EFFECTS OF A LOW GLYCEMIC INDEX DIET ON POST-MENOPAUSAL WOMEN WITH ABDOMINAL OBESITY

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KELLEY SUZANNE BROWN OLREE

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ABSTRACT

THE METABOLIC EFFECTS OF A LOW GLYCEMIC-INDEX DIET ON POST-MENOPAUSAL WOMEN WITH ABDOMINAL OBESITY

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Abdominal obesity has been associated with an increased incidence of insulin resistance, hyperinsulinemia, and hyperlipidemia. Fourteen post-menopausal females with waist-to-hip ratios (WHR) greater than 0.80 participated in a study designed to determine if a low glycemic-index diet would improve the metabolic aberrations associated with abdominal obesity. For two weeks, seven subjects were on a low glycemic-index diet; seven were on a high glycemic-index diet. Both diets were designed for weight maintenance and contained equivalent amounts of carbohydrate, protein, fat, and fiber. The subjects' low density lipoprotein cholesterol (LDL cholesterol), serum fructosamine, serum connecting peptide (C-peptide), and response to oral glucose tolerance tests were measured just before and immediately following the study period. Both groups had a significant reduction ($p<.05$) in LDL cholesterol, C-peptide, and fructosamine values. The differences in pre and post values between groups did not reach significance.

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CHAPTER I

INTRODUCTION

The Surgeon General's Report on Nutrition and Health (1) calls obesity "one of the most prevalent diet-related problems in the United States." Such a statement is supported by the findings of NHANESII: one in four Americans is overweight (85th percentile BMI). Additionally, 9.3 percent of Americans were classified as being severely overweight (95th percentile BMI). The health risks associated with being severely overweight include high blood cholesterol, high blood pressure, and diabetes, and these conditions, in turn, increase the risk of associated diseases: coronary heart disease, neurologic disorders, and kidney diseases. Obesity has been further associated with increased risk of gall bladder disease and some cancers (1). Therefore, the conclusion can be made that obesity is a major threat to the health of Americans and other peoples of the world.

However, many questions still remain concerning the complexities of obesity. Its etiology and most effective treatment have yet to be defined. Some controversy still remains over the definition of the condition itself.

Furthermore, in recent years, two "different" types of obesity have been identified: abdominal or upper body obesity and peripheral obesity. In an editorial in Journal of Internal Medicine, Bjorntorp (2) proposed that only abdominal obesity be considered as "obesity of medical significance". Bjorntorp based his opinions on the numerous studies which have correlated the degree of abdominal obesity with increased risk for those diseases, such as cardiovascular disease and diabetes, that had previously been thought to be associated with increased fat mass irrespective of its distribution (3-7). Results of a study performed by Hartz et al. (3) also led to the conclusion that "obesity cannot be described solely as fat mass, but that the location of fat deposition must be considered when studying the association between obesity and disease".

Proposed pathophysiology of abdominal obesity

Abdominal obesity is often accompanied by glucose intolerance and hyperinsulinemia similar to that found in type II diabetes. This hyperinsulinemic state seems to accompany other metabolic and physiologic aberrations, specifically increased low density lipoprotein cholesterol (LDL cholesterol), hypertension, and elevated blood glucose.

This group of risk factors, including obesity, has been newly identified by some researchers as syndrome X (8).

Many mechanisms have been proposed for the hyperinsulinemic state found in the abdominally obese population. It has been proposed that particular characteristics of the abdominal adipocytes, namely their sensitivity to free fatty acid mobilization, exposes the liver to high concentrations of free fatty acids which, in turn, may inhibit insulin uptake, function, and catabolism by the liver (9). It has also been observed that the hypertrophic adipocytes exhibit more insulin resistance than do the hyperplastic peripheral adipocytes. This insulin resistance can result from either a receptor or post receptor defect. Kolterman et al. (10) have proposed that individuals with moderate obesity possess fewer receptors than non-obese individuals and therefore have decreased insulin sensitivity. These researchers also propose that more severely obese individuals possess fewer receptors as well as post-receptor defects resulting in decreased insulin sensitivity and decreased insulin effectiveness.

The connection between abdominal obesity and increased LDL cholesterol may also be a result of the liver's being exposed to a high concentration of free fatty acids. Studies have demonstrated that secretion of very low density lipoproteins (VLDL), the precursors to LDL cholesterol, is

regulated by the availability of free fatty acids. Thus, if VLDL are secreted from the liver in proportion to the high concentration of free fatty acids available in abdominal obesity, the risk of increased LDL cholesterol is created.

The glycemic-index

In recent years, some individual foods have been classified according to the post-prandial glucose response they create. These glucose responses have been indexed according to the glucose response of white bread, which has been defined to be equal to one hundred. This classification system is commonly known as the "glycemic-index." It has been proposed that planning meals according to the glucose response they create would provide a useful reference for planning a diabetic meal pattern. Meals could be planned to produce the smallest rise in post-prandial blood glucose, thus augmenting the various treatments for the disease, i.e., diet, oral hypoglycemics, and/or exogenous insulin.

Statement of the problem

Abdominal obesity has been identified as a risk factor for cardiovascular disease, cerebrovascular disease, and

type II diabetes in both men and women. Hyperlipidemia, hyperinsulinemia, and hyperglycemia characterize this type of obesity and contribute to the health risks of this condition. Numerous studies have examined the interrelationships of the above conditions and how these conditions are affected by each subject's age, sex, and various anthropometric characteristics. However, these studies have most often included men and/or pre-menopausal women as subjects. Similarly, studies concerning the glycemic-index have focused on certain populations such as type I and type II diabetics and persons with no impairment of glucose tolerance.

To date, no investigator had studied the effects of a diet specifically designed to suppress post-prandial glucose responses on post-menopausal women with abdominal obesity. This type of obesity is common among women in this population as is the tendency to develop impaired glucose tolerance and hyperlipidemia. In light of these facts, a study was performed to determine what, if any, beneficial effects a low glycemic-index diet would have on post-menopausal women with abdominal obesity.

Purpose, objectives, and hypothesis

The purpose of this study was to examine the effects of a low glycemic-index diet on several indices of metabolic function in a specific population: post-menopausal women with abdominal obesity. The study served to provide baseline data for further research with the same subject group on a weight reduction, low glycemic-index diet. Specific objectives of the study were:

1. To design a low glycemic-index diet containing calories needed for weight maintenance.
2. To design a high glycemic-index diet containing calories needed for weight maintenance and amounts of carbohydrate, protein, fat, and fiber equivalent to that found in the low glycemic-index diet.
3. To determine the effects of the diets on insulin secretion and insulin utilization via an oral glucose tolerance test and measurement of serum connecting peptide (C-peptide), insulin, and glycosylated serum proteins.
4. To determine the effects of the diets on lipid metabolism via measurement of low density lipoprotein cholesterol.

The hypothesis of this study was as follows: because hyperinsulinemia has been implicated in the etiology of elevated LDL cholesterol and impaired glucose tolerance in

the abdominally obese, it was proposed that a diet designed to produce a low post-prandial glucose response and reduced insulin secretion (low glycemic-index diet) would also lower serum LDL cholesterol concentrations and improve glucose tolerance.

In the chapter to follow, abdominal obesity will be characterized and the effects of the condition on various metabolic processes will be discussed. The specific health risks associated with abdominal adiposity in post-menopausal women will be reviewed. A proposed dietary treatment (a diet with a low glycemic-index) for the metabolic aberrations accompanying abdominal obesity will be described. Finally, some selected measures of glucose tolerance and hyperinsulinemia will be examined.

CHAPTER II

RELATED LITERATURE

Characteristics of Abdominal Obesity

Abdominal obesity has been defined as enlargement of central or abdominal adipose tissue resulting in a high waist/hip circumference ratio, or WHR (5). Classification of a subject as obese or non-obese is often determined by calculating the subject's body mass index, or BMI. The BMI is expressed as weight in kilograms over height in meters, squared (kg/M^2). Obesity is said to be present if the BMI is equal to or greater than $27kg/M^2$ (11). Likewise, a specific ratio is commonly used to identify abdominal obesity. If a woman's WHR is $\geq .80$, then abdominal obesity is said to be present (7). Both BMI and WHR have been supported in the literature as good anthropometric measures of obesity and abdominal obesity (3,4,12,13,14).

Characteristics unique to abdominal adipocytes have also been identified. First, abdominal adipocytes are extremely sensitive to lipolysis by catecholamines (6). The

location of the adipocytes also has important implications on the metabolic processes of the liver. The metabolites of these adipocytes enter the portal circulation and travel directly to the liver. Elevated concentrations of free fatty acids resulting from an excess of these metabolically active adipocytes has been suggested to be a major factor in the etiology of several metabolic aberrations associated with abdominal obesity (15,5). Abdominal adipocytes have also been characterized as being insulin resistant, a state often attributed to elevation of free fatty acid concentrations (13). Lastly, abdominal adipocytes have been characterized as hypertrophic rather than hyperplastic. Kissebah et al. (6) found the presence of high glucose and high insulin areas to be closely associated with the presence of hypertrophic adipocytes in obese individuals. It was further suggested that hypertrophied abdominal fat cells might play an important role in an obese subject's susceptibility to glucose intolerance, hyperinsulinemia, and hypertriglyceridemia.

