# EFFECT OF DIETARY FIBER ON INSULIN REQUIREMENTS AND SERUM LIPIDS IN JUVENILE-ONSET DIABETES MELLITUS

by

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# DEDICATION

To

Gary

Sharon

Darryl

and

Gay

who sacrificed so much of their time, effort, energy and freedom of daily food choices to make this study possible. I am greatly indebted to them.

- MRH

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# INTRODUCTION

Diabetes mellitus of the juvenile- and adult-onset variety (Type I and Type II, respectively) is associated with alterations in carbohydrate and lipid metabolism. These in turn, have been linked to atherosclerosis, cardiovascular disease, retinopathy, nephropathy, and neuropathy. If glycemic excursions and lipid levels can be reduced in Type I diabetic patients through new vistas in diet modification, this may be of potential value in reducing the incidence of diabetic complications when adhered to over long periods of time.

Recently, studies have revealed evidence that diabetic subjects fed diets high in dietary carbohydrate and fiber show improved glucose tolerance, reduced insulin or sulfonylurea needs, and improvement in the serum lipid picture [1, 2, 3, 4, 5, 6]. When diets high in carbohydrate (without added fiber) are fed to adult diabetic and hypertriglyceridemic subjects, glucose tolerance and fasting plasma glucose are improved [7, 8] although fasting plasma triglycerides are usually increased [9, 10]. This seems to indicate that high levels of dietary fiber modify the hypertriglyceridemic effects of enhanced carbohydrate intake. But studying the physiological effects of increasing dietary fiber, without also increasing the total carbohydrate intake or at least altering the ratio of simple to complex carbohydrate, is difficult because foods with the highest fiber to kilocalorie (kcal) ratios are also very high in complex carbohydrates [11, 12]. Long-term investigations with enhanced fiber as the only dietary variable are therefore difficult to conduct in humans because the food choices are limited, monotonous, and a high level of compliance is difficult to achieve.

Understanding the effects of dietary fiber on glycemic control and serum lipid levels in human diabetic subjects is an important prerequisite

to comprehending the mechanism of action of the high-carbohydrate, high-fiber (HCF) diets which have been so successful.

# LITERATURE REVIEW

## A. Fiber Defined

Interest in dietary fiber has gained increasing recognition in recent years since Burkitt [13] and Trowell [14] first asserted that insufficient dietary fiber may be an etiological factor in the development of a number of 'Western' diseases (Table 1). Trowell observed that diabetes mellitus and ischemic heart diseases are almost non-existant among African tribes who consume diets high in unrefined cereal and grain products. Walker [15, 16] speculated that plant fibers exert protective effects against these disorders and Burkitt has helped to popularize this hypothesis [13, 17]. Extensive research has been conducted in recent years to determine the validity of these assertions [18 - 42]. However, research is plagued by problems of terminology, definition, and analysis [43]. Fiber is composed of a number of polymeric substances [33, 43 - 45] and there is no scientific consensus as to which of these are relevant as fiber in human nutrition [46] ; because the specific components of fiber have not been agreed upon, there is no standard method of analysis for "fiber" and, in turn, there is lack of published analytical data on both total plant fiber and its individual components [43] . The most comprehensive recent publication [12] lists nutritive and fiber contents for only 342 food items.

Efforts are being made to define fiber and several definitions have been proposed in this regard. Analytical methods have been devised to detect the substances comprised under most definitions (Figure 1). Trowell originally defined dietary fiber as "the remnants of vegetable cell walls which are not hydrolyzed by the alimentary enzymes of man" [48]. Because parts of the plant other than the cell wall are not hydrolyzed in the human digestive process, Trowell later redefined it as "plant polysaccharides and

TABLE 1

Western-risk diseases

| Site | Diseases |
|---|---|
| Colonic | Constipation, appendicitis, diverticular disease, hemorrhoids, polyps and cancer of the large bowel, irritable colon, ulcerative colitis. |
| Metabolic | Obesity, diabetes mellitus, ischemic heart disease, peripheral vascular disease, varicose veins, deep vein thrombosis, gallstones, kidney stones, rheumatoid arthritis, multiple sclerosis, senile osteoporosis, osteitis deformans (Paget's), pernicious anemia, most varieties of thrombosis. |
| Endocrine | Thyrotoxicoses, myxedema, Hashimoto's thyroiditis, Addison's hypocorticalism. |
| Others | Dental caries, hiatus hernia, Crohn's disease |

Hypertension and strokes have been rare in population groups if low salt, (1 - 3 g/day) has been combined with high-fiber, very high-starch diets.

