THE EFFECTS OF ACCUMULATED AND CONTINUOUS BOUTS OF AEROBIC EXERCISE AND DIFFERING LEVELS OF EXERCISE INTENSITY ON POSTPRANDIAL LIPEMIA

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THE EFFECTS OF ACCUMULATED AND CONTINUOUS BOUTS OF AEROBIC EXERCISE AND DIFFERING LEVELS OF EXERCISE INTENSITY ON POSTPRANDIAL LIPEMIA

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DISSERTATION ABSTRACT

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The purposes of this investigation were to compare the effects of low- and moderate-intensity exercise and accumulated versus continuous aerobic exercise on postprandial lipemia in males with metabolic syndrome. Fourteen middle-aged males with characteristics of metabolic syndrome (BMI = 34.3 ± 5.6 kg/m^2; % fat = 37 ± 4; waist circumference = 110.2 ± 10.9 cm; TG = 217 ± 84 mg/dL; HOMA = 6.3 ± 3.8) first completed a non-exercise control condition in which they reported to the laboratory in the postabsorptive state for a fasting blood sample, consumed a high-fat test meal and then had postprandial blood samples taken at two-hour intervals for the next six hours. Participants also completed the following exercise conditions in a randomized order by treadmill walking: 1) a continuous moderate-intensity session, 2) a continuous low-

intensity session, 3) two accumulated moderate-intensity sessions. Approximately 500 kcals were expended during all exercise conditions. Participants reported back to the laboratory approximately 13 hours following the completion of exercise for each condition for test meal consumption and serial blood sampling as described for the control condition. A minimum of one week and a maximum of two weeks separated subsequent conditions for each participant. Fasting and postprandial concentrations of triglycerides, insulin and glucose were analyzed using ANOVAs with repeated measures on both condition and time. Additionally, total and incremental area under the curve scores were calculated for both triglycerides and insulin and analyzed using one-ways ANOVAs with repeated measures on condition. The a priori significance level for all analyses was set at $p < 0.05$. The incremental triglyceride area under the curve was reduced by 27% following low-intensity exercise. Triglyceride concentrations were also reduced by 22% and 21% at the four-hour postprandial timepoint following low- and moderate-intensity exercise, respectively. No significant differences in triglyceride parameters were observed following two sessions of moderate-intensity exercise. Also, no significant alterations in insulin or glucose concentrations as a result of any of the exercise conditions were observed in this study. These results indicate that 500 kcals of aerobic exercise is sufficient to alter postprandial lipemia in men with metabolic syndrome. This outcome can be achieved through low- or moderate-intensity exercise performed in a single session. However, accumulating moderate-intensity exercise does not appear to effectively attenuate postprandial lipemia in this population.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER I

INTRODUCTION

Cardiovascular Diseases and Metabolic Syndrome

Cardiovascular diseases (CVD) are the leading cause of death in the United States and (52) epidemiological evidence has been used to identify several modifiable and non-modifiable risk factors for the development of CVD (2, 4). Individuals with a clustering of modifiable risk factors, known as metabolic syndrome, are predisposed to an increased incidence of CVD, type II diabetes and all-cause mortality (128). Metabolic syndrome specifically encompasses abdominal obesity, atherogenic dyslipidemia, glucose intolerance or insulin resistance and hypertension, as well as proinflammatory and prothrombotic states (85). It has been estimated that more than 20% of the U.S. population meets the diagnostic criteria for metabolic syndrome (158). While each of the risk factors associated with metabolic syndrome contributes to its pathogenesis, obesity and adipose tissue-specific disorders are considered to be the main causative factors in its recent rise (85). This is evidenced by data demonstrating that while the prevalence of metabolic syndrome is only approximately 5% in normal weight individuals, it is approximately 60% in those considered to be obese (158). Abdominal obesity is frequently associated with several of the abnormalities that are present in metabolic syndrome. For example, an accumulation of visceral adipose tissue leads to elevations in fasting triglycerides, decreases in high-density lipoprotein-cholesterol (HDL-C) and the

formation of small, dense low-density lipoprotein (LDL) particles (130, 193). Beyond promoting atherogenic dyslipidemia, abdominal obesity is also intimately associated with insulin resistance (159) and hypertension (153).

In addition to the risk factors that are considered direct components of metabolic syndrome, abdominal obesity has also been associated with an exaggerated postprandial triglyceride response (38). Abnormal postprandial lipid metabolism has been proposed as an independent risk factor for the development of CVD (210) because of its direct associations with the formation of atherogenic plaque (164), endothelial dysfunction (200) and atherogenic dyslipidemia (152). The postprandial metabolic perturbations imposed by a single meal are transient in nature; however, most individuals consume several meals throughout the course of a day and thus are in the postprandial state approximately two-thirds of the time (69). Therefore, although fasting triglyceride values are more commonly assessed, evaluations of postprandial triglyceride metabolism provide key insights about the metabolic milieu in which the great majority of time is spent (210).

Lifestyle changes such as increases in physical activity and exercise, which favorably alter components of metabolic syndrome, have been shown to be efficacious in reducing CVD risk (4). The ability of physical activity and exercise to reduce CVD risk is, in part, due to their effects on fasting blood lipids. For example, single sessions of moderate-intensity aerobic exercise have consistently resulted in modest increases in HDL-C (41, 48, 81) and decreases in TG (56, 81) in both active and sedentary populations. Total exercise energy expenditure is considered to be an important factor moderating this response (50).

Several investigations have shown that in addition to the favorable alterations in fasting blood lipid and lipoprotein metabolism, exercise mediates beneficial changes in the postprandial state. For example, acute sessions of aerobic exercise performed prior to the consumption of a high-fat meal have been shown to reduce the lipemic response to the subsequent test meal by 9 to 50% (8, 70, 198). It has been suggested that, as with fasting blood lipids, sufficient total energy expenditure is a key to the exercise-mediated attenuation in postprandial lipemia (197). However, this has primarily been documented by investigations employing doses of exercise that result in relatively high caloric expenditures. It remains less clear how exercise influences postprandial lipemia when the caloric expenditure is approximately 500 kcals or less (107). The effect on postprandial lipemia resulting from caloric expenditures in this lower range needs to be better understood because this amount of exercise is representative of exercise recommendations for individuals with metabolic syndrome (94, 99).

Exercise intensity is also a moderating factor that may influence the lipemic response to fat-laden meal following acute aerobic exercise. Tsetsonis et al. (198) found that low- and moderate-intensity exercise resulted in similar PPL attenuations in physically active, normotriglycerdemic males and females when the total energy expenditure of the exercise conditions was similar. However, discrepant findings have been reported by another investigator using a similar cohort. Katsanos et al. (108) demonstrated that PPL was reduced by moderate, but not low-intensity aerobic exercise when performed one hour prior to the ingestion of a high-fat meal. To date, only one study has investigated how exercise intensity may modulate exercise-induced reductions in PPL in males with metabolic syndrome (205). It was reported that both low and

moderate exercise intensities reduced PPL by similar amounts. However, the investigators did not control for total caloric expenditure in their experimental design and thus each intensity level resulted in a significantly different caloric expenditure. This precludes judgment as to the role of exercise intensity in the response and warrants further study on this issue.

In addition to the intensity of exercise, the activity pattern in which calories are expended may influence the reduction in postprandial lipemia. The Centers for Disease Control and Prevention (CDC), American College of Sports Medicine (ACSM), and the U.S. Surgeon General recommended that every US adult should accumulate 30 minutes (or the equivalent of 200 kcals) or more of moderate-intensity physical activity on most, preferably all, days of the week in order to improve health (160). Despite the inclusion of accumulated sessions of exercise in this recommendation, relatively few attempts have been made to determine the effect of accumulated exercise on PPL. Gill et al. (75) demonstrated that in young, high-fit, normotriglyceridemic males, three sessions of moderate-intensity aerobic exercise accumulated throughout the day were as effective as a single continuous session of exercise at reducing PPL. Additionally, Murphy et al. (150) reported that thirty minutes of brisk walking decreased PPL in men and women by equal amounts whether performed in a continuous session or accumulated in three sessions. While these investigations indicate that accumulated exercise may yield the same benefit as continuous exercise in apparently healthy persons with normal fasting lipid profiles, this has not been explored in individuals who typically demonstrate impaired postprandial lipid metabolism. Given that excessive abdominal adiposity and high fasting triglyceride levels (> 150 mg/dl) are two components of metabolic syndrome

that are considered powerful predictors of excessive PPL (38), further research is needed to compare the respective effects of accumulated and continuous sessions of aerobic exercise in individuals demonstrating these characteristics.

In summary, there is a paucity of information pertaining to how an exercise energy expenditure of 500 kcals impacts postprandial lipemia in men with metabolic syndrome. Additionally, little is known about how differing levels of exercise intensity and methods of expending these calories may influence potential exercise-induced attenuations in postprandial lipemia at this level of caloric expenditure in this population. Therefore, the purposes of this investigation were to determine if this amount of exercise is sufficient to reduce postprandial lipemia in men with metabolic syndrome and to compare the respective effects of low-versus moderate-intensity exercise and continuous versus accumulated exercise on this response.

Hypotheses and Rationale

Research Question 1:

Is a total exercise energy expenditure of 500 kcals resulting from aerobic exercise sufficient to reduce postprandial lipemia in males with metabolic syndrome?

Hypotheses:

H_{O1}: Postprandial lipemia will not be attenuated compared to the control condition as a result of a total exercise caloric expenditure of 500 kcals.

H_{A1}: Postprandial lipemia will be attenuated compared to the control condition as a result of a total exercise caloric expenditure of 500 kcals.

Rationale:

Total caloric expenditure has been shown to be an important factor in determining the extent to which exercise attenuates postprandial lipemia (69). In apparently healthy populations, caloric expenditures of approximately 400 to 500 kcals have been shown to effectively attenuate postprandial lipemia (71, 148). Additionally, the single study using both men with metabolic syndrome and a caloric expenditure within this range demonstrated that this amount of exercise did significantly attenuate the postprandial triglyceride response to a high-fat test meal. Based on these previous findings, it is hypothesized that the total caloric expenditure of the exercise conditions in this study will be sufficient to attenuate postprandial lipemia compared to the control condition.

Research Question 2:

Is a single session of low-intensity aerobic exercise performed at ~ 35 % of $\dot{V}O_{2peak}$ as effective as a single session of moderate-intensity aerobic exercise performed at 60-70% $\dot{V}O_{2peak}$ at reducing postprandial lipemia in males with metabolic syndrome when total energy expenditure is approximately 500 kcals in both conditions?

Hypotheses:

H_{O2}: A single session of aerobic exercise performed at ~ 35 % of $\dot{V}O_{2peak}$ will be equally effective at attenuating postprandial lipemia as a single session of aerobic exercise performed at 60-70% $\dot{V}O_{2peak}$.

H_{A2}: A single session of aerobic exercise performed at ~ 35 % of $\dot{V}O_{2peak}$ will be less effective at attenuating postprandial lipemia than a single session of aerobic

exercise performed at 60-70% $\dot{V}O_{2peak}$.

Rationale:

In other populations, there is conflicting evidence about the influence of exercise intensity on postprandial lipemia. Low-intensity aerobic exercise has been shown to result in similar reductions in postprandial triglyceride concentrations to those seen with moderate-intensity exercise when the total energy expenditure is approximately 1,000 kcals and the high-fat meal is administered 12-16 hours after the cessation of exercise (198). However, some previous studies using low-intensity exercise that resulted in lower caloric expenditures (i.e 500 kcals or less) did not produce significant reductions in PPL (165, 197). Conversely, studies with comparable methodologies using moderate-intensity exercise within this caloric expenditure range have been shown to effectively reduce PPL (70, 71, 148). Therefore, it is hypothesized that low-intensity exercise may not be as effective as moderate-intensity exercise at lowering postprandial lipemia in men with metabolic syndrome when the total caloric expenditure is approximately 500 kcals.

Research Question 3:

Are two sessions of moderate-intensity aerobic exercise performed at 60-70% $\dot{V}O_{2peak}$ as effective as a single session of moderate-intensity aerobic exercise performed at 60-70% $\dot{V}O_{2peak}$ at reducing postprandial lipemia in males with metabolic syndrome when total energy expenditure is approximately 500 kcals in both conditions?

Hypotheses:

H_{O3}: Two sessions of aerobic exercise accumulated throughout the day and performed at 60-70% $\dot{V}O_{2peak}$ will attenuate postprandial lipemia to a similar extent as a single,

continuous session of aerobic exercise performed at 60-70% $\dot{V}O_{2peak}$.

H_{A3}: Two sessions of aerobic exercise accumulated throughout the day and performed at 60-70% $\dot{V}O_{2peak}$ will decrease postprandial TG concentrations to a greater extent than a single, continuous bout of aerobic exercise performed at 60-70% $\dot{V}O_{2peak}$.

Rationale:

Single sessions of moderate-intensity aerobic exercise have been shown to result in substantial reductions in postprandial TG concentrations (166). Likewise, previous investigations in other populations have shown that accumulated exercise sessions are equally effective compared to single sessions at reducing postprandial lipemia (148, 150). A single study has shown that intermittent exercise was more effective at reducing PPL than a continuous session of exercise (9). It was speculated that this was due to an increased metabolic rate following the first intermittent session of exercise that was maintained throughout the measurement period. This indicates that accumulating exercise may result in a greater number of calories being expended over the course of the day. Given that total energy expenditure plays an integral role in determining the postprandial TG response, it is possible that two accumulated sessions of exercise will result in a greater total energy expenditure due to enhanced excess postexercise oxygen consumption. Therefore, it is hypothesized that there will be a greater attenuation in PPL with two accumulated sessions of moderate-intensity exercise compared to a single session of moderate-intensity exercise when the total caloric expenditure is approximately 500 kcals.

Assumptions

1. The males with characteristics of metabolic syndrome sampled from Auburn-Opelika and the surrounding communities are representative of the population response to acute exercise interventions.

2. Participants complied with the instructions to keep dietary intake constant and forego exercise outside of the study for the duration of the protocol.

3. The exercise sessions in this study were practical for this population.

4. Study participants did not have primary dyslipidemias or genetic predispositions for lipoprotein enzyme or transfer protein disorders.

Limitations

1. Dietary intake was quantified using a self-report measure.

2. Participants were recruited only from the Auburn-Opelika area and the surrounding communities.

Delimitations

1. Males with metabolic syndrome were exclusively recruited.

2. Participants did not have known cardiovascular, metabolic or pulmonary diseases.

3. Participants were not taking any medications known to influence lipid or lipoprotein metabolism.

4. Single, continuous low- and moderate-intensity aerobic exercise sessions and two accumulated moderate-intensity aerobic exercise sessions resulting in an approximate caloric expenditure of 500 kcals were used.

Significance of the study

Postprandial lipemia has been proposed to play a significant role in the development of CVD. Although the ability of acute aerobic exercise to reduce postprandial TG concentrations has been well documented in apparently healthy individuals, relatively little data exist for populations with metabolic syndrome. These

results will determine if 500 kcals of total exercise energy expenditure is enough to significantly attenuate postprandial lipemia. Additionally, it is often suggested that total exercise energy expenditure, not exercise intensity, is the major causative factor in exercise-induced reductions in PPL, but there is a lack of empirical evidence to substantiate this claim. These results will be useful in determining the relative effectiveness of low- and moderate-intensity exercise in attenuating exaggerated postprandial lipemia in males with metabolic syndrome. Additionally, this investigation will be the first to compare the effectiveness of accumulated and continuous sessions of moderate-intensity aerobic exercise in males with metabolic syndrome. This will allow for the evaluation of a major physical activity public health recommendation.

CHAPTER II

REVIEW OF LITERATURE

Introduction

This review of literature is intended to provide background information on postprandial lipemia and how it is specifically influenced by aerobic exercise. A brief overview of postprandial lipid and lipoprotein metabolism will be provided. Next, several important factors that moderate postprandial lipemia will be examined. Additionally, evidence establishing a clear link between abnormal postprandial triglyceride metabolism and cardiovascular diseases will be presented. Finally, the role of various acute exercise interventions in favorably altering postprandial lipemia will be discussed in detail.

Postprandial Lipemia – Definition and Methods of Quantification

Postprandial lipemia is the elevation in the concentration of plasma triglyceride levels following the consumption of a meal. Triglycerides typically begin to rise within an hour following meal ingestion, continue to increase until a zenith is reached at approximately four hours and then return to baseline six to eight hours later (162). Given that most individuals consume subsequent meals prior to the complete resolution of the previous meal, the majority of each day is spent in the postprandial state.

Postprandial lipemia is quantified by assessing the temporal triglyceride response to a test meal. A typical assessment requires study participants report to the lab in the

postabsorptive state, consume a fat-laden test meal and have serial blood samples taken every 30-minutes to two hours over the next six to eight hours. Since this test is conceptually similar to an oral glucose tolerance test used to diagnose diabetes, it has been referred to as an oral triglyceride tolerance test.

Most researchers have used test meals where fat is the predominant macronutrient, representing up to 90% of the caloric content of the meal (194, 195, 211). However, some recent investigations have employed mixed meals containing lower amounts of fat that are thought to be more representative of a typical Western diet (117, 118, 167-169). In these cases, the mixed meal often consists of approximately 35% fat. In both methodologies, the test meals are often milkshakes composed of ingredients such as ice cream and heavy whipping cream. However, test meals containing solid foods such as cereal, chocolate, and nuts have also been used to induce postprandial lipemia (166).

Irrespective of the macronutrient content and type of foodstuff used for the test meal, the subsequent lipemic response is most often reported as the total area under the curve (AUC_T) and the incremental area under the curve (AUC_I). Both of these scores are determined using the trapezoidal rule (141). Triglyceride AUC_T is a measurement of the total area under the curve representing the postprandial TG elevations following the consumption of the test meal. The triglyceride AUC_I is a measure where baseline triglyceride concentrations are accounted for by subtracting them from the area under the curve score. Thus, the incremental area under the curve provides a postprandial measure that is relative to baseline TG concentrations. Triglyceride AUC_I is an important tool for comparing postprandial triglyceride responses among individuals with differing baseline

TG values. This score also has utility for comparisons within the same individual prior to and following an intervention that may change fasting triglyceride levels. In addition to area under the curve scores, mean TG responses at peak, as well as the other postprandial timepoints are often reported. The peak TG response gives an indication of the overall magnitude of the lipemic response to a test meal. Analyzing the mean responses to all of the timepoints provides information as to the overall duration of postprandial lipemia, which is an indirect indicator of triglyceride clearance from the vascular space (107).

Triglyceride-Rich Lipoprotein Metabolism

Following the consumption of a meal, the observed rise in plasma triglycerides comes from two primary sources: chylomicrons derived from the small intestine and very-low density lipoproteins (VLDL) derived from the liver (33). Together, these triglyceride carriers are referred to as triglyceride-rich lipoproteins (TRLs).

Dietary triglycerides are ingested and initially broken down into constituent non-esterified fatty acids (NEFAs) and monoglycerides in the small intestine by the enzyme pancreatic lipase. The NEFAs and monoglycerides are then incorporated into mixed micelles which move across the unstirred water layer and the intestinal mucosal cell brush border. Upon entry into the intestinal mucosal cell, NEFAs and monoglycerides are rapidly reesterified into triglycerides. The resulting TGs are packaged with cholesterol esters and phospholipids in the endoplasmic reticulum of enterocytes to form chylomicron lipoprotein complexes, which are the primary carriers of exogenous triglycerides. In addition to these lipids, chylomicrons contain apolipoproteins B-48, A-I, A-II, and A-IV (49).

Following assembly, chylomicrons are secreted from Golgi vesicles and ultimately enter circulation via the lymphatic system (162). Upon entry into general circulation, several important exchanges involving apolipoproteins occur between chylomicrons and HDL particles. These include the transfer of apolipoprotein C-II and E to the outer chylomicron surface, with apolipoprotein A-I being exchanged in the other direction (82). Acquiring these apolipoproteins is necessary for chylomicrons because apolipoprotein C-II is needed for lipoprotein lipase (LPL) activation (184) and apolipoprotein E is involved in uptake of lipoprotein remnants by the liver (79).

VLDL particles are the primary TG carrier in the fasted state, but since these particles are constantly being secreted from the liver, they are present in the postabsorptive and postprandial states (103). The formation of VLDL in hepatocytes is analogous to that of chylomicrons in the intestine, however VLDL particles are released from the liver with apolipoprotein B-100 and apolipoproteins C and E (188). The secretion of VLDL particles is regulated, in part, by the availability of non-esterified fatty acids at the level of the liver (119). Liver sources of NEFAs include adipose tissue lipolysis, uptake of partially hydrolyzed TRL remnants, and possibly de novo synthesis (14). NEFAs produced or extracted by the liver may then be either esterified or oxidized and the extent to which either occurs is dependent upon factors such as feeding status and recent physical activity (106). Following esterification, the resulting TGs may be stored in the liver or packaged with cholesterol esters and apolipoprotein B-100 and secreted into venous circulation through hepatic lymph. By entering general circulation through

the lymphatic system, both VLDL and chylomicrons bypass the initial portal circulation to which other macronutrients are subjected and are made available first to extrahepatic tissues.

In general circulation, the enzyme lipoprotein lipase is the rate-limiting step for the hydrolysis of the TG content of TRLs (121). LPL is bound to the capillary endothelial lumen by a glycoaminoglycan with heparin-like properties (53) and found in several tissues including both adipose and skeletal muscle. Following the consumption of a meal, the activity of lipoprotein lipase is substantially higher in adipose tissue, with a considerably smaller effect on skeletal muscle LPL activity (62). Postprandial increases in the hormone insulin are thought to be responsible for the increase in adipose tissue LPL activity. Conversely, in the postabsorptive state when insulin levels are normally reduced, adipose tissue LPL activity decreases and skeletal muscle LPL activity may increase (45). Therefore, in the postprandial state, insulin-induced increases in adipose tissue LPL activity supply NEFAs for uptake and storage in adipose tissue, but in the postabsorptive state, NEFA uptake may be redirected to skeletal muscle.

Once the triglyceride core of chylomicron or VLDL particles has been at least partially hydrolyzed by LPL, smaller remnant-like particles (RLPs) are formed. It is important to note that while in general circulation, the composition of core lipids within triglyceride-rich lipoproteins and remnant-like particles is subject to change because of dynamic exchanges occurring with other circulating lipoproteins. Specifically, TRLs and RLPs transfer triglycerides to both HDL and LDL particles in exchange for cholesterol esters in a process that is mediated by cholesterol ester transfer protein (CETP) (149). The extent to which these transfers result in appreciable core lipid compositional changes

depends on the length of time that TRLs and RPLs remain in circulation. While the TG content of both TRLs is hydrolyzed by the catalytic action of LPL, the residence time of these particles in general circulation differs due to their respective sizes. Chylomicron triglycerides remain in circulation approximately ten minutes versus fifteen to sixty minutes for those contained in VLDL because the larger chylomicrons are more likely to interact with LPL (78). As discussed in a later section, residence time has a profound impact on the atherogeneticity of these particles and their remnants.

Although the intravascular metabolism of TRLs proceeds similarly for both chylomicrons and VLDL, the catabolism of RLPs can be substantially different. The ultimate fate of chylomicron remnant particles is primarily an apolipoprotein E-mediated receptor uptake and internalization by the liver (188). There is also evidence that this may proceed using a hepatic chylomicron specific remnant receptor called the LDL-like receptor protein (127). As VLDL particles lose TG content, the direction taken by the resulting remnants depends on their size (28). Larger VLDL remnants are taken up by the liver while smaller ones form intermediate-density lipoproteins and are ultimately converted to low-density lipoproteins (LDL) by interactions with hepatic and lipoprotein lipases (188). Following this action, the major lipid component of LDL is cholesterol ester and it becomes the central transport particle in the process of delivering cholesterol to the liver and peripheral tissues.

In the postprandial state, triglycerides are carried in the bloodstream by a mixture of chylomicrons and VLDL and thus TRLs are often said to be in competition for a common saturable lipolytic pathway (23). This results in a postprandial accumulation of primarily endogenous TRLs because of a decreased efficiency of VLDL hydrolysis (181).