As has been mentioned previously, abdominal obesity has been associated with specific metabolic aberrations and increased risk for certain diseases. In a study performed by Krotkiewski et al. (5) using 930 obese, middle-aged men and women, men were found to most often have increased fat deposition in the abdomen while women were found to have

increased fat deposition in the gluteal and femoral regions. Men were also found to have higher triglycerides, blood pressure and fasting glucose and insulin concentrations during a glucose tolerance test. However, a "male risk profile" was seen in women with fat patterning similar to that found in men. The results of the study demonstrated that individuals with abdominal-type obesity were at a higher risk for developing complications related to excess body fat such as abnormal lipid and carbohydrate metabolism.

Numerous studies have further explored the relationship of abdominal obesity to various metabolic aberrations. In this review, the presence of and proposed mechanisms for hyperinsulinemia, insulin resistance, hyperlipidemia, and hypertension in the abdominally obese will be discussed.

Hyperinsulinemia

Hyperinsulinemia has been identified as one of the major metabolic aberrations which characterizes abdominal obesity. Several investigators have demonstrated a relationship between hyperinsulinemia and abdominal obesity and have proposed mechanisms for this relationship (4,6,17-20). Hyperinsulinemia has also been implicated in the etiology of other conditions associated with abdominal obesity, such as hyperlipidemia and hypertension (16).

Kalkhoff et al. (4) and Kissebah et al. (6) observed that increased WHR correlated significantly with increased post-prandial serum insulin concentrations in pre-menopausal women. Despres et al. (17) found subcutaneous trunk fat and abdominal fat cell hypertrophy were correlates of pancreatic insulin secretion in obese, pre-menopausal women and that abdominal obesity was closely associated with reduced hepatic extraction of insulin in these women. Peiris et al. (18) identified a relationship between body fat distribution and insulin clearance in pre-menopausal women. Additionally, reduced insulin clearance in the abdominally obese subjects was observed at plasma insulin concentrations above and below what would be considered maximal.

Peiris et al. (19) also studied splanchnic insulin metabolism in women with upper body obesity. Twenty-two pre-menopausal women were used as subjects for the study. Measurement of C-peptide was used to determine pancreatic insulin secretion. Peripheral insulin turnover was used to estimate total insulin excluding the amount retained by the liver during the first portal passage. The difference between C-peptide and peripheral insulin, thus, quantified hepatic insulin extraction. Women with upper or lower body obesity had equivalent increases in C-peptide during the oral glucose tolerance test, but women with abdominal obesity had significantly greater insulin responses

throughout the glucose challenge. Additionally, women with abdominal obesity were found to have normal extraction rates during the basal state but exhibited a significant reduction in hepatic insulin uptake during oral glucose ingestion. The results of this study led Peiris et al. (19) to conclude that increasing abdominal adiposity was associated with a progressive decrease in hepatic insulin extraction which, in turn, increased post hepatic delivery of the hormone. Thus, this defect, accompanied by an increase in pancreatic insulin production (strongly associated with the overall amount of adiposity), accounted for the degree of hyperinsulinemia found in individuals with abdominal obesity.

Evans et al. (20) found that in healthy, pre-menopausal women, glucose tolerance decreased and plasma insulin concentrations rose as the WHR increased. This relationship was independent of the degree of obesity. In subjects who were obese, WHR remained a significant correlate of impaired glucose tolerance and of basal and post-glucose challenge hyperinsulinemia, but degree of obesity had no predictive value for these effects. Evans et al. (20) proposed that insulin resistance in enlarged abdominal adipocytes could be responsible for diminished glucose tolerance and that compensatory hyperinsulinemia occurs in response to the insulin resistance and elevated blood glucose.

Kissebah et al. (6) proposed a similar mechanism for the hyperinsulinemia present in individuals with upper body obesity. This study was performed using 9 non-obese and 25 obese pre-menopausal women. As was stated previously, the results showed the women with abdominal obesity to have greater fasting hyperinsulinemia and higher insulin concentrations throughout the oral glucose tolerance test. Additionally, the mean insulin area of the women with abdominal obesity was almost twice that of the women with gynoid obesity. Kissebah et al. (6) concluded that hypertrophy of abdominal adipocytes in subjects with abdominal obesity was associated with glucose intolerance and hyperinsulinemia. Determination of fat cell size demonstrated that women with abdominal obesity had abdominal adipocyte cell volumes which were significantly greater than the abdominal adipocyte cell volumes of women with gynoid obesity. The study also demonstrated that these hypertrophic adipocytes were significantly more lipolytic than were the smaller adipocytes. Thus, Kissebah (6) proposed that the excess release of FFA resulting from this increased lipolysis might impair glucose oxidation while the increased cell size may result in reduced numbers of insulin receptors. The combinations of these effects were proposed as potential causes of hyperinsulinemia in individuals with abdominal obesity.

Insulin Resistance

Insulin resistance is perhaps most often associated with the metabolic disturbances present in non-insulin dependent diabetes (NIDDM). However, degrees of insulin resistance have also been identified in subjects with abdominal obesity (21). It has even been postulated that the insulin resistant state associated with abdominal obesity is a precursor for the development of NIDDM since an association between abdominal obesity and the risk for the development of NIDDM have been described by investigators (13).

According to Olefsky and Kolterman (22) the causes of insulin resistance can be placed into three categories: (1) abnormal beta cell secretions (2) circulating insulin antagonists and (3) target tissue defects in insulin action. They further state that target tissue defects are the cause of insulin resistance in obesity and NIDDM. Insulin resistance at the target tissue level can vary according to whether the defect is in the insulin receptor or if the defect includes a post receptor defect. The investigators found that obese individuals with moderate hyperinsulinemia had a mild degree of insulin resistance and that this level of resistance was associated with a decreased number of insulin receptors alone. However, both post-receptor and

receptor defects were found in those subjects with more severe insulin resistance.

Bevilacqua et al. (15) proposed another mechanism of insulin resistance: elevation of free fatty acid concentrations. This hypothesis is especially important in light of the lipolytic nature of hypertrophic abdominal adipocytes which results in such an elevation of free fatty acid concentrations. The investigators studied the effects of free fatty acid elevation in seven women with moderate obesity. The investigators concluded that an "increased supply of fatty fuels" failed to inhibit insulin-controlled glucose removal but that hepatic insulin resistance was induced.

The findings of a study performed by Bolinder et al. (23) also have important implications in the etiology of insulin resistance in the abdominally obese. The difference in insulin action on lipolysis between human omental and subcutaneous tissue was investigated. Other investigators (6) have proposed that metabolic abnormalities associated with abdominal obesity are the result specifically of the enlargement of the omental or visceral abdominal adipocytes. Bolinder et al. found the omental cells to be less sensitive to the antilipolytic effect of insulin than were the subcutaneous adipocytes. Omental adipocytes were also found to have less insulin receptor affinity than that found in

the subcutaneous adipocytes. Thus, increased number and size of omental adipocytes in abdominal obesity could possibly contribute to both higher free fatty acid concentrations through lipolytic activity and decreased insulin receptor affinity which could ultimately result in increased insulin resistance in the omental adipocytes and surrounding tissues.

Insulin resistance has been identified as a metabolic aberration in individuals with abdominal obesity. Evans et al. (20) found WHR and percent body fat to be significantly correlated with insulin resistance. The combined effects of WHR and percent body fat were found to be additive. Evans et al. (20) suggested that the insulin resistance observed was the result of the enlarged adipocytes characteristic of abdominal obesity. Krotkiewski et al. (5) found increased WHR to be associated with decreased glucose tolerance and increased incidence of manifest diabetes. Furthermore, blood glucose, a measure of insulin resistance, was dependent on WHR in stepwise regression but only slightly dependent on body fat. Kissebah et al. (6) also found insulin resistance and glucose intolerance indicative of diabetes to be present in a majority of the obese women with abdominal obesity studied. Ten of the sixteen women with abdominal obesity had glucose tolerance results that indicated the presence of diabetes. None of the women with

lower body obesity were found to be diabetic. The women with abdominal obesity had significantly higher glucose concentrations for all values except the value taken at 180 minutes when compared to the women with lower body obesity. Such an effect suggests a greater degree of insulin resistance in women with abdominal obesity.

Hyperlipidemia

The hyperlipidemia which has been demonstrated to be characteristic of abdominal obesity has often been implicated as a contributing factor in the increased incidence of cardiovascular disease seen in women with this pattern of fat distribution (24). Several investigators who have studied this relationship have suggested a common mechanism for elevated lipid concentrations in individuals with abdominal obesity (6,7). As has been stated previously, omental adipocytes have increased sensitivity to lipolytic stimulation. This increased rate of lipolysis results in an elevation in free fatty acid concentrations in surrounding tissues. As the liver is exposed to the elevated free fatty acids as they enter portal circulation, the liver is induced to excrete increased amounts of very low density lipoproteins (VLDL) resulting in increased circulating concentrations of LDL cholesterol as well.