Source: reference [47]

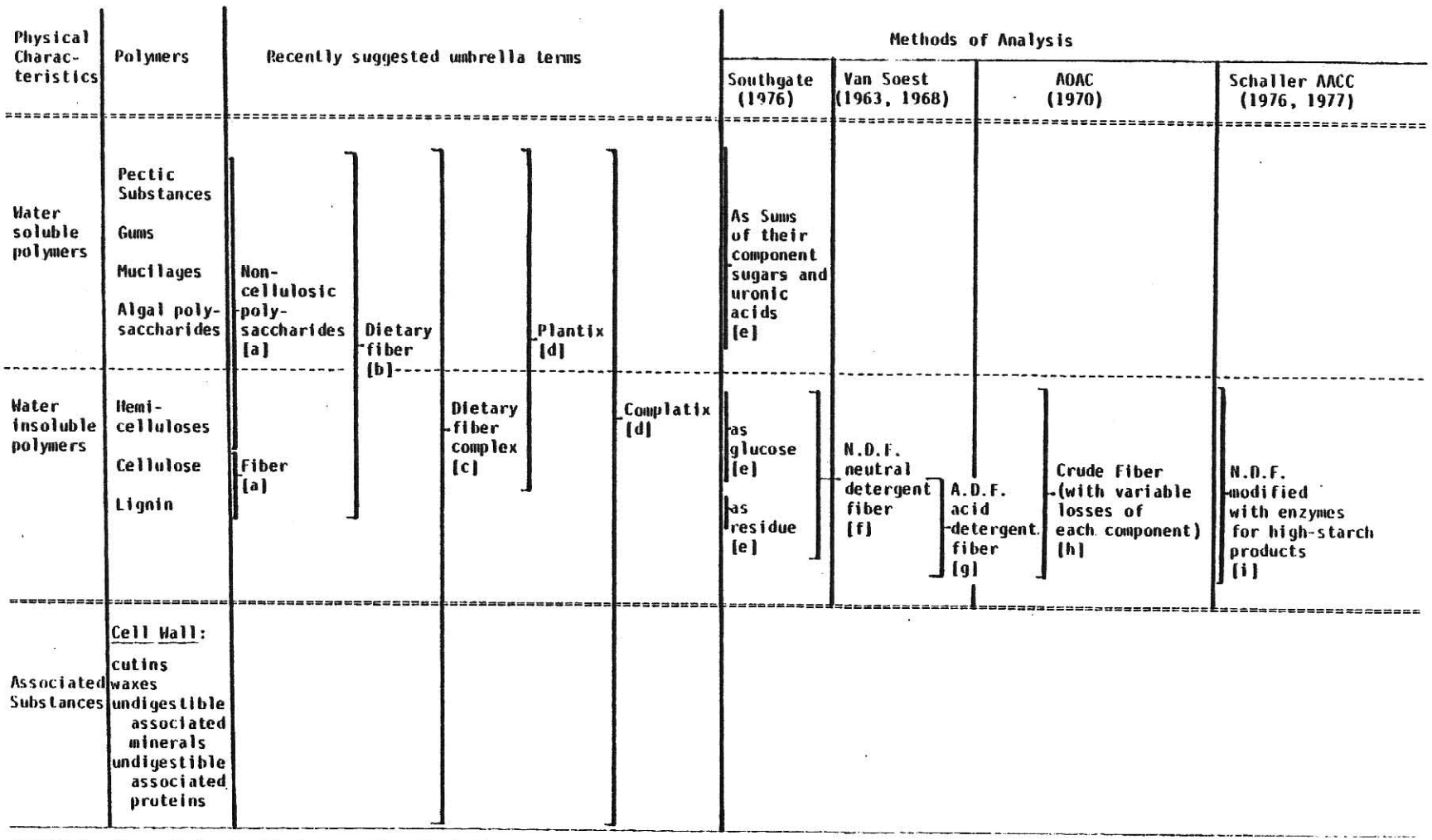


FIGURE 1. Suggested umbrella terms and analytical procedures for dietary fiber or its fraction. [a] Southgate, D.A.T., Bailey, B., Collinson, E., and Walker, A.F.: J. Hum. Nutr. 30: 303-313, 1976. [b] Trowell, H.: Am. J. Clin. Nutr. 25: 926-930, 1972. [c] Trowell, H.: Am. J. Clin. Nutr. 29: 417-426, 1976. [d] Spiller, G.A., Fassett-Cornelius, G., and Briggs, M.: Am. J. Clin. Nutr. 29: 934-935, 1976. [e] Southgate, D.A.T. In: Fiber in Human Nutrition. Spiller, G.A., and Amen, R.J., Edit., New York, Plenum Press, 1976. pp. 73-107. [f] Van Soest, P.J.: J. Assoc. Off. Agric. Chem. 46: 825-829, 1963. [g] Van Soest, P.J., and Wine, R.H.: Assoc. Off. Agric. Chem. 51: 780-785, 1968. [h] AOAC. Official methods of Analysis of the Association of Official Analytical Chemists, 11th ed., Horwitz, W., Edit. Washington, D.C., AOAC 1970, p. 129. [i] Schaller, D.: Food Product Development 11: 70-75, 1972.

Source: reference [43]

lignin which are resistant to hydrolysis by the digestive enzymes of man" [49]. This allowed the inclusion of indigestible substances which are not part of the plant cell wall. Spiller and associates [43] argue that "fiber" and "dietary fiber" are inappropriate terms because many of the components are not fibrous in nature. In addition, "fiber" is an inexact term used in many other fields such as textiles, metals, and anatomy. Spiller prefers the term "plantix" derived from Latin planta (plant) and matrix (matrix) to describe the undigested plant materials that form a matrix in the human digestive system, up to the ileocecal valve. This concept is important, he asserts, because