GLYCEMIC RESPONSE TO A PEANUT BUTTER AND CRACKER SNACK IN NONINSULIN DEPENDENT DIABETICS AND NONDIABETICS

BY

A. ELIZABETH GLYNN, R.D., C.D.E.

Thesis submitted to the Faculty of the

Virginia Polytechnic Institute and State University

in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

in

Human Nutrition and Foods

Approved:

M. A. Novascone

M. A. Novascone, Chair

L. J. Taper

L. J. Taper

F. Gwazdauskas

F. Gwazdauskas

May, 1993

GLYCEMIC RESPONSE TO PEANUT BUTTER AND CRACKER SNACKS IN NONINSULIN DEPENDENT DIABETICS

(ABSTRACT)

The purpose of this study was to observe and compare the blood glucose response of individuals with documented noninsulin dependent diabetes (NIDDM) and controls after they consumed a peanut butter and cracker snack product (Austin "Toasty" crackers). Twenty-one subjects with NIDDM (15 with current NIDDM and 6 with previously abnormal glucose tolerance [PrevAGT]) and 11 controls participated. Height, weight, body mass index (BMI) and age of subjects were recorded and statistically compared. Subjects tested their own blood glucose using the One Touch II glucometer, and participated on two separate occasions which were designated session 1 and session 2.

Blood glucose was measured before eating the test food, every 15 ($\pm$3) minutes for two hours after eating, and at 150 and 180 minutes. Mean peak blood glucose value and the time at which glucose peaked were identified and compared among the groups. Repeated measures ANOVA was used to compare blood glucose response curves of the NIDDM group, the control group, and the PrevAGT group; slope of the line after the peak was of interest. The null hypothesis was that the groups would not differ in their blood glucose responses.

The mean weight and mean BMI of the subjects in the PrevAGT group were between those of the diabetic subjects and the control subjects. Subjects with NIDDM were significantly heavier ($p<0.01$), had significantly higher BMI ($p<0.02$), and were significantly older ($p<0.01$) than control subjects. Subjects with NIDDM were significantly heavier than subjects in the PrevAGT group ($p<0.05$). No statistically

significant differences in characteristics were found between the control group and the PrevAGT group.

Repeated measures ANOVA analyses were performed to verify that no within-group differences existed between session one and session two. Since no such differences in blood glucose responses were found within each group, data from session one and session two were combined for analysis of the blood glucose response curves of the three groups. These curves were compared with the repeated measures ANOVA procedure.

The largest differences in peak values of glucose were seen between the NIDDM and the control groups ($p<0.001$). Mean blood glucose for the PrevAGT group was between those for the NIDDM and control groups, and differed significantly ($p<0.01$) from the value obtained for the NIDDM group. No statistical difference was found between the PrevAGT group and the control group with respect to the mean blood glucose at the peak. However, the mean times at which blood glucose peaked were statistically different (45 vs. 30 minutes, $p<0.005$) for these two groups. The mean time at which the blood glucose of the NIDDM group peaked also was significantly different from the mean time at which the blood glucose of the control group peaked (60 vs. 30 minutes, $p<0.001$).

Comparison of the diabetic with the control group using repeated measures ANOVA showed that an overall time by group effect was present ($p<0.001$). This finding supports the alternative hypothesis that blood glucose response was different between these two groups. Overall time by group effect was not found between the NIDDM group and the PrevAGT group or between the control group and the PrevAGT group.

ACKNOWLEDGEMENTS

> Undoubtedly we have no questions to ask which are unanswerable. We must trust the perfection of the creation so far as to believe that whatever curiosity the order of things has awakened in our minds, the order of things can satisfy.
>
> Ralph Waldo Emerson, Nature, 1836

I would like to acknowledge my parents, Billee and Irving Buckland for creating a home in which curiosity was fostered. "Let's look it up....." was frequently heard during my childhood. Also, my father provided crucial word processing assistance in the eleventh hour.

Thanks are due to the Professors on my committee: Frank Gwazdauskas, Mary Ann Novascone, and Janette Taper. They have all been very helpful, and I appreciate their high standards. Dr. Novascone has given lots of good advice, and has been flexible, imaginative, and supportive in the role of committee chair.

Of course, research could not proceed without the people who volunteer their time, and in the case of this study, their blood. Particular thanks are due to my graduate student colleagues, who gave one of their most precious commodities, time.

My friends, Norm Whitley and Patrick Glynn, have contributed moral support and good advice from a distance. Peter Laws and Clark Gaylord contributed statistical expertise to this project.

Supplies for the project were donated by Bonnie Weiss at Lifescan and Eursula West at Bahlsen Foods. Their support is gratefully acknowledged.

TABLE OF CONTENTS

Introduction

According to statistics from the United States Census Bureau (1), approximately 6 million Americans, or 26 out of every 1,000 people, have been diagnosed with diabetes mellitus. This chronic condition, which is characterized by abnormalities in glucose and lipid metabolism, may profoundly affect the lives of patients with diabetes, inasmuch as they are at increased risk for heart disease, nephropathy, retinopathy, and neuropathy.

It is theorized that prolonged elevated blood glucose (hyperglycemia), a prominent feature of the abnormal glucose metabolism found with diabetes mellitus, may be linked to the microvascular changes associated with long term complications of diabetes. Although the exact role of hyperglycemia remains controversial (2), it is thought that maintaining blood glucose in a range that is close to normal may help prevent microvascular changes. A long term multi-center clinical intervention trial is currently underway to investigate the potential benefits of tightly controlling the blood glucose of diabetics (3).

In an attempt to find foods and meals which help maintain blood glucose in a more normal range, glycemic responses to many individual foods and to some combinations of foods have been measured in both diabetic and nondiabetic individuals. This information may be helpful to diabetic persons who are monitoring their blood glucose closely in order to approximate normal blood glucose (normoglycemia). The American Diabetes Association (4) noted that such information "... may be used, in simplified form, as part of the exchange system." (p.128.)

Individuals with diabetes who are using exogenous insulin or oral hypoglycemic agents may be advised to eat a snack in the mid-afternoon so that adequate glucose is in their blood when the endogenous or exogenous insulin action peaks (5). Avoiding hypoglycemia is important for people with insulin dependent diabetes. People with noninsulin dependent diabetes who use either of the two "second generation" oral hypoglycemic agents (glipizide or glyburide) also are at risk for developing low blood glucose (6). Foods which contain a mixture of protein, carbohydrate, and fat are recommended for the snack; carbohydrate supplies the glucose, and the protein and the fat slow nutrient absorption to avoid a quick peak and a subsequent precipitous drop in blood glucose. For those individuals with NIDDM, small meals and snacks may enhance effectiveness of insulin (7,8). For some individuals who work, taking time to prepare or obtain a snack and then consume it may be difficult. Thus, a snack food which is easily obtainable, easy to transport, and not messy to eat may be desirable.

One food product which meets all of these criteria is crackers with peanut butter on them. Such an item is commercially supplied by several food companies under different brand names. The product is presented as a "sandwich" made from two crackers with peanut butter between the crackers.

Glycemic response to many snack foods, and peanut butter and crackers in particular, has not been tested and reported; information from studies which quantify response of blood glucose to untested foods may prove helpful to diabetics. Thus, the purpose of this study was to observe the blood glucose response to a peanut butter and cracker snack product which is commercially available, and to compare blood glucose response of individuals with documented noninsulin dependent diabetes (NIDDM) to that of individuals without NIDDM (controls). The null hypothesis was that blood glucose response would not be different between these two groups. Clinically important features of the glycemic response such as the peak blood glucose, the slope of the line after the peak, and the time to return to baseline are described using a plot of blood glucose over time.

Review of Literature

Noninsulin Dependent Diabetes Mellitus

Noninsulin dependent diabetes (NIDDM) is considerably more common than insulin dependent diabetes (IDDM). There are about 5.4-5.7 million Americans with this diagnosis, compared with 300,000-600,000 who have been diagnosed with IDDM (9). Noninsulin dependent diabetic subjects were chosen for this study because of the prevalence of this condition in the United States.

Pathogenesis

Development of NIDDM has been linked with lifestyle, heredity, and body weight. It is more likely to occur in adults older than 40, and is more common among African- Americans, Hispanics, Asian-Americans, and among members of some Native American tribes. Prevalence of NIDDM is somewhat higher among women than among men (10).

Pathology

NIDDM is characterized by a derangement of carbohydrate metabolism, and by lipid abnormalities. Elevated blood glucose often is seen along with low, normal or high levels of insulin. Definitive diagnosis is based on an elevated fasting plasma glucose ($\geq$ 140 mg/dl) on more than one occasion, or an elevated plasma glucose of $\geq$ 200 mg/dl two hours after an oral glucose tolerance test of 75 grams of glucose, together with an additional value of > 200 mg/dl at a time before 120 minutes have elapsed (11).

The phrase "insulin resistance" is often used to describe the metabolic abnormalities found in NIDDM. Olefsky and Molina (12) defined insulin resistance as "a state in which a given concentration of insulin produces a less than normal biologic response." (p.121) In other words, peripheral target cells (muscle, liver and fat cells) "resist" insulin which was secreted in response to ingestion of food. This resistance can sometimes be overcome when the individual with NIDDM loses weight.

The insulin receptor is believed to be synthesized as one polypeptide chain which undergoes posttranslational modifications. This receptor is found as a tetramer (with two alpha chains and two beta chains) in the cell membrane. The alpha chains project outside the cell, while the beta chains project through the cell membrane into the cell (13).

Researchers have approached description and quantification of insulin resistance from several perspectives: insulin binding to the insulin receptor (IR), autophosphorylation of the beta subunit of the IR, subsequent substrate phosphorylation by the activated beta subunit, and glucose transport into the cell. More simply, defects in the transduction of the signal from insulin have been categorized as binding- or post-binding defects. An overview of studies which have pursued the mechanisms of insulin resistance is presented below.

Pillay and Makgoba (13) noted that people with NIDDM have fewer insulin receptors, and that the existing receptors are less sensitive (right shift of the insulin dose-response curve) and less responsive (diminished maximal response). They explained that "decreased sensitivity implies a change in receptor number or affinity, while decreased responsiveness implies a change in a rate-limiting step, usually at a post-receptor level." (p.609)

Hjollund et al. (14) studied insulin binding to adipocytes in patients with NIDDM. Weight loss was induced with a diet which was hypocaloric for the subjects (1315 kcal/day with 50% of kcal from carbohydrate, 15% from protein, and 35% from fat). Mean body mass index (BMI) of these diabetics was 31 kg/m^2 before weight loss and 29 kg/m^2 after weight loss (mean weight loss was 8 kg). (BMI of 29 kg/m^2 is still indicative of obesity and is associated with a threefold increase in risk of diabetes, according to the 1985 National Institutes of Health Consensus Statement on Health Implications of Obesity [15]). Mean fasting plasma glucose of the subjects was 207 mg/dl before weight loss, and 124 mg/dl after weight loss.

In cell-binding studies, the investigators found improved binding at 15°C, but not at 37°C after weight loss. The clinical significance of the increase in insulin binding at a nonphysiological temperature is difficult to interpret. The authors explained that at 15°C the insulin is not internalized after binding. In contrast, at 37°C the receptor and the insulin are internalized and processed within the cell. According to Hjollund et al. (14) experiments done at 37°C best represent the whole physiological process, whereas experiments done at 15°C may be better at assessing the status of just the receptor. They concluded that improving the hyperglycemia of the patients did not affect insulin binding to adipocytes.

In view of the fact that the decrease in binding was seen only at a nonphysiological temperature, the authors' conclusions seem justified. Alternatively, the loss of 8 kg. may not have been sufficient to produce an improvement in insulin binding.

The beta subunit of the insulin receptor acquires kinase activity after insulin has bound to the alpha subunit of the receptor. It is then able to phosphorylate itself at specific tyrosine residues (autophosphorylation). After this activation, the receptor catalyzes phosphorylation of an endogenous (and presently unknown) substrate. Ultimate-ly, this sequence results in movement of glucose transporter molecules to the cell surface, and the transport of glucose into the cell (13).