Krotkiewski et al. (5) and Kissebah et al. (6) included investigations of disturbances in lipid metabolism as they relate to body fat distribution in their studies of the impact of abdominal obesity on several parameters of metabolic function. Krotkiewski et al. (5) found that WHR was a better predictor of increased triglyceride concentrations than was epigastric fat cell weight in both men and women. Similarly, Kissebah et al. (6) found that the women subjects with abdominal obesity had significantly higher fasting plasma triglyceride concentrations than those subjects with lower body obesity. Additionally, the women with lower body obesity had serum triglyceride concentrations within the range of the non-obese controls. Fujioka et al. (25) found that subjects with a high ratio of intrabdominal visceral fat to subcutaneous fat (V/S ratio) had significantly higher concentrations of fasting serum triglycerides and total cholesterol than did subjects with a lower ratio. The V/S ratio significantly correlated with serum triglycerides and total cholesterol.

Van Gaal et al. (7) studied the variation in apolipoprotein concentrations in obese subjects as it relates to upper and lower body fat distribution. The study included 123 obese adults: fifty-nine men and sixty-four pre-menopausal women. The results demonstrated that WHR was a significant indicator for most atherosclerotic lipids and

apoproteins in both men and women. In women, WHR was the most important dependent variable in multiple regression analysis, and body mass index was found to make a non-significant contribution to the variable. Furthermore, in men apolipoprotein B concentration was more closely related to age, while in women apolipoprotein B concentration was more closely associated with WHR. The investigators concluded that abdominal obesity in men and women is characterized by serum lipid and apoprotein concentrations which were more predicative of atherosclerotic disease than were the concentrations of individuals with lower body obesity. Hyperinsulinemia, insulin resistance, and increased free fatty acid turnover were proposed as possible contributors to the increased prevalence of lipid abnormalities found in individuals with abdominal obesity.

Despres et al. (26) studied the relationship of abdominal adipose tissue, serum high density lipoprotein cholesterol, serum triglycerides and obesity. This study was performed on 429 male subjects. The study assessed abdominal adiposity by comparing the skinfold measurements of the trunk to the skinfold measurements of the extremities (T/E ratio). Each subject's BMI was also determined. The study found both T/E ratio and abdominal skinfold to be significantly associated with serum lipids and high density lipoprotein cholesterol (HDL cholesterol). Subcutaneous fat

distribution was also found to have an independent effect on serum triglycerides, total cholesterol and HDL cholesterol. The results of this study led the investigators to conclude that both distribution and amount of subcutaneous fat are important predictors of serum lipid and HDL cholesterol concentrations and that the association between abdominal fat and serum HDL cholesterol is independent of total adiposity.

Abdominal obesity in post-menopausal women

In recent years, some investigators have studied abdominal obesity as it related to aging and post-menopausal status in women. Some studies focused mainly on body fat distribution while others also considered the presence of atherogenic risk factors and disease states. The following are brief summaries of articles concerning these topics.

Shimokata et al. (27) studied the effects of age, sex, and obesity on body fat distribution. Seven hundred seventy-one men and four hundred eight women, aged 17 to 96, were included in the study. Numerous anthropometric measurements were made, including WHR. The results of the study showed a dramatic difference in the distribution of WHR values between men and women. Additionally, the WHR grew progressively larger with each age group. In women the

major increase was observed to occur during middle age (40-54) and old age (55 to 69); in men, the age effect was observed to be almost exclusively isolated to the time between the young (under 40) and middle aged (40-54) years. The authors concluded that a progressive trend toward increasing upper and central body fat deposition can be seen as age increases, and, after menopause, women show an acceleration of this trend.

Tonkelaar et al. (28) also studied the factors which influence both BMI and WHR. This study included both pre- and post-menopausal women (n=452) aged 41-75 years. Post-menopausal women were found to have higher BMI, higher WHR and larger circumferences when compared to the pre-menopausal women. In the post-menopausal women, age was associated with WHR and waist circumference. Finally, more of the post-menopausal women were hypertensive, and those post-menopausal women with diabetes had higher WHR than those without the disease.

In another study, Lanska et al. (29) examined factors influencing the body fat distribution in 52,953 women. The women were all members of TOPS, Inc., a nonprofit weight loss company. The study was performed by sending out questionnaires to all chapters of TOPS. WHR were self-reported by the subjects. The results of the study showed

increased age and higher degrees of obesity to be associated with increased WHR.

A study performed by Soler et al. (30) is among those studies which have examined the metabolic characteristics of post-menopausal women and their implications in disease processes. The women (n=75) were all post-menopausal, between the ages of 55 and 70, and in good health. Measurements including BMI and WHR were taken. Fasting insulin, sex hormone binding globulin, estrone, lipids, and lipoproteins were also determined. The investigators found abdominal adiposity and fasting insulin concentrations to be negatively and significantly associated with plasma HDL cholesterol and apolipoprotein A-1. Abdominal adiposity and fasting insulin concentrations were significantly and positively correlated with triglycerides and apolipoprotein B.

In light of similar findings, Haarbo et al. (24) concluded that elderly women with central fat distribution may be at particularly high risk for cardiovascular disease. Ninety-five post-menopausal women, aged 55 to 75 years, were studied. BMI was determined by the standard method (kg/M^2). Fat distribution was determined by dual photon absorptiometry. Additionally, HDL cholesterol, LDL cholesterol, VLDL, total cholesterol and serum triglycerides

were determined. The results included evidence that as obesity increases, per BMI, central adiposity increases. Furthermore, an increase in the fat distribution ratio was accompanied by an increase in serum cholesterol, triglycerides and LDL cholesterol and a decrease in HDL cholesterol. However, BMI and body weight were not strongly related to total cholesterol and an atherogenic lipid profile. Thus, central adiposity in elderly women was found to be positively related to total cholesterol and a lipid profile predictive of heart disease.

Landin et al. (31) examined the role of obesity in metabolic aberrations associated with abdominal adiposity. The subjects consisted of twenty obese post-menopausal women and twenty lean post-menopausal women. Each group was further divided in half according to the body fat distribution: WHR $\geq$ .80 or WHR $<$ .80. Blood pressure, glucose tolerance, insulin, and plasma lipid concentrations were measured for each subject. The study concluded that obesity itself was more closely associated with the metabolic abnormalities but that increased WHR enhanced the effects of obesity on metabolism. Obese women with abdominal obesity had significantly higher systolic blood pressure than obese women without abdominal obesity. Diastolic blood pressure was significantly higher in both groups of obese women when compared to both groups of lean

women. Finally, obese women with abdominal adiposity had significantly higher triglycerides when compared to the lean women and significantly higher cholesterol concentrations when compared to the obese women with WHR < .80.

The Glycemic-Index

In 1981, Jenkins et al. (32) proposed classifying carbohydrate foods according to the post-prandial blood glucose response the foods created. The investigators began this work in an effort to improve upon the efforts of controlling blood glucose in diabetics with diet therapy. Such factors as food form, dietary fiber, and the nature of the carbohydrate had been shown to have important influence on post-prandial glucose response, yet no allowances for these efforts were made when only available carbohydrate was considered in planning diabetic meal patterns. The results of this early study found great differences in the degree to which various carbohydrate sources raise blood glucose. Additionally, no significant relationship was found between glycemic-index and fiber. Both fat and protein were shown to have a significantly negative correlation with glycemic-index. Jenkins and Wolever concluded that classification of foods in such a manner could be beneficial in helping diabetics achieve tighter glucose control by selecting foods

with a low glycemic-index. They also suggested that such a regimen might help post-gastric surgery patients with hypoglycemia and patients with carbohydrate-induced hyperlipidemia. Thus, from the inception of the glycemic-index, its purpose was to augment current attempts at blood glucose control through the use of diet.

The design or method of classifying foods according to post-prandial glucose response has undergone a significant change since the first attempts at classification. Jenkins et al. (31) originally indexed post-prandial glucose responses of food to the post-prandial response of glucose. The glycemic-index of a food was expressed as its percentage of the response to glucose ingestion. However, white bread soon replaced glucose as the reference food. Glucose was found to create greater variation among subjects, possibly due to delayed gastric emptying caused by higher tonicity of the glucose solution (33). Currently the glycemic-index of a food is defined by the following formula:

$$\frac{\text{incremental blood glucose area after test food}}{\text{corresponding area after equicarbohydrate portion of white bread}} \times 100$$

The values used for this equation are based on two hours of data in normal subjects and three hours of data in diabetic

subjects (34). Fifty grams of carbohydrate is the most commonly used amount for the test and reference foods.

Jenkins et al. (33) identified three major issues which have caused objections to be raised concerning the glycemic-index: (1) large individual variation in responses; (2) lack of agreement among different test centers; (3) lack of difference between mixed meals. These issues, however, are largely the result of inadequate standardization in determining the glycemic-index of a food and failure to interpret the post-prandial glucose response to a food correctly.

Individual variation can often be controlled if the relative glycemic effect of different foods is considered (33). Lack of agreement between centers can be explained by such incidences as using different types of potatoes for determining the value for potatoes or rice that has been processed differently for determining the value for rice. Other factors such as the ripeness of fruit or the gelatinization of starch can also cause the "same" food to create very different glycemic responses.

Gannon and Nuttall (35) identified numerous factors which affect the interpretation of glycemic response and insulin areas. These investigators supported the use of the glycemic-index in meal planning for diabetics, but they emphasized many issues that must be considered in the

determination of the values used in the glycemic-index. Issues specifically related to the interpretation of glycemic response included the duration of time over which data is collected, use of absolute versus incremental areas, and the inclusion or exclusion of negative areas if incremental areas are used.