the action of colonic bacteria on this matrix is responsible for many of the physiological effects associated with plantix. "Complantix" could be used to describe plantix-associated materials which may be associated with, or influence, the physiological action of plantix (Figure 1). Routine methods of analysis have not been devised to analyze the plantix-associated compounds and values for them are not included in tables which list the fiber content of foods. For the purposes of this paper, plantix and dietary fiber will be used interchangeably to reflect water-soluble and water-insoluble polymers described in Figure 1.

Following,is a brief description of the components of dietary fiber and their associated physiological effects.

## B. Components of Dietary Fiber/Plantix (see Table 2)

### 1. Cellulose

This is one of several insoluble cell-wall polysaccharides (Table 2) and is the only truly fibrous component of the plant cell wall [44].

TABLE 2

Components of dietary fiber

| Principal sources in the diet | Description | Classical nomenclature |
|---|---|---|
| Structural materials of the plant cell wall | Structural polysaccharides | Pectic substances<br>Hemicelluloses<br>Cellulose |
| | Non-carbohydrate constituents | Lignin<br>Associated substances<br>Cutins<br>Waxes<br>Undigestible associated minerals<br>Undigestible associated proteins |
| Non-structural materials either found naturally, or used as food additives | Polysaccharides from a variety of sources | Pectic substances<br>Gums<br>Mucilages<br>Algal polysaccharides<br>Chemically modified polysaccharides<br>Storage undigested polysaccharides<br>Fungal chitans |

Adapted from [43, 47, 50]