Peak postprandial measurements have demonstrated that almost 80% of the increase in the number of TRL particles in the postprandial state is a result of increases in particles containing apolipoprotein B-100 (181). Despite this, the majority of the postprandial elevation in triglyceride concentration is accounted for by increases in chylomicron TG due to their larger size (132). This accumulation, coupled with diminished hepatic uptake of RLPs (15), results in the elevations in plasma triglycerides that are observed postprandially. The magnitude and duration of this lipemic response is dependent upon several mitigating factors and has important chronic disease implications.

Factors Influencing Postprandial Lipemia

Fasting Triglycerides and HDL-C

Postprandial lipemia is a heterogeneous metabolic abnormality exhibiting high variability between individuals. Several factors influence the extent and duration of postprandial triglyceride elevations, including fasting blood lipid parameters. Early investigations revealed that fasting triglyceride concentrations are one of the most potent predictors of the postprandial TG response (34, 151, 163). Specifically, fasting triglycerides are directly related to postprandial triglycerides and inversely related to triglyceride-rich lipoprotein clearance. Therefore, those with fasting hypertriglyceridemia are also likely to have exaggerated postprandial triglyceride elevations. Linear regression analyses suggest that for each 1 mg/dL increase in fasting triglycerides, triglyceride AUC_T is increased by 8.5 mg/dL/hr (120). These relationships led to the theory that inefficient TRL clearance is reflective of the competition between chylomicrons and VLDL for the same lipolytic pathway (86).

High-density lipoprotein cholesterol is another fasting lipid concentration that warrants consideration in determining postprandial lipemia. Patsch and associates (163) reported that an inverse relationship is present between levels of HDL subfraction 2 and the magnitude of postprandial lipemia. Subsequent studies have yielded conflicting results on this issue. It has been suggested that males with low HDL-C levels have normal (31) or even reduced postprandial lipemia (147). The nature of the role of HDL-C in determining postprandial lipemia may depend on the co-existing levels of fasting triglycerides. Depressed levels of HDL-C may be isolated, but are often found in conjunction with hypertriglyceridemia. Couillard et al. (35) compared the postprandial triglyceride responses in males with isolated HDL-C to those with low HDL-C and concurrent hypertriglyceridemia. It was found that men with isolated low HDL-C displayed a postprandial triglyceride response that was not different from normolipidemic control subjects and significantly lower than those with combined low HDL-C and hypertriglyceridemia. The authors concluded that depressed levels of HDL-C in the absence of elevated triglycerides do not appear to be predictive of exaggerated postprandial lipemia.

Abdominal Obesity

Based on the firmly established relationship between fasting TG concentrations and postprandial lipemia, many conditions often characterized by hypertriglyceridemia also predispose those afflicted to abnormal postprandial triglyceride metabolism. The first such condition is obesity. In recent years, regional body composition analysis has become more frequent due to evidence that abdominal obesity specifically increases CVD risk, in part, because it is associated with elevated fasting triglycerides and insulin

resistance (43). These elevated TG levels are caused by excess release of NEFAs from visceral fat stores which are then directed to liver and result in an overproduction of VLDL. It is therefore reasonable to speculate that the impact of obesity on postprandial lipemia may be dependent on the predominant location of fat storage.

Two cross-sectional studies have shown that abdominal obesity is strongly associated with abnormal postprandial triglyceride responses (177, 203). Additionally, Couillard et al. (38) directly compared postprandial lipemia in males with the same total, but different regional, adiposity. Men with excess visceral adipose tissue had a delayed clearance of triglyceride-rich lipoproteins in comparison to obese men with differing body fat distribution. This metabolic defect in men with excess visceral adiposity was highly correlated with fasting triglyceride levels, suggesting that excess visceral adipose tissue is associated with exaggerated postprandial lipemia partly because of fasting hypertriglyceridemia. In agreement with this contention, Mekki et al. (142) reported that abdominally obese women with fasting hypertriglyceridemia had significantly greater levels of PPL than women matched for abdominal adiposity but without concurrent fasting hypertriglyceridemia.

However, associated hypertriglyceridemia does not entirely explain the impact of abdominal obesity on postprandial lipemia. The study by Mekki et al. also included a group of normotriglyceridemic obese women with a gynoid fat distribution pattern. A comparison of the lipemic responses between this group and the abdominally obese normotriglyceridemic women showed that the latter had an exaggerated response even when matched for baseline triglycerides and total adiposity. This is further supported by a follow-up study by Couillard et al. (36) using abdominally obese males exclusively in

which it was reported that a decreased lipolytic capacity may be a contributing factor in addition to elevations in fasting TG.

Taken together, these studies indicate that adipose tissue distribution may be a more important determinant of postprandial lipemia than obesity per se. It is abdominal adiposity in particular that is associated with a proatherogenic postprandial lipemic response due to a combination of increased fasting triglyceride levels and a decreased lipolytic capacity.

Insulin Resistance and Type II diabetes

Another condition that is frequently associated with fasting hypertriglyceridemia and thus abnormal postprandial triglyceride metabolism is insulin resistance. While insulin resistance is a hallmark of type II diabetes, it may be present and impair metabolism prior to meeting clinically established criteria for the diagnosis of type II diabetes (4). Thus, insulin resistance is a spectrum disorder and it would be expected that those with lower levels of insulin sensitivity would also have impaired postprandial triglyceride metabolism. This relationship has recently been document in middle-aged, apparently healthy men (18).

Lewis and colleagues (131) first noted that the direct relationship between fasting and postprandial triglycerides is also present in those with type II diabetes. The primary reason that those with insulin resistance, including type II diabetics, tend to have elevations in fasting triglycerides is that reductions in insulin sensitivity are frequently associated with hepatic overproduction of VLDL (77). However, the effects of insulin resistance on postprandial lipemia are not limited to hypertriglyceridemia due to liver defects. A secondary issue may be mild reductions in adipose tissue lipoprotein lipase

activity in the postprandial period (155). This reduces the ability to clear postprandial triglycerides and in this way also contributes to an exaggerated postprandial lipemic response.

Insulin resistant individuals are also often obese, making it difficult to discern the effects of insulin resistance on postprandial lipemia that are independent of obesity. A study by Chen and colleagues (29) gives the insight that even when matched for body habitus and fasting triglycerides, type II diabetics still have abnormal postprandial triglyceride metabolism. This study matched participants on the basis of body mass index, so the effect of regional body composition on this relationship was not adequately addressed. Blackburn et al. (17) attempted to determine the contribution of visceral adipose tissue to abnormal postprandial triglyceride responses accompanying impaired glucose tolerance. They found that males with impaired glucose tolerance, but not visceral adiposity, did not show a different postprandial triglyceride response in comparison to lean males with normal glucose tolerance. While these authors did not directly assess insulin resistance, this indicates that visceral adipose tissue does play an important role in the impaired postprandial triglyceride response seen in those with metabolic abnormalities associated with insulin resistance.

Sex Differences

Postprandial triglyceride concentrations generally have been shown to be significantly elevated in males compared to females (65). Since this has been related to sex differences in fasting triglyceride concentrations, conditions promoting fasting hypertriglyceridemia have been implicated as causative factors. Males typically tend to be predisposed to accumulation of visceral adipose tissue compared to females. Thus, it

is plausible that this sex dimorphism in regional body composition is at least partly responsible for this response. Couillard et al. (37) studied 88 males and females with a wide range of body fat values and distributions and found that in accordance with previous reports, males did demonstrate a significantly higher lipemic response compared to females. Further analysis revealed that when the sexes were matched for amount of visceral adipose tissue, sex differences in postprandial lipemia were completely eliminated.

While the aforementioned findings suggest a strong role for visceral adipose tissue and fasting triglycerides in sex differences in postprandial lipemia, such differences have still been found even when normal-weight men and women are matched for fasting triglyceride levels (100). Variations in metabolic processes pertaining to triglyceride-rich lipoproteins may explain this. Knuth and Horowitz (115) reported that the concentration of exogenous triglycerides remains elevated substantially longer in lean men versus lean women. Another contributing factor may be postprandial triglyceride clearance in skeletal muscle. Horton et al. (97) discovered enhanced postprandial skeletal muscle TG clearance in women compared to men with similar levels of fasting TG. Thus, it appears that while fasting triglyceride concentrations and visceral adipose tissue may play roles in the commonly seen sex-based differences in postprandial lipemia, other metabolic factors reduce the atherogenic potential of each meal in women.

Dietary Variables

There is considerable debate as to the optimal dietary macronutrient composition to reduce cardiovascular disease risk. Reducing dietary fat content has long been suggested as an effective strategy because this is known to reduce concentrations of

LDL-C (30). However, when dietary fat content is replaced by carbohydrates, increases in fasting plasma triglycerides and reductions in HDL-C have been consistently shown to result (143). The unfavorable fasting lipid changes as a consequence of high-carbohydrate diet translate into exaggerated postprandial lipemia as well (123). This side effect should not completely discount this dietary regimen because it may be offset by participation in exercise. For example, although endurance athletes typically consume a high percentage of dietary carbohydrates with respect to fat, their fasting triglycerides are often lower and HDL-C concentrations higher than non-exercisers (51). Exercise seems to have a similar effect postprandially. Koutsari et al. (122) demonstrated that increases in postprandial lipemia resulting from a low-fat, high-carbohydrate diet were completely negated with the addition of aerobic exercise.

In addition to macronutrient composition, consumption of alcohol influences postprandial lipemia. Acute consumption of alcohol has been associated with increases in magnitude and duration of postprandial lipemia (57). This may be due to increases in fasting triglyceride concentrations as well as reduced chylomicron lipolysis (171). Thus, although moderate alcohol consumption has been regarded as cardioprotective in some respects, its consumption may have a negative impact on postprandial lipemia.

Medications

Numerous pharmacologic therapies are widely prescribed for the treatment of dyslipidemias. Many of these medications also influence postprandial lipemia. Fibrates have a major effect on triglyceride metabolism due to an increase in both lipoprotein lipase activity and enhanced hepatic fatty acid oxidation (102). As expected, this class of medication also creates substantial reductions in postprandial lipemia that range from

approximately 30-60% (54, 58). Niacin (Vitamin B_3) also profoundly decreases fasting triglyceride concentrations and has been shown to reduce postprandial lipemia by as much as 45% (113). Finally, although HMG-CoA reductase inhibitors (statins) are primarily prescribed for their ability to reduce LDL-C, they also modestly reduce postprandial lipemia in both normotriglyceridemic and hypertriglyceridemic patients by approximately 30% (156, 157).

Aging

The aging process has been shown to have a negative influence on postprandial lipemia, with older persons demonstrating an exaggerated response compared to younger ones (34). More specifically, Krasinski et al. (124) reported that chylomicron residence time was nearly twice as long in men and women over age 60 compared to those aged 18-30. This suggests that aging is associated with delayed clearance of intestinally-derived triglyceride-rich lipoproteins.

Cigarette smoking

Cigarette smoking is another variable that has been associated with exaggerated postprandial lipemia. Sharrett et al. (187) found that smokers had significantly elevated levels of apolipoprotein B-48, but not apolipoprotein B-100, in response to a high-fat test meal compared to non-smokers. This suggests that the elevated levels of postprandial triglycerides were a result of increases in chylomicrons. The authors also reported that unlike many of the other factors influencing postprandial lipemia, this relationship was independent of fasting triglyceride levels.

Fasting Lipids, Lipoproteins and CVD

Fasting plasma lipid levels are often measured to assess the future risk of cardiovascular diseases. Epidemiological studies have found a direct relationship between total cholesterol (TC) levels and coronary heart disease (CHD) rate (27) and mortality (191) in men and women. However, it has been noted that although individuals afflicted with CHD tend have higher TC levels, almost half have plasma cholesterol levels as low or lower than non-diseased persons (64). Thus, while elevated total cholesterol levels have been identified as an independent CVD risk factor, additional components of the blood lipid profile are needed for more clinically useful assessments of CVD risk.

Levels of low-density lipoprotein cholesterol are also directly associated with coronary artery disease (186). In support of this epidemiological evidence, several major clinical trials have convincingly demonstrated that reductions in LDL-C are associated with decreases in cardiovascular events and mortality (126). For example, the use of statins to pharmacologically induce reductions in LDL-C has been associated with 30% reductions in CVD risk (6, 46, 178). These findings have led the National Cholesterol Education Program (NCEP) to issue guidelines calling for the aggressive lowering of LDL-C in both primary and secondary settings (4).

Reductions in LDL-C are not the only favorable blood lipid change that can occur to reduce CVD risk. The cholesterol content of high-density lipoprotein cholesterol must also be considered when assessing CVD risk because an inverse relationship between HDL-C and CVD has been established for both men and women (59). It has been estimated that for every 1 mg/dL increase in HDL-C, cardiovascular disease risk may be

reduced by 2 to 3 percent (21). Importantly, recent work has demonstrated that increases in HDL-C, without alterations in LDL-C, yielded a 22% reduction in the risk of a recurrent cardiovascular event (175). Findings such as these have made targeting low levels of HDL cholesterol an increasingly popular strategy for reducing cardiovascular disease risk.

Fasting plasma triglycerides are another lipid parameter that has been associated with cardiovascular disease. In the Framingham Heart Study, an increased risk for CHD was found in those with elevated triglycerides (26). This finding was more pronounced in women compared to men. Elevations in fasting triglycerides are often associated with low levels of HDL-C, which has presented difficulties in determining the independent effect of increased levels of triglycerides on CVD risk. This has lead some investigators to speculate that the main culprit is decreased levels of HDL-C, as opposed to increased levels of TG (12). However, there is also ample evidence to support the notion that fasting hypertriglyceridemia is independently associated with increased CVD risk (95, 154).

Measurement of plasma lipid concentrations is done routinely as part of comprehensive clinical assessments of cardiovascular disease risk. While these measurements provide valuable information, new insights have indicated that lipoprotein particle size may also play an important role in determining the atherogenic potential of lipoproteins. LDL particles were originally thought to be homogenous, but have now been shown to be heterogeneous (125) with small, dense particles being considered more atherogenic than larger, more buoyant particles (16).

LDL particle size is related to traditional lipid parameters as it is positively correlated with HDL-C and negatively correlated with TG (63). These associations preclude definitive statements as to whether or not small, dense LDL particles are an independent risk factor for CVD or merely reflective of a more broad pathological metabolic state. Nonetheless, the combination of small, dense LDL particles, depressed levels of HDL-C and elevated TG has been termed the atherogenic lipoprotein phenotype (11) and small, dense LDL particle size has been accepted as an emerging lipoprotein risk factor by the NCEP-ATP III (4).

In summary, several plasma lipid and lipoprotein parameters are significantly involved in the development and progression of cardiovascular disease. These include traditional measures such as total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides. The information provided by these measures may be supplemented by assessment of lipoprotein particle sizes.

Postprandial Lipemia and CVD

In addition to the CVD risk imposed by various fasting dyslipidemias, an exaggerated postprandial lipemia response is thought to contribute significantly to the development of atherosclerosis. This postulation was first advanced by Zilversmit in 1979 (209) and has been substantiated in recent years by cross-sectional studies and clinical trials, as well as mechanistic investigations that demonstrate biological plausibility.

Several cross-sectional studies have demonstrated a direct relationship between postprandial triglyceride concentrations and the presence and severity of coronary artery disease in males (84, 105, 145, 164). This relationship has been shown to remain

significant even after accounting for fasting triglyceride levels. In fact, it has even been suggested that postprandial triglycerides are a superior predictor of CAD compared to fasting triglycerides (164). The results from several case-control studies also show that those with documented coronary artery disease have elevations in plasma TG in the postprandial period compared to controls (98, 145, 192). The consistency seen from these two types of studies lends credence to the association between PPL and CVD. However, because abnormal postprandial lipemia often occurs in conjunction with several other established CVD risk factors, some investigators have questioned its independence (119). Future prospective studies are needed to more conclusively delineate the independent role of impaired postprandial triglyceride metabolism in the development of cardiovascular diseases.

Potential mechanistic links between postprandial metabolism and CVD include both direct effects of triglyceride-rich lipoproteins as well as indirect effects they may have on other lipoproteins in circulation. TRLs and their subsequent remnants have been implicated in the initiation of the atherosclerotic process because they may directly infiltrate arterial walls and participate in the cascade of events leading to the formation of atherogenic plaque (209). This assertion by Zilversmit was predicated on the assumption that these lipoprotein species are small enough to penetrate the endothelium. Later studies using human participants have shown that this is not the case for the majority of, but not all, chylomicrons and their remnants because they are removed from the plasma compartment prior to achieving a reduction in size that will allow them to localize subintimally (104, 129). However, deposition of cholesterol identified as being from VLDL has been found in human arterial specimens (173). Therefore, the flux of

lipoproteins and their remnants appears to be inversely related to the size of the particles. Although this relationship dictates that the majority of this process may be specifically attributed to RLPs originating from the VLDL subfraction, it is possible that sufficiently small chylomicron remnants may also participate.

In addition to arterial wall penetration, triglyceride-rich lipoproteins may also directly contribute to cardiovascular disease processes through nonatherogenic effects on the vascular wall (61). For example, postprandial endothelial dysfunction has been shown to occur in both apparently healthy populations (200), as well as in patients with documented CAD (208). The exact mechanisms responsible for this response remain unclear, yet several hypotheses have been advanced. For example, it has been speculated that the by-products produced during TRL lipolysis, such as NEFAs, may impair endothelial function and simultaneously enhance uptake of LDL particles (176).

Beyond the direct effects that triglyceride-lipoproteins and remnant-like particles have on the vasculature, lipoprotein modifications they participate in indirectly influence atherosclerotic risk. The primary example of this is the cholesterol enrichment of RLPs. In the postprandial state, the previously described exchange of core lipids between TRLs and other lipoprotein species is enhanced (103). Owing to the competition with chylomicrons for the catalytic activity of lipoprotein lipase, VLDL particles remain in circulation for a prolonged period of time following a meal, which provides increased opportunity for the CETP-mediated transfer of triglycerides to low- and high-density lipoproteins in exchange for cholesterol esters. This results in TG-enriched LDL and HDL particles. Once the TG content of these particles has been hydrolyzed by hepatic lipase, atherogenic small, dense LDL particles are formed (83), as well as small, dense

HDL particles that are cleared from circulation more rapidly than unmodified particles (174). The extent to which this CETP-mediated exchange occurs is directly related to the particle residence time (139), which suggests that individuals with impaired postprandial metabolism are more susceptible to these atherogenic lipoprotein modifications.

Despite these commonly recognized deleterious effects suggesting exaggerated postprandial lipemia plays an important role in the development of cardiovascular diseases, several difficulties have prevented oral triglyceride tolerance testing from becoming commonplace as a clinical screening tool. Principal among these is a lack of normative data to define what is considered a normal versus an exaggerated lipemic response. Additional methodological issues include standardization of blood sampling timepoints and test meal macronutrient content. Once these problems are resolved, the clinical relevance of postprandial triglyceride metabolism can be more firmly established.

Exercise Mechanisms

Exercise has been shown to be an important lifestyle modification for reducing postprandial lipemia. This reduction may result from an enhanced rate of removal of TRL, a diminished rate of their release into general circulation, or some combination of the two.

Skeletal Muscle Lipoprotein Lipase Activity and Triglyceride Clearance

Increased triglyceride clearance has been shown to occur following single sessions of exercise of extended duration (10, 179). The primary mechanism responsible for this enhanced clearance capacity is thought to be an increase in skeletal muscle lipoprotein lipase activity (69). While lipoprotein lipase is found in capillary beds of many extrahepatic tissues, it appears that the upregulation resulting from exercise is

specific to skeletal muscle lipoprotein lipase activity (SM LPLa) (182). Following single sessions of intense, prolonged aerobic exercise, SM LPLa may be increased by as much as 240% over baseline (133, 134). This occurs in a delayed fashion, with increases in activity seen from 4 to 18 hours after exercise (111).

These elevations in skeletal muscle lipoprotein lipase activity are thought to result from postexercise increases in gene expression. Seip et al. (183) reported that SM LPL mRNA increases immediately postexercise, reaches an apex at four hours postexercise and then declines by 8 hours postexercise. Increases in SM LPL mRNA were also associated with increases in SM LPL protein mass that peaked more than 8 hours after the cessation of exercise. Both SM LPL mRNA and protein mass returned to baseline by 20 hours postexercise. These findings have been corroborated by another investigative team who also established a similar time course for postexercise changes in SM LPL (189).

The time courses of the transient increase in SM LPLa and the reduction of postprandial triglyceride levels following single sessions of exercise parallel each other. Several studies have shown that exercise undertaken from 12 to 16 hours prior to a high-fat test meal significantly reduces postprandial triglyceride elevations (166). Therefore, the postprandial challenges in these studies were all well within the reported range for postexercise increases in SM LPLa. The congruence of these time frames suggests that the increase in triglyceride lipolytic capacity in skeletal muscle may be a key factor in reducing postprandial lipemia.

Although the mechanisms for the postexercise increases in SM LPLa are beyond the scope of this review, it should be stated that changes in concentrations of circulating

hormones such as insulin may play a role in determining this important response. As previously discussed, insulin reciprocally regulates adipose tissue and skeletal muscle LPL. In the postprandial state, insulin reduces the activity of skeletal muscle LPL (112), while simultaneously increasing the activity of adipose tissue LPL (170). Insulin sensitivity can be improved in response to a single session of exercise (146), and thus insulin concentrations have been shown to be reduced postprandially following an exercise session (68, 74). Therefore, reductions in the concentration of insulin, a hormone that reduces SM LPLa, may play a permissive role in facilitating increases in triglyceride clearance in the postprandial state.

While increased SM LPLa is considered an important factor in reducing postprandial lipemia, its role is not unquestionable. This is particularly true in the context of low- and moderate-intensity exercise since exercise of insufficient volume and/or intensity may not result in the increases in SM LPLa that have been reported for more exhaustive exercise (184). Studies examining changes in both postprandial lipemia and lipoprotein lipase activity support this because decreases in postprandial lipemia have been demonstrated without concurrent reductions in post-heparin lipoprotein lipase activity (73, 108). In a study specifically designed to address the role of increases in SM LPLa, Herd et al. (92) found that 90 minutes of moderate-intensity cycling reduced the lipemic response to a high-fat test meal 16 hours later, but tissue biopsies revealed that this occurred without concurrent increases in SM LPLa. Although mean SM LPLa values were not significantly changed in this study, there were significant correlations between the magnitude of PPL reduction and increases in SM LPLa. In addition to studies with direct measures of LPLa, other investigations have shown that exercise-

induced reductions in PPL were not the result of enhanced skeletal muscle triglyceride uptake (136) or even whole-body triglyceride clearance (74). It can be concluded from these studies that increases in SM LPLa are not solely responsible for the consistent reductions in postprandial lipemia following single sessions of exercise.

Rate of Chylomicron Appearance and Hepatic VLDL-TG Release

While it is theoretically possible that exercise may alter the rate of chylomicron appearance into general circulation, it does not appear that this is the case because exercise does not result in a delay in the time it takes for chylomicron-TG concentration to peak (68, 136). Furthermore, the rate of gastric emptying is not altered postprandially the day after an exercise session (74). This had led to speculation that exercise may reduce secretion of VLDL-TG from the liver. In animal models, it has been shown that chronic exercise training reduces VLDL secretion and increases markers of hepatic fatty acid oxidation (60). This indicates that exercise may reduce hepatic fatty acid esterification into triglycerides and secretion in VLDL particles in favor of increased utilization of fatty acids as a fuel. The direct evidence for this is lacking in humans, but increased markers of hepatic fatty acid oxidation have been observed concurrently with decreases in VLDL-TG concentrations following single sessions of exercises in studies using human participants (68, 136).

The available evidence from these mechanistic studies indicates that exercise likely reduces postprandial lipemia by complementary mechanisms. Increases in SM LPLa, along with increased insulin sensitivity, mediate increases in triglyceride clearance in response to exercise. However, it is also apparent that these transient adaptations do not explain the entire phenomenon. Decreases in hepatic VLDL secretion

are also likely a contributing factor. Thus, it seems that exercise reduces postprandial lipemia by a combination of an increasing lipolytic capacity and reducing the number of triglyceride-rich VLDL particles in circulation.