Lastly, the application of the glycemic-index to a mixed meal has been greatly disputed (34,35). As was the case with other objections, often discrepancies in methodology or interpretation were to blame when the glycemic-index of individual foods were not shown to influence the glycemic-index of the complete meal (33).

Wolever et al. (36) and Chew et al. (37) have demonstrated the glycemic-index's utility in predicting glycemic responses to mixed meals. Wolever et al. examined the effect of mixing carbohydrate foods with different glycemic-indexes in the absence of fat and protein. The observed glycemic-index of the mixed meal was within two percent of the predicted value. The meals used in the study by Chew et al. were of various ethnic origins and contained fat and protein. Significant differences were found among the meals, and the predicted glycemic indices significantly correlated with the observed glycemic responses.

Effects of a low glycemic-index diet on conditions associated with abdominal obesity

Jenkins et al. (37,38) completed studies concerning the effects of a low glycemic-index diet on non-diabetic subjects. One study assessed the effects on six healthy men while an earlier study assessed the effects on twelve hyperlipidemic patients. Both studies found a low glycemic-index diet to have significantly beneficial effects on the parameters examined. The following is a review of these two studies and their results.

The effects of low glycemic-index foods on hyperlipidemia were measured in nine men and three women with hyperlipidemia. The subjects were selected based on a health screening and a history of compliance with the lipid clinic diet. The study was performed over a three month period. During the first and third months, the subjects consumed the lipid clinic diet under close supervision. During the second month, carbohydrates with a low glycemic-index were substituted for more commonly consumed carbohydrates. The glycemic-index of the meals consumed during the second month was approximately twenty percent lower in glycemic-index than the control diets.

The mean of the serum cholesterol and triglyceride results before and after the control periods was almost exactly the same as the concentrations maintained by the

patients throughout the preceding year. However, during the low glycemic-index phase, total serum cholesterol and serum triglycerides fell significantly from the concentrations maintained during the first month and rose again to the same concentrations during the third month. During the low glycemic-index period, serum cholesterol fell by 9 ± 2%, and serum triglycerides were reduced by 16 ± 3%. There was also a mean reduction of LDL cholesterol by 10 ± 4%, but no change was observed in HDL cholesterol concentrations.

Because the low glycemic-index diet represented no significant alteration in fiber or macronutrient content, it was concluded from the above results that a diet composed of carbohydrate foods low in glycemic-index may be beneficial in the dietary treatment of hyperlipidemia. Reduced stimulus of hepatic triglyceride synthesis via the minimizing of elevations in glucose and insulin concentrations was proposed as the mechanism for the observed effect.

In a more recent and more comprehensive study, the effects of low and high glycemic-index diets on the glucose and lipid metabolism of six healthy men were assessed. The six subjects were all within range of their ideal body weights and exhibited normal glucose tolerance. Each subject participated in two, two-week dietary programs in random order. One of the two-week periods consisted of a

diet high in glycemic-index, the other diet being low in glycemic-index.

Several methods of assessing glucose and lipid metabolism were employed. Fasting blood samples were drawn at the beginning of each period and at days 7, 14 and 15. On day 14, an intravenous glucose tolerance test was given to three subjects before breakfast. Capillary blood samples were analyzed by a glucose oxidase method, and venous blood samples were analyzed for glycosylated serum proteins by use of a fructosamine test. Urine C-peptide was measured, and the fractional hepatic extraction of insulin was calculated. Total cholesterol, LDL cholesterol, and triglycerides were also determined.

The results of the study demonstrated significant effects on almost all of the areas examined. Serum fructosamine, the twelve hour blood glucose profile, total serum cholesterol, and twenty-four hour urinary C-peptide concentrations were all significantly reduced. The reduction in C-peptide concentrations and improvement in glucose tolerance suggests a reduction in insulin secretion and improvement in insulin utilization. These results, as well as those of the previous study, suggest that a diet low in glycemic-index may be useful in improving the hyperinsulinemia, insulin resistance, and lipid profiles associated with abdominal obesity.

Determination of pancreatic insulin secretion and short-term glycemic control

The determination of serum C-peptide concentrations has been established as a reliable measure of pancreatic insulin secretion (40-42). Evaluation of beta-cell function by radioimmunoassay of C-peptide provides two advantages: first, it remains accurate in insulin-treated patients in whom the presence of insulin antibodies interferes with an insulin radioimmunoassay; second, it measures only endogenous secretions of the pancreas. Comparing C-peptide concentrations to the results of an insulin radioimmunoassay in non-diabetic subjects can indicate the hepatic insulin extraction as well.

The degree of nonenzymatic glycosylation of serum proteins has been used to assess the duration of hyperglycemia over time. Specifically, glycosylated hemoglobin has been found to be especially indicative of long-term glycemic control due to hemoglobin's extended half-life (43-45). However, glycosylation of serum proteins with half-lives shorter than that of hemoglobin have been shown to reflect changes in glycemic control after as little as one week (44).

A simplified and accurate method for determining concentrations of glycosylated protein has been developed. This method utilizes the protein's ketoamine ability to

reduce nitroblue tetrazolium. The assay has been termed the "fructosamine assay" (46). This method of determining glycosylated serum proteins can be performed by the use of simple colorimetry and requires the addition of only one reagent. Because of the sensitivity of this assay to short-term changes in glycemia and the relative simplicity of performing the procedure, serum fructosamine has been recommended for use in determining short-term changes in glycemia (45).

CHAPTER III

EXPERIMENTAL PROCEDURES

Subject recruitment and screening

During the last two weeks of September, 1990, advertisements regarding the present study were placed in the Texas Woman's University paper and in the Denton newspaper. Additionally, flyers were posted in grocery stores in Denton, Texas and in TWU faculty mail boxes. Respondents were screened by telephone regarding weight, height and the time since last menses. Those respondents that were identified as obese and post-menopausal were scheduled for further screening which occurred September 27 through October 2, 1990. During this screening, the potential subjects' weight and height were measured. Weight was measured with a beam balance scale. The potential subjects were weighed in street clothes, without shoes. Each potential subject, without shoes, then stood on a platform with a measuring board attached to it. The board was brought to rest on the top of each respondent's head and the height was measured. Waist and hip measurements were made using a flexible measuring tape. Waist measurements

were made between the last rib and the iliac crest, above the umbilicus. Hip circumference was measured at the greatest girth of the hip area. At this same screening session, respondents were also asked to fill out a health questionnaire (Appendix A). Possible risks and benefits of the study were reviewed orally, and written consent was obtained from each respondent.

Subjects

After the completion of the screening sessions, twenty-four subjects meeting the inclusion requirements were selected for the study. Inclusion requirements are listed in Table 1. The subjects were divided into two groups: one group was to follow a high glycemic-index diet, the other group was to follow a low glycemic-index diet. Each subject was assigned to her group in an attempt to match the groups according to BMI and medication use. Two subjects were allowed to change groups based on food preferences. Seven of the subjects either never began the study or withdrew from the study by the end of the first week. Three of these subjects withdrew because of medical problems unrelated to the study. Two subjects were excluded from the study after

TABLE 1

Inclusion Criteria

Caucasian female
Waist to hip ratio (WHR) > .80
Body mass index (BMI) > 27 kg/M^2
Post-menopausal
No personal history of diabetes mellitus
In generally good health

one week because of abnormal glucose tolerance tests. One subject's data was excluded from the data analyses because she failed to maintain her weight within plus or minus two pounds during the first week of the study. The characteristics of those subjects who completed the study are shown in Table 2.

Experimental design

The experiment was approved by the Human Subjects' Review Committee of Texas Woman's University. The study period spanned approximately two weeks, from October 8, 1990 to October 23, 1990. During the two week period, the subjects followed either a high or a low glycemic-index diet containing calories for weight maintenance.

Prior to beginning the diet and immediately following the end of the diet, the subjects underwent a 75 gram, oral glucose tolerance test (OGTT) at the Student Health Services at TWU. Fasting venous blood samples were taken from all subjects. The subjects' body composition was determined using bioelectrical impedance analysis (RJL Systems). The calculation of the subjects' maintenance calorie needs was based on the results of these analyses.

TABLE 2

Subject Characteristics (mean ± SD)

	Group A (High Glycemic-Index Diet)	Group B (Low Glycemic-Index Diet)
Weight	87.1 ± 10.9	88.4 ± 16.4
WHR	.91 ± .05	.87 ± .05
BMI	33.4 ± 4.1	33.7 ± 5.1
Age	62.9 ± 8.1	60.0 ± 6.3

The subjects were provided with the appropriate breakfast following the completion of the OGTT. During the first series of testing, the subjects were also provided with a sack lunch. The subjects were instructed concerning how to follow the diets and the importance of keeping accurate food records. Questions were also answered concerning appropriate products to be purchased for following the diet, i.e., whole wheat bread, sugar free peanut butter, etc.

The subjects met with the author one week into the study period to be weighed and to participate in a brief behavior modification program regarding taking control of eating behaviors. If a subject's weight had changed ± two pounds, the calorie concentrations was adjusted appropriately. The subjects' weight was taken again at the end of the study. A time line summarizing both the pre-study and study events is presented in Table 3.