Freidenberg and coworkers (16) studied IR purified from adipocytes of three groups of patients: lean, obese without NIDDM, and obese with NIDDM. For three days before the study, subjects received an isocaloric diet. (The authors did not specify whether this meant a weight maintenance diet or whether it meant that all the subjects received the same number of calories.) In the absence of insulin, no differences in autophosphorylation were seen among the groups. However, when maximally stimulating concentrations of insulin were added to the receptor preparations (at 4°C), receptors from individuals with NIDDM were only 46% as active in the autophosphorylation reaction as those from the lean controls. Again, since these results were obtained under nonphysiological conditions, their significance is difficult to interpret. However, studies such as this one provide good justification for continuing to investigate events which occur along the pathway of insulin signal transduction.

Thies et al. (17) obtained similar results in a study which also used IR isolated from human adipocytes. The subjects in this study were lean and obese individuals without NIDDM, and obese individuals with NIDDM. The investigators compared the ratio of autophosphorylated IR to total IR (at 37°C) and found that a statistical difference in this measurement did not exist between the lean and obese subjects without NIDDM, but that this ratio was about 50% lower in the obese diabetics ($p<0.02$).

In the same study, substrate phosphorylation also was tested. As noted above, the substrate for the second phosphorylation has not yet been definitely identified. However, the investigators isolated a polypeptide (pp185) which may be an endogenous substrate for the activated beta subunit of the insulin receptor. A comparison also was made of the ratio of activated beta insulin receptors to phosphorylated pp185 molecules in samples taken from diabetic, obese nondiabetic, and control individuals. No differences were found in these ratios among the groups. Thus, the authors identified a decrease in autophosphorylation of the bound insulin receptors in NIDDM, but no parallel decrease in the phosphorylation of the possible substrate identified as pp185.

Lipid Abnormalities

People with NIDDM frequently have an elevated plasma triglyceride value and a depressed HDL-cholesterol value. The elevation in triglycerides correlates with elevated blood glucose, and diminishes when blood glucose approaches the normal range. The issue of whether elevated triglycerides constitute an independent risk factor for cardiovascular disease has not been resolved (2). However, this correlation between elevations in blood glucose and elevations in blood triglycerides contributes to the rationale for normalizing the blood glucose of the diabetic individual.

Complications of Diabetes

Although NIDDM is seldom acutely life-threatening, individuals with this disorder still may develop the long-term complications seen in individuals with IDDM. At the present time, the mechanisms involved in the genesis of these complications are incompletely understood. A discussion of theories regarding the causes of the major long term complication of diabetes will follow.

Cardiovascular complications account for 74% of the cost of hospitalizations for diabetic complications. An individual with diabetes is 8.3 times more likely to be hospitalized for myocardial infarction than an individual without diabetes (18). A possible mechanism for this acceleration of the disease process will be discussed below.

Because people with diabetes have consistently high levels of blood glucose, nonenzymatic glycosylation of proteins in the blood (and elsewhere) occurs. Researchers hypothesize that, over time, this glycosylation leads to cross-linking of proteins, and a concomitant decrease in protein function. For example, enzymatic activity, recognition of protein macromolecules (such as LDL), and protein immunogenicity all may be affected by glycosylation (2).

Cross-linked proteins may become imbedded in the endothelial layer of a blood vessel. These altered proteins may be perceived by the immune system as non-self, and thus may be immunogenic. Circulating monocytes then might be attracted to arterial sites where cross-linked proteins (such as LDL) have been deposited, and chemoattractant substances may be produced as part of the immune process. The monocytes then may oxidize the LDL. The oxidized LDL becomes even more antigenic, hence attracting more monocytes to the area. As more monocytes and oxidized LDL molecules accumulate, foam cells form. Thus the scenario of atherogenesis described by Steinberg and Witztum (19) may be initiated in diabetic individuals (see Figure 1).

Diet Recommended for Individuals with Diabetes

Generally, nutritionists strive to design diets which meet both the therapeutic and lifestyle needs of an individual. They begin with guidelines provided by professional organizations such as the American Diabetes Association

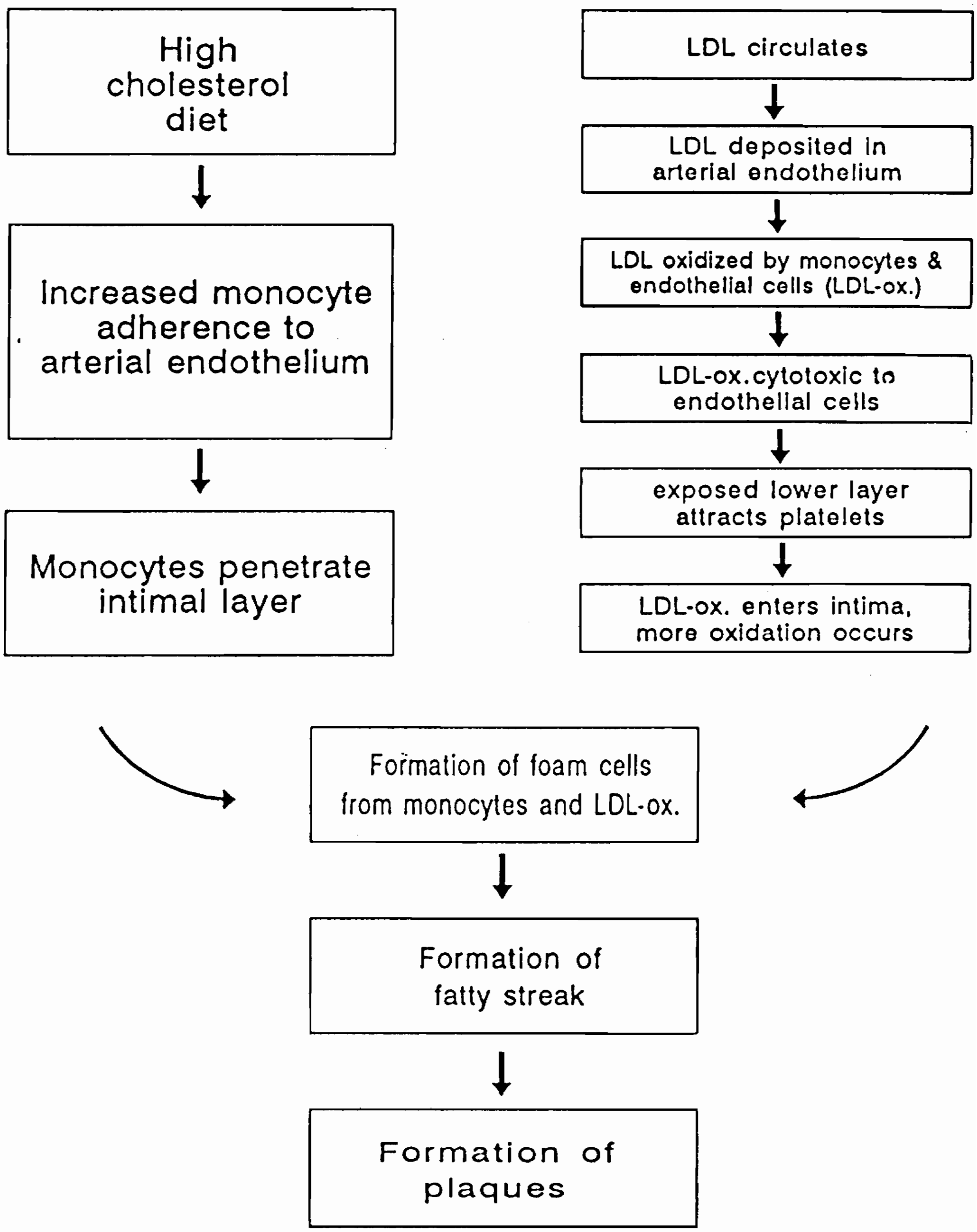

FIGURE 1
FORMATION OF ATHEROMAS

as described by Steinberg and Witztum (19) and the American Association of Diabetes Educators. The nutritionist then individualizes dietary recommendations to suit the patient's medical needs and personal preferences.

Currently, the American Diabetes Association (ADA) (4) recommends that the diet for diabetics be designed to include a caloric level which will achieve or maintain a reasonable body weight. Furthermore, they promote a diet which has calories distributed as follows: 55-60% from carbohydrate, 12-20% from protein, and $\leq$ 30% from fat. The calories from fat may be roughly equally distributed among saturated, polyunsaturated and monounsaturated fats.

In addition, the following goals of nutritional therapy are proposed by the American Association of Diabetes Educators (10).

> 1. Restore as near-normal blood glucose levels as is feasible, and attain optimal blood lipid [cholesterol, triglycerides and high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very-low-density lipoprotein (VLDL)] levels....
>
> 5. Determine an appropriate meal plan for an individual's lifestyle based on his/her diet history.
>
> 6. Provide assistance in weight management for people with NIDDM.
>
> 7. Improve overall health through optimal nutrition. (p.14)

Although neither of these two organizations specifically addresses the issue of simple carbohydrates versus complex carbohydrates, most nutritionists recommend complex carbohydrates (polysaccharides) over simple sugars (mono- and di-saccharides). This approach may be a bit confusing, since some foods (dairy products and fruits) which are acceptable for use contain simple sugars. An alternative way of conceptualizing this issue is refined (or concentrated) sugars versus naturally occurring sugars. Hollenbeck and Coulston (20) observed that consumption of sucrose resulted in postprandial elevations of blood glucose, insulin, and triglycerides. Elevations in fasting triglycerides and cholesterol also were found.

Recommendations for the high carbohydrate diet (50-60% of energy from carbohydrate) were instituted in view of the increased risk of cardiovascular disease which diabetics face. A diet which ameliorates risk of heart disease might be expected to produce a decrease in the blood lipids which have been connected to risk of heart disease, such as total, HDL-, and LDL-cholesterol. Thus studies which investigate desirable proportions of macronutrients in the diet for diabetes also have measured the effect of the diet on blood lipids.

Recently, investigators have studied the effects of diets with calories distributed as favored by the ADA. In patients with NIDDM, Chen et al. (21) found that a diet with 60% of calories from carbohydrate and 25% of calories from fat led to the same level of postprandial triglycerides as a diet with 40% of calories from carbohydrate and 45% of calories from fat. This study measured only effects that occurred within 24 hours of the meal. The authors did not specify the amount or type of fiber which was in the test diet.

In a similar study with diabetic subjects, Coulston et al. (22) compared the effects of a high carbohydrate diet (60% of calories from carbohydrate, 20% of calories from fat, 18.1 grams dietary fiber/day) to the effects of a low carbohydrate diet (40% calories from carbohydrate, 40% of calories from fat, 14.3 grams dietary fiber/day). Subjects followed each diet for a period of six weeks. On the high carbohydrate diet, day-long plasma glucose and insulin concentrations were higher than those found when the subjects consumed the low carbohydrate diet ($p<0.001$). Triglycerides also were elevated when the subjects ate the high carbohydrate diet ($p<0.001$). Since elevated triglycerides may contribute to risk of developing heart disease, and since elevated blood glucose may contribute to the development of complications associated with diabetes, the authors noted "...it seems reasonable to suggest that the routine recommendation of low-fat high-carbohydrate diets for patients with NIDDM be reconsidered." (p. 94)

Glycemic Response

Many factors affect glycemic response to a given food or meal, and much effort has been expended to identify all the factors which play a role. Factors which influence glycemic response to a food may be broadly classified as related to external conditions or as related to the person who ingests the test food. For example, time of meal ingestion, and variables related to the specific food or meal may be considered external factors. On the other hand, age and/or sex of the subject, body weight of the subject, and distribution of the subject's body fat (peripheral vs. abdominal) all have been studied as possible influences on blood glucose responses.