Exercise and Postprandial Lipemia

Consistently engaging in exercise is known to substantially reduce the risk for the development of several chronic conditions, including cardiovascular diseases (116). Several lines of investigation suggest that a portion of this risk reduction is a result of favorable exercise-induced alterations in postprandial lipid and lipoprotein metabolism (107).

Cross-Sectional, Detraining and Longitudinal Exercise Training Studies

Much of the early evidence that exercise has a favorable effect on postprandial lipemia comes from cross-sectional reports demonstrating that postprandial lipemia is lower in habitually physically active individuals compared to their sedentary counterparts (32, 90, 93, 110, 144, 204, 211). The magnitude of this reduction ranges from 27 to 74%. Similar findings have been reported from longitudinal exercise training studies. Chronic exercise training without concomitant weight loss has been reported to increase triglyceride-rich lipoprotein catabolism by as much as 37% (201). Please see Tables 1 and 2.

While these studies suggest that consistent exercise training reduces PPL, the timing of the last bout of exercise prior to the postprandial challenge was either close enough that its effect on PPL can not be excluded (32, 144, 201, 211) or was not reported (90, 110, 204). In the latter studies, it is reasonable to assume that exercise-trained individuals will continue to engage in their regimens unless specifically instructed not to,

so recent exercise likely influenced these reports. The acute effect of the most recent exercise session must be taken into account because a single session of exercise has been shown to reduce postprandial lipemia (69). Therefore, in these cross-sectional and longitudinal exercise training studies, it may be the effect of the most recent bout of aerobic exercise that is responsible for the attenuation of postprandial lipemia attributed to habitual exercise.

Detraining studies, where interruptions of exercise training have been introduced, have been used to investigate the respective influences of acute exercise and exercise training on postprandial lipemia. Please see Table 2. Only one study has directly compared the PPL response in cohorts of different training statuses. Herd et al. (93) evaluated sprint- and strength-trained, endurance-trained and untrained males and females after sixty hours without engaging in exercise and found that there were no significant differences among any of these groups in response to a high-fat test meal. It should be noted that there were also no significant differences in age, percentage body fat, or fasting triglyceride levels among any of the groups. This provides strong evidence that in the absence of recent exercise, individuals of contrasting training statuses, but alike in other respects, exhibit similar postprandial lipemia responses.

Other detraining investigations have been aimed at establishing a temporal sequence for this rapid reversal in postprandial triglyceride metabolism following exercise cessation. The first authors to report on this were Mankowitz et al. (138) and they found that 14-22 days of detraining altered metabolism of chylomicrons and chylomicron remnants unfavorably in males who typically ran 30-40 miles per week. Several studies since this initial report have examined time frames closer to the last

session of exercise. For example, Hardman et al. (89) administered a postprandial challenge to endurance athletes 15 hours after the most recent bout of aerobic exercise and then again at 60 hours and 6.5 days postexercise. It was reported that the PPL response was 35% higher 60 hours postexercise compared to 15 hours following the cessation of exercise training. There was no statistically significant difference between the 60-hour and 6.5 day trials. In support of this, Herd et al. (91) reported that 13 weeks of endurance training reduced the lipemic response to an oral fat tolerance test 15 hours following the last training session; however, after two and a half days without exercise the lipemic response of endurance-trained individuals comparatively rose by 37% and was not significantly different from pre-training levels. Finally, Aldred et al. (7) demonstrated that in previously inactive women, 12-weeks of aerobic exercise training significantly increased aerobic power but did not reduce PPL significantly compared to the pre-training response 48 hours after the most recent exercise session.

Collectively, these studies suggest that physically active individuals only have a reduced lipemic response when recent exercise has been performed. This effect may be absent within 48 to 60 hours of discontinuation of exercise, suggesting that frequent sessions of aerobic exercise are required to maintain the anti-atherogenic improved tolerance to a fat meal often demonstrated in regular exercisers.

Acute Effects of Exercise

Recent aerobic exercise consistently reduces the lipemic response to a test meal by 9 to 39%. Please see Table 3. The wide range seen in this response may be explained by several considerations including total energy expenditure, exercise intensity, pattern of

activity, participant characteristics, fasting triglyceride changes, test meal timing and composition, and modality of exercise.

Total Exercise Energy Expenditure and Dose-Response

The health-related benefits derived from consistent physical activity are thought to accrue in a dose-dependent fashion, with higher energy expenditures resulting in greater cardiovascular disease risk reduction (116). The current consensus is that total energy expenditure is the key factor in determining the reduction in postprandial lipemia (69, 166), thus it should be determined if this occurs in a dose-response manner. This can be accomplished by partitioning acute exercise studies into the following three doses based on total energy expenditure: 1) < 500 kcals, 2) 500-1,000 kcals, 3) > 1,000 kcals.

Energy Expenditures of < 500 kcals

Current public health recommendations suggest a minimum physical activity energy expenditure of approximately 200 kcals per day on most, if not all, days of the week (160). Therefore, total energy expenditures in this range are of critical importance because they represent the minimum doses of exercise purported to reduce CVD risk.

The lowest caloric expenditure studied to date is approximately 250 kcals. Altena et al. (9) reported that this level of energy expenditure resulted in a 10% reduction of triglyceride AUC_T in young males and females, although this finding was not statistically significant. Another report indicated that a similar amount of exercise also reduced this same outcome significantly by 12% (150). The effectiveness of energy expenditures within this range is also supported by the findings of Gill et al. (71), who reported that approximately 350 kcals of moderate-intensity treadmill walking reduced the triglyceride AUC_T and AUC_I scores by 9% and 11%, respectively. Finally, in strong support of a

dose-response effect within this total energy expenditure category, studies increasing caloric expenditures to between 400 and 450 kcals have reported proportionately larger reductions in PPL in the range of 16-18% (70, 197).

Energy Expenditures Between 500-1,000 kcals

Most of the studies on the influence of acute exercise on postprandial lipemia have used total energy expenditures within this range and report reductions in the triglyceride AUC_T and AUC_I scores in response to a high-fat meal that are typically between 19-40% (8, 13, 66-69, 71-74, 109, 148, 190, 194, 195, 197, 199, 205-207). Comparing this range to the previous caloric expenditure category lends credence to exercise-induced reductions in postprandial lipemia occurring in a dose-response fashion. There is also direct evidence to support this from Gill et al. (71), who found that ~760 kcals of exercise reduced PPL by 23% compared to a 9% reduction for an exercise session with half of the caloric expenditure. Additionally, Tsetsonis et al. (199) demonstrated a 32% reduction in PPL in trained females compared to a 16% reduction in untrained females, who expended roughly one-third fewer kcals during a 90-minute exercise session. Both of these studies suggest that further increases in caloric expenditure result in greater reductions in PPL.

Energy Expenditures of >1,000 kcals

Several studies have used prolonged moderate-intensity exercise sessions lasting up to three hours and requiring total energy expenditures of at least 1,000 kcals (75, 92, 108, 136, 137, 198). Within this category, reductions in triglyceride AUC_T and AUC_I ranging from 28-42% are typically reported, suggesting that increases in caloric expenditure beyond 1,000 kcals create further reductions in PPL. Although not studied

extensively, there may be an upper limit to this response. Protocols using approximately 1,100 kcals yield responses in the typical range for this category (108, 198), but those increasing caloric expenditure beyond this have not found additional benefit (136).

Based on the available evidence, there is a strong dose-response relationship for aerobic exercise-induced reductions in postprandial lipemia. Total exercise energy expenditures ranging from ~250 to ~1,110 kcals typically reduce the triglyceride response to a high-fat test meal from 9-42% in a dose-dependent fashion. Further work is needed to decisively determine what the minimum necessary total energy expenditure is to reduce postprandial lipemia.

Exercise Energy Expenditure Compared to Caloric Restriction

That total energy expenditure appears to be of critical importance in the ability of exercise to reduce PPL implies that it may be possible to achieve a similar benefit through caloric restriction. Gill and Hardman (70) compared energy intake restriction to exercise and found that exercise significantly reduced triglyceride AUC_T and AUC_I by 18%, whereas a hypocaloric diet resulted in non-significant 9% and 7% reductions in these scores, respectively. From this it can be concluded that although exercise may produce an energy deficit, its effects on postprandial lipemia are distinct from and superior to energy deficits achieved through caloric restriction.

Physical Fitness Status

Although physical fitness status does not appear to influence postprandial lipemia beyond the most recent sessions, it may have an indirect impact by influencing the rate of energy expenditure. Tsetsonis et al. (199) compared the effects of a single session of aerobic exercise on postprandial lipemia in trained and untrained women and found that 1

hour of moderate-intensity exercise reduced PPL only in the endurance-trained women. In this study, both cohorts were given the same amount of time to exercise at 60% of their respective maximal aerobic capacities. As expected, the mean aerobic power was significantly higher in the trained group, leading to substantially higher exercise energy expenditures in these women. These results can't be directly attributed to training status because total energy expenditure was not taken into account. However, it does illustrate that endurance-trained individuals have an advantage in achieving exercise-induced reductions in PPL because they can expend greater amounts of energy per unit of time than those who are untrained.

Exercise Intensity

Although total energy expenditure is an important postprandial determinant, the intensity at which exercise is performed will influence rate of caloric expenditure and is thus also worth consideration. While moderate- and high-intensity aerobic exercise will invariably result in greater caloric expenditures than lower intensities in a given time period, low-intensity exercise has been shown to promote exercise adherence in older, more sedentary populations (39). Therefore, a broad spectrum of intensities needs to be examined in order to prescribe aerobic exercise for diverse populations.

The majority of the postprandial lipemia studies pertaining to exercise have used moderate-intensity exercise. To date, only four studies have made direct comparisons of low- and moderate-intensity exercise (108, 197, 198, 205). The first study to address the issue found that 90 minutes of treadmill walking at 60%, but not 30%, of maximal aerobic power resulted in significant PPL reductions. Although the authors concluded that low-intensity exercise was ineffectual compared to moderate, it must be considered

that the total energy expenditure was significantly greater in the moderate-intensity trial. Based on this discrepancy, it is not possible to determine if exercise intensity or total caloric expenditure is responsible for these results. This same miscalculation was made in a more recent investigation into the issue of aerobic exercise intensity (205). Failure to maintain a consistent total caloric expenditure in these protocols effectively invalidates their findings with respect to exercise intensity.

To date, only two studies manipulating exercise intensity using isocaloric exercise sessions have been performed. In the first such study, Tsetsonis and Hardman (198) had physically active men and women walk on a treadmill for 1.5 hours at moderate-intensity or for 3 hours at low-intensity. This protocol required a total exercise energy expenditure of approximately 1,000 kcals and the lipemic response to a high-fat test meal was lowered by similar amounts the day after exercise, irrespective of intensity. These findings have frequently been cited as direct evidence that exercise intensity is not an important moderator of the postprandial lipemic response to exercise if total energy expenditure is held constant.

Despite this, there are still remaining issues to be resolved with respect to exercise intensity and postprandial lipemia. First, it appears that the total energy expenditure achieved in an exercise protocol may alter the effectiveness of low-intensity exercise. In contrast to the previously mentioned findings, two previous studies using low-intensity exercise resulting in caloric expenditures of approximately 400 kcals did not produce significant reductions in PPL (165, 197). In comparable studies, similar total caloric expenditures performed at a moderate-intensity have frequently been shown to have this effect (70, 71, 148). This leaves open for debate whether or not low-intensity exercise is

as effective as moderate-intensity exercise at lower levels of energy expenditure. This question is ultimately of practical importance for public health considerations because this amount (i.e. 400 kcals) of aerobic exercise is consistent with what older, inactive individuals are most likely to perform (5).

Another intensity-related inconsistency in the current literature was revealed when Katsonos et al. (108) recently showed that an exercise energy expenditure of 1,100 kcals performed at low-intensity (25% of $\dot{V}O_{2max}$) failed to attenuate PPL in active males. When the same caloric expenditure was achieved through moderate-intensity exercise (65% of $\dot{V}O_{2max}$), PPL was significantly reduced compared to the non-exercise control condition. This suggests a more complex role for exercise intensity in determining postprandial lipemia at higher energy expenditures than previously reported. Methodological differences may explain these discrepant findings. Although the total energy expenditure in this study was similar to that of Testsonis and Hardman (198), the timing of the test meals was different. In the former, the test meal was provided approximately 16 hours after the completion of the exercise session, while in the latter the test meal was administered 1 hour later. Test meal timing is a moderator that will be discussed in detail later in this section.

In summary, low-intensity exercise has been shown to be as effective as moderate exercise when the total caloric expenditure is high and the test meal occurs approximately 16 hours after the exercise session. The effectiveness of low-intensity exercise is less certain at lower caloric expenditures or when performed 1 hour prior to a high-fat test meal.

Pattern of Activity - Accumulated and Intermittent Exercise

Major public health recommendations from several governing bodies have endorsed accumulating exercise throughout the day as being equally effective as continuous exercise for the reducing cardiovascular disease risk (160). Some investigations of this claim have used accumulated exercise protocols where several hours elapsed between sessions, whereas others have used intermittent activity patterns with 20 minutes or less separating each session.

To date, there has only been one study to investigate the effects of accumulated exercise on the lipemic response to a single high-fat test meal (75). In this protocol, apparently healthy young males completed both a single session of treadmill running for 90 minutes and three 30-minute sessions at a moderate-intensity. Both exercise conditions required a total energy expenditure of roughly 1,100 kcals. Mean reductions in total triglyceride area under the curve scores of approximately 18% were reported for both trials. Since there was no difference between the two trials, it was concluded that accumulating exercise throughout the day was equally effective at reducing postprandial lipemia as a single, continuous session of equal caloric expenditure. It should be noted that the notion of accumulating exercise throughout the day is a physical activity recommendation that is mainly targeting older, previously sedentary individuals who likely have poor cardiorespiratory fitness (87). Given that this study used a high-fit, apparently healthy population, more studies are needed to fully examine the effectiveness of this public health recommendation at lower doses of exercise in less healthy populations.

Murphy et al. (150) also assessed the impact of accumulated exercise on postprandial lipemia using an unconventional protocol. Participants in this study performed treadmill walking for 30 minutes prior to consuming breakfast in one trial and then performed 10 minutes of treadmill walking prior to breakfast, lunch and dinner in a separate trial. In both conditions participants were not fed a single test meal, but three meals throughout the course of a single day. Additionally, the postprandial challenge in this study was a mixed meal comprised of 47% fat. Nonetheless, postprandial triglyceride concentrations were reduced equally as a result of exercise in both conditions.

Based on these two studies, accumulating moderate-intensity exercise over the course of the day seems to reduce PPL to the same extent as a continuous session of exercise the following day, as well as throughout the day the exercise is performed.

Altena and colleagues (9) were the first to report on the influence of intermittent activity patterns on postprandial lipemia. This group had moderately-fit young males and females complete a single 30-minute session of exercise and three 10-minute sessions of exercise each separated by 20 minutes of rest. The intermittent exercise condition resulted in a significant reduction in the incremental triglyceride area under the curve score, whereas the continuous exercise condition was not different from the control trial. As yet, this is the only finding that suggests that intermittent patterns of exercise may actually be more effective than single sessions of similar caloric expenditure at reducing postprandial lipemia. The authors hypothesized that intermittent activity may amplify resting metabolism in the recovery period due to excess postexercise oxygen consumption. This may have caused intermittent exercise to have a different influence on

lipoprotein lipase activity than continuous exercise, although no data to support this were presented.

In contrast to the previous findings, Miyashita et al. (148) recently reported that ten 3-minute sessions of moderate-intensity exercise separated by 30-minute rest intervals reduced PPL the following day to a similar degree as a single, continuous session of exercise. These are the first data to demonstrate that this particular CVD risk factor may be favorably altered by exercise sessions shorter in duration than the recommended minimum of 10 minutes. However, the practicability of these findings to exercise prescription for public health is questionable. Although the age group, as well as the duration and intensity of exercise were similar in both intermittent protocols, the fitness levels of the participants used by Miyashita et al. were substantially higher than those used by Altena et al. As a result, the approximate caloric expenditure was almost twice as high in the former study compared to the latter. This may explain the inconsistent results of the two studies.

In addition to structured sessions of intermittent exercise, the effect of intermittent games activity on PPL has been documented (13). The authors had study participants engage in intermittent physical activity in 15-minute intervals with 3-minute rest periods between each interval using a shuttle test. This was intended to simulate the pattern of activity that sports such as tennis, soccer or hockey may produce. In a second exercise trial, participants completed equivalent intervals of continuous treadmill walking. Intermittent physical activity reduced PPL to a similar extent as treadmill walking. The implication of this study is that intermittent games may also reduce postprandial

triglyceride concentrations in a similar fashion to what has been shown for traditional structured exercise.

Collectively, these studies indicate that intermittent patterns of structured exercise or physical activity games are as or possibly even more efficacious for reducing PPL compared to continuous exercise sessions of similar caloric expenditure.

Participant Characteristics

The participants in the majority of the exercise studies described in this section were lean, normotriglyceridemic, and at least moderately physically fit. These are not characteristics of individuals who would be expected to display exaggerated postprandial lipemia. Additionally, the acute exercise interventions in these studies often require total caloric expenditures well in excess of the recommendations for public health (160) and even weight reduction (94). These issues present difficulties in extending the current knowledge about the influence of exercise on postprandial lipemia to sedentary populations with characteristics of metabolic syndrome.

Currently, only a few studies have attempted to determine how metabolic syndrome factors may alter the previously described relationship between aerobic exercise and postprandial lipemia. Gill et al. (66) specifically compared the effects of moderate-intensity exercise on PPL in lean and centrally obese males. Both groups performed 90-minutes of treadmill walking 16 hours prior to a high-fat test meal which resulted in 25% reductions in postprandial TG concentrations the following day. Although this suggests an equal exercise stimulus resulted in parallel reductions in both groups, total energy expenditure was not controlled. Due to lower levels of aerobic fitness, the centrally obese males expended 30% fewer calories (~700 vs. ~900 kcals) in

the same time period to achieve this reduction. Based on this, it may be that inactive, obese males with hypertriglyceridemia have a lower caloric threshold than healthy males to achieve similar PPL reductions. While this requires further study with respect to postprandial lipemia, this is similar to what has been shown for reductions in fasting lipid concentrations. Crouse et al. (40) demonstrated that significantly lower amounts of acute aerobic exercise were necessary to alter fasting lipid and lipoprotein metabolism in sedentary males compared to previous reports using habitually active persons (56).

Zhang and co-workers (206) also looked into how exercise alters postprandial lipemia in obese, hypertriglyceridemic males. Participants exercised for 1 hour at 60% of their maximal aerobic power resulting in an approximate caloric expenditure of 650 kcals. This reduced triglyceride AUC_I by 33% the following day. In a follow-up study by the same authors (205), a similar group of participants was assigned to exercise to total caloric expenditures of approximately 450, 650 and 750 kcals. Triglyceride AUC_I concentrations were reduced by 30%, 31% and 39%, respectively.

The reductions in postprandial lipemia in the three studies using males with characteristics of metabolic syndrome appear to be consistent with what may be expected with similar acute exercise interventions in other populations. However, this should be directly investigated using isocaloric exercise sessions. Based on these studies, it appears that aerobic exercise is also effective in attenuating PPL in males with characteristics of metabolic syndrome. The caloric expenditure threshold for producing this response, as well as other issues of exercise prescription, such as exercise intensity and accumulated exercise, remain unclear in this population.

Acute Exercise Effect on Fasting Triglycerides

Single sessions of aerobic exercise have consistently been shown to reduce fasting triglyceride concentrations by 20%, on average (49). Although this lowering effect does not seem to be present immediately after exercise (55), TG reductions have been reported 24 to 48 hours postexercise (56, 96). These transient reductions in triglyceride concentrations are thought to be associated with the previously mentioned postexercise increase in skeletal muscle lipoprotein lipase activity (101).

Given the importance of fasting TG levels in determining the postprandial TG response, it is reasonable to suspect that a portion of the reduction in total triglyceride area under the curve scores the day after an acute exercise session may be due to reductions in fasting triglycerides. Indeed, several postprandial investigations have reported reductions in fasting triglycerides 12 to 18 hours after exercise that are within the same range as the reported reductions in triglyceride AUC_T (66, 74, 198). For example, Gill et al. (66) reported that exercise 18 hours prior to a test meal resulted in 25% reductions in both fasting TG and triglyceride AUC_T the next day. Thus, part of the reason that acute exercise reduces postprandial lipemia may be due to a reduction in fasting triglycerides, which in turn reduces the total number of triglyceride rich lipoproteins in circulation during the postprandial period.

Test Meal Timing

Investigators have administered test meals at different timepoints in relation to the most recent exercise session and this may influence postprandial lipemia. The preponderance of experimental designs have evaluated the influence of aerobic exercise 12 to 16 hours prior to a test meal (9, 13, 68-70, 72, 75, 76, 92, 118, 136, 137, 148, 195,

198, 199, 206, 207); however, some investigators waited as long as 24 hours after exercise (206, 207). Fewer investigations have used prior exercise performed one hour or less prior to the test meal (108, 109, 168, 194, 207). Finally, the effects of postmeal exercise has also been determined (109, 207).

Zhang et al. (207) directly compared the effects of different timing schemes on postprandial lipemia and reported that exercise 12 hours prior and 1 hour prior to the test meal reduced triglyceride AUC_I by 51% and 38%, respectively. The difference between the two protocols was not statistically significant, so it was concluded that both time frames were equally effective in attenuating PPL. While this is the only study to make a direct comparison, it appears that, if all else is equal, moderate-intensity exercise sessions undertaken anywhere from 1 to 16 hours prior to a meal will help equally to diminish elevations in postprandial triglycerides (166). Thus, within the range of 1 to 16 hours, timing of the test meal with respect to prior moderate-intensity exercise does not appear to be a critical consideration. From a practical vantage point, this has led to the suggestion that morning aerobic exercise may be optimal because it will reduce postprandial lipemia throughout the course of the day (107). As previously stated, this may not hold true for low-intensity exercise because as yet, only low-intensity exercise undertaken 12 to 16 hours prior to the test meal has been shown to attenuate postprandial lipemia (8, 198, 205).

Timing of the test meal has been shown to be of more concern when the test meal is 24 or more hours after the end of the most recent exercise session (166). Another timing study by Zhang et al. (206) compared exercise undertaken 12 versus 24 hours prior to a postprandial triglyceride challenge. In this case, exercise preceding the meal by

12 hours lowered PPL, but not exercise 24 hours prior. Although skeletal muscle lipoprotein lipase activity was not measured in this study, the findings may emphasize the importance of the documented transient increase in SM LPLa thought to occur after a single session of exercise, but decline by 20 hours postexercise (184). The postprandial period in this study protocol ranged from 24-32 hours postexercise. Therefore, it is possible that exercise sessions this far in advance do not result in reductions in PPL because the time sequence does not optimally overlap with postexercise increases in SM LPLa.

While the majority of studies have focused on premeal exercise, there have also been a few efforts to understand the effect of postmeal exercise on PPL. When Zhang et al. (207) directly compared exercise 1 and 12 hours prior to a meal versus 1 hour postmeal, only the premeal exercise conditions resulted in a statistically significant attenuation of PPL. Although these findings suggest that premeal exercise is ineffective, there is contrasting evidence. Katsanos et al. (109) had participants commence exercise 90 minutes following meal ingestion on one occasion and 30 minutes prior to a meal on another. Postprandial lipemia was reduced by similar amounts in both trials, indicating that exercise undertaken during the postprandial period reduces PPL as effectively as premeal exercise. These findings are in agreement with others (88, 114, 180), and thus the majority of the available evidence suggests that exercise initiated up to 90 minutes after meal consumption may reduce postprandial lipemia.