Sample collection and analyses

The subjects were instructed to fast, with the exception of water, after the evening meal prior to sample collection. A fasting blood sample was drawn and was analyzed for serum insulin, serum connecting peptide (C-peptide), serum glucose, LDL cholesterol concentrations

TABLE 3

Time Line for Study

Pre-study	
Week 1	Subject recruitment began.
Week 2	Research committee met to design study diets.
Week 3	Subjects were screened and selected.
Study	
Week initial	All subjects underwent an oral glucose tolerance test. Fasting samples were drawn for C-peptide, insulin, LDL cholesterol and glucose analyses. Diets were individualized for each subject's calorie needs. Diet instructions were given; subjects began diets.
Week 1	Subjects met with investigators to review diet records, weigh in, and ask questions. Subjects participated in a behavior modification class.
Week 2	Subjects completed the last week of the isocaloric diets. Biochemical and bioelectrical impedance analyses were repeated. Post study weights were measured.

Each subject then ingested 75 grams of glucose. Blood samples were drawn at 30, 60, 90, and 120 minutes. These samples were analyzed to determine serum insulin and serum glucose concentrations. Additionally, one of the five samples from each subject was analyzed for serum fructosamine concentration. The LDL cholesterol and serum glucose analysis were performed at Medical Laboratories in Denton, Texas. All other analyses were performed by the author with technical assistance from Chuck Zammutt (Diagnostic Products Corporation) and Steve Barrett (Rouche Diagnostic Systems).

Serum glucose concentrations were determined using the Paramax Analytical Systems glucose reagent (Baxter Healthcare Corporation). This particular method is a modification of the coupled enzymatic method of Slein (47). LDL cholesterol was determined using the Lipid Analyst® bench top chemistry system (Dupont, Wilmington, DE).

For serum C-peptide, serum insulin, and serum fructosamine determination, serum was collected with disposable pipettes after whole blood samples had undergone refrigerated centrifugation, at 4700 RPM, for fifteen minutes. The serum samples were stored in disposable, plastic cuvettes at -20°C for no more than three weeks prior to analysis. Serum C-peptide was determined by analyzing fasting serum samples with C-Peptide Double Antibody

Radioimmunoassay (DPC, Los Angeles, CA). Serum insulin concentrations were determined using Coat-A-Count Insulin Radioimmunoassay (DPC, Los Angeles, CA). Serum insulin was determined in all five samples from each subject. These analyses were performed at the Allied Laboratories in Hurst, Texas by the author and Chuck Zamutt. Samples were diluted for analysis using the DPC Delta Robotic Sampler/Diluter; the assays were performed using the Genesy Gamma Counter 7000.

Serum fructosamine analysis was performed using one of the five samples from each subject. For this analysis, the ROTAG Fructosamine Glycated Protein Assay was performed using the Cobas Fara (Rouche Diagnostic Systems, Nutley, NJ). was used for the analysis. A specific sample of the five samples was not indicated since glucose values up to 1400 mg/dl do not interfere with testing. This analysis was performed by the author and Steve Barrett.

Diets

The subjects were on either a high or low glycemic-index diet, designed for weight maintenance, for two weeks. The diets consisted of a seven day menu cycle. The day one menu for the 1500 calorie, high glycemic-index diet is presented in Table 4; the day one menu for the 1500 calorie,

TABLE 4[a]

Sample Menu for High Glycemic-index Diet

Calories	1477 Kc
Carbohydrate	226.8 Gm
Protein	74.01 Gm
Fat	39.68 Gm
Cholesterol	33.51 Mg
Dietary Fiber	41.19 Gm

Meal Pattern	Food Name	Serving
Breakfast	Milk-nonfat-fluid	1.0 Cup
	Bananas-raw-peeled	0.5 Item
	Margarine-diet-Mazola	1.5 TBSPS
	Bread-whole wheat-soft	2.0 Slices
	Cereal-wheat-shred-biscuit	2.0 Ounces
Lunch	Jam/preserve-straw-low cal	2.0 TSPS
	Jam/preserve-straw-low-cal	1.0 TSP
	Peanut Butter-old fashion	1.0 TBSP
	Bread-whole wheat-soft	2.0 Slices
Dinner	Broccoli-froz-boil-drain	2.0 Cups
	Ham-can-extra lean-4% fat	3.0 Ounces
	Margarine-diet-Mazola	2.0 TBSPS
	Milk-nonfat-fluid	1.0 Cup
	Potato-baked-peel after	1.0 Item
	Corn-froz-boil-kernels	0.5 Cup
Snack	Raisins-seedless	2.0 TBSPS

[a]Diets were analyzed using Nutritionist III, Version 4.5, Computing Analytic Software, Salem, Oregon.

TABLE 5[a]

Sample Menu for Low Glycemic-index Diet

Calories	1505 Kc
Carbohydrate	213.1 Gm
Protein	84.95 Gm
Fat	39.77 Gm
Cholesterol	80.19 Mg
Dietary Fiber	30.80 Gm

Meal Pattern	Food Name	Serving
Breakfast	Milk-nonfat-fluid	1.0 Cup
	Grapefruit-raw-pink & red	0.5 Item
	Bread-pumpernickel	2.0 Slices
	Margarine-diet-Mazola	1.5 TBSPS
	Cereal-oatmeal-cooked	1.0 Cup
Lunch	Peanut Butter-old fashion	1.0 TBSP
	Bread-pumpernickel	1.0 Slice
	Bread-pumpernickel	1.0 Slice
	Jam/preserve-straw-low cal	1.0 TBSP
Dinner	Vegetable oil-olive	1.0 TSP
	Milk-nonfat-fluid	1.0 Cup
	Garlic-raw-clove	1.0 Item
	Margarine-diet-Mazola	1.0 TBSP
	Macaroni-cooked-tender-hot	1.5 Cups
	Chick-breast-no skin-roast	3.0 Ounces
	Lemon Juice-raw	1.0 TBSP
	Broccoli-froz-boil-drain	2.0 Cups
Snack	Apple juice-canned/bottled	0.5 Cup

[a]Diets were analyzed using Nutritionist III, Version 4.5, Computing Analytic Software, Salem, Oregon.

low glycemic-index diet is presented in Table 5. The diets provided an average of at least 75% of the RDA for all micronutrients, excluding zinc.

The appropriate calorie level for each subject was determined based on the results of bioelectric impedance analysis (RJL Systems). Twelve hundred calorie diets were planned as a basis for the diets used during the present study. The diets were planned using the exchange system (48). The majority of the foods included in the meal plans had previously determined glycemic-index values (49). When a food without a pre-determined glycemic-index value was used, it was included in both diets in equivalent amounts. The average meal glycemic-index for the high glycemic-index diet was 89.63; the average meal glycemic-index for the low glycemic-index diet was 59.07. The glycemic-index for each meal was calculated according to the method described by Wolever (48). The 1200 calorie diets were modified to meet each subject's needs by adding the appropriate amount of calories. These modifications contained the same percentage of calories from carbohydrate, protein, and fat as the original 1200 calorie diets contained. All of the meal plans, regardless of caloric content, contained an average of 57% of calories from carbohydrate, 23% from fat, and 20% from protein, and contained 18 grams of dietary fiber/1000 calories. The subjects received a seven day menu and food

diary and recipes for combination dishes included in the meal plans (Appendix B). The subjects' compliance to the diet was calculated by comparing the food diaries to the diets and was expressed as the percentage of the foods on the meal plan which were eaten each day.

Statistical analysis

Analysis of variance and covariance was used to determine if a difference existed between trials and if a difference existed between trials by group for the following dependent variables: fasting insulin, fasting glucose, fasting glucose, C-peptide, area under the curve insulin (AUC insulin), area under the curve glucose (AUC glucose), fructosamine, LDL cholesterol, and weight. Area under the curve was calculated using the following equation (50): fasting value/2 + 30 minute value + 60 minute value + 90 minute value + 120 minute value/2.

CHAPTER IV

RESULTS

Results of biochemical analyses

All fourteen subjects had normal glucose tolerance tests. The mean serum fasting glucose, the mean serum C-peptide, the mean serum fructosamine, and the mean serum fasting insulin were also all within normal limits for both groups prior to beginning the study.

In Figure 1, ten of the subjects' pre-diet insulin responses to oral glucose tolerance tests were compared to the population normals published by Kraft (51) (Table 6). Three subjects had missing insulin values and therefore could not be used in this comparison. One subject's values were elevated above the range of the assay. BMDPAM - Description and Estimation of Missing Data (BMDP Statistical Software, Inc.) was used to determine missing values used for the subjects' for use in determining group means.

