. Cholesterol – The major sterol in animal tissues. An amphipathic molecule with a polar head group and a nonpolar hydrocarbon body. A component of cell membranes, cholesterol also serves as precursors of bile acids, steroid hormones, and vitamin D.

3. Lipoprotein – a molecular structure consisting of a hydrophobic core containing triacylglycerols and cholesterol esters and a hydrophilic surface consisting of a layer of amphipathic molecules, such as cholesterol, phospholipids, and apolipoproteins.

4. High-Density Lipoprotein (HDL) – This small, dense lipoprotein is derived from both intestinal and hepatic sources and associates with apolipoproteins A-I, A-II, C-II, and E. HDL is the key lipoprotein involved in reverse cholesterol transport and the transfer of cholesterol esters between lipoproteins.

5. Low-Density Lipoprotein (LDL) – This class of lipoprotein carries the majority of the cholesterol in the blood, while associating with apolipoprotein B-100, and delivers the cholesterol to peripheral and hepatic cells of the body through receptor-mediated endocytosis.

6. Very Low Density Lipoprotein (VLDL) – Large, buoyant lipoprotein complex secreted by the liver which contain large amounts of TG and smaller amounts of cholesterol ester, and phospholipids; associated with apo B-100, apo C-I, C-II, C-III, and apo E.

7. Triglyceride (TG) – A molecule composed of three fatty acids each in ester linkages with a single glycerol backbone.

8. Lipoprotein Lipase (LPL) – A glycoprotein, that is synthesized in both adipose and muscle tissue; it hydrolyzes 1(3) ester-linkages of triglycerides in chylomicrons and VLDLs, generating 2-monoacylglycerol and unesterified fatty acids which are taken up and utilized by the surrounding peripheral tissues.

9. Hepatic Triglyceride Lipase (HTGL) – A glycoprotein, synthesized primarily in the liver; it hydrolyzes triglycerides and phospholipids in the hepatic circulation.

10. Lecithin: Cholesterol Acyltransferase (LCAT) – A glycoprotein that is secreted into the plasma from the liver. LCAT catalyses esterification of plasma cholesterol and acylation of lysophosphatidylcholine. LCAT is most effectively activated by apo A-I.

11. Cholesterol Ester Transfer Protein (CETP) – A hydrophobic glycoprotein synthesized by the liver, spleen, adipose tissues, small intestine, adrenal gland, kidney, heart and skeletal muscles. CETP facilitates the transfer of CE from HDL to chylomicrons, VLDL, IDL, and LDL. TG is transferred in the opposite direction in exchange for the CE. CETP is not considered an enzyme; the CE transfer from HDL is influenced by the composition of acceptor lipoproteins (VLDL, LDL). Ability of VLDL to accept CE is enhanced when it contains more TG and surface components than CE.

12. Reverse Cholesterol Transport – the process by which cholesterol is removed from the tissues and returned to the liver for removal from the body.

13. Forward Cholesterol Transport – The process by which exogenous and endogenous cholesterol is transported to extrahepatic cells.

14. Primary Prevention of CHD – A process by which preventive actions are employed to prevent the development of CHD in people without established cardiovascular disease.

15. Secondary Prevention of CHD – A process by which preventive actions are employed by people with established CHD, with the purpose of preventing any future cardiovascular events.

VITA

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Education

B.S., Kinesiology, The Ohio State University, 1994

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Ph.D., Kinesiology, 2008

Research and Professional Experience

2007-present	Texas A&M University	Lecturer Fitlife Program Coordinator
2003- 2007	Scott & White Clinic	Clinical Exercise Physiologist
1996 - 2003	Texas A&M University	Graduate Assistant
1996 - 1997	St. Elizabeth Hospital	Fitness Specialist
1995 -1997	St. Elizabeth Hospital	Clinical Exercise Physiologist

Professional Organizations

American College of Sports Medicine, Member	Member # 519026
National Strength and Conditioning Association	Member # 97-01-28-007