Time of administration of an oral glucose tolerance test (50 grams of glucose given as a beverage) was studied by Jarrett et al. (23). They gave patients on an orthopedic ward the glucose tolerance test at 9 A.M., 3 P.M., and 8 P.M. The results of the afternoon and evening tests were similar, and both tests were significantly higher than the test in the morning. The results of this study were somewhat confounded by the fact that 26 of the 28 subjects in the study were being treated for musculoskeletal disorders, and may have been taking medications which might either increase or decrease glucose tolerance (specifics of the medications which the subjects were taking were not reported). However, the majority of studies which examine blood glucose response to feedings of various types have been administered in the morning, after an overnight fast (25-48). Apparently the authors of these studies have chosen to accept the results from the study by Jarrett et al. (23), despite the possible confounding factor introduced by the medications.

As noted above, various characteristics of subjects have been considered with regard to their effect on glucose tolerance. Relationships among age, body weight, body fat distribution, and physical fitness (as measured by VO_2max) were examined by Coon et al. (24). Men with normal glucose tolerance were studied in two age ranges: older (47-73 years old) and younger (19-36 years old). Glucose disposal rate (GDR) was measured under conditions where blood insulin was maintained at an elevated level (hyperinsulinemic clamp), and blood glucose was held at a normal level (euglycemic clamp). These conditions made it possible to examine in vivo processing of glucose by target cells, with the insulin and glucose inputs controlled.

The investigators found that in older men with normal glucose tolerance, GDR was not different from that in younger men. A significant negative correlation between GDR and waist-hip ratio (r=-0.77), and with percent body fat (r=-0.46) was found. A significantly positive correlation between VO_2max and GDR was reported (r=0.54), and age by itself was reported not to be correlated with GDR (r=-0.38).

Results from this study must be viewed with caution. A highly artificial environment was created because the disposal of glucose at the level of the target cells is near the end of the process of digestion, absorption, and nutrient delivery. Consequently, to study GDR, unnatural control mechanisms had to be employed. Findings from research such as this are best used in the context of other studies which make use of less artificial methods. Thus, since increased adiposity has been a well-documented correlate of diminished glucose tolerance, the results of this study may be viewed as a further clarification in that line of research.

Rasmussen et al. (25) fed two test meals (60 grams white rice alone and 100 grams white bread plus cucumber and tomato; grams of available carbohydrate were not reported) to males and females with NIDDM. Subjects were matched with respect to age, duration of diabetes, and body mass index. Glycemic responses to the test meals were not different between the men and women studied. The authors concluded that sex of the subject did not influence glycemic response when age and body mass index were controlled.

Because "tight control" of blood glucose is believed to be highly beneficial for diabetics (3), interest and research have focused on variables which influence nutrient absorption, particularly digestion and absorption of carbo-hydrate. Investigators have looked into such food-related variables as the type of fiber and amount of fiber present in the diet, degree of food processing before cooking, and length of cooking time. In these studies subjects consumed the test food and appearance of glucose in the blood over time was measured. Investigators often have constructed a glucose and/or insulin response curve to depict results. An important consideration in studying the rate of glucose absorption after feeding is the degree to which the glucose tolerance of the subjects is abnormal. In other words, glycemic response of nondiabetic subjects may be sufficiently different from that of diabetics to warrant extreme caution when considering application of this information.

Using the coefficient of variation (CV), Wolever et al. (26) compared between- and within-subject variability in glucose absorption of normal individuals, persons with NIDDM, and persons with IDDM. The magnitude of this statistic, which depends on the relationship between a mean and the standard deviation associated with it, indicates the degree of variability in a given measurement. The authors reported the following results: individuals with NIDDM had the smallest within-subject variability (CV=16%), normal individuals had intermediate within-subject variability (CV=22%), and people with IDDM had the highest variability (CV=29%). Between-subject variability was lowest in normal individuals (CV=24%), and equivalent in people with NIDDM and IDDM (CV=34% for both). Again, it would seem important to separate data obtained from normal subjects from data derived from diabetic subjects.

Jenkins et al. (27) proposed use of a "glycemic index" to assess the effects of ingestion of various types of carbohydrates on individuals with and without diabetes. The glycemic index (GI) was defined as the area under the blood glucose response curve of a test food divided by the area under the blood glucose response curve of a standard food. (Initial studies used a glucose solution containing 50 grams glucose for the standard food; a few years later white bread was substituted as the standard food, since many subjects became nauseated when consuming the glucose solution.) The quotient was then multiplied by 100, to give a percent. Jenkins et al. (27) reported GI values for many foods when eaten alone. For example, the following GI values were published: spaghetti from white flour, 50%; new potatoes, 70%; kidney beans, 29%; and peanuts, 13%.

Food-related Factors which Influence Glycemic Response

Conflicting reports regarding effects exerted by different types of fiber on glycemic response may be found in the literature. Type of fiber appears to have an effect on speed of glucose absorption in diabetic and normal individuals. Foods containing fiber which forms a viscous gel (soluble fibers) in the gastrointestinal tract have been shown to elicit a lower glycemic response than foods with fiber which is insoluble (28). In contrast, Wolever et al. (29) reported that more variation in the GI was explained by the uronic acids in insoluble fiber than by soluble fiber content. Behme and Dupre (30) found that area under the glucose response curve for a meal, which included cereal containing insoluble fiber (All Bran with 19 g total dietary fiber), was 40% less than the area under the glucose response curve for a low fiber meal which included Corn Flakes (0.5 g total dietary fiber). Thus, wheat bran does exert some effect on glycemic response.

In addition to the type of fiber fed, the amount of fiber fed may exert an important influence on the rate of glucose absorption. In a review of absorptive consequences of high fiber meals, Hollenbeck and Coulston (20) noted that in studies in which subjects were fed very large daily doses of fiber (70-100 grams fiber/day) significant decreases in glycemic response were found. On the other hand, diets containing moderate doses of fiber (30-50 grams/day) provoked a smaller response. O'Dea et al. (31) reported a decrease in fasting plasma glucose after 14 days on a 53 g fiber/day diet in which the fiber was a mixture of soluble and insoluble fibers in foods.

Degree of food processing has been examined as a variable affecting glucose absorption. If grains are milled to a fine texture, and the surface area available to digestive enzymes is increased, then the absorptive rate also is increased. Thus, Jenkins et al. (27) reported lower glycemic index values for whole kernel brown and white rice than for ground brown and white rice. Golay et al. (32) compared glycemic responses to white beans whose cells were either ruptured or intact, and found that if cell walls remain intact, then the absorption of glucose is slowed.

In a similar vein, Sud et al. (33) compared glycemic responses to whole foods (potato, rice, bread, and green gram) with glycemic responses to formulated mixtures of corn flour, casein, corn oil, and ispaghula husk. The formulations contained the same amounts of the macronutrients as the whole foods. Not surprisingly, the authors reported that "nutrient composition is a poor predictor of glycaemic response." (p. 5)

The effect of length of cooking time and heat processing (such as canning) on starch hydrolysis was investigated by Wong et al. (34). The rate of starch hydrolysis was increased when cooking disrupted the cell walls within foods. However, Bornet et al. (35) found that if a starch was already fairly accessible to digestive enzymes, as is the case in some pastas, then duration of cooking time did not affect glycemic response.

Presence of sodium (1600 mg) has been reported by Thorburn and colleagues (36) to affect glycemic response of normal individuals when added to bread or lentils. However, this finding has not been replicated by other investigators (37,38) who added similar amounts of sodium to similar amounts of carbohydrate (50 grams).

Macronutrient Interactions

The effects of coingestion of protein and/or fat with carbohydrate have been studied. Nuttall et al. (39) fed liquid glucose solutions (50 grams carbohydrate) alone or in combination with 10, 30, or 50 grams of protein (given as hamburger with 6.5% fat) to subjects with NIDDM. This "meal" was served in the morning, after an overnight fast (exact time was not specified). Area under the glycemic response curve was computed for each of the above conditions. With each increment of protein fed there was a decrease in area, but the only condition which evoked a statistically significant difference between glucose alone and glucose plus protein was the addition of 50 grams of protein. Since the height of the peak from glucose alone was comparable to the height of the peak from glucose, protein, and fat combined, and since both peaks occurred at the same time, the authors concluded that the inclusion of fat did not unduly influence glycemic response. Insulin response to the glucose and protein condition was significantly higher than the insulin response to glucose alone (233 microUnits x h/ml vs. 93 microUnits x h/ml).

Blood glucose response to exactly the same nutrient sources later was tested by Westphal et al. (40) with normal subjects; they obtained contrasting results. In subjects with normal glucose tolerance, the addition of protein did not evoke a statistically different serum glucose response. The subjects in this study also were fed after an overnight fast; the meal was given at 8 A.M. Insulin response to the glucose plus protein feeding was significantly higher than insulin response to the glucose alone (100 microUnits x h/ml vs. 75 microUnits x h/ml).

The results obtained regarding glucose response of subjects with NIDDM (Nuttall et al., 39) are not consistent with those obtained by Westphal et al. (40) from nondiabetic individuals. However, both groups of investigators found similarly enhanced secretion of insulin in response to the glucose plus protein feeding. The different glucose response of the diabetic subjects may be a demonstration of insulin resistance.

Wolever et al. (41) fed 50 grams of carbohydrate as pasta to subjects with NIDDM and with IDDM after an overnight fast (time of feeding not reported). They found an insignificant drop in glycemic index when the pasta was enriched with a small amount of protein (2.3 grams), and served with 32 grams cheese (including about 9 grams fat; total protein content of meal was 11.4 grams) and tomato. Glycemic index of a combination of spaghetti, cheese, and tomato was 45%; GI of a protein-enriched spaghetti, cheese and tomato combination was

38%.

Wolever and coworkers (41) referred to the results found by Nuttall et al. (39) when they concluded that the total amount of protein added was probably not enough to significantly increase the GI of the meal. Since both of these studies used subjects with NIDDM, these results from Wolever et al. (41) provide further evidence that small amounts of protein (11 grams and less) added to carbohydrate-containing meals do not decrease the blood glucose response to the meal. The authors of this study, by using solid food as the vehicle for the carbohydrate, also extended the findings of Nuttall et al., (39), who used a glucose-containing solution.

Villaume et al. (42) reported that equivalent amounts of protein from different food sources (14 grams protein from ham versus 12 grams protein from egg) elicited differently shaped curves in normal subjects. The test proteins were fed in a multi-food meal where all other foods were identical (54 grams carbohydrate from bread and saccharose and 16.8 grams of fat from butter and the protein source). Although the curves were shaped differently, the areas under the curves were not statistically different. The integrated blood glucose response elicited by the ham meal was 1303 mmol/min/L; the integrated blood glucose response of the egg meal was 1349 mmol/min/L. The peak blood glucose of the ham meal was significantly higher (about 140 mg/dl at 40 and 50 minutes) than that of the egg meal (108 mg/dl at 65 minutes). Since the subjects were nondiabetic individuals and the glucose responses were within the normal parameters, it is unlikely that the differently shaped curves have a biological significance.

As noted above, Jenkins et al. (27) reported GI values for many carbohydrate containing foods when eaten alone. Other investigators have used these results while posing this follow-up question: can glycemic response to mixed meals be manipulated (and predicted) by choosing carbohydrate sources which, when fed individually, elicit a high, intermediate, or low glycemic response? These studies represent an effort to move towards evaluating conditions which simulate "real life" more closely and to examine the practicality of using results from blood glucose response studies as a meal-planning tool for diabetic patients.