The mean LDL cholesterol concentrations were elevated in both groups (Table 7). After the two week study period,

FIGURE 1

Subjects' Pre-study Insulin Responses to OGTT
Compared to Kraft's Population Means

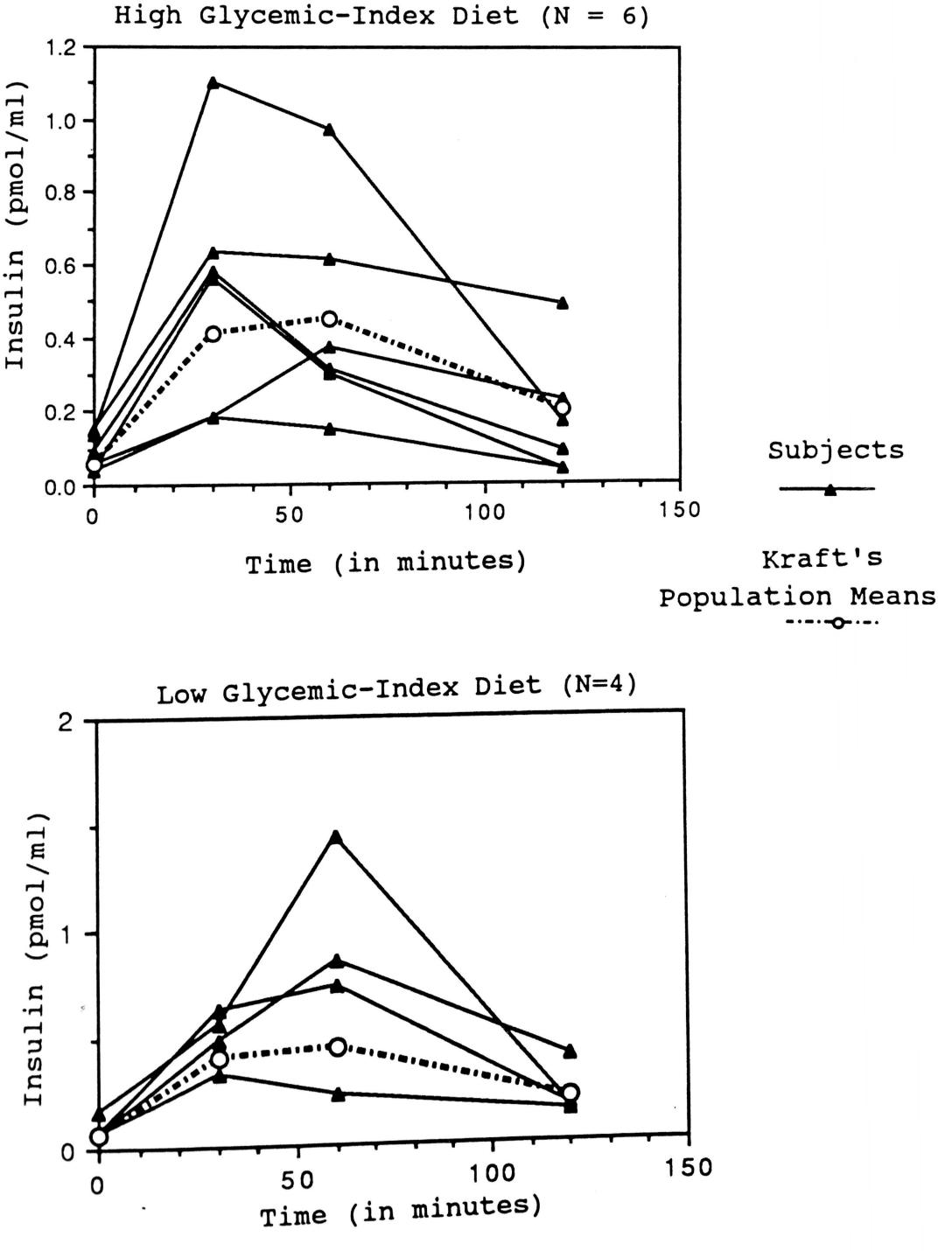

TABLE 6

Mean Normal Insulin Values (N=1889)

Fasting	.055 (pmol/ml)
½ hour	.411 (pmol/ml)
1 hour	.447 (pmol/ml)
2 hour	.199 (pmol/ml)

LDL cholesterol concentrations were reduced significantly. The difference in the reduction between diets was not significant, however. Likewise, serum C-peptide (Table 7) and fructosamine concentrations (Table 8) fell significantly, but the difference between diets was not significant. In Figure 2 and Figure 3, the subjects' pre- and post-study insulin and glucose curves were graphed; the differences between trials and diets were not significant. No other pre/post study differences were significant between trials or between diets (Table 9).

Subjects' compliance with the diets

The subjects' average percent compliance during the two week study are listed on Table 10. Each subject's compliance was > 90%; this level of compliance was considered acceptable for the purpose of this study.

TABLE 7 (N=14)

Fasting Values (±SD)

	Diet I (High GI)			Diet II (Low GI)		
	Pre	Post	%Change	Pre	Post	%Change
LDL* (mmol/L)	4.5 (±1.345)	4.0 (±1.279)	-12%	4.0 (±1.335)	3.4 (±1.270)	-15%
Insulin (pmol/L)	.08 (±.05146)	.08 (±.02736)	0%	.11 (±.05478)	.09 (±.03118)	-18.2%
Glucose (mmol/L)	5.38 (±.70759)	5.38 (±.62758)	0%	6.0 (±.94285)	5.42 (±.71070)	-3.2%
C-peptide (pmol/L)	.99 (±.33507)	.89 (±.25054)	-10.2%	1.17 (±.29483)	1.01 (±.23426)	-13.7%

*Low density lipoprotein cholesterol

TABLE 8 (N=14)

Glucose Tolerance Measures

	Diet I (High GI)			Diet II (Low GI)		
	Pre	Post	%Change	Pre	Post	%Change
AUC* Insulin	1.5 (±.86608)	1.5 (±.35441)	0%	3.5 (±2.5544)	3.5 (±2.4756)	0%
AUC Glucose	25.8 (±6.0132)	27.9 (±6.0721)	+8%	30.9 (±7.7976)	28.4 (±4.9898)	-8.1%
Fructosamine (mmol/L)	2.5 (±.07559)	2.4 (±.12150)	-4%	2.5 (±.19024)	2.4 (±.18898)	-4%