Test Meal Composition - Mixed Meals

Some recent studies have used mixed test meals with a lowered fat content compared to traditional high-fat test meals. In these cases, test meals often have 35% of

their calories from fat, and may have as little as 15-30 g of absolute fat content. Despite being substantially less than what is contained in a high-fat meal, these amounts of dietary lipid are sufficient to induce postprandial lipemia (47). Aside from the macronutrient composition of the test meal, all other aspects of the experimental design are similar to those of protocols using high-fat test meals. The rationale for this methodology is that mixed meals are more representative of standard Western diets and the results obtained give a better indication of how exercise impacts postprandial lipemia in free-living conditions (168).

The major difference seen in mixed-meal protocols is that exercise energy expenditures on the lower end of the spectrum do not seem to produce reductions in postprandial lipemia. Two studies using caloric expenditures of 250 kcals did not show diminished triglyceride responses the next day (167, 168). The authors of these studies have concluded that protocols using high-fat test meals overstate the actual benefit of exercise in this caloric expenditure range on postprandial lipemia in real-life settings.

In contrast, exercise energy expenditures of 550 kcals (118) and 1,000 kcals (117) were associated with 26% and 35% reductions in triglyceride $AUC_{T.}$ These responses are consistent with those found in response to a high-fat test meal when similar amounts of exercise energy expenditure were attained. Based on the limited available evidence, it appears that the impact of exercise on postprandial lipemia only varies in response to differing test meal composition at lower levels of energy expenditure.

Other Exercise Modalities - Resistance Exercise

While aerobic exercise has been the modality of exercise most frequently studied for its ability to reduce CVD risk, resistance training has also been recognized for this

purpose (1). In accordance, the postprandial triglyceride response to a single session of resistance exercise has begun to receive attention as well; however, the findings have been far less consistent than for aerobic exercise. Studies have suggested that resistance exercise reduces (165), has no effect (25, 185), or even increases PPL (24) . Please see Table 4. The estimated energy expenditure and volume of exercise was comparable in these protocols and therefore these issues do not clearly explain the discrepant findings. Participant training status may explain part of the differences. Petitt et al. (165) reported significant attenuations with resistance-trained participants, whereas Shannon et al. (185) and Burns et al. (25) studied resistance-naïve participants and both reported that resistance exercise didn't significantly alter PPL. It has been hypothesized that initial bouts of resistance exercise in untrained persons may actually result in impaired TG clearance (24). Nonetheless, this is unlikely to explain the entire phenomenon because in a second study by Burns et al. (24), resistance-trained individuals also demonstrated an increased lipemic response to a high-fat test meal. More studies incorporating resistance exercise are needed for a full understanding of how this modality of exercise impacts PPL.

Summary

Postprandial lipemia is the elevation in plasma triglyceride levels that occurs following the consumption of a meal. An exaggerated postprandial triglyceride response has been shown to be closely associated with cardiovascular disease risk. Individuals with metabolic syndrome, a clustering of CVD risk factors that includes abdominal obesity, hypertriglyceridemia, insulin resistance, low levels of HDL-C, and hypertension are particularly susceptible to postprandial triglyceride abnormalities.

It is clear that aerobic exercise consistently reduces postprandial lipemia. This effect appears to be solely the result of recent, acute sessions of aerobic exercise, as opposed to habitual exercise training. The primary physiological mechanisms mediating this response are thought to be increases in skeletal muscle LPL activity and reduced hepatic VLDL-TG secretion.

While the efficacy of aerobic exercise in terms of postprandial triglyceride reductions is beyond question, several issues pertaining to participant characteristics and exercise prescription remain unanswered. The great majority of the acute exercise studies have used young, apparently healthy, normotriglyceridemic individuals as participants. There is much more limited evidence about how exercise affects PPL in people who are physically inactive, obese, and hypertriglceridemic. Additionally, the doses and intensities of the acute exercise sessions the current literature may not be palatable to less physically fit populations. To date, no investigations using participants with characteristics of metabolic syndrome have been conducted to compare the effects of exercise intensity and accumulated versus continuous sessions of aerobic exercise at doses that are recommended for public health and weight loss. Further investigation into these issues is warranted because these individuals likely have impaired triglyceride metabolism and thus may respond differently to exercise intervention than the populations previously studied.

Table 1. Selected cross-sectional studies

Study Characteristics				
Author	Design	Participants	Last EX	Δ AUC_T
Cohen et al., 1989 (32)	characterize PPL in athletes vs. sedentary	30 M, 15 T, 15 UT; age 26 ± 4 (T) 22 ± 2 (UT) AP NR % fat NR BTG 61 ± 18 (T) 70 ± 26 (UT)	W/I 24 hr	-59% (T) vs. (UT)
Hartung et al., 1993 (90)	comparison of PPL in runners vs. untrained	27 M, 14 R, 13 UT; age 38.6 ± 8 (R) 30.6 ± 6 (UT) AP NR % fat NR BTG 68 ± 21 (R) 119 ± 52 (UT)	NR	-27% (R) vs. (UT)^{NS}
Herd et al., 2000 (93)	examine PPL in athletes vs. sedentary males and females	32 M, 20 F; age 24.2 ± 4.3 20 ET, 10 ST, 22 UT AP 70.2 ± 8.9(EM) 57.2 ± 4.4 (EF) 58.2 ± 5.8 (SM) 51.3 ± 4.6 (UM) 38.9 ± 4.2 (UF) % fat 14 ± 5 (EM) 22 ± 4 (EF) 15 ± 5 (SM) 15 ± 4 (UM) 27 ± 6 (UF) BTG 96 ± 5 (EM) 75 ± 11 (EF) 93 ± 3 (SM) 90 ± 7 (UM) 75 ± 11 (UF)	> 60 hr	-8% (EM) vs. (UM)^{NS} -11%(SM) vs. (UM)^{NS} +2% (EM) vs (SM)^{NS} +26% (EF) vs. (UF)^{NS}
Katzel et al., 1994 (110)	comparison of PPL in older adults with and w/o SI	25 M, 12 control, 13 SI; age 50-75 active AP 40-55 % fat 5-24 BTG 23-113	NR	-27% C vs SI

Study Characteristics				
Author	Design	Participants	Last EX	Δ AUC_T
Merrill et al., 1989 (144)	characterize PPL in trained vs. untrained males	16 M; age 22-34 9 T, 7 UT AP 67.4 ± 8.8 (T) 51.6 ± 6.2 (UT) % fat 13 ± 4 (T) 20 ± 7 (UT) BTG 64 ± 15 (T) 69 ± 35 (UT)	W/I 24 hr	-74% (T) vs. (UT)
Yanes et al., (204)	compare PPL in CR patients vs controls with CAD	13 M, 6 CR, 7 control; age 56.4 ± 5 AP 30 ± 2.5 (CR) % fat 26 ± 2 (CR) 34 ± 2 (C) BTG 113 ± 11 (CR) 279 ± 85 (C)	NR	-28% (CR) vs. (C)
Ziogas et al., 1997 (211)	characterize PPL in sedentary, active and endurance trained	54 M F; age 30-53 16 T , 21 RA, 17 S AP 50.2 ± 7.4 (T) 41.5 ± 5.8 (RA) 50.2 ± 7.4 (S) % fat 15 ± 5 (T) 20 ± 5 (RA) 24 ± 6 (S) BTG 57 ± 20 (T) 62 ± 22 (RA) 75 ± 29 (S)	No Vig EX W/I 36 hr	-38% (RA) vs.(S)^{NS} -61% (T) vs. (S) -36% (T) vs. (RA)^{NS}

AP = aerobic power; **BTG** = baseline triglycerides; **C** = control; **CAD** = coronary artery disease; **CR** = cardiac rehabilitation; **EF**= endurance-trained females; **EM** = endurance-trained males; **EX** = exercise; **F** = females; **hr** = hour; **M** = males; **NS** = not statistically significant; **NR** = not reported; **PPL** = postprandial lipemia; **R** = runners; **RA** = recreationally active; **S** = sedentary; **SI** = silent ischemia; **SM** = strength-trained males; **T** = trained; **UF** = untrained females; **UM** = untrained males; **UT** = untrained; **Vig** = vigorous; **W/I** = within.

Age is reported in years; AP is reported in mL/kg/min; BTG is reported in mg/dL.

Table 2. Selected exercise training and detraining studies

Study Characteristics				
Author	Purpose	Participants	Last EX	Δ AUC_T
Aldred et al., 1995 (7)	effects of 12 wk brisk walking training	24 F, 11 EX, 13 C age 40-59 previously inactive AP NR BMI 23 ± 2 BTG 65 ± 8	48 hr prior	+8% walkers^{NS} +3% control^{NS}
Gill et al., 2003 (67)	effects of 1 wk detraining	8 M; age 27.8 ± 12.1 endurance-trained AP NR % fat 17 ± 3 BTG ~70 mg/dL	1 wk prior	+53%
Hardman et al., 1998 (89)	effects of brief detraining	9 M, 1 F; age 18.3-55.4 endurance trained AP NR BMI 20.4-29 BTG NR	15 hr 60 hr 6.5 days	+27% 60 hr vs. 15 hr +32% 6.5 d vs. 15 hr
Mankowitz et al., 1992 (138)	effects of detraining	8 M; age 34 ± 6 endurance trained AP 58 ± 7 % fat 15.5 ± 5 BTG 99 ± 32	14-22 d prior	No Δ (data NR) +42% (CH) +36% (CR)
Paton et al., 2006 (161)	effects of 6 d training	8 M F; age 58.9 ± 4.7 AP 27 ± 2.5 % fat ~37 BTG 102 ± 20	24-36 hr prior	-9%

AP = aerobic power; **BMI** = body mass index; **BTG** = baseline triglycerides; **C** = control; **CH** = chylomicrons; **CR** = chylomicron remnants; **d** = days; **EX** = exercise; **F** = females; **hr** = hour; **M** = males; **NS** = not statistically significant; **NR** = not reported; **wk** = week; **W/I** = within.

Age is reported in years, AP is reported in mL/kg/min; BTG is reported in mg/dL; BMI is reported in kg/m^2.

Table 3. Selected acute aerobic exercise studies

Study Characteristics					
Author	Design	Participants	Protocol	Δ AUC_T	Δ AUC_I
Aldred et al., 1994 (8)	15 hr prior low-int. EX	6 M, 6 F; age 25.8 ± 1.2 active AP 48.6 ± 3 %fat 20 ± 2 BTG 87 ± 5	TM walking; I = 30% D = 120 min TEE = 623 kcals	NR	-31%
Altena et al., 2004 (9)	12 hr prior IE vs. CE	7 M, 8 F; age 25 ± 1.8 inactive AP 38.4 ± 1.5 % fat 17 ± 2 M % fat 26 ± 2 F BTG 92 ± 10	TM running; I = 60% D = 30 min CE =30-min, 1X IE =10-min, 3X TEE = 245 kcals	-13% (IE)^{NS} -10% (CE)^{NS}	-27% (IE) -16% (CE)^{NS}
Barrett et al., 2006 (13)	16 hr prior games vs. CE EX	12 M; age 21.1 ± 0.4 active AP 53.0 ± 1.5 %fat NR BTG 83 ± 5	TM walking; Intermittent games; I = 62% (C) I = 72% (G) D = ~60 min TEE = 740 kcals	-25% (G) -19% (CE)	-33% (G) -21% (CE)^{NS}
Dalgaard et al; 2004 (42)	16 hr prior vs. postmeal EX on a mixed meal	12 M T2D; age 59.3 ± 10.4 activity level NR AP 28 ± 6 BMI 27.9 ± 2.8 BTG 246 ± 175	Cycle erg; I = 40% D = 40 min TEE = NR	-3% (PO)^{NS} +7% (PE)^{NS}	+9% (PO)^{NS} +20% (PE)^{NS}
Gill et al., 2001 (68)	15 hr prior EX	11 M; age 51.7 ± 6.1 active AP 38.9 ± 5.6 % fat 27 ± 6 BTG 90 ± 10	TM walking; I = 60% D = 90 min TEE = 805 kcals	-23%	-27%
Gill et al. 2000 (70)	16 hr prior EX vs. IR	11 PM F; age 60.2 ± 3.8 active AP 30.7 ± 3.2 % fat ~35.7 BTG 88 ± 8	TM walking; I = 60% D = 90 min TEE = 413 kcals	-9% (IR)^{NS} -18% (EX)	-7% (IR)^{NS} -18% (EX)

Study Characteristics					
Author	Design	Participants	Protocol	Δ AUC_T	Δ AUC_I
Gill et al., 2002 (72)	16 hr prior EX	38 M 43 F; age 21-64 yr active AP 41.2 ± 9.9 BMI 23.9 ± 2.3 BTG 78 ± 4	Cycle erg or TM; I = 60% D = 90 min TEE = NR	-22%	-22%
Gill et al. 1998 (75)	14 hr prior AE vs. CE	18 M; age 30.6 ± 9 active AP 57.8 ± 5.5 BMI 23.1 ± 1.4 BTG 78 ± 7	TM running; I = 60% D = 90 min AE = 3 30-min bouts CE = 1 90-min bout TEE = 1,125 kcals	-18% (AE) -18% (CE)	NR NR
Gill et al., 2004 (76)	16-18 hr prior EX in lean vs. obese	10 obese M, 10 lean M; age 48 ± 8 (O) 47 ± 11 (L) AP 41 ± 7 (O) 44 ± 6 (L) WC 107 ± 8 (O) 82 ± 5 (L) BTG 153 ± 18 (O) 75 ± 4 (L)	TM walking; I = 50% D = 90 min TEE (O) = 884 kcals TEE (L) = 693 kcals	-25% (O) -25% (L)	-28% (O) -34% (L)
Gill et al. 2002 (71)	dose-response effect of 18 h prior EX	11 F; age 21.3 – 40.5 activity level NR AP 39.7 BMI 18.9-30.1 BTG 61 ± 5	TM walking; I = 50% D_1 = 1 hour D_2 = 2 hours TEE_1 = 358 kcals TEE_2 = 740 kcals	-9.3% (D_1) -22.8% (D_2)	-10.6% (D_1) -31.8% (D_2)
Gill et al., 2003 (73)	18 hr prior EX	9 F; age 27.4 ± 7 active AP 42 ± 6.7 % fat 26 ± 5 BTG 59 ± 18	TM walking; I = 50% D = 120 min TEE = 765 kcals	-23%	-42%
Gill et al., 2001 (74)	16 hr prior EX	8 M; age 48.3 ± 7.3 active AP 39.0 ± 6.1 % fat ~ 29 ± 12 BTG 120 ± 19	TM walking; I = 60% D = 90 min TEE = NR	-18%	17%

Study Characteristics					
Author	Design	Participants	Protocol	Δ AUC_T	Δ AUC_I
Herd et al., 2001 (92)	16 hr prior EX	8 M; age 27 ± 4.2 active AP NR BMI 24.5 ± 1.3 BTG 67 ± 17	Cycle erg; I = 60% D = 90 min TEE = 1,075 kcals	-28%	-42%
Katsanos et al., 2004 (108)	1 hr prior EX at Low and Mod intensity	13 M; age 23.8 ± 0.9 active AP 49.5 ± 2 % fat 11.9 ± 1.7 BTG 70.5 ± 4.0	TM W/R I (Mod) = 65% I (Lo) = 25% D (Mod) = 91 min D (Lo) = 238min TEE = 1,100 kcal	NR NR	-39% (Mod) -8% (Lo)^{NS}
Katsanos et al., 2004 (109)	prior vs. postmeal EX	10 M; age 25.2 ± 0.9 untrained AP 46.6 ± 3.0	TM walking; I = 50% D = 90 min TEE = NR	NR NR	-49% (PE) -52% (PO)
Kokalas, et al., 2005 (117)	14 hr prior EX on a mixed meal	8 F: age 18-25 active AP 49.5 ± 2 BMI 22.9 ± 0.5 BTG 23-70	Rowing erg; I = 55% D = 80 min TEE = 1,003 kcals	-35%	-36%
Kolifa et al., 2004 (118)	15 hr prior EX on a mixed meal	9 M; age 20-25 activity level NR AP NR BMI 24.7 ± 0.8 BTG 65	Cycle erg; I = 70-75% D = 60 min TEE = 549 kcals	-26%	-18.5%^{NS}
Koutsari et al., 2001 (122)	prior EX and HC diet	9 M; age 33 ± 4 active AP 54 ± 7 BMI 24.4 ± 1.2 BTG 96 ± 41	TM walking; I = 60% D = 30 min F = 1x day for 3 d TEE = 377 kcals	+ 35% (HC) + 6% (EX)	+30% (HC) -13% (EX)
Malkova et al., 1999 (137)	15 hr prior EX with Acipomox	12 M; age 21 – 36 active AP 58.6 ± 6.5 BMI 24 ± 2.5 BTG 81 ± 40	TM running; I = 60% D = 90 min TEE = 1,154 kcals	-18% (PL) -18% (ACX)	-28% (PL) -28% (ACX)

Study Characteristics Author	Design	Participants	Protocol	Δ AUC_T	Δ AUC_I
Malkova et al., 2000 (136)	16 hr prior EX	8 M; 21-46 yr active AP 56.8 ± 5.3 % fat 18 ± 5 BTG 80 ± 8	TM running; I = 60% D = 120 min TEE = 1,722 kcals	-34%	NR
Miyashita et al., 2006 (148)	17 hr prior IE vs. CE	10 M; age 21-32 active AP 56.3 ± 1.8 % fat 9 ± 1 BTG 118 ± 25	TM running; I = 70% D = 30 min CE = 1, 30 min bouts IE = 10, 3-min bouts TEE = 478 kcals	-22% (IE) -24% (CE)	-31 (IE) -32 (CE)
Petridou et al., 2004 (167)	immediately prior EX on a mixed meal	11 M; age 21.7 ± 0.6 inactive AP NR BMI 22.5 ± 0.5 BTG ~ 61	Cycle erg; I = 60 – 65% D = 45 min TEE = 263 kcals	-17%^{NS}	-8%^{NS}
Pfeiffer et al., 2005 (168)	dose-response effect of immediately prior EX on mixed meals	16 M; age 24.8 ± 0.8 inactive AP 41.2 ± 0.8 BMI 21.1 ± 0.5 BTG 90 ± 8	TM walking; I = 50% D_1 = 30 min TEE_1 = 210 kcals D_2 = 60 min TEE_2 = 430 kcals D_3 = 90 min TEE_3 = 628 kcals	+2 (D_1)^{NS} -4 (D_2)^{NS} -4 (D_3)^{NS}	+2% (D_1) -14% (D_2)^{NS} -15% (D_3)^{NS}
Smith et al., 2004 (190)	12 hr prior EX and N3 fatty Acids	10 M; age 25 ± 1.5 active AP 53.1 ± 1.7 % fat 10 ± 1 BTG ~ 95	TM running; I = 60% D = 60 min TEE = 734 kcals	-18% (EX)^{NS} -42% (N3)	-40% (EX) -58% (N3)
Thomas et al., 2000 (194)	1 hr prior EX and N-3 fatty acids	12 M; age 25.8 ± 6.8 inactive AP 39.9 ± 3.5 % fat 26 ± 4 BTG 137 ± 73	TM running; I = 60% D = 60 min TEE = 619 kcals	NR	-3% (N3)^{NS}

Study Characteristics Author	Design	Participants	Protocol	Δ AUC_T	Δ AUC_I
Thomas et al., 2001 (195)	12 hr prior EX with MCT	12 M, 13 F; age 30.4 ± 8.8 active (N=12) inactive (N=12) AP 42.8 ± 11.0 % fat 18 ± 9 BTG 89 ± 52	TM running; I = 60% D = 60 min TEE = 606 kcals	NR	-35%
Tsetsonis et al.. 1996 (197)	16 hr prior EX at low and mod intensity	6 M, 6 F; age 27 ± 3.8 active AP 43.6 ± 5.7 BMI 23.7 ± 1.7 BTG ~60	TM walking; I_1 = 30% I_2 = 60% D = 90 min TEE_1 = 413 kcals TEE_2 = 829 kcals	-16% (Lo)^{NS} -26% (Mod)	-15% (Lo)^{NS} -31% (Mod)
Tsetsonis et al., 1996 (198)	16 hr prior EX at low and mod intensity	5 M, 4 F; age 25-32 active AP 31.5-67.2 BMI 20.3-27.7 BTG 83 ± 16	TM walking; I_1 = ~30% D_1 = 3 hours I_2 = ~60% D_2 = 1.5 hours TEE = ~1,000 kcals	-33% (Lo) -32% (Mod)	-30% (Lo) -30% (Lo)
Tsetsonis et al., 1997 (199)	16 hr prior EX in trained vs. untrained	19 F; age 42.4 ± 3.9 AP 50.3 ± 5.9 (T) 31.7 ± 3.6 (UT) % fat ~25 (T) ~30 (UT) BTG 59 ± 5 (T) 66 ± 8 (UT)	TM walking; I = 60% D = 90 min TEE = 812 kcals (T) 549 kcals(UT)	-32% (T) -16% (UT)	-33 (T) -10% (UT)
Zhang et al., 2006 (205)	12 hr prior at differing intensities	10 M; age 40.1± 2.2 inactive AP 37.0 ± 1.7 % fat 21.7 ± 1.7 BTG 263 ± 25	TM walking; I_1 = 40% I_2 = 60% I_3 = 70% D = 60 min TEE_1 = 423 kcals TEE_2 = 649 kcals TEE_3 = 722 kcals	NR NR NR	-30% (I_1) -31% (I_2) -39 % (I_3)
Zhang et al., 2004 (206)	12 and 24 hr prior EX	10 M; age 40.3 ± 2.2 inactive AP 36.7 ± 1.8 % fat 22 ± 2 BTG 291 ± 29	TM walking; I = 60% D = 60 minutes TEE = 639.6 kcals	NR NR	-33% (12hr) -4% (24hr)^{NS}

Study Characteristics					
Author	Design	Participants	Protocol	Δ AUC_T	Δ AUC_I
Zhang et al., 1998 (207)	effects of EX timing	21 M; age 27 ± 1.7 active AP 48 ± 1.0 % fat 16 ± 1 BTG 86 ± 9.1	TM running; I = 60% D = 60 min TEE= ~700 kcals	NR NR NR	-51% (12H) -38% (PE) -5% (PO)^{NS}

AP = aerobic power; **ACX** = acipomox; **AE** = accumulated exercise; **BTG** = baseline triglycerides; **CE** = continuous exercise; **D** = duration; **erg** = ergometry; **EX** = exercise; **F** = females; **G** = games activity; **HC** = high-carbohydrate diet; **hr** = hour; **I** = intensity; **IE** = intermittent exercise; **IR** = intake restriction; **L** = lean; **Lo** = low-intensity; **M** = males; **MCT** = medium-chain triglycerides; **min** = minutes; **Mod** = moderate-intensity exercise; **N3** = N-3 fatty acids; **NS** = not statistically significant; **NR** = not reported; **O** = obese; **PE** = prior exercise; **PO** = postmeal exercise; **T2D** = type II diabetes; T = trained; TEE = total energy expenditure; **TM** = treadmill; **UT** = untrained; **W/R** = walk/run.

Age is reported in years, AP is reported in mL/kg/min; BTG is reported in mg/dL; BMI is reported in kg/m^2.