Coulston and coworkers (43) pursued this question by feeding mixed meals containing 15 grams protein (in lean turkey meat), 17.8 grams fat (as margarine), and 45 grams carbohydrate (in a starch, a fruit and a vegetable). The high glycemic response carbohydrate foods were rice, banana, and carrots. The intermediate glycemic response foods were spaghetti, orange, and beets. Lentils, apple, and frozen peas were served in the low glycemic response condition. The investigators reported that "plasma glucose responses after the meals did not vary as a function of their glycemic potency in...NIDDM subjects." (p.395)

Gulliford et al. (44) also explored coingestion of protein, carbohydrate, and fat in subjects with NIDDM. The objective of their study was to determine whether glycemic responses to different carbohydrate-containing foods (25 grams carbohydrate as either potato or spaghetti) were equally influenced by coingestion of 25 grams protein (given as tuna fish) or coingestion of 25 grams protein plus 25 grams fat (given as margarine). When potato and tuna fish were consumed, the glycemic response was significantly lower ($p<0.05$) than when potato was eaten by itself. Addition of fat elicited an even lower glycemic response when compared with glycemic response to potato alone ($p<0.001$). However, glycemic response to spaghetti plus tuna fish was not significantly lower than that to plain spaghetti, and the addition of fat did not alter this result. Thus, coingestion of protein or protein and fat affected the glycemic response to only one of the two test carbohydrates (potato). The authors noted that "the physical structure of carbohydrate-containing foods can influence the rate of starch hydrolysis and this, in turn, can influence postprandial blood glucose responses." (p.776). They attributed absence of a diminished blood glucose response to the spaghetti plus protein or spaghetti plus protein plus fat to the relatively low response to spaghetti alone. These investigators concluded that "...if differences in glycemic responses are to be used in a quantitative way, further information would be required to define the effects of coingestion of protein and fat." (p.776)

Hermansen et al. (45) examined the same question, while studying glycemic responses to potato and spaghetti in subjects with IDDM. In this experiment, the subjects were brought to normoglycemia through the use of an artificial pancreas. (The authors explained that the artificial pancreas was used in this study to control for the high variability in blood glucose response seen in people with IDDM.) Each subject's blood glucose was within the normal range for one hour prior to the consumption of the test meals. The meals consisted of 47 or 48 grams of carbohydrate (potato or spaghetti), 23 or 26 grams of protein, and 18 grams of fat. The source of protein and fat was Bolognese sauce in both the potato and spaghetti treatments. These investigators found that "blood glucose increment after white spaghetti and Bolognese sauce was only about 50% of that seen in response to potato and Bolognese sauce." (p.401) Thus, in this study, the GI of the carbohydrate was predictive of the glycemic response to a meal containing a mixture of protein, carbohydrate and fat.

While it may seem that the use of the artificial pancreas in this study severely limits the applicability of the results, the investigators were attempting to clarify the responses of people with IDDM, in the absence of a potentially confounding factor. In addition, since the use of the insulin pump is becoming more widespread, there is a population to whom results of such a study may be applicable.

Collier and O'Dea (46) devised a protocol to assess the effect of coingestion of carbohydrate and fat. Fifty grams of carbohydrate were fed as potato either alone or in combination with 50 grams of fat (butter). Subjects had normal glucose tolerance. Addition of the fat was found to significantly decrease postprandial glucose response ($p<0.005$).

In a similar investigation, the same group (47) repeated the potato alone or potato with butter condition, but changed the amounts fed (75 grams of carbohydrate and 37.5 grams of fat). They also fed lentils alone (75 grams carbohydrate) or lentils plus fat (37.5 grams). Again potato alone was found to elicit a glucose response which was significantly higher than the response to potato plus fat ($p<0.05$). Lentils alone also elicited a higher glycemic response than lentils plus fat. ($p<0.05$).

Several investigators have studied the effects of ingestion of peanuts or peanut butter. Results from these studies are summarized below, in Table 1.

TABLE 1: GLYCEMIC RESPONSE TO INGESTION OF PEANUTS

Investigators	Subjects	Source	Results
Jenkins et al. (27)	healthy n=5-10	25 g. peanuts vs. 50 g. OGTT*	GI=13% of glucose ($p<0.001$)
Jenkins et al. (48)	11 NIDDM	50 g. PB** with 50 g. bread vs. plain bread	area with PB** smaller ($p<0.01$)
	6 IDDM	same foods	areas not different
Oettle et al. (49)	healthy n=10	23 g. peanuts with raisins or bananas vs. candy bar or cola with potato chips	response to peanuts and fruit less than response to processed snack

*oral glucose tolerance test
**peanut butter

These results demonstrate that addition of peanuts or peanut butter to a primarily carbohydrate food can blunt the blood glucose response. Jenkins (48) speculates that the differences found between NIDDM and IDDM subjects with respect to GI after peanut butter and bread "...is a reflection of the greater degree of variability in the results of the IDDM compared with the NIDDM." (p.979) Responses to the peanut plus fruit snacks were not statistically different from responses to the processed snacks. Again, since this study was done with nondiabetic subjects, findings should not be taken to apply to diabetic people, especially since Jenkins (48) did find a different response in subjects with NIDDM.

Gregersen et al. (50) investigated whether ingestion of water (two volumes, 90 ml or 600 ml) with a meal had an effect on glycemic response. Subjects with NIDDM ate a meal (40 grams carbohydrate and approximately 10 grams fat) with or without water. The researchers reported that the addition of water to the meal did not change the area under the blood glucose curve.

Methodological Issues

In pursuing glycemic response information, the investigator faces certain choices. To what degree should experimental conditions approximate reality? Should an environment which is highly controlled or an environment which simulates reality be created? What are the implications of each as far as interpretation and application of the results? Some relevant issues will be discussed below.

Many factors must be considered when designing a glycemic response study. In the initial studies of this type, investigators opted for maximal standardization of conditions, in order to provide the most controlled assessment of blood glucose response of their subjects. In this way, individual variables which affect blood glucose response could be most clearly delineated. Blood glucose response of nondiabetic individuals is a good starting point, but results obtained in such studies may not always be replicated by similar studies done with diabetic subjects, as was seen with results from Nuttall et al. (39) and Westphal et al. (40). Thus, application of findings obtained from studies of nondiabetic individuals should be avoided when possible. However, findings from studies with nondiabetic individuals have given direction to research related to feeding the athlete before, during, and after endurance competitions such as marathons (51).

Another factor which contributes to a highly controlled environment in a blood glucose study is the time that the food or meal is given to the subjects. Some evidence (Jarrett et al. 23) from a study of nondiabetic individuals indicated that giving the food or meal in the morning elicits a lower glycemic response than feeding later in the day. Since the factors which contribute to this phenomenon have not been completely elucidated, many investigators have chosen to conduct their studies in the morning. However, since diabetic individuals also need to eat in the afternoon and evening as well, physicians and dietitians are interested in studying glycemic responses later in the day. Ultimately, the goal is to understand how external factors and factors related to the individual interact at all times of the day, so that blood glucose control may be optimized.

Findings from very controlled or "best case" scenario studies have provided the foundation of our understanding of glycemic response to foods. However, since such tightly controlled conditions exist only in research, the applicability of these results may be limited. Thus, in subsequent years, some researchers have chosen to create a test environment which more closely approximated reality. For example, Coulston et al. (22) studied response to a noon meal, and Oettle et al. (49) studied response to snacks offered at 3 P.M. In these investigations, researchers still exerted a fair amount of control by feeding the subjects known meals earlier in the day. Findings from studies which try to approximate realistic conditions may be used to check the relative contribution of factors studied under more tightly controlled situations. For example, relative contribution of time of day as a factor could be studied by feeding the same food or meal for breakfast, lunch and dinner. Day-to-day variation could be assessed by repeating this process for two to three days in a row. Results from a study such as this may identify a new factor which may need to be initially studied under tightly controlled conditions. Thus, the process of research is an ongoing one; results from a study may clarify one issue, but will often raise related questions for further investigation.

Systematic study of blood glucose response to meals and foods began in the mid-1970s (52), and dozens of GI and glycemic response studies have been conducted since that time. As noted above, the American Diabetes Association (4) has approved use of information from glycemic response studies in conjunction with the exchange system. On the other hand, the National Institutes of Health (53), has recommended against using this information. Wolever (52) described the issues involved in the debate about the practicality of using information from GI studies in the following way. "The concern revolves around four major issues: (1) large individual variation in response; (2) lack of agreement between different centers; (3) lack of difference between mixed meals, and (4) lack of demonstration of long-term benefits of low GI foods." (p.125)

Several investigators have studied the problem of variability of glycemic response to foods, and have divided it into between-subject and within-subject components. For results from glycemic response studies to be useful as a dietary management tool for diabetics, these components should be quantified.

Wolever (52) noted that lack of agreement among different centers may be largely attributed to differences employed in methodologies; he advocated use of the glycemic index (as opposed to measuring area under the glycemic response curve alone) as a way to deal with between-subject variability. However, some investigators (22) have proposed use of average day-long glycemia as a method for revealing the blood glucose milieu over an extended time period. This method makes sense if the ultimate goal is the control of blood glucose throughout the day.

Although some investigators (43) have reported results indicating that glycemic response to a meal (as opposed to response to a single food) cannot be predicted based on the composition of the carbohydrate components of the meal, others, such as Clark et al. (54) have found GI to be useful as a predictor. In addition, Clark and coworkers addressed the issue of possible long-term benefits of using low GI foods.

At the 1992 Annual Meeting of the American Dietetic Association, Clark et al. (54) presented results of a meta-analysis of the usefulness of the glycemic index as a predictor of blood glucose response to foods and meals. They reported that "...the glycemic response of a mixed meal is a useful predictor of the glycemic response to that mixed meal ($p<0.05$)...consumption of low-glycemic-index foods was shown to significantly reduce serum total cholesterol ($p<0.005$), LDL-cholesterol ($p<0.005$), triglycerides ($p<0.05$), and glycosylated hemoglobin ($p<0.05$)." (p. A28). HDL-cholesterol was not affected.

Overview studies such as the one done by Clark et al. (54) will probably play an important role in future evaluations of glycemic response for use as a meal-planning tool. These determinations will be made by policy-making groups such as the American Diabetic Association and the National Institutes of Health.

Individual studies, such as the ones reviewed here, also will be considered, of course.

Issues Related to Glucometers

Questions regarding the accuracy and precision of patient-performed measurements have been investigated by several researchers. Hunt and Alojado (55) compared accuracy of the "One Touch" system (LifeScan, Milpitas, CA) to the accuracy of a standard glucose analyzer used in laboratories (YSI Model 23A) when patients performed the tests. Regression of the mean glucose results from the One Touch compared with the YSI system yielded a correlation coefficient (r) of 0.999 ($p<0.001$). Jovanovic-Peterson et al. (56) also compared results obtained by diabetics using the "One Touch" to results from the YSI Model 23A Glucose Analyzer. One hundred percent of results from the One Touch were within 15% of the YSI values when the blood glucose values were in the 101-200 mg/dl range. When the blood glucose values were in the 201-300 mg/dl range, 96% of the results were within 15% of the YSI values.

Tate et al. (57) conducted a study in which accuracy of five brands of home blood glucose monitors was compared by laboratory technicians. They used multiple regression analysis and found that the "One Touch" best predicted laboratory assays done by the Du Pont Dimension 380E, which used the hexokinase method to determine blood glucose values.

Burritt et al. (58) assessed accuracy of the "One Touch" glucometer when testing was performed by laboratory technicians. Results were compared with values obtained from a Beckman Astra-8 Glucose Analyzer. Correlation coefficient (r) was found to be 0.979 when the "One Touch" system results were plotted against the results from the Beckman instrument.

Precision of the "One Touch" system was tested by the three groups noted above. Each group reported precision in terms of coefficient of variation. Results of their studies are summarized in Table 2.

TABLE 2: PRECISION OF THE "ONE TOUCH" GLUCOMETER

Investigator	Coefficient of Variation, %
Jovanovic-Petersen et al. 1988 (56)	5.9
Hunt and Alojado 1989 (55)	4.5
Burritt et al. 1990 (58)	2.8-4.6

Burritt and his colleagues (58) concluded that the variability in the results produced by the "One Touch" glucometer was acceptable. They advocated its use in their Phlebotomy Service.