*Area under the curve

FIGURE 2

Pre- and Post-Study Insulin Curves

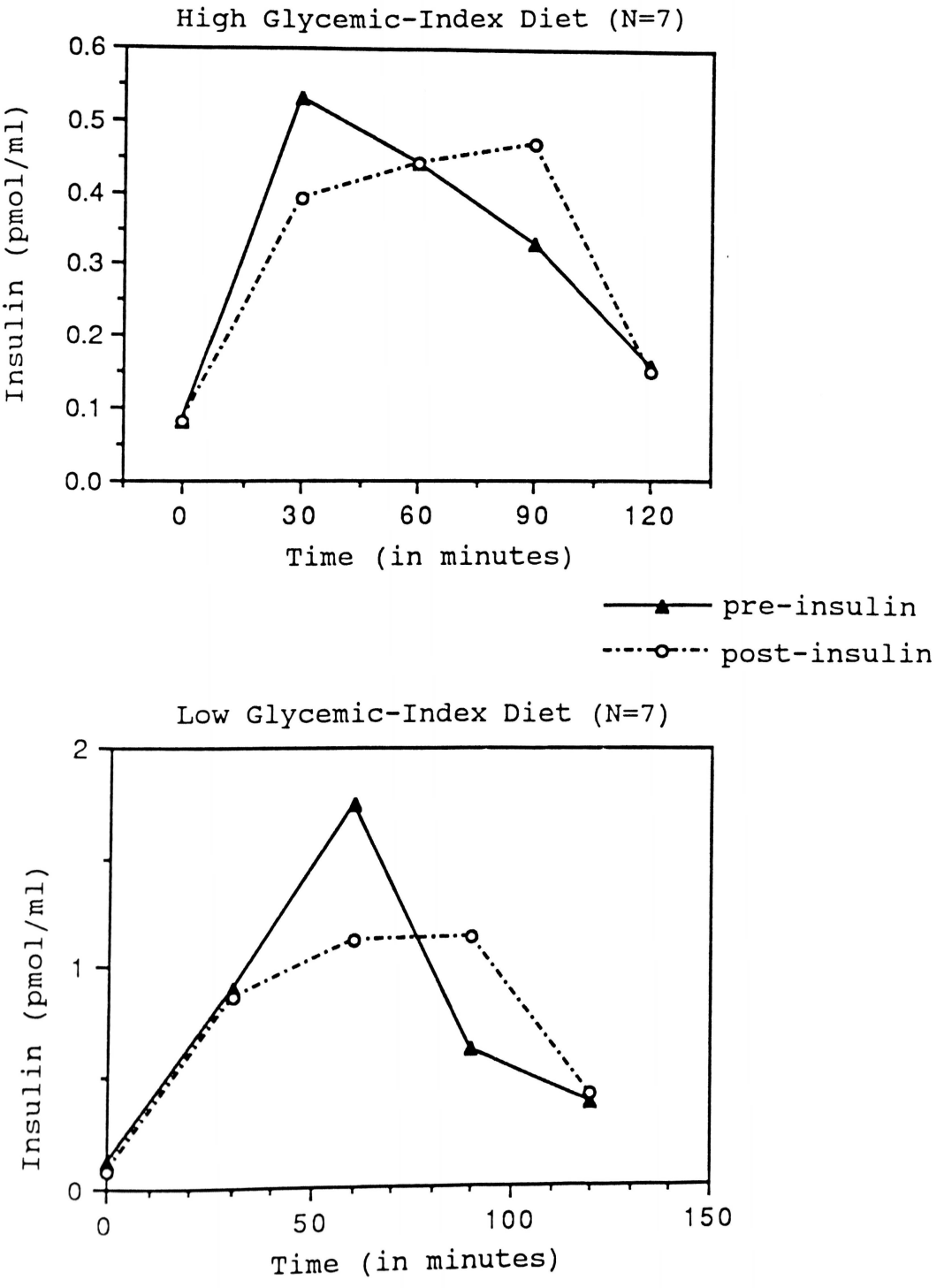

FIGURE 3

Pre- and Post-Study Glucose Curves

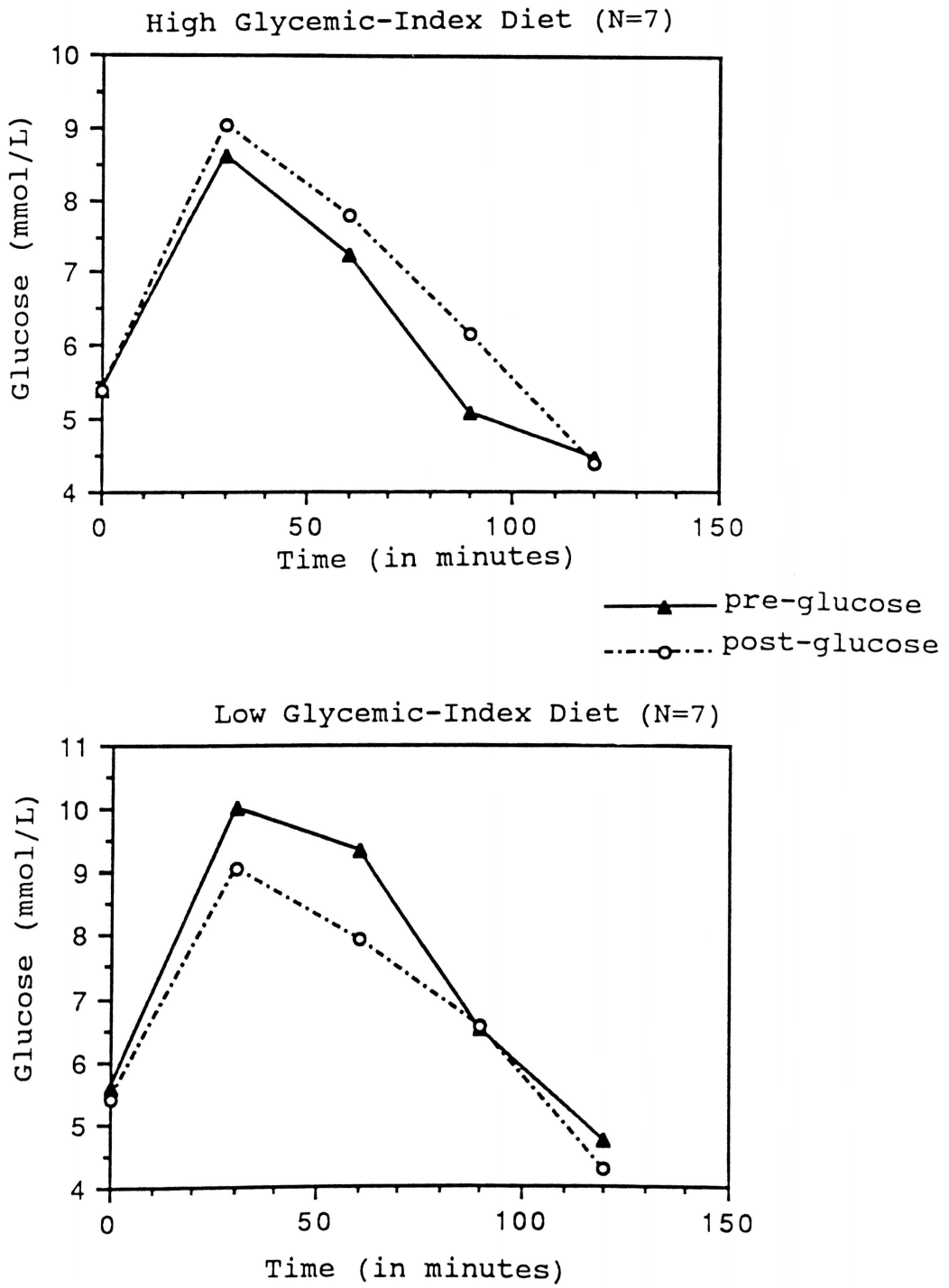

TABLE 9 (N=14)

Analysis of Variance and Covariance with Repeated Measures

Fasting Insulin

Source	DF	SS	F	P
Trials	1	0.00111	1.19	0.2959
Trials by group	1	0.00073	0.78	0.3931
Error	12	0.01111		

Fasting Glucose

Source	DF	SS	F	P
Trials	1	5609.77013	.38	.55
Trials by group	1	5609.76322	.38	.55
Error	12	77982.60386		

C-Peptide

Source	DF	SS	F	P
Trials	1	.12403	8.03	.0151
Trials by group	1	.00611	.40	.5410
Error	12	.18530		

*AUC Insulin

Source	DF	SS	F	P
Trials	1	588.47470	0.05	.8260
Trials by group	1	341.79412	0.03	.8669
Error	12	139902.44584		

TABLE 9 (continued)

*AUC Glucose

Source	DF	SS	F	P
Trials	1	114.00893	1	.8493
Trials by group	1	12201.43750	1	.0677
Error	12	36306.17857	12	

Fructosamine

Source	DF	SS	F	P
Trials	1	.05143	5.47	0.0375
Trials by group	1	.00571	.61	0.4508
Error	12	.11286		

**LDL

Source	DF	SS	F	P
Trials	1	2860.32143	15.25	.0021
Trials by group	1	10.32143	.06	.8185
Error	12	187.57143		

Weight

Source	DF	SS	F	P
Trials	1	9.67392	.92	.3570
Trials by group	1	.74279	.07	.7952
Error	12	126.51631		

*Area under the curve
**Low density lipoprotein cholesterol

TABLE 10

Subject's Compliance to Diets

Subject No.	% Compliance
High Glycemic-index Diet	
2	94.3
10	99.4
14	91.9
17	97.2
18	92.1
19	100
20	100
Low Glycemic-index Diet	
4	95.1
7	93.1
8	91.4
9	95.2
11	97.5
16	92.2
21	98.2

CHAPTER V

DISCUSSION AND CONCLUSION

At the completion of this study, all subjects, regardless of diet, had significant reductions from pre-study concentrations in LDL cholesterol, serum fructosamine, and serum C-peptide. The reduction in LDL cholesterol is not surprising given the extremely low percentage of calories provided by fat and saturated fat in both diets. The decrease in serum fructosamine indicates that serum glucose concentrations were maintained at lower concentrations than those maintained prior to the study thereby decreasing the amount of glycosylated serum proteins. This decrease in serum fructosamine may simply be a function of the minimum amount of simple sugars consumed during the study period. The reduction in serum C-peptide, which reflects a decrease in pancreatic insulin secretion, could also be reflective of the subjects' low intake of simple sugars. However, some investigators also suggested that the high fiber content of the diets was an important factor in the reduction of the aforementioned biochemical parameters (52,53).

There was not a significant reduction in fasting insulin in either group. This result is puzzling in light of the significant reduction in C-peptide secretion. Jenkins et al. (38) in their study of the effects of a low glycemic-index diet on normal weight men, had similar findings. These authors proposed that, for an unknown reason, hepatic extraction of insulin fell while the subjects were on the low glycemic-index diet. The results of this present study seem to support that observation.

Failure to produce a significant change in AUC insulin during OGTT may also be a function of hepatic insulin extraction. Vansant et al. (11) proposed that the increased number of abdominal adipocytes seen in the abdominally obese exposes the liver to increased concentrations of free fatty acids. Vansant et al. (11) further hypothesized that when the liver was exposed to free fatty acids, the hepatic extraction of insulin was decreased. Because the diets in the present study were designed for weight maintenance, the size of the abdominal adipocytes was not effected. Thus, the liver's exposure to free fatty acids was likely not decreased. Maintenance of the abdominal adipocytes may have prevented an increase in hepatic insulin extraction.

Glucose tolerance, as determined by fasting glucose and OGTT, did not improve significantly. These findings are consistent with the results of the fasting insulin and AUC

insulin analyses. Depres et al. (17) found deep abdominal fat to be positively correlated with AUC glucose and serum C-peptide concentrations. The highly lipolytic activity and insulin resistance of those abdominal adipocytes were named as important factors in the observed correlation. Again, maintenance of the subjects' abdominal adipocytes in the present study may have prevented improvement in these parameters.

In two previous studies, Jenkins et al. (37,38) demonstrated beneficial effects of a low glycemic-index diet on both lipid and carbohydrate metabolism. In this study, no significant difference between diets was seen. However, there were many differences in design and subject populations among this study and the studies by Jenkins et al. (37,38).

First, the subjects studied previously had normal glucose tolerance and were not obese. The fourteen women included in this study were abdominally obese and seven subjects had elevated insulin responses to an OGGT. The low glycemic-index diet alone may not be as effective in abdominally obese subjects. The results of this study indicated that while pancreatic secretion of insulin was reduced (in both groups), post-hepatic or total insulin concentrations were not. Thus, these subjects may require reduction of abdominal adipocytes (weight loss) in order to

increase hepatic insulin extraction via a reduction in hepatic exposure to free fatty acids. Such weight loss may be required before this population would be sensitive to changes in the glycemic-index of their diets.