Table 4. Acute resistance exercise studies

Study Characteristics					
Author	Design	Participants	Protocol	Δ AUC_T	Δ AUC_I
Burns et al., 2006 (24)	1 hr prior EX	10 M; age 22-31 resistance trained % fat 17 ± 4 BTG 97± 9	10 exercises 3 sets, 12 reps I = 80% of 12-RM D = 90 min TWL = 12,951 TEE = 389 kcals	+48%	+89%
Burns et al., 2005 (25)	16 hr prior EX	11 M; age 18-40 resistance naïve % fat 14 ± 2 BTG 90 ± 11	11 exercises 4 sets, 10 reps I = 80% of 10-RM D = 88 min TWL = 14,214 TEE = 550 kcals	-5%^{NS}	+4%^{NS}
Petitt et al., 2003 (165)	15 hr prior R vs. A	10 M, 4 F; age 24.3 ± 2.9 yr trained % fat 20 ± 7 BTG 89 ± 42	10 exercises 3 sets, 10 reps I = 100% of 10-RM D = 88 ± 3 min TWL = NR TEE_{RE} = 408 kcals TEE_{AE} = 382 kcals	-18% R vs A -14% R vs C +5% A vs C^{NS}	NR NR NR
Shannon et al., 2005 (185)	dose-response	4 M, 6 F; age 23.4 ± 2.5 resistance trained % fat 23 ± 1.8 BTG 78 ± 8	8 exercises 1 set, 3 sets, 5 sets 10 reps (all) I = 75% of 1-RM D = 20, 48, 90 min TEE_1 = 136 kcals TEE_2 = 411 kcals TEE_3 = 616 kcals	-15% 1 set^{NS} -12% 3 sets^{NS} -17% 5 sets^{NS}	NR NR NR

A = aerobic exercise; **BTG** = baseline triglycerides; **C** = Control; **D** = duration; **EX** = exercise; **F** = females; **I** = intensity; **Kg** = kilograms; **M** = males; min = minutes; **R** = resistance exercise; **RM** = repetition maximum; reps = repetitions; **TEE** = total energy expenditure; **TWL** = total weight lifted.

Age is reported in years; BTG is reported in mg/dL.

CHAPTER III

METHODS

Study Overview

Fourteen males completed a non-exercise control condition and three aerobic exercise conditions to elucidate the respective effects of low- and moderate-intensity exercise and accumulated sessions versus a single session of moderate-intensity aerobic exercise on postprandial lipemia. For the non-exercise control condition, participants consumed a high-fat test meal and subsequently had blood samples taken every two hours for the next six hours. Participants also completed each of the following aerobic exercise conditions in a randomized order by walking on a treadmill: 1) a continuous session performed at moderate-intensity, 2) a continuous session performed at low-intensity, 3) two sessions of moderate-intensity exercise performed on the same day but separated by three to five hours. Each condition required participants to expend approximately 500 kcals during exercise. Participants returned to the laboratory twelve to fourteen hours after completing the exercise for each condition for the high-fat test meal and blood sampling as described for the control. There was a minimum of one week and maximum of two weeks between subsequent conditions for each participant.

Participants

Volunteer recruitment

Volunteers were recruited from Auburn University and the Auburn-Opelika community by posted flyers (Appendix A), newspaper advertisements and campus departmental mailings. Male volunteers aged 25 to 60 meeting the following inclusion criteria were invited to enroll in the study: 1) obese - waist circumference > 40 inches, body mass index (BMI) ≥ 30 kg/m^2 and body fat % below the 50th percentile for their age, 2) hypertriglyceridemic - 150 mg/dL< fasting triglyceride levels < 350 mg/dL, 3) non-cigarette smoker, 4) physically inactive - operationally defined as not meeting the U.S. Surgeon General's physical activity recommendations for at least the previous six months. Volunteers taking prescription medications with known effects on lipid or carbohydrate metabolism or those with known cardiovascular, pulmonary or metabolic diseases were excluded from the study. Additionally, volunteers with total cholesterol levels above 240 mg/dL or triglyceride levels greater than 350 mg/dL were referred to an independent physician for medical clearance and release to exercise prior to matriculation into the study.

Preliminary Procedures and Assessments

Preliminary Screening

Preliminary screening was done by telephone interview or e-mail (Appendix B). Qualifying volunteers were scheduled for an initial visit to the Exercise Technology Laboratory for further screening. Upon arrival, volunteers were verbally informed about the study, provided with an opportunity to ask questions and signed an institutionally-approved informed consent document prior to any screening processes (Appendix C).

Next, anthropometric measurements including height, weight and waist circumference were obtained. Height was determined to the nearest 0.25 inch with a stadiometer and weight was measured to the nearest 0.25 pound using a calibrated balance scale. BMI was calculated from these measures as weight (kg)/height (m^2) (202). Waist circumference was measured to the nearest 0.5 cm at the narrowest portion of the torso above the umbilicus and below the xyphoid process of the sternum (135). Finally, a fasting venous blood sample was drawn and sent to a reference laboratory for a blood lipid panel, complete blood count, as well as liver function testing. These measures were used to verify the lipid inclusion criteria and exclude participants with signs of metabolic disorders. Volunteers meeting all of the inclusion criteria were invited to return to the lab for a physiological assessment.

Physiological Assessment

Following the initial screening, qualifying volunteers returned to the laboratory for a physiological assessment. Body composition and bone mineral density were assessed during this visit using Dual Energy X-Ray Absorptiometry (DEXA) (General Electric, Lunar Prodigy, Fairfield, CT). Participants also performed a graded exercise stress test with 12-lead electrocardiography monitoring on motor-driven treadmill using the Bruce Protocol (22). Oxygen consumption was measured using breath-by-breath analysis and averaged over 30-second intervals with an automated metabolic testing system (Ultima Exercise Stress Testing System, Medical Graphics, Minneapolis, MN). The highest observed oxygen uptake was considered the peak oxygen consumption ($\dot{V}O_{2peak}$) or maximal oxygen consumption ($\dot{V}O_{2max}$) if a minimum of two of the following criteria were met: 1) maximal heart rate within ± 10 beats per minute of age

predicted maximum, 2) respiratory exchange ratio (R) ≥ 1.15, 3) rating of perceived exertion on the Borg scale ≥ 18. The results of the DEXA scan and graded exercise stress test were reviewed by laboratory personnel and following final clearance, volunteers were invited to participate in the study.

Dietary Records

Participants were asked to complete a 3-day dietary record following the completion of all screening procedures and then subsequent records for the three days prior to each high-fat test meal (Appendix E). The initial dietary record served as a representative baseline for caloric intake and macronutrient composition. While this protocol did not intervene in the dietary patterns of the participants, each participant was instructed not to alter his current dietary habits for the duration of the study. All dietary records were analyzed for total caloric intake, and macronutrient content including protein, carbohydrate, fat, and polyunsaturated to saturated fat ratio by a Registered Dietician with a commercially available software package (NutritionCalc Plus, ESHA Research, Inc., Portland, OR). The dietary records were statistically analyzed to ensure that any extraneous influence from nutritional variation was minimal.

Experimental Procedures

Participants first completed a non-exercise control condition, followed by three aerobic exercise conditions completed in a randomized order. Three days prior to the high-fat test meal in all experimental conditions, participants began a dietary record and were asked to discontinue outside physical activity other than activities of daily living.

On the morning of the non-exercise control condition, participants reported to the lab for a fasting blood draw followed immediately by the consumption of a high-fat test

meal. Subsequent blood sampling occurred at two-hour intervals for six hours after the consumption of the test meal. Each of the three aerobic exercise conditions required two days to complete. On the morning of the first day of each aerobic exercise condition, participants reported to the lab in the fasted state for a fasting blood draw and then returned to the lab later in the day for their exercise session(s). Participants walked on a treadmill until approximately 500 kcals were expended in each of the following aerobic exercise conditions: 1) a continuous session performed at moderate-intensity (Mod-1), 2) a continuous session performed at low-intensity (Low-1), 3) two accumulated sessions performed at moderate-intensity (Mod-2). Both sessions in the accumulated exercise condition resulted in an approximate caloric expenditure of 250 kcals and were separated by three to five hours. Additionally, the last accumulated exercise session was scheduled to end at approximately the same time of day as the single exercise sessions in the other two exercise conditions. Participants returned to the lab twelve to fourteen hours after the completion of exercise for each condition for a fasting blood draw and high-fat test meal followed by blood sampling at two-hour intervals for six hours. At least one week, but no more than two weeks, separated subsequent conditions (Please see Figures 1 and 2).

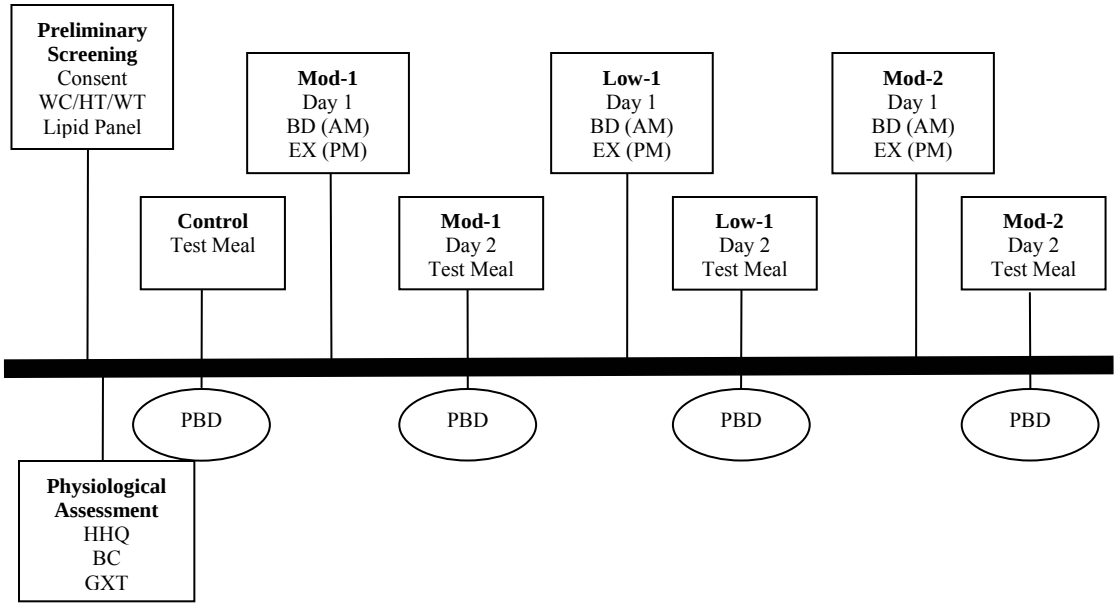

Figure 1. Experimental schematic

Following preliminary screening and a physiological assessment, qualifying volunteers completed each of the four experimental conditions. The control condition required a fasting blood draw, consumption of a high-fat test meal and serial blood sampling every two hours for a six hour period. Mod-1 required a single session of moderate-intensity exercise. Low-1 required single session of low-intensity exercise. Mod-2 required two sessions of moderate-intensity exercise. The exercise for each condition was completed twelve-fourteen hours prior to the consumption of the high-fat test meal. Serial blood samples were taken every two hours for the six hours following the test meal. WC = waist circumference; HT = height; WT = weight; HHQ = Health History Questionnaire; BC = body composition; GXT = graded exercise test; BD = blood draw; EX = exercise; PBD = postprandial blood draws.

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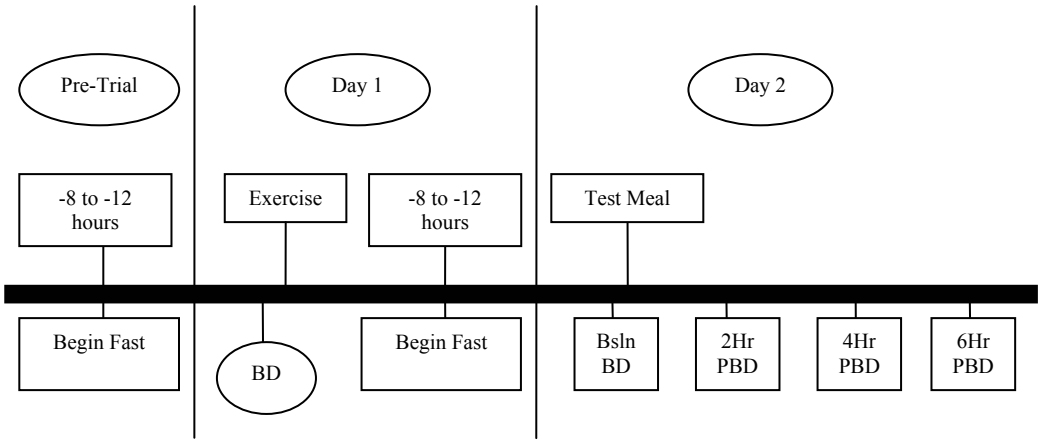

Figure 2. Experimental blood sampling schematic

For the control condition, participants reported to the lab in the fasted state for the baseline blood draw, high-fat test meal and subsequent postprandial blood draws. Prior to each exercise condition, participants reported to the lab in the fasted state for a blood draw and returned later in the day to complete the exercise session(s). Twelve to fourteen hours after completing the final exercise session of each condition, participants returned to the lab for the high-fat test meal and postprandial blood sampling. BD = blood draw; Hr = hour; PBD = postprandial blood draw.

High-Fat Test Meal

The high-fat test meal used in all four experimental conditions was prepared by blending 65 g of vanilla ice cream and 270 mL of heavy whipping cream into a 16 oz. shake. This meal consisted of approximately 1000 kcals, 100g of fat, 17g of carbohydrate, and 3g of protein (207). Participants were given a 10-minute time period to consume the meal and blood samples were taken two, four and six hours following consumption.

Exercise Conditions

The approximate total caloric expenditure for each of the aerobic exercise conditions was 500 kcals. Caloric expenditure for all exercise sessions was estimated by multiplying a standard caloric equivalent of 5 kcals/L of oxygen consumed by the

corresponding absolute $\dot{V}O_2$. The duration of all exercise sessions was determined by dividing 500 kcals by the estimated rate of caloric expenditure.

Participants performed a standardized 3-minute warm-up on the treadmill at 2.0 miles per hour and 2.0% grade and then the treadmill speed and grade were adjusted to elicit the appropriate intensity for each condition. Heart rate and respiratory gas analysis values were checked at 15-minute intervals throughout all exercise sessions to verify intensity and estimate energy expenditure. Treadmill speed and grade were adjusted during the exercise sessions to maintain the appropriate intensity.

Blood Sampling Procedures

Participants were asked to report to the lab following an 8-12 hour fast for each fasting blood sampling timepoint. Additionally, all fasting blood draws occurred at approximately the same time of day for each participant. Body weight was measured prior to each high-fat test meal and participants completed a pre-blood draw questionnaire to verify compliance with instructions (Appendix F). An intravenous catheter (Becton Dickson Infusion Therapy Systems, Sandy, UT, 22G x 1.0) was inserted into an antecubital vein and then capped with an intermittent injection port (Kawasumi Laboratories, Inc., Tampa, FL) immediately prior to each high-fat test meal. Blood samples were drawn into two red-top, non-additive 10.0 mL serum vacutainer tubes (Becton Dickinson Vacutainer, Franklin Lakes, NJ, 13 x 100 mm) on the morning of the day of the exercise sessions and at baseline and two, four, and six hours following consumption of each high-fat test meal. Catheter patency was maintained by a 2 mL injection of sodium heparin lock flush (Abbott Laboratories, North Chicago, IL, 10 USP U/mL) following each blood sampling timepoint and again as needed.

Hemoglobin and hematocrit were determined immediately following each blood sample using a minute portion of the whole blood sample; the remainder of the sample clotted prior to centrifugation at 1500 X g for 10 minutes for isolation of serum. Serum aliquots were isolated in 2.0 mL ultracentrifuge tubes and stored at – 70 ºC for subsequent analysis.

Two 10.0 mL serum tubes were collected in the morning on the day of the exercise sessions and at baseline, 2, 4, and 6 hours following consumption of the high-fat meal for each of the four conditions. The total amount of blood volume for this experiment was approximately 204 mL and minimum of four needle sticks and four catheter insertions were required to obtain the blood samples. Participants reported to the laboratory for 13 visits throughout the study requiring an approximate time commitment of 31 hours.

Analysis of Dependent Variables

Hemoglobin and hematocrit concentrations from whole blood samples were used to estimate plasma volume shifts resulting from the aerobic exercise sessions or high-fat test meals (44). Serum concentrations of triglycerides were determined by an enzymatic TG reagent (Raichem, San Diego, CA, Order # 85424). Concentrations of glucose were determined with a glucose oxidase and modified Trinder color reaction (Raichem, San Diego, CA, cat # 80039). Insulin concentrations were determined with a human insulin specific radioimmunoassay kit (LINCO Research, St. Charles Missouri, Cat # HI-14K). Homeostasis model assessment (HOMA) scores and the ratio of glucose to insulin were calculated for baseline blood samples to evaluate insulin resistance. HOMA scores were calculated by multiplying fasting glucose concentration (mg/dL) by fasting insulin

concentration (μU/mL) and dividing the result by 22.5 (140). The intra- and inter-assay coefficients of variation for triglycerides were 1.6% and 2.2%, respectively. The intra- and inter-assay coefficients of variation for glucose were 1.3% and 1.9%, respectively. For insulin concentrations, all samples for a single participant were analyzed with a single kit. The intra-assay coefficient of variation for insulin was 5.9%.

Statistical Procedures

Mean responses over the six-hour postprandial period were determined for triglyceride, insulin and glucose concentrations. Also, total (AUC_T) and incremental (AUC_I) area under the curve scores were calculated for triglycerides and insulin as follows (141):

$$AUC_T \text{ (mg/dL x 6Hr)} = n_B + 2[n_2 + n_4] + n_6$$

$$AUC_I \text{ (mg/dL x 6Hr)} = 2[n_2 + n_4] + n_6 - 5n_B$$

Where n_2, n_4 and n_6 are representative of postprandial concentrations and n_B is representative of baseline concentrations. The constant 2 was used to represent the 2 hours for the n_2 and n_4 sampling timepoints.

This experiment was a within-subjects design with each participant serving as his own control. Group characteristics were reported as means ± sd. Multiple four (condition) x four (time) analysis of variance (ANOVAs) with repeated measures on both condition and time were used to compare mean postprandial triglyceride, insulin and glucose responses to the high-fat test meals. A one-way ANOVA with repeated measures

on condition was used to determine significant differences in AUC_I, AUC_T, as well as peak concentrations for both triglycerides and insulin.

The independent variables for this experiment are as follows: condition (control, Mod-1, Low-1, Mod-2) and all of the fasting and postprandial blood sampling timepoints (pre-exercise, baseline, 2 Hr, 4 Hr, 6 Hr). The dependent variables included height, weight, BMI, waist circumference, % body fat, baseline and postprandial concentrations of TG, insulin, glucose, HOMA score and ratio of glucose to insulin. AUC_T and AUC_I for triglycerides and insulin were also dependent variables. Significant between-group differences were further explored with Duncan's New Multiple Range Test. The a priori significance level for this study was $p < 0.05$. Data analysis was completed with the Statistical Analysis System (SAS for Windows, version 9.1, SAS Institute, Cary, NC).

CHAPTER IV

RESULTS

Participant Selection

Forty-eight individuals inquired about the study in response to recruiting methods. Thirteen of these individuals did not reply when their phone calls and/or e-mails were returned. An additional ten volunteers were excluded based on the initial telephone screening due to prescription medications, known metabolic disease, habitual physical activity, or cigarette smoking. Finally, seven volunteers were excluded after the preliminary screening because they did not meet the triglyceride entry criteria. In total, 18 volunteers met the study inclusion criteria and agreed to participate in the study. Two participants completed the initial, preliminary and physiologic screenings but discontinued the study prior to any of the experimental conditions. Both individuals cited the time commitment as the reason. Another two participants completed all requirements up to and including the control condition, but dropped out of the study prior to completing any of the exercise conditions. These participants did not offer an explanation for ending their participation and did not respond to attempts to contact them. The remaining 14 participants began and completed the entire study protocol. Thirteen of the 14 participants were of Caucasian decent and one was of Asian descent. Please see Figure 3.

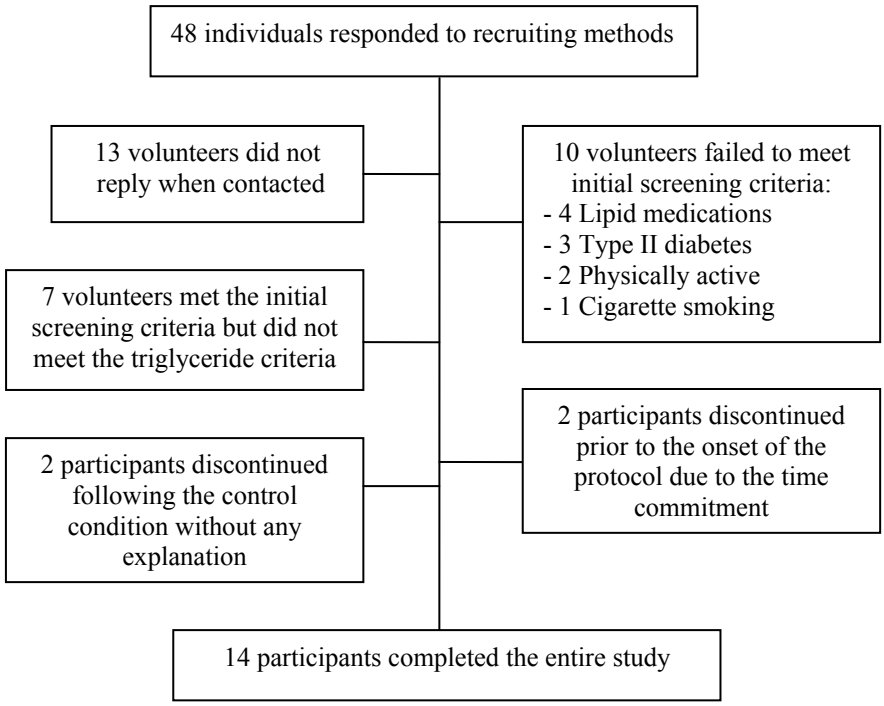

Figure 3. Participant recruitment

Baseline Physiological Characteristics

Participant baseline physiological characteristics and blood variables are presented in Tables 5 and 6, respectively. During the preliminary screening process, a single participant exhibited TG levels that exceeded 350 mg/dL, but were less than 500 mg/dL. This individual was included in the study only after receiving clearance from his primary care physician. Seven participants had borderline elevated total cholesterol concentrations, but none exceeded 240 mg/dL. Although HDL-C levels were not depressed on average, four individuals displayed baseline HDL-C concentrations that were less than 40 mg/dL. Following preliminary screening, all participants completed the graded exercise test to volitional fatigue without exhibiting signs or symptoms indicative of cardiovascular diseases or other health-related problems that would preclude participation in the study.

Table 5. Baseline physiological characteristics

Variable	Mean ± SD	Minimum	Maximum
Age (yrs)	43 ± 9	27	56
Height (cm)	177.1 ± 7.1	166.4	191.1
Weight (kg)	107.3 ± 17.1	90.1	141.8
BMI (kg/m^2)	34.3 ± 5.6	27.9	46.9
Body fat (%)	37 ± 4	33	44
Waist (cm)	110.2 ± 10.9	94.0	133.4
SBP (mmHg)	120 ± 12	104	148
DBP (mmHg)	76 ± 10	62	100
$\dot{V}O_{2peak}$ (L/min)	2.7 ± 0.6	1.6	3.8
$\dot{V}O_{2peak}$ (mL/kg/min)	26.3 ± 6.2	17	38.1

All values are presented as mean ± standard deviation and minimum and maximum values. BMI = Body mass index; Waist = Waist circumference; SBP = Systolic blood pressure; DBP = Diastolic blood pressure.

Table 6. Baseline blood variables

Variable	Mean ± SD	Minimum	Maximum
TG (mg/dL)	217 ± 84	110	398
TC (mg/dL)	202 ± 29	161	238
HDL-C (mg/dL)	44 ± 7	34	54
LDL-C (mg/dL)	115 ± 24	81	153
Insulin (μU/mL)	24.1 ± 14.3	8	58
HOMA score	6.3 ± 3.8	2.1	15.7
G/I ratio	5.7 ± 3.0	1.9	13.0

All values are presented are reported as mean ± standard deviation and minimum and maximum values. TG = triglycerides; TC = Total cholesterol; HDL-C = High-density lipoprotein cholesterol; LDL-C = Low-density lipoprotein cholesterol; HOMA = Homeostasis model; G/I = Glucose/Insulin.

Exercise Intervention

All participants were able to complete each of the three exercise conditions. One participant stopped for approximately 5 minutes during the single session of moderate-intensity exercise to stretch because of Achilles tendonitis. He was then able to complete the remainder of the session without interruption. Outside of this, there were no adverse events during any of the other exercise sessions.