Table 3 displays some aspects of blood sampling schedules used by investigators in this field. Sampling interval can be seen to be the most varied aspect of the schedules. Clearly, a more frequent sampling interval will allow construction of a more accurate curve. A fair amount of agreement appears to exist with respect to the appropriate duration of sample collection. Time at which blood glucose peaked after consumption of the test food can be seen to be variable. Thus, the peak of the glycemic response curve may be difficult to predict in an untested food, and frequent sampling intervals will help pinpoint the time at which blood glucose will peak.

TABLE 3: COMPARISON OF BLOOD SAMPLING SCHEDULES

Investigator	Sampling Interval	Peak	Duration
Bukar et al. 1990 (59)	every 20 minutes	80-120 minutes	3 hrs.
Cohen et al. 1990 (60)	every 15 minutes first hr., then every 30 minutes thereafter	30 minutes	5 hrs.
Coulston et al. 1987 (43)	every 30 minutes first hr., then hourly	60 minutes	3 hrs.
Indar-Brown et al. 1992 (61)	every 30 minutes first hr., then hourly	60 minutes	3 hrs.
Jenkins et al. 1984 (48)	every 30 minutes	30-60 minutes	3 hrs.
Oettle et al. 1987 (49)	every 10 minutes first hr., then every 15 minutes second hr., then every 30 minutes	30 minutes	3 hrs.
Thorburn et al. 1986 (36)	every 15 minutes first hr., then every 30 minutes	30 minutes	3 hrs.

Materials and Methods

Subjects

Twenty-one individuals with NIDDM were recruited from local medical practices, the Cardiac Rehabilitation Program at Virginia Tech, and through the New River Valley Diabetes Association. Eleven individuals without diabetes were recruited for participation in a control group. The study procedure was verbally explained to each subject, and each subject was required to sign a consent form (Appendix A). As part of the informed consent, subjects with NIDDM were required to affirm that their physicians had been apprised of their participation in this study.

Height, weight, age, sex, and medications (diabetic and other types) taken by subjects were recorded (Data Collection Form, Appendix B), and each subject's body mass index was computed. Each diabetic subject was instructed to follow his or her usual treatment regimen (diet alone or diet plus oral hypoglycemic agents) (25). Individuals with known gastroparesis were excluded from participation.

Test Food

The Austin brand ("Toasty") peanut butter and cracker product was used in this study. This product (and other similar versions, Table 4) is available in

TABLE 4: NUTRIENT COMPOSITION OF SAMPLE PEANUT BUTTER AND CRACKER PRODUCTS

Brand Name	Na, mg.	CHO, g.	PRO, g.	Fat, g.	% Kcals from fat
Lance	160	17	5	10	50
Austin	330	22	5	10	45
Moore	N/A*	21	6	10	45
Keebler	N/A*	27	6	9	38

*N/A, not available

packages which contain six peanut butter and cracker "sandwiches." Each subject consumed one such package per session of this study.

Equipment

Blood glucose was measured from whole blood using the "One Touch II" glucometer (LifeScan, Milpitas, CA). This instrument employs an assay which uses the glucose oxidase method (56) to quantify blood glucose and is designed for home use by diabetic patients. Whole blood samples were obtained from the subject's finger using the Penlet II Automatic Blood Sampler (LifeScan, Milpitas, CA). If an individual was unfamiliar with this type of glucometer, training regarding its use was provided prior to the experimental sessions.

Methods

The following procedures were approved by the Institutional Review Board of Virginia Polytechnic Institute and State University prior to the initiation of the study. Subjects fasted overnight (no food or beverages after midnight) and they came in for the testing session at 8 AM. Subjects tested their own blood glucose. It was tested when the subject first arrived (fasting), and every fifteen minutes ($\pm$ 3 minutes) for the first two hours after eating one package of the peanut butter and crackers. After 120 minutes, samples were taken at 30 minute intervals until the 180th minute. Each subject participated on two separate occasions (session one and session two).

Subjects consumed the peanut butter and crackers immediately after the fasting blood test; the peanut butter and crackers were eaten within a period of five minutes. When the subjects finished eating, they notified the investigator, and the time was noted. The timing of the 15 minute intervals commenced when the subject finished eating. Subjects were allowed to drink up to 240 ml water after consuming the test food.

If a subject had experienced symptoms of hypoglycemia, or if the glucometer reading was $\leq$ 50 mg/dl (62), 20 grams oral glucose in tablet form would have been given to elevate blood glucose. Brodows et al. (63) found that this treatment corrected low blood glucose without rebound hypoglycemia. However, none of the subjects experienced hypoglycemia during participation in this study.

Statistical Analysis

As noted above, body weight, height, and age were recorded for each subject; body mass index was calculated for each. Descriptive statistics (mean and standard deviation) were calculated for each parameter, and these were compared for statistical differences using the Wilcoxon Rank Sum Test. This nonparametric measure was chosen because of the small number of subjects in each group.

Peak value and the time at which blood glucose peaked were of interest. Foods which lead to moderate increases in post meal blood glucose are thought to be more appropriate for diabetics than foods which lead to large increases in post meal blood glucose (10). Thus, group means for peak value and the time at which blood glucose peaked were calculated. The group means were assessed for statistical differences using the Wilcoxon Rank Sum Test. Between-subject variability for the peak blood glucose values also was computed using the coefficient of variation in order to compare variability of the blood glucose response found in this study with the variability of blood glucose responses reported in other investigations.

A blood glucose response curve was constructed from the mean values of blood glucose responses of each group at each time interval. Repeated measures analysis of variance (ANOVA) was used to compare control, PrevAGT, and NIDDM subjects in terms of the slopes of the glucose response curves. This analysis allowed comparison of the slopes of lines for each of the ten time intervals which comprised the three hour test session. If any of the subjects had developed hypoglycemia, the slope of that individual's blood glucose response curve would have been interesting to compare with the rest of the group. In addition, the repeated measures ANOVA tested for time by group effect.

Results and Discussion

Analytical Considerations

It was not possible for some subjects to perform the blood glucose test within the specified time interval (15 $\pm$ 3 minutes). Since the repeated measures ANOVA could not be executed on a data set with missing values, three data points out of 704 (0.4%) were interpolated. In addition, blood glucose values which were obtained outside the 15 ($\pm$ 3) minute intervals were used, even though they fell outside the specified time range. Forty-three out of 704 data points (6%) fell into this category. The use of these points may be justified on the following grounds. First, the ultimate goal of this study was to construct the blood glucose response curves for the three groups. The fact that 6% of the points were outside the time intervals did not mean that they did not represent a "true" part of the blood glucose response curve, and thus their inclusion in the data was acceptable. Second, they represented a small percentage of the total number of points, so that their ability to "deform" the "true" shape of the curve was quite limited.

As discussed previously, the data from each subject were collected in two sessions. It would be desirable to combine the data from session one with that from session two in order to increase the power of the analysis by increasing the number of observations on which it would be based. However, this combination would be inappropriate without prior verification of the absence of differences between the sessions within each of the three groups. Thus, within-group between-session repeated measures ANOVA analyses were performed. Results of these analyses are displayed in Table 5. No between-session differences in blood glucose responses within the groups were found.

Characteristics of Subjects

As noted above, 21 subjects with NIDDM indicated interest in participating in this study. During participation, six of these individuals were found to have fasting blood glucose values below the diabetic range (120 mg/dl for whole blood) (62). Upon questioning, it was found that these subjects had experienced significant and planned weight loss (12-45 kg.) since the time of their diagnosis, and several of them exercised or walked several times per week. They were asked not to exercise on the days they participated in the study (as were all subjects), and they were included in the analyses. This subset of six individuals formed a third treatment group, designated as previous abnormal glucose tolerance (PrevAGT) (11).

TABLE 5: WITHIN-GROUP BETWEEN-SESSION REPEATED MEASURES ANOVA

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	50002.7	50002.7	3.0	0.09
Group	2	12494.2	6247.1	0.4	0.69
Error	29	482713.8	16645.3		

The body weight, height, and age of each subject was recorded. Body mass index (BMI) was calculated for each subject from the height and weight data. Eleven of the 15 subjects in the NIDDM group were taking oral hypoglycemic agents, the remaining four were treated with diet alone. Table 6 displays the characteristics of the subjects and statistical comparisons of subjects' characteristics. It shows the mean weights and body mass indices of the three groups; the mean weight and mean BMI of the subjects in the PrevAGT group were between those of the diabetic subjects and the control subjects. Subjects with NIDDM were significantly heavier ($p<0.001$), had significantly higher BMI ($p<0.02$), and were significantly older ($p<0.001$), than control subjects. Subjects with NIDDM were significantly heavier than subjects in the PrevAGT group ($p<0.05$). No statistically significant differences in characteristics were found between the control group and the PrevAGT group.

Since Rasmussen et al. (25) concluded that sex of the subject in and of itself did not influence glycemic response, subjects were not divided by sex within the groups. A separate analysis was not performed to check this, since there was no evidence to suggest that it may affect the results of the study.

Glucose tolerance has been reported to decline as age advances. Templeton (64) noted that "Although fasting plasma glucose levels change only slightly with advancing age, postprandial glucose tolerance decreases appreciably." (p.353) She listed several possible mechanisms for this physiological change.

TABLE 6: CHARACTERISTICS OF SUBJECTS*

Group	NIDDM	PrevAGT	Control
Sample size	15	6	11
Sex			
females	7	3	9
males	8	3	2
Body Wt., kg.	87.7±12.5[a,c]	74.5±8.0	68.4±12.2
BMI, kg/m²	29.8±5.0[b]	26.5±3.6	24.7±3.9
Age, years	61±10[a]	56±19	38±20

*mean, ± standard deviation
NIDDM, noninsulin dependent diabetes mellitus
PrevAGT, previous abnormal glucose tolerance
BMI, body mass index
[a] significantly different from controls, $p<0.001$
[b] significantly different from controls, $p<0.02$
[c] significantly different from PrevAGT, $p<0.05$

Among them were decreased synthesis of insulin, decreased uptake of glucose in the periphery, altered body composition such that lean body mass decreases and fat tissue increases, changes in the foods eaten, and a decline in physical activity. Although Coon et al. (24) used highly artificial conditions (hyperinsulinemic euglycemic clamps) for their study of the relationship of age to insulin sensitivity, their study may be taken to provide preliminary evidence that advanced age, per se, will not necessarily incline a person towards insulin resistance. They found that increased central adiposity (as indicated by waist-hip ratio) was correlated with decreased glucose disposal in their subjects. In the present investigation of glycemic response to peanut butter crackers, there was no way to discriminate between an effect due to the age of the subject and an effect which may have been due to the body composition of the subject.

Mean Blood Glucose at Peak

Data from session one and session two also were combined for the analysis of mean peak blood glucose. Table 7 shows the results of the analyses related to the mean blood glucose. Mean peak blood glucose for the PrevAGT group (118 ± 20 mg/dl) was between those for the NIDDM and control groups (181 ± 41 and 113 ± 15 mg/dl, respectively) and differed significantly ($p<0.005$) from the

TABLE 7: MEAN TIME AT WHICH BLOOD GLUCOSE PEAKED AND MEAN PEAK BLOOD GLUCOSE VALUE

	NIDDM	PrevAGT	Control
Mean* Peak Blood Glucose, mg/dl Combined sessions	181±41 [a,b]	118±20	113±15
Mean Peak Time, minutes** Combined sessions	60 [a,b]	45 [c]	30
Between-Subject CV, Mean Peak Blood Glucose Combined sessions	23%	17%	13%
Published Between-Subject CV Values			
Wolever (26)	34%	NA	24%
Rasmussen (65)	33%	NA	NA

*mean; ± standard deviation
**identified on blood glucose response curves
NIDDM, noninsulin dependent diabetes mellitus
PrevAGT, previous abnormal glucose tolerance
[a] significantly different from controls, $p<0.0001$
[b] significantly different from PrevAGT, $p<0.005$
[c] significantly different from controls, $p<0.0001$
CV, coefficient of variation
NA, not assessed

value obtained for the NIDDM group. The NIDDM group's mean blood glucose was statistically different from that of the control group ($p<0.0001$). No statistical difference was found between the PrevAGT group and the control group with respect to the mean blood glucose at the peak.