Second, the degree of control exerted over the subjects' and their intake varied among studies. Subjects in previous studies either had been on a regimented diet for some time prior to the study (38) or had their meals provided to them during the study (39). Because the method of preparation of a food can alter its glycemic index (49), failure to prepare foods as directed could alter the glycemic-index value of a meal. It is possible that since these subjects purchased and prepared their own foods, the glycemic-index values of the diets were altered and the intended differences between diets were not achieved.

Finally, subject number must be considered. At the conclusion of the study, seven subjects per diet remained. This translates into less than two subjects per dependent variable. It has been recommended that a study include a minimum of four subjects per dependent variable in order to protect against Type II errors (54). Therefore, it is possible that the differences between diets did not reach significance because of the number of metabolic parameters studied in a relatively small sample and that a Type II error was made.

In conclusion, the results of this study point to a need for further research regarding the role of diet therapy in the treatment of abdominal obesity. Future studies that include a larger sample and exert more control over that sample could possibly identify beneficial effects of a low glycemic-index diet on this population. The effect of long term, significant weight loss in combination with changes in the glycemic-index of dietary intake should be investigated, as well.

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APPENDIX A

SUBJECT QUESTIONNAIRE

WEIGHT LOSS STUDY
FALL 1990

Complete this questionnaire if you want to be considered as a participant in the weight loss study.

Name: _____ Code #:_____

Address: _____

Telephone: Day_____ Evening_____

Social Security #: _____ Date of Birth: _____

OCCUPATION: (Select one most appropriate answer)

1. Professional ____
2. Manager or Administrator ____
3. Sales Worker ____
4. Clerical ____
5. Craftsman ____
6. Operator or Laborer ____
7. Service Worker ____
8. Self-employed ____
9. Not employed ____
10. Homemaker ____
11. Student ____
12. Retired ____
13. Other ____

POSITION OR TITLE_____

Have you had or do you have any of the following:

	YES	NO	DO NOT KNOW	IF YES WHEN OR ONSET
1. High Blood Pressure	___	___	____	_____
2. Heart Attack or	___	___	____	_____
Coronary within:	___	___	____	_____
0-1 yr___,1-2 yrs___,	___	___	____	_____
2-5 yrs___, or over	___	___	____	_____
5 yrs___	___	___	____	_____
Comments:_____				
3. Chest Pain or discomfort	___	___	____	_____

Comments: _____

	YES	NO	DO NOT KNOW	IF YES WHEN OR ONSET
4. Shortness of Breath				
1) with exertion	___	___	___	_____
2) while sitting still	___	___	___	_____
3) when lying down	___	___	___	_____
Comments: _____				
5. Asthma	___	___	___	_____
Comments: _____				
6. Bronchitis	___	___	___	_____
Comments: _____				
7. Emphysema	___	___	___	_____
Comments: _____				
8. Daily Cough or Raising Phlegm: persisting 3 Months or longer	___	___	___	_____
Comments: _____				
9. Anemia	___	___	___	_____
Comments: _____				
10. Abnormal Bleeding or Clotting Time	___	___	___	_____
Comments: _____				
11. High Cholesterol (value, if known_____)	___	___	___	_____
Comments: _____				
12. High Triglycerides or Blood Fats: (value, if known_____)	___	___	___	_____
Comments: _____				
13. Diabetes	___	___	___	_____
Comments: _____				
14. High Blood Sugar	___	___	___	_____
Comments: _____				
15. Low Blood Sugar	___	___	___	_____

Comments:_____

	YES	NO	DO NOT KNOW	IF YES WHEN OR ONSET
16. Thyroid Trouble	___	___	___	_____
Comments:_____				
17. Stroke	___	___	___	_____
Comments:_____				
18. Dizziness	___	___	___	_____
Comments:_____				
19. Double Vision or Blurred Vision	___	___	___	_____
Comments:_____				
20. Fainting	___	___	___	_____
Comments:_____				
21. Epilepsy, Seizures or Convulsions	___	___	___	_____
Comments:_____				
22. Frequently or chronically depressed or anxious	___	___	___	_____
Comments:_____				
23. Hospitalized for a Nervous Disorder	___	___	___	_____
Comments:_____				
24. Psychiatric or Psychological Consultation	___	___	___	_____
Comments:_____				
25. Stomach Trouble such as heartburn, indigestion, pain, fatty food intolerance	___	___	___	_____
Comments:_____				
26. Cirrhosis	___	___	___	_____
Comments:_____				
27. Constipation, Diarrhea				

blood in stool, hemorrhoids or colitis ___ ___ ____ _____
Comments:_____

	YES	NO	DO NOT KNOW	IF YES WHEN OR ONSET
28. Any Kidney Problem such as stones, blood in urine, burning, infection, etc.	___	___	____	_____
Comments:_____				
29. Hearing Problem	___	___	____	_____
Comments:_____				
30. Any Kind of Cancer (specify:_____ _____)	___	___	____	_____
31. Allergies: Hay fever, Skin, Other(_____) (Reactions_____ _____)	___	___	____	_____
Comments:_____				
32. Food intolerance	___	___	____	_____
Comments:_____				

33. Do you have any other medical problems no previously mentioned? Yes_____ No_____

34. What prescribed or self-described medications are you taking now? (include oral contraceptive and dietary supplements)

MEDICATIONS	DOSAGE	FREQUENCY/DAY	WHEN STARTED
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____

35. When did you last menstruate? Year_____

36. FAMILIAL DISEASES: Have your parents, grandparents, sisters or brothers, aunts or uncles, or you children developed any of the following? Exclude cousins, relatives by marriage or adoption, and half relatives. (Please check appropriate responses and write on corresponding lines.)

YES	NO		FAMILY RELATION	AGE OF ONSET	HEALTH NOW
___	___	Heart attacks under age 50	_____	_____	_____
___	___	Heart attacks between 50 and 70	_____	_____	_____
___	___	Heart attacks at 70 or over	_____	_____	_____
___	___	Strokes under age 50	_____	_____	_____
___	___	High blood pressure	_____	_____	_____
___	___	Elevated cholesterol	_____	_____	_____
___	___	Diabetes	_____	_____	_____
___	___	Obesity (20 or more lbs. overweight)	_____	_____	_____

38. Do you currently smoke? Yes_____ No_____
(If no, go to question 39)
a. How often?_____
b. When did you start?_____

39. WEIGHT & HEIGHT
What do you consider a good weight for yourself?_____

What is the most you have ever weighed (including when pregnant?_____lbs. At what age?_____

WEIGHT: Now____lbs. One year ago:____lbs. At age 21_____
HEIGHT: _____inches

40. Number of meals you usually eat per day:_____

41. Do you ever drink alcoholic beverages? Yes___ No ___
If yes, how many drinks per week?

Beer (12 oz.) _____
Wine (3 oz. glass _____
Hard liquor (2 oz.) _____

42. Did you engage in any of the flowing physical activities in the last month?

YES	NO	
___	___	Walk, run, jog - miles per workout____; time per mile_____(min.); _____(sec.) number of workouts per week _____.
___	___	Stationary running - steps per min._____; average duration of workout_____(min.); number of workouts per week_____.
___	___	Bicycling (outdoors) - miles per workout_____; average duration of workout____(min.); number of workouts per week_____.
___	___	Stationary cycling - bike load (.5 to 4.5)___; or average heart rate_____; you weight in lbs. _____; average duration of workout____(min.); number of workouts per week_____.
___	___	Treadmill - speed in mph___; per elevation___; time walked on treadmill____(min.); number of workouts per week_____.
___	___	Swimming - yards swum per workout____; average duration of workout_____(min.); number of workouts per week_____.
___	___	Golf (walking) - number of holes per week____.
___	___	Calisthenics or weight lifting - average duration of workout____; number of workouts per week_____

43. What activities are included in your exercise program that have not been listed in the preceding questions? Please specify event, time of year (if seasonal), duration and miles per workout (if applicable), and number of workouts per week.

_____

_____

_____

_____

44. Briefly state why you are interested in participating in this research study.

APPENDIX B

SAMPLE FOOD DIARY
(1500 calories)

Meal plan		Food Diary	
Breakfast:		Description	Activity
1 cup	oatmeal		
1 cup	skim milk		
1 half	grapefruit		
2	slices pumpernickel		
1½	Tbsp diet margarine		
Lunch:			
1	Tbsp Natural peanut butter		
1	Tbsp Estee Jelly		
2	Slices pumpernickel		
Dinner:			
*Pasta Shells with Chicken and Broccoli			
1 cup	Skim milk		
Snack:			
½ cup	Apple Juice		

*Refer to recipe

APPENDIX C

REFERENCE VALUES*
(conversion factor)

INSULIN (x .007241)	2 to 25 uU/mL 0.014482 to 0.181025 pmol/ml
C-PEPTIDE (x. 331)	1 to 4 ng/mL 0.331 to 1.324 pmol/ml
GLUCOSE (÷ 18.014)	70 to 108 mg/dL 3.886 to 5.995 mmol/L
FRUCTOSAMINE	1.5 to 2.7 mmol/L
LDL (÷ 38.66976)	< 130 mg/dl < 3.3618

* All reference values taken from the protocols for each analysis.