All exercise conditions required an approximate caloric expenditure of 500 kcals. For the low-intensity exercise condition, participants walked on the treadmill at relative intensities ranging from 33 to 59% of $\dot{V}O_{2peak}$ for 79 to 120 minutes. By design, the single session and accumulated sessions of moderate-intensity exercise were performed at a higher range of intensities (52 to 75% of $\dot{V}O_{2peak}$) than the low-intensity session and therefore required less time to achieve the target caloric expenditure (45 to 84 minutes). There were no significant differences in exercise intensity ($F_{1,13} = 0.49$; $p = 0.50$) or total exercise time ($F_{1,13} = 0.57$; $p = 0.46$) between the two moderate-intensity exercise conditions. Participants reported back to the laboratory for the test meal 13 ± 0.2 hours following the completion of each exercise condition. There was no statistically significant difference in the number of hours between the end of exercise and the test meal among the three exercise conditions ($F_{2,13} = 1.24$; $p = 0.31$). Exercise intervention data are presented in Table 7.

Exercise Effect on Fasting Blood Variables

There were no significant differences in pre-exercise versus 12-hour postexercise fasting blood variables among any of the three exercise conditions (TG, $F_{1,13} = 0.12$; $p = 0.74$; HDL-C, $F_{1,13} = 0.71$; $p = 0.42$; Insulin, $F_{1,13} = 0.92$; $p = 0.36$;

Glucose, $F_{1,13} = 1.39$; $p = 0.26$; HOMA, $F_{1,13} = 0.75$; $p = 0.40$; GIR, $F_{1,12} = 0.23$; $p = 0.64$). Please see Table 8.

Table 7. Exercise session data

Variable	Low-1	Mod-1	Mod-2
$\dot{V}O_2$ (L/min)	1.0 ± 0.4	1.7 ± 0.1	1.7 ± 0.1
$\dot{V}O_2$ (mL/kg/min)	9.5 ± 0.5	16.4 ± 1.0	15.9 ± 1.0
% $\dot{V}O_{2peak}$	38.6 ± 2.2	63.5 ± 5.7	63.1 ± 1.5
HR (bpm)	105 ± 3	135 ± 4	133 ± 4
% HR_{peak}	61.5 ± 2.6	77.8 ± 2.4	73.0 ± 5.3
Total time (min)	102.8 ± 4.3	60.2 ± 3.3	61.6 ± 3.3
Hours b/t	13.0 ± 0.2	12.8 ± 0.2	13.2 ± 0.2

All values are presented as mean ± standard error. Mod-2 values are reported as the average for the two exercise sessions. $\dot{V}O_2$ = peak oxygen uptake; % $\dot{V}O_{2peak}$ = percentage of peak oxygen uptake; HR = heart rate; % HR = percentage of peak heart rate; Total time = total exercise time to reach 500 kcals; Hours b/t = hours between end of exercise and test meal.

Table 8. Pre- and 12-hr post-exercise fasting blood variables

Variable	Pre-Exercise	Post-Exercise	P-Value
TG (mg/dL)	204 ± 11	207 ± 11	0.74
HDL-C (mg/dL)	48 ± 8	48 ± 7	0.42
Insulin (μU/mL)	22.9 ± 1.7	23.8 ± 1.7	0.92
Glucose (mg/dL)	104 ± 1.3	105 ± 1.3	0.26
HOMA score	6.0 ± 0.5	6.3 ± 0.5	0.40
G/I ratio	5.5 ± 0.3	5.6 ± 0.4	0.64

All values are presented as mean ± standard error. Means were collapsed across exercise conditions. No statistically significant differences were detected between pre and post timepoints. TG = triglycerides; HOMA = Homeostasis model; G/I = Glucose/Insulin.

Effect of Exercise on Postprandial Blood Variables

Triglycerides

Plasma volume was not significantly altered during any of the four conditions ($F_{3,39} = 2.39$; $p = 0.08$), thus all analyses were completed using unadjusted data. Plasma volume data are presented in Table 9. The total triglyceride area under the curve was not significantly different from the control condition in any of the three exercise trials ($F_{3,39} = 1.85$; $p = 0.15$). Please see Figure 4. However, the incremental triglyceride area under the curve was significantly diminished by 27% the day after low-intensity exercise was undertaken ($F_{3,39} = 3.52$; $p = 0.02$). Similarly, a single session of moderate-intensity exercise reduced the triglyceride AUC_I the following day by 20%. Although the reduction resulting from one session of moderate-intensity exercise was not significantly different from that of the low-intensity exercise condition, it was also not significantly different from the control condition. In contrast, two sessions of moderate-intensity exercise did not produce a significant attenuation in triglyceride AUC_I ($p > 0.05$). Please see Figure 5 for triglyceride AUC_I responses.

Table 9. Plasma volume changes by condition

Condition	2 Hr	4 Hr	6 Hr
Con	-0.8 ± 1.9	1.2 ± 1.3	-0.6 ± 0.7
Low-1	2.7 ± 2.0	0.5 ± 1.5	-1.6 ± 1.7
Mod-1	0.6 ± 1.9	0.6 ± 1.7	-1.5 ± 1.4
Mod-2	-1.1 ± 1.1	-1.2 ± 1.4	-3.3 ± 0.9

Plasma volume values are reported as percentage changes (from baseline) ± standard error. Con = Non-exercise control; Low-1= single session of low-intensity exercise; Mod-1 = single session of moderate-intensity exercise; Mod-2 = two sessions of moderate-intensity exercise. Plasma volume was not significantly altered during any of the conditions.

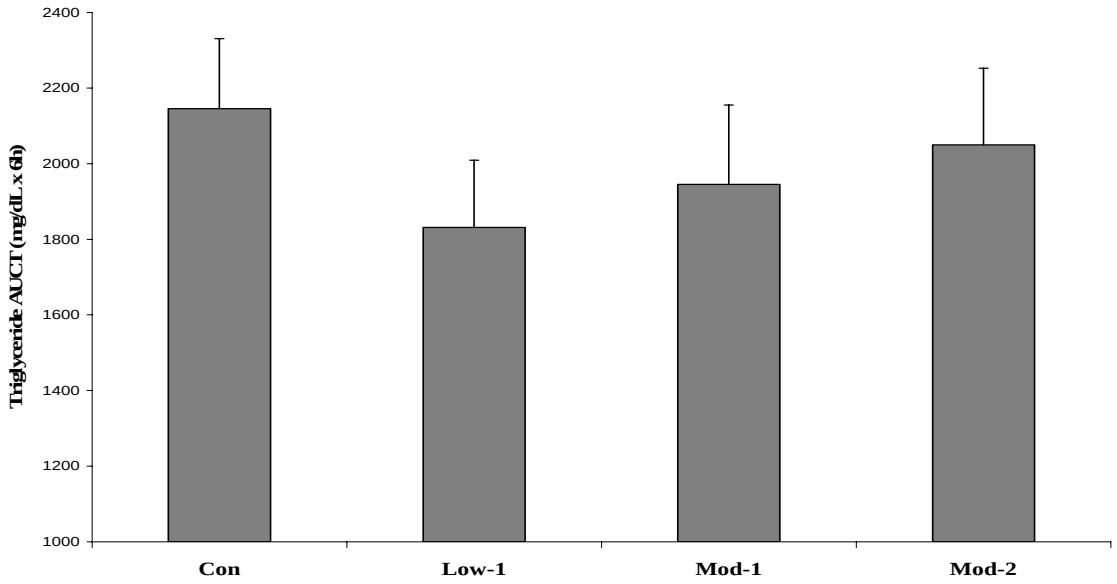

Figure 4. Total triglyceride area under the curve by condition

Values are reported as mean ± standard error. AUC_T was calculated using $n_B + 2\ [n_2 + n_4] + n_6$, where n_2, n_4 and n_6 = postprandial timepoints and n_B = baseline. None of the exercise conditions were significantly different from control. Con = Control; Low-1= single session of low-intensity exercise; Mod-1 = single session of moderate-intensity exercise; Mod-2 = two sessions of moderate-intensity exercise.

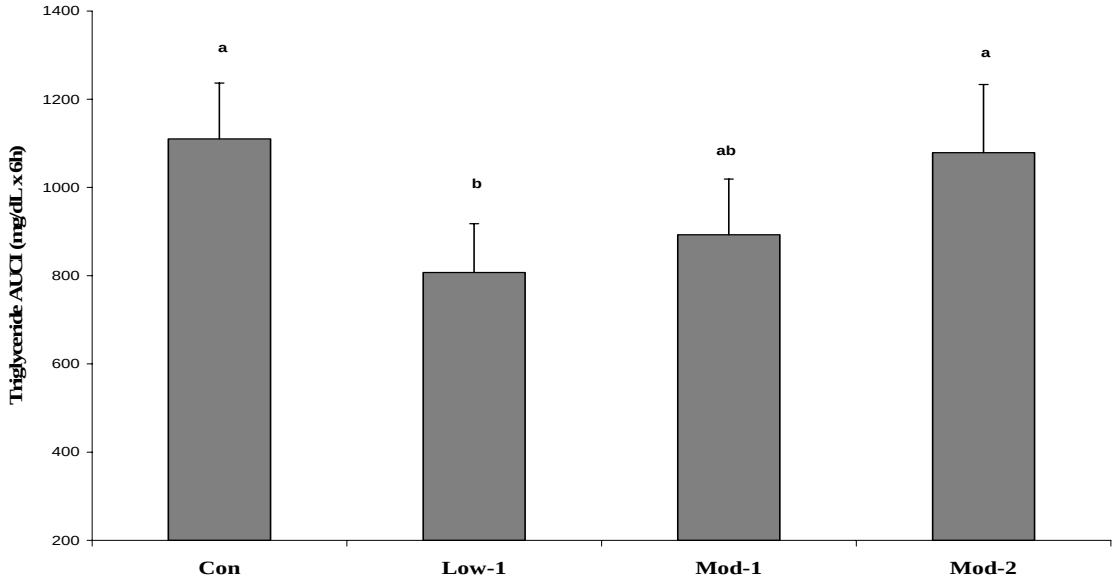

Figure 5. Incremental triglyceride area under the curve by condition

Values are reported as mean ± standard error. AUC_I was calculated using $2[n_2 + n_4] + n_6 - 5n_B$, where n_2, n_4 and n_6 = postprandial timepoints and n_B = baseline. Means with the same letter are not significantly different. Con = Control; Low-1= single session of low-intensity exercise; Mod-1 = single session of moderate-intensity exercise; Mod-2 = two sessions of moderate-intensity exercise.

Single sessions of low- and moderate-intensity exercise reduced triglyceride concentrations at the 4-hour postprandial timepoint by 22% and 21% compared to control, respectively ($F_{3,156} = 5.08$; $p < 0.05$). In contrast, two sessions of moderate-intensity exercise resulted in a non-significant 9% reduction compared to the control condition at this same timepoint ($p > 0.05$). Triglyceride concentrations were not significantly altered from control at baseline or at 2 and 6 hours after the test meal during any of the exercise conditions. The average time to reach peak TG concentration (4.1 ± 0.1 hours) was not significantly different among any of the conditions ($F_{3,39} = 1.68$; $p = 0.19$). Participants did not return to baseline TG concentrations at the end of the test meal in any of the conditions. On average, TG levels remained 72% higher than fasting levels 6 hours after consuming the test meal. Please see Figure 6.

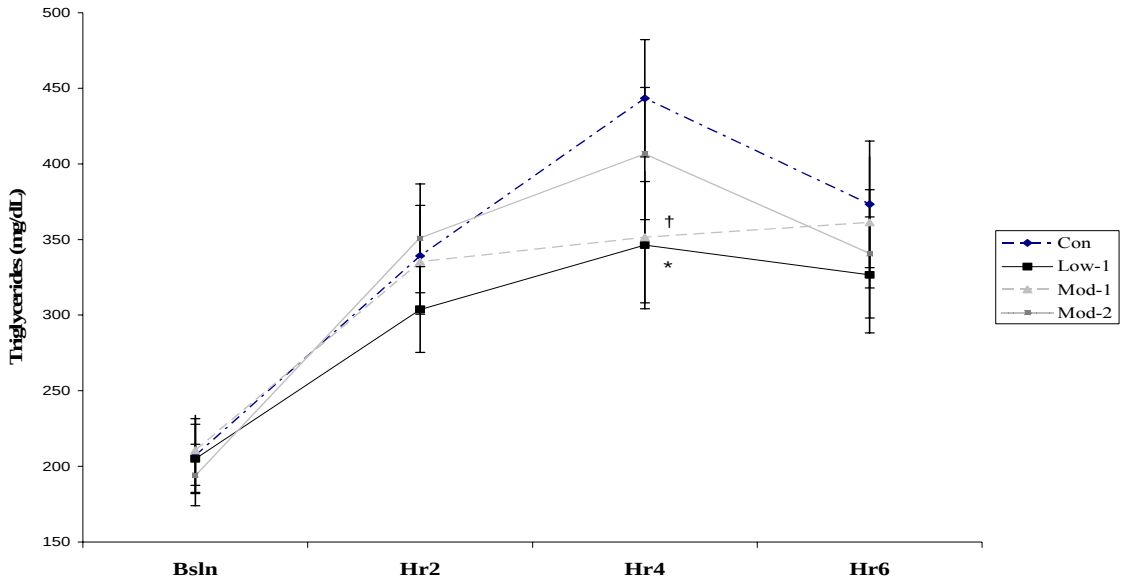

Figure 6. Temporal postprandial triglyceride response by condition

Values are reported as mean ± standard error. * = significant difference from control and Mod-2 at Hr4. † indicates significant difference from Con at Hr4 . Con = Control; Low-1= single session of low-intensity exercise; Mod-1 = single session of moderate-intensity exercise; Mod-2 = two sessions of moderate-intensity exercise.

Glucose

Glucose concentrations did not differ significantly among the four conditions at baseline or any of the postprandial timepoints ($F_{3,39} = 2.47$; $p = 0.08$). Means collapsed over condition were also not significantly different over the postprandial period ($F_{3,39} = 1.81$; $p = 0.16$). Please see Table 10 and Figure 7.

Table 10. Postprandial temporal glucose response by condition

Condition	Bsln	2Hr	4Hr	6Hr
Control	104 ± 2	106 ± 3	105 ± 3	102 ± 3
Low-1	104 ± 3	101 ± 2	103 ± 3	100 ± 3
Mod-1	101 ± 3	107 ± 3	103 ± 3	102 ± 3
Mod-2	105 ± 3	107 ± 4	108 ± 3	102 ± 3

All values are presented as mean ± standard error. Means between conditions were not significantly different. Low-1= single session of low-intensity exercise; Mod-1 = single session of moderate-intensity exercise; Mod-2 = two sessions of moderate-intensity exercise.

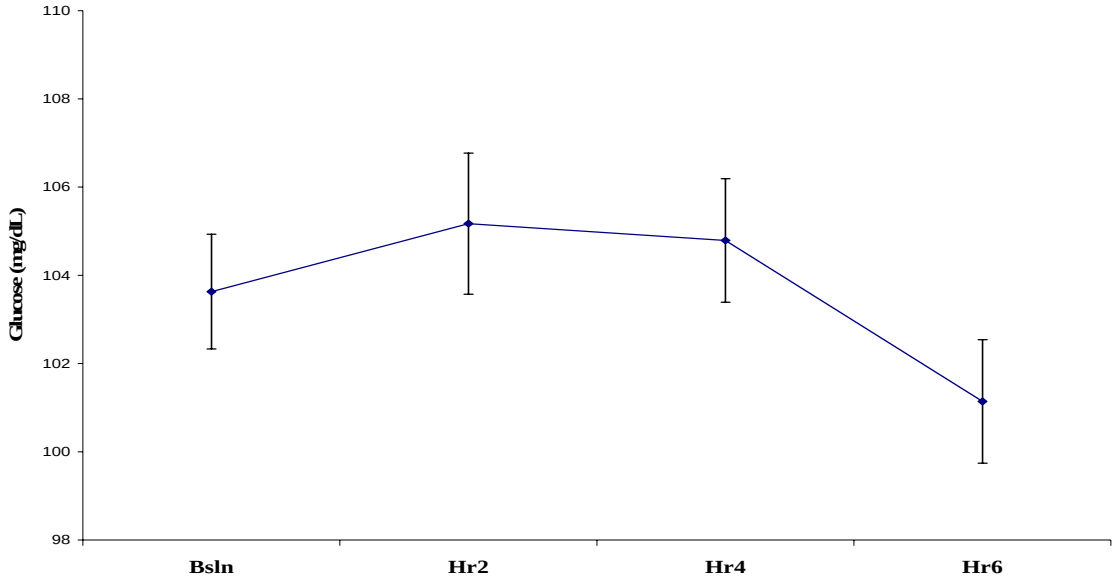

Figure 7. Temporal postprandial glucose response

Values are reported as mean ± standard error. Means are collapsed across condition. None of the postprandial timepoints were significantly different from baseline.

Insulin

Insulin concentrations rose significantly by 32% two hours after the consumption of the test meal ($F_{3, 36} = 0.23$; $p = 0.0002$). Insulin concentrations subsequently decreased at hour 4 and were ultimately 24% lower than baseline at the end of the 6-hour postprandial period, although this difference was not statistically significant ($p > 0.05$). Mean insulin responses to the test meal did not differ among any of the conditions ($F_{3,36} = 0.71$; $p = 0.55$). Please see Table 11 and Figure 8.

The total insulin area under the curve ranged from 43.6 to 356.7 μU/mL x 6 hr and was not significantly altered from the control in any of the exercise conditions ($F_{3,36} = 0.34$; $p = 0.80$). The incremental insulin area under the curve ranged from ranged from -95.6 to 146.4 μU/mL x 6 hr and was also not significantly changed by any of the exercise interventions ($F_{3,36} = 0.71$; $p = 0.55$). The total and incremental insulin area under the curve data are presented in Figures 8 and 9, respectively.

Table 11. Postprandial temporal insulin response by condition

Condition	Bsln	2Hr	4Hr	6Hr
Control	24.1 ± 3.9	29.3 ± 4.2	20.0 ± 3.4	18.2 ± 2.9
Low-1	24.7 ± 4.2	28.6 ± 5.4	23.8 ± 3.8	19.8 ± 3.4
Mod-1	22.5 ± 3.2	30.3 ± 5.4	20.3 ± 3.4	16.2 ± 2.8
Mod-2	20.4 ± 2.2	32.2 ± 6.9	21.3 ± 2.9	15.5 ± 2.0

All values are presented as mean ± standard error. Means between conditions were not significantly different at any timepoint. Con = Control; Low-1= single session of low-intensity exercise; Mod-1 = single session of moderate-intensity exercise; Mod-2 = two sessions of moderate-intensity exercise.

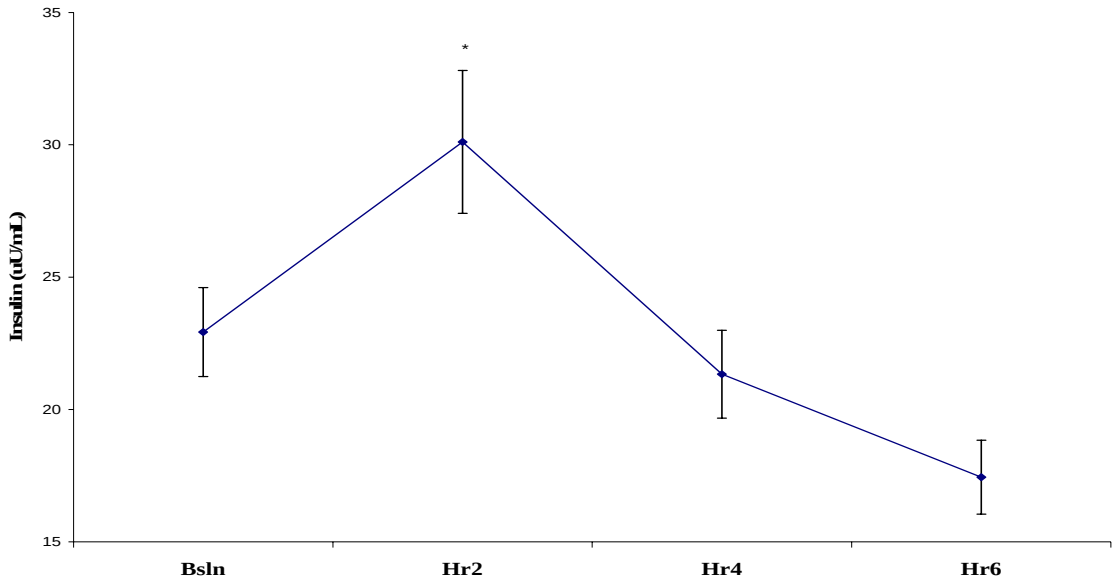

Figure 8. Temporal postprandial insulin response

Values are reported as mean ± standard error. Means are collapsed across condition. * = significant difference from Bsln.

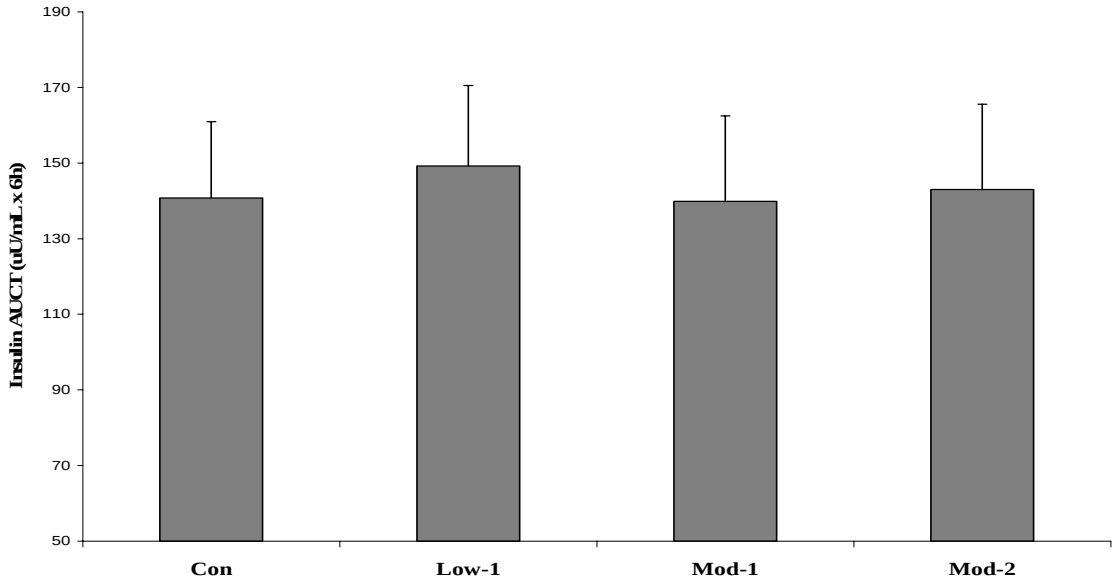

Figure 9. Total insulin area under the curve by condition

Values are reported as mean ± standard error. AUC_T was calculated using $n_B + 2\ [n_2 + n_4] + n_6$, where n_2, n_4 and n_6 = postprandial timepoints and n_B = baseline. None of the three exercise conditions were significantly different from control. Con = Control; Low-1= single session of low-intensity exercise; Mod-1 = single session of moderate-intensity exercise; Mod-2 = two sessions of moderate-intensity exercise.