Between-subject variability, as measured by the coefficient of variation (CV), is shown in Table 7. Variability was highest in the NIDDM group, intermediate in the PrevAGT group, and lowest in the control group. Variability of control and NIDDM subjects in this investigation appears to be somewhat lower than in other published studies. Information on variability of individuals with PrevAGT has not been published. The differences in the between-subject variability found in this study and the between-subject variabilities published by Wolever et al. (26) and Rasmussen et al. (65) have no obvious explanation. It may be that the subject population studied here was more genetically homogeneous, and therefore less variable. A comparison of the adiposity or at least the BMI of the subjects also may be useful in identifying possible differences among subjects in these studies.

Rasmussen et al. (65) reported the mean BMI of subjects as 26.4 kg/m^2; Wolever et al. (26) did not report BMI of the subjects in this paper. The mean BMI reported by Rasmussen was relatively low, and thus did not help explain the differences found in variability between their study and the present one.

Variability of glycemic response was noted as an important factor by Wolever (52). However, if the larger goal of quantifying day-long glycemia is to be attained, variability of responses should not prevent research in this area. The present study contributes information which can best be considered preliminary data regarding glycemic response to ingestion of the peanut butter and crackers.

Mean Time at which Blood Glucose Peaked

The mean peak value observed for the NIDDM group, 181 mg/dl, actually occurred at 45, 60, and 75 minutes. For statistical analysis, the middle time was used, since this is equivalent to averaging 45, 60, and 75. Table 7 displays the times at which blood glucose peaked. Blood glucose peaked first in the control group (30 minutes), second in the PrevAGT group (45 minutes), and third in the NIDDM group (60 minutes). Time of peak was significantly different between the NIDDM and control groups ($p<0.0001$), between NIDDM and PrevAGT groups ($p<0.005$), and between the PrevAGT and control groups ($p<0.0001$).

Peak blood glucose elicited by crackers and peanut butter may be compared with that reported for other foods. Peak blood glucose values elicited by other foods and time at which blood glucose peaked are displayed in Table 8. The test food, peanut butter and crackers, can be seen to elicit a lower blood glucose response than orange slices and orange juice (67), two foods which are commonly accepted for use in the diabetic diet. So, using the criterion of physiological effect on blood glucose, this food may be acceptable for inclusion in the diabetic diet. However, this criterion is only one way to evaluate a food for inclusion in the diet for a person with diabetes. Other considerations include nutritional contribution of the food (benefits and risks), potential effects of consuming the food on the diabetic's lipid profile, whether the individual is trying to lose weight, and other factors relating to that individual's needs and habits. For example, ice cream (59) elicited a relatively low peak blood glucose, but it does not contribute many vitamins, minerals, or much fiber to the diet. It also contains a substantial amount of fat which is largely saturated fat. And ice cream is not usually recommended as an integral part of weight loss meal plans. How should it be judged for use in the diet for someone with diabetes? The final guideline in the list published by the American Association of Diabetes Educators, that of individualizing the meal plan, blocks the issuance of blanket statements. However, most nutritionists would agree that frequency of consumption of a particular food is an important factor to consider, and most would not recommend frequent consumption of ice cream for a person with NIDDM.

TABLE 8: BLOOD GLUCOSE RESPONSE OF SUBJECTS WITH NIDDM TO VARIOUS FOODS

Peak Blood Glucose, mg/dl	Time of Peak, minutes	Food
157	40	under-ripe banana (21 g CHO) (66)
164	40	over-ripe banana (20 g CHO) (66)
181	60	peanut butter and crackers (22 g CHO)
185	55	white bread (20 g CHO) (66)
190	120	ice cream (50 g glucose) (59)
~ 220	90	glucose (50 g) (59)
~ 222	120	tofu frozen dessert (51 g glucose) (59)
225	60	orange slices (27 g CHO) (67)
245	60	Coke (27 g CHO) (67)
247	60	orange juice (27 g CHO) (67)
288	60	glucose (50 g) (61)

Should peanut butter and crackers be recommended to individuals with NIDDM for consumption as a snack? Fiber content of this product has not been published. This information would be helpful for evaluating the appropriateness of the peanut butter and cracker snack for use in the diabetic diet, since type of fiber and the amount of fiber appears to have an effect on the blood glucose response to ingestion of a food.

This type of snack product is fairly high in fat content (45% of calories), as can be seen in Table 4. The manufacturer reports that, of the ten grams of fat in the product, two grams are saturated, two grams are polyunsaturated, and the remaining six grams are monounsaturated. Some nutritionists may feel that use of this product should be discouraged in the diabetic diet because of its fat content. However, since the majority of the fat is either polyunsaturated or monounsaturated, this product may be acceptable for occasional use.

More information, such as the blood lipid reaction to consumption of this food, would be desirable before making a definitive pronouncement. The individual lipid profile, as well as lifestyle needs of the potential consumer, also are important considerations.

Repeated Measures ANOVA

Overall time by group effects were measured in this analysis. Statistically significant differences were found using Wilks' Lambda ($p<0.01$). This finding supported the alternative hypothesis that blood glucose response was different somewhere among the three groups. Further statistical manipulations (also using Wilks' Lambda) revealed that the difference existed only between the diabetic group and the control groups ($p<0.001$); no time by group differences were found between the control group and the PrevAGT group or between the diabetic group and the PrevAGT group.

Santiago et al. published (68) a case in which symptoms of hypoglycemia were reported by a diabetic when blood glucose dropped from 200 mg/dl to 100 mg/dl in the course of an hour. This is noteworthy because the subject's blood glucose was still above the textbook definition of hypoglycemia [<45-50 mg/dl, (62)]. This phenomena is familiar to clinicians, and is known as "relative hypoglycemia." If any of the subjects had experienced hypoglycemia, it would have been interesting to look at the rate at which the blood glucose had dropped during that interval, i.e. the slope of the line for that interval. However, none of the subjects reported symptoms of low blood glucose, and the actual measurements were above 50 mg/dl.

Nonetheless, slopes of the lines during each of the intervals for each of the groups were compared using the repeated measures ANOVA. The slopes of the three lines were found to be statistically different during only one interval; this was between 30 and 45 minutes, after the control group's glucoses had peaked, but the other two groups' glucoses were still climbing. Table 9 displays the results

TABLE 9: DIFFERENCES IN SLOPES AMONG GROUPS DURING THE THIRD INTERVAL

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	504	504	2.5	0.13
Group	2	9115	4558	22.2	0.0001
Error	29	5951	205		
Contrast	DF	Contrast SS	Mean Square	F	Pr>F
Groups*					
1 vs. 2	1	8995	8995	44	0.0001
1 vs. 3	1	515	515	2.51	0.12
2 vs. 3	1	2764	2764	13	0.001

*Group 1 vs. 2, NIDDM vs. Control
Group 1 vs. 3, NIDDM vs. PrevAGT
Group 2 vs. 3, Control vs. PrevAGT

of this analysis. Statistical differences were found between the NIDDM and control groups ($p<0.0001$) and between the PrevAGT and control groups ($p<0.001$). Comparisons of the slopes in the other intervals are listed in Appendix E.

Figure 2 displays blood glucose response data graphically.

One noteworthy feature of the PrevAGT curve was that a second peak occurred at 120 minutes. This second peak was an unexpected finding and was caused by a second peak in blood glucose experienced by four of the six subjects with PrevAGT. Although the second peak was not anticipated, Oettle et al. (49) reported a similar finding in a study done with normal subjects. In contrast, Bukar et al. (59), who studied subjects with NIDDM and sampled at similar intervals, did not show a second peak.

Three possible explanations exist for this second peak. First, it could be due to the effects of counterregulatory hormones such as glucagon or growth hormone. Since these were not measured, one can only speculate about whether this was indeed the case. A second alternative was that the second peak could be due to experimental error in the sampling procedure. If red blood cells became lysed during the sampling, then intracellular glucose would have joined the extracellular glucose and produced an artificially high value. However, it seems unlikely that this source of error would emerge only in the PrevAGT

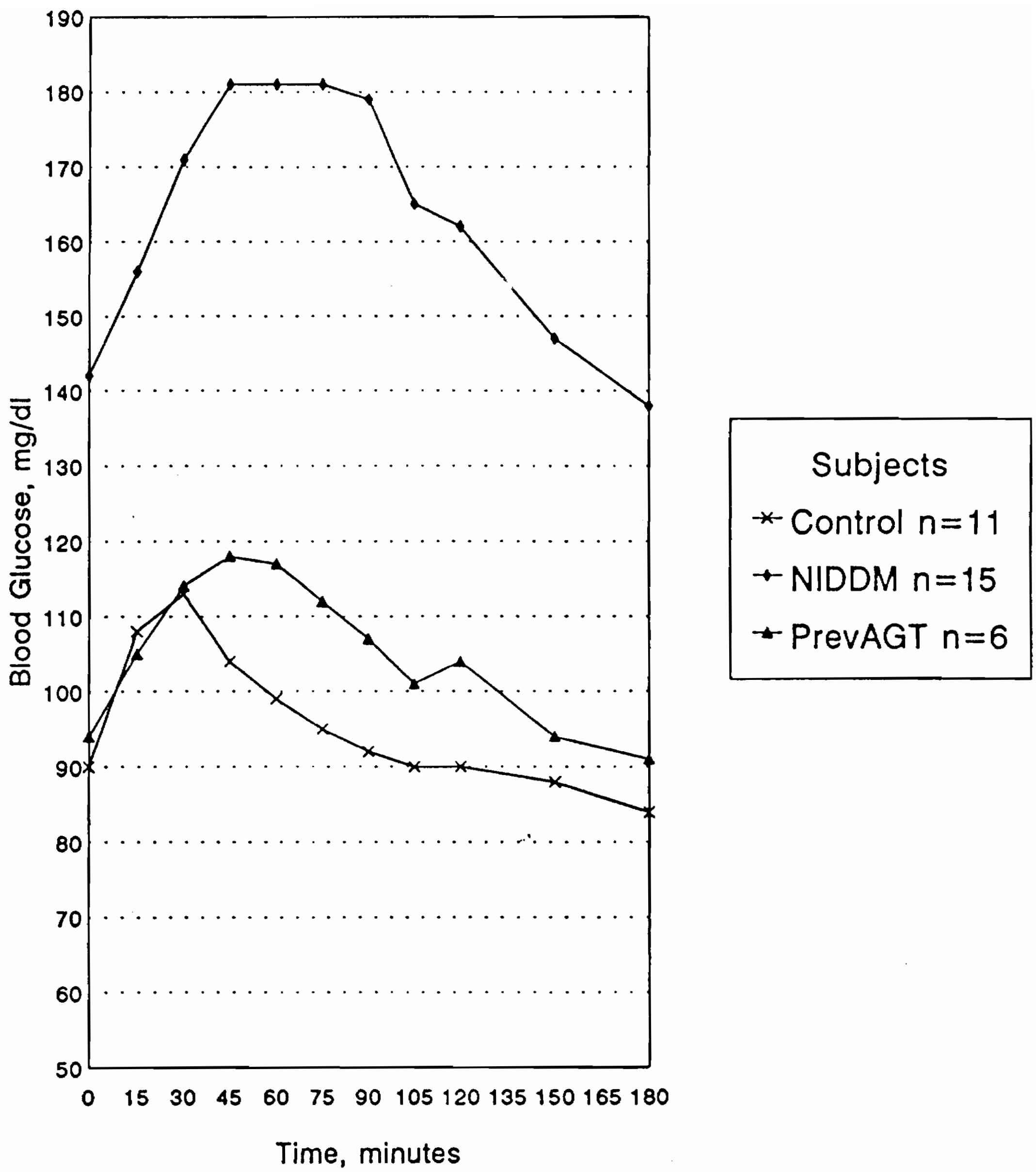

Figure 2: Blood Glucose Response to Peanut Butter Crackers
Combined Data from Session 1 and Session 2

group. A third possible cause of the second peak in blood glucose would be hepatic glucose output (which was insensitive to the ambient blood glucose environment). Unfortunately, there was no way to identify the cause of the second peak.