Long, unbranched chains (3,000 to 100,000 units) of glucose linked in a β-1→4 manner are arranged in crystalline form and contribute to the fibrousness of this compound [19, 51]. Structural stability and crystallinity are conferred by extensive inter- and intra-molecular hydrogen bonding [44]. This is the β-isomer of starch [52], resistant to human pancreatic amylase, but probably suseptible to bacterially-produced colonic cellulases. Human metabolic studies reveal that cellulose is degraded to a variable extent in the human colon [33, 53 - 56] but an average of 40% degradation is suggested as reasonable [44]. The variability in cellulose digestion (degradation) has been attributed to differences in intestinal transit time between human subjects [55]; those with the longest transit times show the greatest apparent digestibility of cellulose [57]. A reasonable explanation for this phenomenon is that longer transit times provide bacterial enzymes increased time to act on the fiber; this is consistent with the observation that cellulose digestibility is proportional to laxation rate [58].

Physiologically, cellulose has been shown to reduce blood glucose levels in carbohydrate-sensitive individuals [29, 59] as well as normal man and animals [60, 61]. Hypocholesterolemic effects have been small or non-existent in some studies [59, 62 - 65] but significant in others [66 - 68]. Cellulose binds bile acids [64, 66, 69], decreases intestinal transit time[70], and provides protection against tumor induction in animals [71]. Increased fecal excretion of magnesium, zinc, calcium, phosphorus, or iron has accompanied ingestion of cellulose in some studies [64, 70, 72, 73] but not others [74 - 76].

2. Hemicelluloses

The hemicelluloses encompass a great variety (at least 250) of

cell-wall polysaccharides, composed of two or more different sugars and a chain length of 150 - 200 sugar units [44, 45]. As a broad generalization, xylose sugars form the backbone of these molecules, with various substitutions and degrees of branching [33, 77]. Hemicelluloses are degraded in the colon to a greater extent than cellulose [52, 54, 78]. Three properties of hemicelluloses may hold significance in human physiology: their capacity to bind ions, hold water, and their digestibility [33, 44, 54, 57, 72, 78]. However, metabolic studies are difficult to conduct with the hemicelluloses because these substances are almost impossible to isolate without damaging their structure [45].

3. Pectic Substances

The typically amorphous character of the pectic substances makes "fibrous" a very inaccurate term to describe their physical properties [45]. Included in this group is the water-insoluble protopectin, in addition to the water-soluable pectinic acids and pectin [52]. The "parent" molecule is a polymer of 1-4,β-D-galacturonic acid with variable degrees of esterification [33, 44]. Purified pectin is added to supplement the natural fruit pectin in jam-making to make the product "jell". The gel-forming property of the pectic substances has been well-documented [33, 45]. Physiologically, these hold water (gel formation), bind cations and organic materials (bile acids), and lower serum cholesterol [18, 33, 44, 45, 68]. Pectins are almost completely degraded in the colon [33].

4. Lignins

The lignins are the only major plant fibers which are not polysaccharides [33]; chemically they are very inert [52] and resistant to enzymatic

digestion. The lignins are neither digested nor absorbed in the human gastrointestinal tract [33], because lignin is normally metabolized aerobically [55]. Physiologically, lignins bind bile salts and may decrease absorption of fiber-associated nutrients in the small intestine [33].

5. Gums [44]

The plant gums are a group of highly-branched polymers containing uronic and galacturonic acids. They are non-structural plant materials which form sticky exudates at the site of injury to plants, then dry to produce nodules which are hard and protective. Commercially, these can be obtained by inflicting injury to the plant and collecting the fluid that drains. In addition to being consumed in natural foodstuffs, they are commercially added to processed foods as stabilizers, emulsifiers and thickeners, and to pharmaceutical preparations marketed as laxatives. Many gums are degraded by bacterial enzymes in the human colon [79]. Carageenan, konjac mannan and locust bean gum lower serum cholesterol in man and animals [68].

6. Mucilages

This group of plant fibers exhibit structural similarity to the hemicelluloses [52] but they are located in the endosperm of seeds, mixed with digestible polysaccharides, rather than in the cell wall. Botanically, they retain water in the seed to prevent its desiccation. Physiologically, mucilages bind water and bile salts and exert hypocholesterolemic effects [44]. The cholesterol-lowering property of guar gum is well-documented [18, 32, 80, 81], even when cholestyramine has proved ineffective [82]. Mucilages are fermented in the human colon by bacterial enzymes [79].