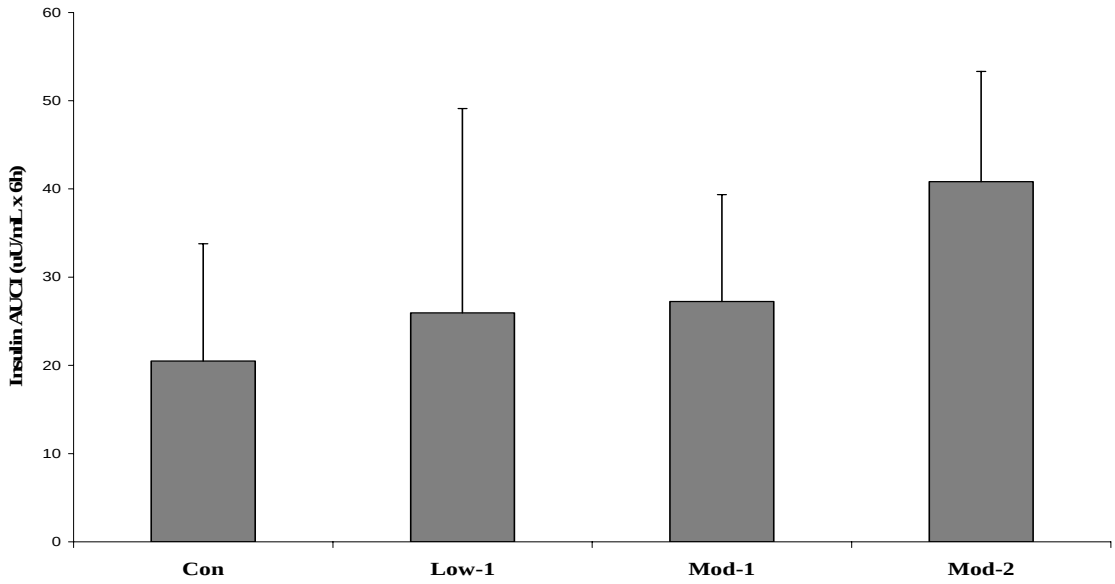

Figure 10. Incremental insulin area under the curve by condition

Values are reported as mean ± standard error. AUC_I was calculated using $2[n_2 + n_4] + n_6 - 5n_B$, where n_2, n_4 and n_6 = postprandial timepoints and n_B = baseline. None of the three exercise conditions were significantly different from control. Con = Control; Low-1= single session of low-intensity exercise; Mod-1 = single session of moderate-intensity exercise; Mod-2 = two sessions of moderate-intensity exercise.

Correlations

Fasting triglyceride concentrations were predictive of the total triglyceride area under the curve score ($r = 0.73$; $p < 0.001$), but not the incremental triglyceride area under the curve score ($p = 0.43$). Abdominal adipose tissue relative to total adipose tissue was significantly correlated with the change in triglyceride AUC_I from the control condition to the low-intensity exercise condition ($r = -0.29$; $p = 0.04$) and the single session of moderate-intensity exercise ($r = -0.52$; $p < 0.0001$).

Extraneous Influences

Body Weight

All participants completed the protocol within six weeks of commencement. Body weight was measured immediately prior to each postprandial challenge and did not significantly differ over the course of the study protocol ($F_{3,39} = 0.64$; $p = 0.59$).

Dietary Variables

Analysis of dietary records indicated no significant differences in total caloric intake or major macronutrient content among any of the study conditions (Total kcals, $F_{3,36} = 0.67$; $p = 0.57$; Cho, $F_{3,36} = 0.97$; $p = 0.42$; Pro, $F_{3,36} = 1.17, 0.34$; Fat, $F_{3,36} = 0.14$, $p = 0.93$; P/S ratio, $F_{3,36} = 0.53$; $p = 0.66$). Please see Table 12.

Physical Activity

Although outside physical activity was not directly quantified, participants were also asked to refrain from all physical activity outside of the study for the duration of the protocol. Verbal compliance was documented prior to beginning each condition.

Table 12. Caloric intake and macronutrient composition

	Total Kcals	Cho (g)	Pro (g)	Fat (g)	P/S ratio
Control	2019 ± 130	250 ± 23	78 ± 5	79 ± 7	0.3 ± .06
Low-1	2124 ± 154	257 ± 25	85 ± 5	79 ± 8	0.3 ± .05
Mod-1	2114 ± 181	261 ± 25	79 ± 5	83 ± 8	0.3 ± .04
Mod-2	2354 ± 301	308 ± 56	92 ± 8	87 ± 8	0.3 ± .05

Values are reported as mean ± standard error. No significant differences were found among any of the conditions. Low-1= single session of low-intensity exercise; Mod-1 = single session of moderate-intensity exercise; Mod-2 = two sessions of moderate-intensity exercise.

CHAPTER V

DISCUSSION

The purposes of this study were to determine the respective effects of low- versus moderate-intensity exercise and continuous versus accumulated exercise on postprandial lipemia in men with metabolic syndrome. This is one of the first studies to demonstrate that an exercise caloric expenditure as low as 500 kcals reduces postprandial lipemia in men with metabolic syndrome and that this effect can be achieved through a single session of low-intensity exercise. Additionally, this is this first study to directly compare the effect of low-intensity exercise on postprandial lipemia to that of a similar amount of moderate-intensity exercise in this population. Our data uniquely show that the attenuation produced by low-intensity exercise was not significantly greater than that produced by a single session of moderate-intensity exercise. This suggests that expending 500 kcals in a single session of exercise reduces postprandial lipemia in men with metabolic syndrome to a similar degree whether performed at a low- or moderate-intensity. In contrast, performing two sessions of moderate-intensity exercise that resulted in a similar total caloric expenditure did not significantly ameliorate postprandial lipemia. This indicates that accumulating exercise throughout the day may not be as effective as single sessions of exercise for reducing postprandial lipemia in this population. Thus, the public health recommendation purporting the efficacy of accumulating exercise throughout the day for health-related benefits appears to be

specific to some health characteristics and may not include postprandial lipemia in men with metabolic syndrome.

Participants

Many exercise studies evaluating postprandial lipemia have used apparently healthy, lean, normotriglyceridemic individuals (8, 9, 13, 68, 70, 71, 75, 92, 108, 109, 136, 137, 148, 190, 195, 197, 198, 207); while fewer exercise studies have used participants with attributes of metabolic syndrome (66, 205, 206). Our focus was to recruit participants from the latter population. Based on waist circumference, fasting triglycerides and insulin resistance, our middle-aged participants met the criteria for metabolic syndrome (85). The average waist circumference was indicative of excessive abdominal obesity and places these participants at high-risk for the development of CVD and type II diabetes (20). The cohorts' average BMI can be categorized as class I obesity (3). Also, average body fat percentage was below the 10^{th} percentile ranking for men of similar ages (202). In addition to being obese, triglyceride values at the preliminary screening were indicative of hypertriglyceridemia (4). Finally, fasting insulin levels and HOMA score were both above threshold values for insulin resistance (172). Although low levels of HDL-C and hypertension are also components of metabolic syndrome, they were not observed in the present cohort.

The participants in this study were considered to be physically inactive because each self-reported that he did not consistently engage in more than 30 minutes of regular exercise on three or more days per week. Participants also demonstrated low levels of cardiorespiratory fitness, with an average peak aerobic power value that places them below the 10^{th} percentile for men their age (202).

Exercise Effect on Postprandial Lipemia

Acute sessions of aerobic exercise are consistently capable of reducing postprandial lipemia in a dose-response manner. The key variable mediating this response appears to be total energy expenditure, as higher total exercise energy expenditures typically result in larger reductions in PPL (69). However, the majority of these investigations have used single sessions of at least moderate-intensity exercise that resulted in relatively high total exercise energy expenditures (166). Given that these intensities and amounts of exercise may be undesirable for populations with metabolic syndrome; our investigation is one of the first efforts to elucidate the effects of differing exercise intensities and accumulated exercise at the lower end of the caloric expenditure and exertional intensity spectrum in this population.

Exercise Intervention

Since all exercise conditions resulted in the same approximate caloric expenditure of 500 kcals and were completed approximately 13 hours prior to the consumption of the test meal, the influence of differences in caloric expenditure or test meal timing on the parameters of interest was likely minimal. Also, the average time between the last exercise session of each condition and the test meal the next morning falls within the established time frame of 1-18 hours that typically results in significant attenuations of postprandial lipemia (107).

Triglyceride Response

We found that baseline fasting TG levels were significantly correlated with total triglyceride area under the curve score in the control condition. This is in agreement with the widely-held idea that fasting TG levels are directly related to postprandial TG

concentrations (163). Despite this, exercise did not significantly reduce triglyceride AUC_T compared to the control condition (Figure 4). Past investigations have shown that total triglyceride area under the curve scores are frequently lower as a result of prior acute sessions of aerobic exercise (166). This decrease typically ranges from 9 to 39% and is most consistently seen in apparently healthy populations at caloric expenditures that exceed 500 kcals (107). To date, the only published report on triglyceride AUC_T using men with metabolic syndrome found that it was reduced by approximately 24% 18 hours following moderate-intensity exercise (66). The total caloric expenditure in this report was 40% higher than in our exercise conditions. Therefore, it is possible that we did not see significant reductions in triglyceride AUC_T because of the lower level of exercise energy expenditure.

While our results appear dissimilar to previous findings, it should be noted that there was considerable variability between individual responses for triglyceride AUC_T, with scores ranging from 782 to 3,571 mg/dL x 6hr. Closer analysis of the triglyceride AUC_T scores indicates that reductions of 15% and 9% are present in the low- and moderate-intensity exercise conditions, respectively. By comparison, two accumulated sessions of moderate-intensity exercise resulted in only a 4.5% decrease. Although it is recognized that none of these results were statistically significant, the reductions due to low- and moderate-intensity exercise are comparable to the 9 to 18% significant reductions found in other populations when similar caloric expenditures were used (70, 71, 199). This may indicate that although these results did not achieve statistical significance, they may still be of physiological significance. Thus, these non-statistically significant reductions in triglyceride AUC_T may represent a trend towards improved

triglyceride clearance and metabolic health during the postprandial period following low- and moderate-intensity exercise.

Despite the non-significance of the triglyceride AUC_T, the incremental triglyceride area under the curve score was significantly diminished by 27% compared to the control condition following low-intensity exercise. A single session of moderate-intensity exercise also attenuated triglyceride AUC_I by 20%. While this reduction was not significantly different than that of low-intensity exercise, it was also not significantly different than that of the control condition. Furthermore, low-and moderate-intensity exercise performed in a single session significantly reduced triglyceride concentrations 4 hours after the consumption of the test meal by 22% and 21%, respectively. These findings are similar to those of Zhang et al. (205), who reported that triglyceride AUC_I was attenuated by 30% in men with metabolic syndrome following an exercise energy expenditure of 425 kcals at 40% of $\dot{V}O_{2max}$. Thus, our findings substantiate that this amount of total caloric expenditure is sufficient to favorably alter postprandial lipemia in men with metabolic syndrome.

Low-intensity exercise successfully attenuated postprandial lipemia in our cohort, as evidenced by the reductions in both triglyceride AUC_I and TG concentrations at the 4-hour timepoint compared to the control values. The aforementioned findings of Zhang et al. (205) compliment those of the current study and, taken together, suggest that low-intensity exercise effectively reduces postprandial lipemia in men with metabolic syndrome when caloric expenditure ranges from 400-500 kcals. This is contrary to some previously published reports for low-intensity exercise in other populations. In these studies, similar caloric expenditures performed at low-intensities did not yield significant

reductions in triglyceride AUC_I or the temporal TG response (165, 197). To date, the lowest amount of low-intensity exercise shown to reduce triglyceride AUC_I in a healthy population is approximately 625 kcals (8). Thus, while low-intensity exercise in the range of 400-500 kcals may be sufficient to attenuate PPL in men with metabolic syndrome, additional caloric expenditure may be required for apparently healthy populations to gain this effect at low intensities of exercise. This is similar to what has been seen for other health parameters when comparing groups of differing health statuses. For example, significant modifications in fasting blood lipid concentrations have been reported in sedentary men with exercise caloric expenditures as low as 350 kcals (41), whereas substantially larger caloric expenditures (i.e. 800 kcals or more) may be required to produce such changes in high-fit males (56). Therefore, although this has yet to be compared directly, high-fit individuals may require greater energy expenditures than low-fit individuals to achieve similar attenuations in postprandial lipemia via low-intensity exercise.

This is the first study to compare isocaloric sessions of low- and moderate-intensity exercise in men with metabolic syndrome. Our findings demonstrate that approximately 500 kcals of low-intensity aerobic exercise is sufficient to attenuate postprandial lipemia and that this response is equally, but not more, effective than that produced by a similar amount of moderate-intensity exercise performed in a single session. Previous reports directly comparing the effects of low- and moderate-intensity exercise on postprandial lipemia have typically used apparently healthy populations and greater total exercise caloric expenditures. For example, Testsonis et al. (198) reported that both low- and moderate-intensity exercise yielding caloric expenditures of over

1,000 kcals attenuated triglyceride AUC_I by approximately 20% and reduced TG concentrations 4 hours after the test meal by approximately 43%. However, Katsanos et al. (108) also used a similar dose of exercise for high-fit young adults and found that moderate, but not low-intensity, exercise reduced triglyceride AUC_I. It is difficult to directly compare these two studies because Tsetsonis et al. had participants consume the test meal 16 hours after completing exercise, whereas Katsanos et al. served the test meal 1 hour after exercise. Thus, the results of the current study are consistent with previous work demonstrating that low- and moderate-intensity exercise of equal caloric expenditure have similar effects on the postprandial triglyceride response the day after exercise. Our results extend these observations to a lower caloric threshold and to men with metabolic syndrome.

Our finding that 500 kcals of low-intensity exercise is equally effective compared to a similar volume of moderate-intensity exercise in this population is novel, but is strengthened by comparison to results of studies using only moderate-intensity exercise. We have recently shown a 32% reduction in triglyceride AUC_I in males with metabolic syndrome following 500 kcals of moderate-intensity exercise (unpublished data). Additionally, Miyashita et al. (148) reported a 32% decrement in triglyceride AUC_I with approximately 500 kcals of moderate-intensity exercise in lean, normotriglyceridemic males. Although these studies did not directly compare low- and moderate-intensity exercise, the quantified reductions in triglyceride AUC_I resulting from 500 kcals of moderate-intensity exercise are strikingly similar to what was found in our low-intensity exercise condition. This enhances our contention that low-intensity exercise is equally, but not more, effective at reducing postprandial lipemia than moderate-intensity exercise.

These comparisons also reveal that unlike low-intensity exercise, moderate-intensity exercise of 500 kcals may yield similar benefits in both high-fit males and males with metabolic syndrome.

Although triglyceride concentrations were significantly reduced at the 4-hour timepoint by single sessions of low- and moderate-intensity exercise, they were not reduced at the 6-hour timepoint in any of the exercise conditions compared to the control condition. Additionally, triglyceride concentrations were still significantly above baseline values by an average of 72% at the 6-hour timepoint. The average elevation in triglyceride concentrations at the 6-hour timepoint in our study can be cautiously compared to other studies with similar volumes of exercise. Zhang et al. (205) reported that, in men with metabolic syndrome, TG concentrations remained approximately 56% above baseline values 6 hours into the postprandial period. In healthy populations, three studies using high-fat test meals and exercise amounts ranging from approximately 415 to 475 kcals also reported a range of elevations in triglyceride concentration above baseline from 63% to 83% six hours after the test meal (70, 148, 197). Thus, it appears that while triglyceride concentrations are higher in absolute terms 6 hours after a high-fat test meal in men with fasting hypertriglyceridemia, the relative increase in triglyceride concentration over baseline may be similar to what is seen in healthy populations.

Although we found that 500 kcals of exercise was sufficient to reduce postprandial lipemia when performed in a single session, this was not apparent for two sessions of accumulated moderate-intensity exercise. We did not find any significant alterations in the triglyceride area under the curve scores or temporal triglyceride response following this condition. Our findings indicate that public health

recommendations advising accumulation of moderate-intensity exercise throughout the day do not seem to apply to postprandial lipemia in men with metabolic syndrome at this level of caloric expenditure. This is not consistent with the one previous postprandial lipemia study using accumulated exercise. Gill et al. (75) demonstrated that triglyceride AUC_T was 18% lower following 3 sessions of moderate-intensity exercise accumulated throughout the day and that this manner of expending calories was equally effective compared to a single session. Key differences in study design may offer an explanation for our contrasting findings. The participants in Gill's study expended approximately 1,125 kcals over 3 exercise sessions spaced apart by 4 hours. By comparison, participants in the current study expended only 500 kcals over 2 sessions separated by approximately 4 hours. Thus, it is possible that accumulated exercise may only reduce postprandial lipemia at higher caloric expenditures and/or if the exercise is distributed over more than 2 sessions.

Triglyceride Correlations

As previously mentioned, fasting TG concentrations directly correlated with total triglyceride area under the curve in the control condition. However, we also found that fasting TG levels were not predictive of the incremental triglyceride area under the curve ($p > 0.05$). This suggests that fasting TG levels do not predict the postprandial triglyceride response to a high-fat test meal when the area under the curve score is normalized for baseline TG levels. In addition to fasting triglyceride concentrations, another common correlate of postprandial lipemia is abdominal obesity. We demonstrated that those with lower levels of adipose tissue expressed relative to total adiposity had greater changes in triglyceride AUC_I from the control to the low-intensity

exercise and to the single session of moderate-intensity exercise. Although these correlations are relatively modest, they suggest that those with higher levels of abdominal adiposity were less responsive to these exercise conditions.

Mechanisms of the Triglyceride Response

This study did not directly assess the mechanisms by which exercise attenuates postprandial lipemia. However, based on available evidence from the composite body of work on postprandial lipemia and exercise, it is likely that the reductions in PPL seen in this study are a result of two complementary mechanisms. First, exercise may reduce hepatic VLDL-TG secretion (68, 136). Second, increases in skeletal muscle lipoprotein lipase activity following a single session of exercise may mediate increases in triglyceride clearance (10, 179).

Effect of Exercise on Postprandial Insulin and Glucose

Insulin

To the extent that insulin may influence skeletal muscle lipoprotein lipase activity, we examined insulin and glucose responses to the test meal to assess the role of insulin in attenuating postprandial lipemia. Our finding that the temporal insulin response, as well as the total or incremental insulin areas under the curve, was not significantly altered from control by any of the exercise conditions is in opposition to some, but not all previous reports. It has been previously reported that similar volumes of exercise have created significant reductions in total and incremental insulin AUC scores in healthy populations (70, 71) as well as in men with metabolic syndrome (205). However, there are also other studies that have failed to show postprandial changes in measures of insulin with 500 kcals of moderate-intensity exercise (148), or with even

greater amounts (92). Comparison of these studies does not lead to a readily apparent rationale for the incongruence. It should be recognized that while decreases in insulin concentration during the postprandial period following exercise have been proposed to have a role in the attenuation of postprandial lipemia, this does not appear to be a major factor mediating this response. Indeed, Gill et al. (72) reported that when postprandial reductions in insulin and triglycerides coincide, they are not related to one another in apparently healthy individuals. Our finding of reductions in postprandial lipemia following low- and moderate-intensity exercise in the absence of reductions in insulin concentrations provides evidence that PPL may be reduced without changes in postprandial insulin concentrations in men with metabolic syndrome as well.

Glucose

We did not see, nor expect to see, a significant rise in glucose concentrations during the postprandial period because the carbohydrate content of the high-fat test meal was only 3 grams. This finding is similar to what has been previously reported for postprandial glucose concentrations following high-fat test meals (92, 199). Thus, postprandial alterations in glucose metabolism were not likely to have influenced the differences observed in postprandial lipemia.

Exercise Effect on Fasting Blood Variables

Triglycerides and HDL-C

We did not find that any of the exercise conditions significantly reduced fasting triglycerides or increased HDL-C concentrations 13 hours after exercise was completed. Although acute sessions of exercise within this caloric expenditure range have been shown to reduce fasting triglycerides and increase HDL-C concentrations, this is not

always the case. For example, Grandjean et al. (80) reported that a single session of exercise with a total caloric expenditure of 350 kcals did not produce these changes. Additionally, these transient changes have been commonly seen 24 to 48 hours postexercise (49). Thus, 13 hours may have been insufficient to promote these responses.

Insulin

As for fasting triglycerides, fasting insulin concentrations and clinical indices of insulin sensitivity (HOMA score and glucose/insulin ratio) were both unaltered by our exercise conditions. Insulin sensitivity has been shown to transiently improve for up to 48 hours after a single session of aerobic exercise (19); however, the required intensity and caloric expenditure to produce this response have not been consistently defined (196). It is possible that more vigorous exercise sessions than the ones in this study would have reduced fasting insulin concentrations and improved the clinical indices of insulin sensitivity; however, attempting to change these metabolic variables was not a specific aim of this investigation.

Glucose

Glucose concentrations were also unchanged 12 hours after the exercise conditions. The average glucose concentration at baseline for these participants was below the threshold for impaired glucose tolerance, and thus it would not be expected that exercise would profoundly impact glucose homeostasis.

Outside Variability

Participants in this study maintained free-living conditions throughout the entire protocol. To limit variation in study outcomes due to extraneous elements, participants were given instructions at the onset of the study and were also given reminders prior to

the start of each condition pertaining to dietary and physical activity regimens. Participants were asked to refrain from making any dietary changes throughout the duration of the study protocol. Dietary records indicated that there were no significant differences in caloric intake or major macronutrient composition among any of the experimental conditions (Table 12). Participants were also asked to refrain from engaging in outside physical activity and/or exercise throughout the study. Compliance was documented verbally prior to each condition. Given that there were no significant changes in the dietary records and that participants were weight stable during the study, it is unlikely that outside variation influenced the present findings. Additionally, the significant changes reported in this study overcame any variation due to free-living conditions.

Conclusions

This is one of the first studies to demonstrate that 500 kcals of exercise attenuates postprandial lipemia in men with metabolic syndrome. Low-intensity exercise reduced the triglyceride AUC_I by 27% and triglyceride concentrations at the 4-hour timepoint by 22%. Importantly, neither of these effects was greater than that resulting from the same amount of moderate-intensity exercise performed in a single session. These results show, for the first time, that low-intensity exercise is as effective as moderate-intensity exercise in reducing postprandial lipemia in this population. The practical implication of these findings is that prescribing this dose of exercise reduces postprandial lipemia in a population with a clustering of risk factors that predisposes them to the development of cardiovascular disease. Also, it appears that this effect may be obtained by exercising at a low-intensity, which may be more palatable for this population.

We also found that two sessions of moderate-intensity exercise were not able to effectively reduce postprandial lipemia. This is not consistent with current physical activity recommendations for public health. These recommendations have stated that the health benefits conferred by aerobic exercise are similar whether the exercise is performed in a continuous manner or accumulated throughout the day. Based on our findings, it appears that accumulating exercise throughout the day is not an effective method of exercise prescription to reduce postprandial lipemia in men with metabolic syndrome. It is possible that accumulated exercise may be more effective at higher total caloric expenditures or if the exercise is partitioned into more than two sessions.

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APPENDICIES

APPENDIX A

Research Study
Aerobic Exercise and Cholesterol

We are seeking male volunteers between the ages of 25 and 60 to participate in a study to investigate the effects of intermittent vs. continuous aerobic exercise on blood lipid responses to a high-fat meal

You don't have be a current exerciser to participate!