Summary

In this study, the blood glucose responses of subjects (with and without NIDDM) to a peanut butter and cracker snack product were compared. Diabetic subjects' responses were found to be different from control subjects' responses with respect to peak blood glucose and time at which blood glucose peaked. None of the subjects reported subjective experience of low blood glucose, and low blood glucose values were not documented in any subject.

An important point to emphasize here is that the peanut butter and crackers were tested under "best case" conditions, that is, in the morning, when blood glucose response was likely to be lowest. It was desirable to get the "best case" information first, as has been done in most of the glycemic response studies which have preceded this one (25-48).

Results from this study should be viewed as preliminary, since the study was executed under "best case" conditions. Future research investigating glycemic response to this food (and other snacks recommended to people with NIDDM) when eaten in the afternoon will provide useful information.

REFERENCES

1. U. S. Bureau of the Census, Statistical Abstract of the United States: 1991. (111th edition.) Washington, DC,1991.

2. Moltich, ME. Complications of diabetes mellitus. In: Handbook of diabetes nutritional management. Powers, M. ed Rockville: Aspen Publishers, Inc. 1987. pp.36-39.

3. DCCT Research Group. Diabetes control and complications trial (DCCT) update. Diabetes Care 1990;13:427-33.

4. American Diabetes Association Policy Statement. Nutritional recommendations and principles for individuals with diabetes mellitus: 1986. Diabetes Care 1987;10:126-32.

5. Franz M. Consistency: the nutrition key in type I diabetes. In: Learning to Live Well with Diabetes. Jensen NCM, and Moore MP eds. Minnetonka: International Diabetes Center, 1987. pp.161-2.

6. Gerich JE. Sulfonylureas in the treatment of diabetes mellitus--1985. Mayo Clin Proc 1985;60:439-43.

7. Franz M, Monk A. Type II diabetes nutrition: in search of a desirable weight. In: Learning to Live Well with Diabetes. Jensen NCM, and Moore MP eds. Minnetonka: International Diabetes Center, 1987. p.199.

8. Jenkins DJA, Ocana A, Jenkins AL, Wolever TMS, Vuksan V, Katzman L, et al. Metabolic advantages of spreading the nutrient load: effects of increased meal frequency in non-insulin-dependent diabetes. Am J Clin Nutr 1992;55:461-7.

9. Beebe CA,Rubenstein AH. Classification diagnosis and treatment of diabetes. In: Handbook of diabetes nutritional management. Powers, M. ed Rockville: Aspen Publishers, Inc. 1987. p.3.

10. Guthrie DW, ed. Diabetes Education: A Core Curriculum for Health Professionals.American Association of Diabetes Educators;1988: p.6,p.257,p.14.

11. National Diabetes Data Group. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance.Diabetes 1979;28:1039-57.

12. Olefsky JM, Molina JM. Insulin resistance in man. In: Rifkin H, Porte D Jr, eds. Ellenberg and Rifkin's Diabetes Mellitus. New York: Elsevier;1990;p.121.

13. Pillay TS, Makgoba MW. Molecular mechanisms of insulin resistance. South Afr Med J 1991;79:607-13.

14. Hjollund E, Pederesen O, Sorensen NS. Adipocyte insulin binding and action in moderately obese NIDDM patients after dietary control of plasma glucose: reversal of postbinding abnormalities. Diab Care 1987;10:306-12.

15. Burton BT,Foster WR.Health implications of obesity: an NIH Consensus Development Conference.J Am Diet Assoc 1985;85: 1117-21.

16. Freidenberg GR, Henry RR, Klein HH, Reichart DR, Olefsky JM. Decreased kinase activity of insulin receptors from adipocytes on non-insulin-dependent diabetic subjects. J Clin Invest 1987;79:240-50.

17. Thies RS, Molina JM,Ciaraldi TP,Freidenberg GR,Olefsky JM. Insulin-receptor autophosphorylation and endogenous substrate phosphorylation in human adipocytes from control, obese, and NIDDM subjects. Diabetes 1990;39:250-9.

18. Jacobs J, Sena M, Fox N. The cost of hospitalization for the late complications of diabetes in the United States. Diabebic Medicine 1991;8 symposium:S23-29.

19. Steinberg D, Witztum JL. Lipoproteins and atherogenesis.JAMA 1990;264(23):3047-51.

20. Hollenbeck CB, Coulston AM.Diabetes Mellitus. In: Brown ME, ed. Present knowledge in nutrition. Washington, DC: International Life Sciences Institute-Nutrition Foundation, 1990:362-70.

21. Chen YDI, Skowronski R, Coulston AM, Pietarinen J, Hollenbeck CB, Reaven GM. Effect of acute variations in dietary fat and carbohydrate intake on retinyl ester content of intestinally derived lipoproteins. J Clin Endocrinol Metab 1992;74:28-32.

22. Coulston AM, Hollenbeck CB, Swislocki ALM, Reaven GM. Persistence of hypertriglyceridemic effect of low-fat high-carbohydrate diets in NIDDM patients. Diab Care 1989;12:94-101.

23. Jarrett RJ,Baker IA,Keen H,Oakley NW.Diurnal variation in oral glucose tolerance: blood sugar and plasma insulin levels morning, afternoon, and evening.Brit Med J 1972; January 22:199-201.

24. Coon PJ,Rogus EM,Drinkwater D,Muller D,Goldberg AP.Role of body fat distribution in the decline in insulin sensitivity and glucose tolerance with age.J Clin Endocrinol Metab 1992; 75:1125-32.

25. Rasmussen OW, Gregersen S,Dorup J, Hermansen K.Blood glucose and insulin responses to different meals in non-insulin-dependent diabetic subjects of both sexes.Am J Clin Nutr 1992;56:712-15.

26. Wolever TMS, Nuttall FQ, Lee R, Wong GS, Josse RG, Csima A, Jenkins DJA. Prediction of the relative blood glucose response of mixed meals using the white bread glycemic index.Diab Care 1985;8:418-28.

27. Jenkins DJA,Wolever TMS,Taylor RH,Barker H,Fielden H,Baldwin JM,Bowling AC,Newman HC,Jenkins AL,Goff DV.Glycemic index of foods: a physiological basis for carbohydrate exchange.Am J Clin Nutr 1981;34:362-6.

28. Nishimune T, Yakushiji T,Sumimoto T,Taguchi S,Konishi Y, Nakahara S, Ichikawa T,Kunita N. Glycemic response and fiber content of some foods. Am J Clin Nutr 1991;54:414-9.

29. Wolever TMS.Relationship between dietary fiber content and composition in foods and the glycemic index.Am J Clin Nutr 1990;51:72-5.

30. Behme MT, Dupre J. All bran vs corn flakes: plasma glucose and insulin responses in young females. Am J Clin Nutr 1989;50:1240-3.

31. O'Dea K,Traianedes K, Ireland P,Niall M,Sadler J,Hopper J, De Luise M.The effects of diet differing in fat, carbohydrate, and fiber on carbohydrate and lipid metabolism in Type II diabetes.J Am Diet Assoc 1989;89:1076-86.

32. Golay A,Coulston AM,Hollenbeck CB,Kaiser LL,Wursch P, Reaven GM.Comparison of metabolic effects of white beans processed into two different physical forms.Diab Care 1986;9:260-6.

33. Sud S, Siddhu A, Bijlani RL, Karmarkar MG. Nutrient composition is a poor determinant of the glycaemic response. Brit J of Nutr 1988;59:5-12.

34. Wong S,Traianedes K,O'Dea K.Factors affecting the rate of hydrolysis of starch in legumes.Am J Clin Nutr 1985;42:38-43.

35. Bornet FRJ,Cloarec D,Barry J,Colonna P,Gouilloud S,Laval JD, Galmiche J. Pasta cooking time: influence on starch digestion and plasma glucose and insulin responses in healthy subjects.Am J Clin Nutr 1990;51:421-7.

36. Thorburn AW, Brand J, Truswell AS. Salt and the glycaemic response. Brit Med J 1986;292:1697-99.

37. Gans ROB, Heine RJ, Donker AJM, van der Veen EA. Influence of salt on glycaemic response to carbohydrate loading. Brit Med J 1987;294:1252-3.

38. O'Donnell LJD, Emmett P, Heaton KW. Failure of salt to increase starch digestibility and glycaemic response. Brit Med J 1988;296:394.

39. Nuttall FQ, Mooradian AD, Gannon MC, Billington C, Krezowski P. Effect of protein ingestion on the glucose and insulin response to a standardized oral glucose load. Diab Care 1984;7:465-70.

40. Westphal SA, Gannon MC, Nuttall F. Metabolic response to glucose ingested with various amounts of protein. Am J Clin Nutr 1990;52:267-72.

41. Wolever TMS, Jenkins DJA, Kalmusky J, Giordano C, Giudici S, Jenkins AL, Thompson LU, Wong GS, Josse RG. Glycemic response to pasta: effect of surface area, degree of cooking, and protein enrichment. Diab Care 1986;9:401-4.

42. Villaume C, Beck B, Rohr R, Pointel JP, Debry G. Effect of exchange of ham for boiled egg on plasma glucose and insulin responses to breakfast in normal subjects. Diab Care 1986; 9:46-9.

43. Coulston AM, Hollenbeck CB, Swislocki ALM, Reaven GM. Effect of source of dietary carbohydrate on plasma glucose and insulin responses to mixed meals in subjects with NIDDM. Diab Care 1987;10:395-400.

44. Gulliford MC, Bicknell EJ, Scarpello JH. Differential effect of protein and fat ingestion on blood glucose responses to High- and low-glycemic-index carbohydrates in noninsulin-dependent diabetic subjects. Am J Clin Nutr 1989; 50:773-7.

45. Hermansen K, Rasmussen O, Arnfred J, Winther E, Schmitz O. Glycemic effects of spaghetti and potato consumed as part of mixed meal on IDDM patients. Diab Care 1987;10:401-6.

46. Collier G, O'Dea K. The effect of coingestion of fat on the glucose, insulin, and gastric inhibitory polypeptide responses to carbohydrate and protein. Am J Clin Nutr 1983; 37:941-4.

47. Collier G, McLean A, O'Dea K. Effect of co-ingestion of fat on the metabolic responses to slowly and rapidly absorbed carbohydrates. Diabetologia 1984;26:50-4.

48. Jenkins DJA, Wolever TMS, Wong GS, Kenshole A, Josse RG, Thompson LU, Lam KY. Glycemic responses to foods: possible differences between insulin-dependent and noninsulin-dependent diabetics. Am J Clin Nutr, 1984;40:971-81.

49. Oettle GJ, Emmett PM, Heaton KW. Glucose and insulin responses to manufactured and whole-food snacks. Am J Clin Nutr 1987;45:86-91.

50. Gregersen S, Rasmussen O, Winther E, Hermansen K. Water volume and consumption time: influence on the glycemic and insulinemic responses in non-insulin-dependent diabetic subjects. Am J Clin Nutr 1990;52:515-8.

51. Thomas DE,Brotherhood JR,Brand JC.Carbohydrate feeding before exercise: effect of glycemic index.Int J Sports Med 1991;12:180-6.

52. Wolever TMS.The glycemic index. In: Aspects of Some Vitamins, Minerals, and Enzymes in Health and Disease.Bourne GH ed. World Rev Nutr Diet. 1990;62:120-85.

53. Diet and exercise in noninsulin-dependednt diabetes mellitus. National Institute of Health Consensus Development Conference Statement.Bethesda, NIH, 1986;6(8).

54. Clark SL,Nowbar LA,Sexton GJ,Hagan DW.A meta-analysis of the usefulness of the glycemic index in control of diabetes mellitus.J Am Diet Assoc (Supplement) 1992;92(9):A28.

55. Hunt JA, and Alojado NC. A new, improved test system for rapid measurement of blood glucose. Diabetes Res and Clin Prac 1989;7:51-5.

56. Jovanovic-Peterson L, Peterson CM, Dudley JD, Kilo C, Ellis B. Identifying sources of error in self-monitoring of blood glucose. Diab Care 1988;11:791-4.

57. Tate PF, Clements CA, Walters JE. Accuracy of home blood glucose monitors. Diab Care 1992;15:536-8.

58. Burritt MF, Klee GG, Hanson E, Converse JT, Forsman R. Evaluation of the One Touch glucose meter for use by a phlebotomy team. Laboratory Med 1990;21:512-16.

59. Bukar J, Mezitis NHE, Saitas V, Pi-Sunyer FX. Frozen desserts and glycemic response in well-controlled NIDDM patients. Diab Care 1990;13:382-5.

60. Cohen C, Wylie-Rosett J, Shamoon H. Insulin response and glycemic effects of meals in non-insulin-dependent diabetes. Am J Clin Nutr 1990;52:519-23.

61. Indar-Brown K, Norenberg C, Madar Z. Glycemic and insulinemic responses after ingestion of ethnic foods by NIDDM and healthy subjects. Am J Clin Nutr 1992;55:89-95.

62. Zeman FJ. Clinical Nutrition and Dietetics. 2nd ed. New York:Macmillan Publishing Co.,1991. p.458,p.418.

63. Brodows RG, Williams C, Amatruda JM. Treatment of insulin reactions in diabetics. JAMA 1984;252:3378-81.

64. Templeton CL.The older person: nutrition and diabetes.In: Handbook of diabetes nutritional management. Powers, M. ed. Rockville: Aspen Publishers, Inc. 1987. p.353.

65. Rasmussen OW, Gregersen S, Dorup J, Hermansen K. Day-to-day variation of blood glucose and insulin responses in NIDDM subjects after starch-rich meal.Diab Care 1992;15:522-4.

66. Hermansen K,Rasmussen OW, Gregersen S,Larsen S.Influence of ripeness of banana on the glood glucose and insulin response in Type 2 diabetic subjects.Diab Med 1992;9:739-43.

67. Sullivan MJ, Scott RL. Postprandial glycemic response to orange juice and nondiet cola: is there a difference? Diab Educ 1991;17:274-8.

68. Santiago JV, Clarke WL, Shah SD, Cryer PE. Epinephrine, norepinephrine, glucagon, and growth hormone release in association with physiological decrements in the plasma glucose concentration in normal and diabetic man. J Clin Endocrinol Metab 1980;51:877-83.

APPENDIX A: CONSENT FORM

CONSENT FOR PARTICIPATION IN THE BLOOD SUGAR STUDY
DEPARTMENT OF HUMAN NUTRITION AND FOODS
VIRGINIA POLYTECHNIC INSTITUTE AND STATE UNIVERSITY
BLACKSBURG, VIRGINIA

I have received an oral explanation of the blood sugar study. I understand the following:

I will not consume any food or beverage after midnight on the day prior to the day of the study.

I will be asked to report to Wallace Hall Annex at 8 AM in a fasting condition on the day of the study. I can expect to finish the session by noon. I am willing to participate in the study on two separate occasions.

My blood sugar will be measured using a glucometer, which I will operate myself. I am willing to participate in training to learn how to use the One Touch II.

Blood sugar measurements will be taken every 15 minutes for the first two hours, and on the half hour thereafter. (11 finger sticks)

After the first blood sugar measurement is taken I will consume one package of peanut butter and cracker "sandwiches."

If I am a diabetic, I have obtained clearance for participation from my physician.

I will follow my usual treatment regimen and take my usual medicines (if applicable).

If I feel symptoms of low blood sugar, or if glucometer reading is less than or equal to 50 mg/dl glucose, then participation will be terminated, and I may choose to take oral glucose tablets to counteract the hypoglycemia.

If at any time I believe that my health may be impaired or jeopardized, I may cease to participate in this study.

I understand the above and agree to participate in the blood sugar study to be conducted at Virginia Polytechnic Institute and State University during the summer of 1992.

____
signature and date

Investigators: Elizabeth Glynn, R.D. (951-4171), Graduate Student/HNF

Dr. Mary Ann Novascone (231-5778), Academic Advisor/HNF

APPENDIX B: DATA COLLECTION FORM

Date:
Subject name:
Gender: Ht.: Wt.: BMI:
Medications taken today: Gastroparesis:

sequence	time	BG
FBS		
Done Eating	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	
t-15		
t-30		
t-45		
t-60		
t-75		
t-90		
t-105		
t-120		
t-150		
t-180		

sequence	time	BG
FBS		
Done Eating	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	
t-15		
t-30		
t-45		
t-60		
t-75		
t-90		
t-105		
t-120		
t-150		
t-180		

APPENDIX C: RAW BLOOD GLUCOSE DATA FROM SESSION 1

FBG	15	30	45	60	75	90	105	120	150	180	Group
					(Above: Time in Minutes)						
172	157	180	173	178	174	192	197	201	183	177	1
79	162	188	205	196	223	218	221	205	185	171	1
162	202	199	216	216	209	196	182	176	156	141	1
192	221	243	267	285	232	227	218	173	208	199	1
131	150	159	172	161	160	156	143	136	118	108	1
203	195	238	270	241	244	239	265	184	237	156	1
101	99	114	109	106	97	103	104	103	90	90	1
185	192	216	205	210	244	253	211	218	206	209	1
105	117	106	133	160	145	129	132	116	124	109	1
67	86	85	111	105	111	110	96	81**	66	62	1
161	165	181	217	213	236	278	225	247	176	174	1
76	91	115	136	140	135	102	129	119	102	90	1
135	141	146	154	151	147	143	127	123	112	111	1
161	162	170	152	189	169	164	159	173	146	164	1
151	181	214	251	206	222	208	172	156	140	136	1
86	116	109	84	73	82	85	82	80	80	80	2
89	113	106	87	85	96	83	89	78	86	91	2
89	108	102	100	97	87	80	90	97	87	85	2
83	114	136	121	93	89	89	90	95	87	93	2
89	97	105	101	95	92	93	87	89	87	70	2
96	123	118	107	103	88	70	93	86	90	91	2
101	114	113	102	94	91	95	95	96	91	82	2
81	88	92	77	78	75	83	75	73	77	81	2
99	106	133	134	139	147	143	130	114	106	92	2
70	96	118	111	113	113	93	85	87	87	91	2
92	93	108	99	105	95	91	92	95	90	89	2
85	101	111	104	80	82	78	77	80	76	77	3
109	117	119	128	137	116	126	101	143	119	90	3
89	104	109	99	96	94	98	84	87	86	88	3
104	105	122	140	140	126	115	102	93	92	91	3
128	128	125	144	163	162	153	158	149	131	120	3
90	105	110	103	108	101	96	92	91	97	89	3

FBG, Fasting Blood Glucose
Group 1, NIDDM
Group 2, Control
Group 3, PrevAGT
** Interpolated Value

APPENDIX D: RAW BLOOD GLUCOSE DATA FROM SESSION 2

(Above: Time in Minutes)

FBG	15	30	45	60	75	90	105	120	150	180	Group
172	153	164	171	163	167	184	180	179	158	166	1
175	179	203	211	213	207	192	178	186	154	143	1
121	164	179	178	160	151	141	129	116	108	97	1
164	183	203	200	224	232	211	162	218	189	175	1
139	140	126	136	137	144	149	129	145	137	119	1
151	186	210	189	208	196	186	158	159	147	129	1
166	149	159	179	191	204	209	191	194	170	160	1
169	169	178	183	184	180	192	138	180	157	157	1
178	168	213	212	216	227	219	200	215	198	176	1
72	93	103	112	134	105	100	94	95	66	57	1
83	113	128	133	126	132	135	127	121	108	88	1
180	194	225	227	233	240	256	225	212	200	201	1
178	206	232	249	199	229	222	219	205	200	192	1
133	147	131	150	164	154	144	137	131	101	107	1
112	113	129	143	129	113	108	102**	96	80	79	1
100	130	149	147	134	119	106	90	89	90	88	2
89	120	116	112	110	93	92	88	91	91	91	2
79	106	102	86	90	82	85	83	85	80	74	2
95	118	135	117	92	84	85	90	91	90	89	2
93	96	97	94	88	88	89	81	84	80	80	2
89	113	106	87	85	96	83	89	78	86	91	2
77	90	75	77	81	79	79	80	82	81	75	2
86	103	115	112	108	109	100	92	93	79	85	2
89	99	110	95	100	103	98	96	100	100	84	2
103	121	121	137	109	109	102	95	93	100	94	2
81	102	98	87	79	74	80	84	86	84	77	2
74	84	99	105	98	90	76	81	69	62	79	3
90	123	115	132	125	147	127	117	126	98	86	3
82	88	98	95	93	97	86**	75	85	86	69	3
92	107	129	126	132	122	116	125	110	72	96	3
99	111	131	146	142	127	131	125	127	115	116	3
80	87	95	98	87	81	86	77	83	91	87	3

FBG, Fasting Blood Glucose
Group 1, NIDDM
Group 2, Control
Group 3, PrevAGT
** Interpolated Value

APPENDIX E: COMPARISONS OF SLOPES DURING EACH TIME INTERVAL

Interval 1: 0-15 minutes

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	23259	23259	32.7	0.00
Group	2	956	478	0.67	0.52
Error	29	20628	711		

Interval 2: 15-30 minutes

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	10162	10162	18.6	0.00
Group	2	2890	1445	2.65	0.09
Error	29	15824	546		

Interval 3: 30-45 minutes

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	504	504	2.5	0.13
Group	2	9115	4558	22.2	0.0001
Error	29	5951	205		

Contrast	DF	Contrast SS	Mean Square	F	Pr>F
Groups*					
1 vs. 2	1	8995	8995	44	0.0001
1 vs. 3	1	515	515	2.51	0.12
2 vs. 3	1	2764	2764	13	0.001

*Group 1 vs. 2, NIDDM vs. Control
Group 1 vs. 3, NIDDM vs. PrevAGT
Group 2 vs. 3, Control vs. PrevAGT

Interval 4: 45-60 minutes

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	591	591	1.79	0.19
Group	2	628	314	0.95	0.40
Error	29	9545	329		

Interval 5: 60-75 minutes

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	942	942	3.07	0.09
Group	2	470	235	0.77	0.47
Error	29	8896	y307		

Interval 6: 75-90 minutes

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	1230	1230	5.68	0.02
Group	2	123	61	0.28	0.76
Error	29	6284	217		

Interval 7: 90-105 minutes

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	5915	5915	9.84	0.00
Group	2	3791	1896	3.15	0.06
Error	29	17440	601		

Interval 8: 105-120 minutes

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	0	0	0.00	1.00
Group	2	547	273	0.35	0.71
Error	29				

Interval 9: 120-150 minutes

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	8745	8745	13.5	0.00
Group	2	4040	2020	3.12	0.06
Error	29	18789	648		

Interval 10: 150-180 minutes

Source	DF	Type III SS	Mean Square	F	Pr>F
Mean	1	2902	2902	5.84	0.02
Group	2	1265	633	1.27	0.29
Error	29	14399	497		

Vita

Liz was born in North Carolina but didn't live there long enough to develop a Southern accent. She grew up in California, where she attended Stanford University (B.A. in sociology) and University of California (B.S. in clinical nutrition).

After graduation, Liz worked as a dietitian for about 10 years, then opted to continue her education at Virginia Tech. Professional goals include adding to the body of knowledge about nutrition in diabetes, and continuing to work with people who live with diabetes.

A E Glynn