If you meet the inclusion criteria for the study you will receive a free:

- Cholesterol, triglyceride and glucose screening at rest and following a meal
- Resting and exercise blood pressure assessment
- Body composition and bone mineral density analysis
- Maximal graded exercise test to evaluate your current level of fitness
- Exercise prescription to improve fitness and lose weight

If you are interested in participating in this study please contact:

Michael Mestek
Exercise Technology Laboratory
Department of Health and Human Performance
Auburn University
(334) 844-1482 or (334) 332-6561
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APPENDIX B

Initial Screening Questionnaire

1. Name: _____ Age: _____
2. Contact information:
   Home phone: _____ Work phone: _____
   E-mail:_____ Cell phone:_____

3. Have you participated in any form of leisure-time or occupational physical activity or structured exercise in the past 6 months? _____
   Frequency/intensity/duration:_____
   _____

4. Do you have a history of cardiovascular disease, lung disease, or diabetes?
   _____
   Description:_____
   _____

5. Do you know your current TG or TC level? _____

6. Are you currently taking a prescription medications, vitamins, over-the-counter medications dietary supplements?
   Description:_____
   _____

8. Are you a current cigarette smoker or have you quit within the last 6 months?
   _____

9. Do you have orthopedic (or other) problems that would interfere with exercise?
   _____
   Description:_____
   _____

APPENDIX C

A Copy of the INFORMED CONSENT used

FOR

THE RESEASRCH STUDY ENTITLED:

"The Effects of Accumulated and Continuous Aerobic Exercise and Exercise Intensity on Postprandial Lipemia"

Principal Investigator:	Michael L. Mestek, M.S.
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1. Study Purpose

You have been invited to participate in a study to evaluate the effects of exercise intensity and single versus multiple bouts of exercise performed in one day and exercise intensity on lipid concentrations that appear in your blood in the hours after a meal (postprandial lipemia). Lower postprandial blood responses have been shown to occur after a single bout of exercise. However, there is limited information available on the effect of exercise on postprandial lipids when performed two times per day or at differing exercise intensities. Current exercise recommendations from the U.S. Surgeon General, the Centers for Disease Control, the American College of Sports Medicine, and American Heart Association suggest that moderate-intensity exercise accumulated in multiple sessions compared to one long session may provide similar improvements in fitness, body composition, weight loss, and blood pressure at similar caloric expenditures. Yet there is little information about how effective multiple daily exercise sessions or low-intensity exercise sessions are for reducing postprandial lipemia. This is a particularly interesting area of research since we spend most of our day in the postprandial state. In addition, exercise performed over multiple short sessions may also be more practical for many individuals who have limited time to exercise during the day. **You have been**

asked to participate in this study because you are a male between the ages of 25-60 with no physical conditions or medical conditions that would prevent you from exercising or providing blood samples safely.

2. Procedures Used to Address the Purpose

Preliminary Procedures

We will provide an overview of the study protocol and answer any questions that you may have about this project. If you volunteer and provide your informed consent to be a participant in this study, you will be given a health history questionnaire and physical activity questionnaire to complete. You are encouraged to answer the questionnaires to the best of your knowledge to ensure your safety as a participant. Subsequently, we will measure your height and weight, calculate your body mass index and measure your waist circumference. Next, we will obtain a blood sample to determine fasting total cholesterol, high and low-density lipoprotein cholesterol, triglycerides, and blood sugar (glucose). This visit will take approximately 1 hour. **To be included in the study, you must meet each of the following: 1) age 25-60 yrs, 2) physically inactive – not engaging in regular exercise in your occupation or leisure-time, 3) overweight – body mass index > 30 kg/m^2 and waist circumference > 40 inches, 4) fasting triglyceride levels > 150 mg/dL, and 5) Non-smoker. If you have abnormal fasting cholesterol or blood glucose or excessively high triglyceride levels, you will not be allowed to participate in the study**. **Additionally, you must be otherwise healthy, and not taking any medications that are known to influence fat or carbohydrate metabolism.**

If you meet all of the initial criteria, you will be asked to return to the Exercise Technology Laboratory for a physical examination by a physician, which will take approximately 1 hour. We will determine your body composition (lean, fat tissue and bone density) with a total body x-ray (DEXA). You will then be asked to perform an exercise test on a motor driven treadmill to determine your cardiovascular fitness and to screen for underlying cardiovascular disease. This test is sometimes called a $\dot{V}O_{2max}$ test, or a stress test, and the treadmill will begin at a comfortable walking pace and progressively increase both the speed and elevation. We will ask you to continue the test as you are able but you may discontinue the test at any point due to exhaustion or other reasons. Throughout the test, you will breathe through a mouthpiece to measure your oxygen uptake and carbon dioxide production. Heart rate, ECG, blood pressure and ratings of perceived exertion will be monitored throughout the test by trained technicians. Please report any unusual symptoms such as lightheadedness, dizziness, faintness, chest pain or other signs or symptoms during the course of the testing procedures. The information gathered in this test will be used to individually tailor the exercise sessions you will be asked to perform in this study.

You will then be provided with instructions regarding the dietary and physical activity requirements of the study. You will be asked to return 3-day dietary and physical activity records within 7 days of the second visit. We will use the dietary information to

determine your average daily caloric intake and the nutritional composition of your diet. This information will be used to construct an individualized diet for you to follow on the days of the exercise conditions. Throughout the study, you will be asked to fill out additional dietary records so that we can check the type and amount of food you are eating. **It is important that you adhere to the dietary habits as closely as possible to maintain your current body weight and to stabilize your blood lipid concentrations throughout the experimental protocol. The physical activity record will be used to determine how much physical activity you typically perform. Since you are not currently physically active, any sudden increase in physical activity or exercise outside of this research could alter the results of the study.** At this point, we will try to determine a schedule for you to return for the additional testing requirements.

Experimental Procedures

You will be asked to complete 4 different experimental conditions with a minimum of 5 days between each condition. You will be asked to consume a high-fat meal during each condition and have blood samples taken at 2-hour intervals for 6 hours during each condition to measure postprandial lipemia. The first condition is a baseline, or control, and you will not be asked to exercise for this condition. The 3 exercise conditions are as follows: 2) one session of moderate-intensity exercise, 3) one session of low-intensity exercise, 4) two sessions of moderate-intensity exercise with a minimum of 4 hours between each session. The goal of each of the exercise sessions is to expend 500 calories in a single session or over 2 exercise sessions. We will randomly determine the order of the exercise sessions you will perform prior to your visit and inform you of your assignment the day before your first exercise session.

You will be asked to record your diet for 3 days prior to each experimental condition. After 3 days on a standardized diet, you will be asked to return to the laboratory (visit 3) to begin the experimental protocol. You will also be asked to eat your standardized diet and refrain from any moderate or strenuous physical activity for 72 hours (3 days) prior to the start of the protocol.

During each session you will asked to walk or jog on a treadmill at an intensity of either 35% or 70% of your maximal aerobic capacity for a length of time required to burn 500 total calories of energy accumulated in one or two exercise sessions. This will take approximately 45 minutes for the 70% session and 90 minutes for the 35% session. These submaximal exercise bouts will be personalized so that you will exercise on a treadmill at a level that is most comfortable for you. Twelve hours after the completion of the final exercise session of each exercise condition, or on the day of the control condition, you will be asked to report to the lab after an 8-10 hour fast for blood sampling. Upon arrival, we will measure your body weight and then insert a venous catheter into the most prominent vein site in your lower arm and obtain a blood sample equal to about 2 tablespoons (10mL). You will then be asked to consume a milkshake consisting of whipping cream (20tbsp) and vanilla ice cream (1/2 cup) within 15 minutes. This meal is high in fat and contains approximately 1000 calories, 100g of fat, 17g of

carbohydrate, and 3 g of protein. After you consume the meal, you will be asked to remain in the lab to have blood samples taken at 2-hour intervals up to 6 hours for a total of 5 blood samples and 6 tbsps of blood (including the baseline blood sample). Approximately 0.5 tablespoon of blood (7 mL) will be drawn at each of the 2-hour intervals. While you will be asked to remain in the lab over the 6-hour period, you will be allowed to performing light activities such as writing, reading, watching television, computing, etc. The catheter will be removed from your vein immediately following the last blood sample at 6 hours.

The total number of visits to the Exercise Technology Laboratory will be 13 for a total time commitment of approximately 32 hours.

3. Discomforts or Risks to be Reasonably Expected

The following few paragraphs provide information about the potential risks and discomforts that you may experience as a participant in this study.

The risks associated with the graded exercise test are comparable to those you face when you perform hard exercise, which causes you 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 instances, heart attack, or death. In addition, there is a risk of falling on the treadmill that could cause cuts, scrapes or bruises. You could also suffer orthopedic injuries, such as ankle, knee, hip or muscle strains and sprains, or rarely fracture bones. Studies have shown that your risk of death during this type of test is about 0.5 in 10,000 and your risk of harmful effects is about 5 to 8 in 10,000. We will make every effort to minimize these risks by carefully reviewing your health history form and having your undergo a physical examination by a physician. All of these procedures will be done before you are allowed to exercise. If we find physical problems that, in our judgment, make exercise risky, we will not invite you to exercise in the study.

During the graded exercise test, we will ask you to wear a mouthpiece so that we can measure the amount of oxygen you consume and the amount of carbon dioxide you produce. The primary risk involved is contamination of the mouthpiece or tubing. The risk will be minimized by using mouthpieces that will be cleansed with anti-bacterial, germ killing solutions with each use.

Ten electrodes will be placed on your skin to measure the electrical activity of your heart during a procedure called an electrocardiogram (ECG). Each electrode's site will be prepared by rubbing the skin with an abrasive material and then cleansed with an alcohol pad. These procedures may cause some irritation and a mild stinging sensation. There is a slight possibility that you will be allergic to the gel used in the electrodes. This may cause some itching and redness of the area that might last for several days. All equipment used meets all safety specifications to minimize risk of electrical shock. The procedures are performed with strict adherence to guidelines by the American College of Sports Medicine.

Venous blood sampling requires the introduction of a small gauge catheter to a forearm vein to acquire the blood sample. Risks of the procedure are minimal and rare, but may result in moderate bruising and stiffness around the affected site. In addition, as with any similar procedure disrupting the skin barrier, there is a risk of contracting an infection. The risk to you will be minimized through the use of accepted universal precautions for blood sampling and handling which include: (1) latex surgical gloves by the technician; (2) antiseptic cleansing (70% alcohol) of the involved site prior to the puncture; (3) use of sterile equipment and instruments for each sample; and (4) proper dressing of the wound following sample collection. Dr. Grandjean will supervise all phlebotomy procedures. All investigators have completed updated training in blood sampling, blood sample handling, and blood-borne pathogens (Auburn University Biosafety Office 2003).

4. Precautions and available medical treatment

We will make every effort to minimize all of the risks listed above by carefully reviewing your health and medical history questionnaire, your physical activity questionnaire and evaluating your risk factors for cardiovascular disease. All of these procedures will be done before you are allowed to exercise. If we find physical problems that, in our judgement, make exercise risky, for your own protection we will not invite you to participate in this study. Compensation, including medical costs for physical injury or adverse effects is not available. The participant is responsible for the cost of medical care needed as a result of participating in the study. Michael Mestek and other trained graduate students will be in charge of conducting all of the lab and exercise measurements. In addition, Dr. Grandjean, Ph.D. will supervise all of the exercise testing procedures and will be available in the event of an emergency. Dr. Grandjean, Ph.D. and all individuals involved with the testing procedures are trained in CPR. Dr. Jack Mahurin, D.O. will provide medical supervision for all graded exercise testing and review all health history questionnaires and graded exercise test results prior to entry into the study. The emergency equipment and emergency plans for the Exercise Technology Laboratory meets standards that are recommended by the American College of Sports Medicine for non-medical exercise testing facilities.

All investigators will closely follow the emergency plans and procedures that have been previously established for the laboratory. The 7th edition of the American College of Sports Medicine's Guidelines for Exercise Testing and Prescription (2006) will be observed throughout all body composition assessment and graded exercise test procedures.

5. Benefits of participation

You will receive a physician examination and maximal graded exercise test with 12-lead electrocardiography. Body composition measurements such as waist circumference and DEXA will provide valuable information regarding your percentage fat, body weight distribution and bone mineral density. You will also receive a determination of individualized report with your baseline lipids, as well blood lipid responses to a meal. Additionally, you will receive an individualized participant report detailing all the measurements we obtained for you how these responses compared to the group averages.

6. Right to privacy

All individual information obtained in this study will remain confidential and your right to privacy will be maintained. Data collected will be used for research purposes only and will be limited to access by the investigators of this study. Only data reported as group means or responses will be presented in scientific meetings and published in scientific journals. Confidential data will be destroyed following the project. If this project lasts for more than one year, a new protocol will be submitted to the Office of Human Subjects Research.

7. Consent

Participation is entirely voluntary. The decision to participate or not will not jeopardize your relationship with the Department of Health and Human Performance or Auburn University. Refusal to participate involves no penalty. You may withdraw your consent and discontinue participation at any time for any reason.

8. Questions concerning the research and the procedures

As investigators, it is our obligation to explain all of the procedures to you. We want to make sure that you understand what is required of you and what you can expect from us in order to complete this research project.

Please do not hesitate to inquire about the research, rights and responsibilities of the participant and the investigator now or at any time throughout the study.

9. Additional information regarding your rights as a research participant

For more information regarding your rights as a research participant you may contact the Auburn University Office of Human Subjects Research or the Institutional Review Board by phone (334) 844-5966 or e-mail at hsubjec@auburn.edu.

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 FOR MY OWN RECORDS.

_____ _____

Participant's Signature **Date**

_____ _____

Investigator Obtaining Consent **Date**

APPENDIX D

HEALTH & LIFESTYLE HISTORY

Please complete this form as accurately and completely as possible. The information you provide will be used to evaluate your health by the principle investigators who will oversee the conductance of this study. All information will be treated as privileged and confidential.

NOTE: This information is being collected for use in the study entitled, "The Effects of Accumulated and Continuous Bouts of Aerobic Exercise and Differing Levels of Exercise Intensity on Postprandial Lipemia". All information obtained in this document will be destroyed upon completion of the study.

1. IDENTIFICATION & GENERAL INFORMATION

Name			Today's Date	
			/ / 06	
Age	Date of Birth	Gender	Occupation	
	/ /			
Home Address		City	State	ZIP
Home Phone	Work Phone	e-mail		
Emergency Contact	Phone	Physician	Phone	

Please check the box that applies to you:

Race or Ethnic Background

☐ White, not of Hispanic origin	☐ American Indian / Alaskan native	☐ Asian
☐ Black, not of Hispanic origin	☐ Pacific Islander	☐ Hispanic

2. ILLNESS & MEDICAL HISTORY

Check all of 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 hand margin after the date.

Medical Condition	Check if Applicable	Date Diagnosed (M / Yr)	Current?
AIDS			
Allergies			
Arthritis			
Osteoarthritis			
Rheumatoid			

Medical Condition	Check if Applicable	Date Diagnosed (M / Yr)	Current?
Asthma			
Bronchitis (chronic)			
Bone Fracture			
Cancer			
Breast			
Cervix			
Colon			
Lung			
Prostate			
Skin			
Other Cancer			
Cataracts			
Cirrhosis (liver)			
Colitis (ulcerative)			
Depression			
Eating Disorders (anorexia, bulimia)			
Emphysema			
Epilepsy			
Frequent Bleeding			
Gallstones / Gallbladder Disease			
Glaucoma			
Gout			
Hearing Loss			
High Anxiety / Phobias			
Hepatitis Type:			
Osteoporosis			
Pneumonia			
Tuberculosis			
Renal / Kidney Problems			
Sleeping Problems			
Stomach / Duodenal Ulcer			
Substance Abuse Problems			
Rectal Growth or Bleeding			
Metabolic Problems Diagnosed	Check if Applicable	Date Diagnosed (M / Yr)	Current?
Thyroid Problems			
Diabetes			
Cardiovascular Problems Diagnosed	Check if Applicable	Date Diagnosed (M / Yr)	Current?
Angina			
Anemia (low iron)			
Coronary Disease			
Disease of the Arteries			
Enlarged Heart			
Heart Attack			
Heart Murmur			
Heart Rhythm Problem			
Heart Valve Problem			
Heart Problem (other)			

Heart Problem (other)			
High Blood Pressure (controlled)			
High Blood Pressure (uncontrolled)			
Medical Condition	Check if Applicable	Date Diagnosed (M / Yr)	Current?
Peripheral Vascular Disease			
Phlebitis or Emboli			
Rheumatic Fever			
Rheumatic Heart Disease			
Pulmonary Emboli			
Have you ever had:	Check if Applicable	Date Diagnosed (M / Yr)	
An abnormal chest x-ray?			
An abnormal electrocardiogram (ECG)?			
An exercise stress test?			
An abnormal exercise stress test?			
Orthopedic Problems	Check if Applicable	Date Diagnosed (M / Yr)	
Low Back Pain			
Shoulder Pain			
Elbow Pain			
Wrist or Hand Pain			
Hip Problems			
Knee Problems			
Ankle or Foot Problems			

3. SYMPTOMS or SIGNS SUGGESTIVE of DISEASE

Do you presently have or recently had (Check if Applicable):

Yes	Description	Yes	Description
	Have you experienced unusual pain or discomfort in your chest, neck, jaw, arms, or other areas that may be due to heart problems?		Do you suffer from swelling of the ankles (ankle edema)?
	Have you experienced unusual fatigue or shortness of breath at rest, during usual activities, or during mild-to moderate exercise (e.g., climbing stairs, carrying groceries, brisk walking, cycling?		Have you ever experienced an unusual and rapid throbbing or fluttering of the heart?
	Have you had any problems with dizziness or fainting?		Have you ever experienced severe pain in your leg muscles during walking?
	When you stand up, or sometimes during the night while you are sleeping, do you have difficulty breathing?		Has your doctor told you that you have a heart murmur?

☐	Have you ever experienced a seizure?	☐	Have you ever had unexpected weight loss of 10 lbs or more?

4. CHRONIC DISEASE RISK FACTORS

Do you presently have or recently had (Check if Applicable):

Yes	Description	Yes	Description
☐	Are you a male over 45 years of age, or a female over 55 years of age who has experienced premature menopause and is not on hormone replacement therapy?	☐	Is your total serum cholesterol greater than 200 mg/dL, or has your doctor ever told you that your cholesterol is at high-risk level?
☐	Has your father or brother had a heart attack, cardiac revascularization surgery, or died suddenly of heart disease before age 55; has your mother or sister experienced these heart problems before age 65?	☐	Is your HDL cholesterol low (< 40 mg/dL for males, < 50 mg/dL for females) , or has your doctor ever told you that your HDL cholesterol is at high-risk level?
☐	Are you a current cigarette smoker?	☐	Are your triglyceride levels > 200 mg/dL, or has your doctor ever told you that your triglycerides are at high-risk level?
☐	Has a doctor told you that you have high blood pressure (more than 140 / 90 mmHg), or are you on medication to control your blood pressure?	☐	Are you physically inactive and sedentary (little physical activity on the job or during leisure time)?
☐	Do you have diabetes mellitus?	☐	Do you weigh more than 20 lbs more than you should?

Additional Family History Information

Check all of the conditions or diseases for which any member of your immediate family, including grandparents, have been diagnosed and/or treated. Also provide their age and the date of occurrence or diagnosis if known.

Medical Condition	List Relative & Age at Diagnosis	Date Diagnosed
High Blood Pressure before age 40		
High Cholesterol		
Obesity		
Diabetes		
Stroke under age 50		
Heart Attack under age 50		
Heart Operation		
Cancer under age 60		

Physical Activity Information

Please check the box that best describes you.

1. In general, compared to other persons your age, rate how physically fit you are:

Not at all fit	Slightly below average fitness	Average fitness	Slightly above average fitness	Extremely fit
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. Outside of your normal work, or daily responsibilities, how often do you engage in physical exercise?

☐ 5 or more times per week ☐ 3 - 4 times per week ☐ 1 - 2 times per week

☐ Less than 1 time per week ☐ Seldom or never

3. On average, how long do you exercise on each occasion?

☐ 10 - 20 min ☐ 20 - 30 min ☐ 30 - 40 min ☐ 40 - 50 min ☐ > 50 min

4. On a scale of 1 to 10 (1 being the lowest, 10 being the highest), how would you rate your exercise intensity ?

☐ Very Low (1 - 2) ☐ Low (3 - 4) ☐ Moderate (5 - 6) ☐ Mod. - High (7 - 8) ☐ High (9 - 10)

5. How much strenuous physical work is required on your job?

☐ A great amount (> 60%) ☐ A moderate amount (30 - 50%)

☐ A little (< 30%) ☐ None

6. How often does your work entail repetitive pushing and pulling or lifting while bending or twisting, leading to back pain?

☐ All of the time ☐ Most of the time

☐ Some of the time ☐ Rarely or never

Body Weight Information

1. What is the most you have ever weighed? When?

2. Are you currently trying to:

☐ Lose weight ☐ Gain weight

☐ Stay the same ☐ Not trying to do anything

Substance Use

1. How would you describe your tobacco use habits?

   ☐ Never smoked

   ☐ Used to smoke (How long ago did you quit?): _____

   ☐ Still smoke (How many cigarettes / day?): ___

2. How many alcoholic drinks do you consume? (A "drink" is one glass of wine, a wine cooler, a bottle / can of beer, a shot glass of liquor, or a mixed drink).

   ☐ Never use alcohol ☐ Less than 1 per week ☐ 1 - 6 per week

   ☐ 1 per day ☐ 2 - 3 per day ☐ More than 3 per day

Stress Index

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 5 as indicated below.

1. In general, I seem to have many responsibilities but little authority.

Strongly disagree	Somewhat disagree	Undecided	Somewhat agree	Strongly agree
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. I rarely have enough time to do a good job, accomplish what I want or for family, social obligations or personal needs.

Strongly disagree	Somewhat disagree	Undecided	Somewhat agree	Strongly agree
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. Most of the time I have little control over my life at work, school, or home.

Strongly disagree	Somewhat disagree	Undecided	Somewhat agree	Strongly agree
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

4. On average, how many hours of sleep do you get in a 24-hour period?

   ☐ Less than 5 ☐ 5 to 7

   ☐ 8 to 10 ☐ More than 10

5. MEDICATIONS

Please indicate any medications, prescription or "over the counter" by providing the name and dosage:

Medication Type	Name of Medication	Dosage
Heart Medicine		
Blood Pressure Medicine		
Blood Cholesterol Medicine		
Insulin		
Other Medicine for Diabetes		
Thyroid Medicine		
Medicine for Breathing / Lungs		
Medicine for Weight Loss / Weight Control		
Hormones		
Painkiller Medicine		
Arthritis Medicine		
Medicine for Depression		
Medicine for Anxiety		
Medicine for Ulcers		
Allergy Medicine		
Other (please specify)		

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 your overall health and well being? If so, please give an explanation below.

APPENDIX E

3 – DAY FOOD RECORD

- RECORD EVERYTHING YOU EAT AND DRINK INCLUDING SNACKS AND BEVERAGES.
- RECORD IMMEDIATELY AFTER FOOD IS CONSUMED
- INDICATE PORTION SIZES. MEASURE AMOUNTS OF EACH FOOD USING MEASURING CUPPS OR SPOONS WHEN IT IS PRACTICAL. RECORD PORTION SIZES IN GRAMS, OUNCES, CUPS, TABLESPOONS, TEASPOONS, OR PIECES. (example: 8 oz orange juice, 1 piece wheat bread, 1 tbsp butter)
- INDICATE THE BRAND NAME. (3 oz Ruffles BBQ Potato Chips, 1 cup Uncle Ben's Long Grain Rice, McDonald's Large French Fries)
- INDICATE FORM OF PURCHASE. (fresh, frozen, canned, etc..)
- RECORD TIME OF MEAL
- RECORD AND CHECK THE NUMBER OF SERVINGS FOR EACH ITEM LISTED (ST= Starch (bread, pasta, cereal, rice, etc); MT= Meat (poultry, beef, fish, eggs, nuts); V=Vegetable; FR= Fruit; D= Dairy (milk, yogurt, cheese, etc..); FT= Fat (butter, oil, sugar, jelly); B= Beverage (regular soft drinks, sweet tea, sports drinks, etc..)

PLEASE BE AS SPECIFIC AND AS COMPLETE WITH YOUR RECORDS AS YOU POSSIBLY CAN. THANK YOU.

If you have any questions, please contact:

Michael Mestek

(334) 844-1482

mesteml@auburn.edu

Time	Food/Beverage	Quantity	Calories	Protein (g)	Fat (g)	CHO (g)

APPENDIX F

Pre-Blood Draw Questionnaire

Participant: _____ Visit:_____

Date: _____ Time: _____

Please answer 'YES' or 'NO' to each of the following questions and provide the requested information.

_____ 1. Have you fasted overnight (8-12 hours)?
If no, when was your last meal? _____

_____ 2. Have you had anything to drink in the last 12 hours?
If yes, list the amount and type of drink: _____

_____ 3. Are you taking any medications to thin your blood?
If yes, please list: _____

_____ 4. Do you currently have any medications "on board"?
If yes, please list: _____

_____ 5. Have you engaged n any strenuous physical activity for the past two days?
If yes, list the amount and type: _____

_____ 6. Do you experience fainting or dizziness when you have your blood drawn?
If yes, please describe:_____