7. Algal and indigestible storage polysaccharides

These consist of branched or linear molecules containing a variety of pentose and hexose sugars. Few, if any, studies have examined the physiologic effects of this class of plantix components, although it is thought to be readily hydrolyzed in the gut [44].

8. Fiber associated substances

The fiber-associated substances are a group of indigestible compounds associated with the plant cell wall. These include proteins, minerals, cutins, and waxes [44].

C. Analytical Methods

The fiber values most often reported in the literature are crude fiber (CF) and dietary fiber (DF). In recent literature, values for dietary fiber are increasingly reported over those for crude fiber. Delineation between them is important because they contain different percentages of the various fiber components. Since this distinction must be made if meaningful conclusions are to be drawn from research, both will be reviewed briefly, here.

1. Crude fiber

Crude fiber was first analyzed by Einhof in 1806 [51] and was considered an estimate of the indigestible fraction of animal feed, an important prerequisite in determining the nutritional value of the feed. Although a modification of the Einhof method is still used today to analyze fiber in human foods and is still reported in food composition tables (United

States Department of Agriculture Handbook Number 8 [83]), it probably has no real significance in human nutrition. The method is very insensitive at the low levels which are found in foods and it measures variable and underestimated proportions of plant cell-wall constituents [44]. In general, it recovers only 50 - 80% of the cellulose, 20% of the hemicelluloses and 10 - 50% of the lignin [44, 51, 84, 85].

2. Dietary Fiber

Although crude fiber analysis is conducted by internationally agreed-upon methods, there is no such agreement for dietary fiber methodology. Acid detergent fiber analysis proposed by Saunders [86 (Saunders)] recovers most of the cellulose and lignin, but virtually none of the other plantix components. Neutral detergent fiber analysis (American Association of Cereal Chemists) recovers virtually all of the celluloses, hemicelluloses and lignin [33, 86], which are major constituents of dietary fiber, but fails to measure the water-soluble polymers (Figure 1). Southgate has developed a series of complex methods for recovering both water-soluable and water-insoluable plant polymers [87]; this provides the most useful information for studying the metabolic effects of dietary fiber. However, this method is slow, tedious, and expensive, and food fiber values analyzed by this technique are rare in the literature. Because methods of analyses for dietary fiber recover a greater percentage of plantix components, values for dietary fiber are generally two to five times the crude fiber values [84].

D. Effects of Fiber on Metabolic Parameters of Glucose and Lipid Metabolism

Subsequent to Burkitt and Trowell's proposed link between low fiber diets and diabetes mellitus, extensive studies have been conducted to ascertain the effects of high-fiber diets on parameters of glycemic control in normal and carbohydrate-sensitive individuals. Investigations have focused on the addition of fiber, variation of fiber type, as well as simultaneous elevation of fiber and carbohydrate while necessarily limiting fat.

1. Effect on Glycemic Response

a. Fiber from mixed dietary sources: Human studies have shown hypoglycemic and/or hypoinsulinemic response when high-carbohydrate and high-fiber are combined as part of the dietary regimen. When seven healthy young adults were fed two isocaloric high (70%) carbohydrate diets, either with low (1 g crude) or high (18 g crude) fiber, the endogenous insulin response to the high-fiber diet was only half as great ($P < 0.05$ at 30 minutes and 2 hours) as the low fiber diet with an equivalent amount of carbohydrate Blood glucose was not significantly altered [3]. Anderson [2] has shown that both insulin and glucose responses are lower in Type II diabetics fed high-fiber (70 g dietary), high-carbohydrate (60 - 75%) compared to low (44%) carbohydrate, high (70 g dietary) fiber diets. Postprandial and fasting blood glucose levels are almost always lower on high-carbohydrate, high-fiber diets than conventional diabetic diets of lower carbohydrate (40-45%) and fiber (20 g dietary/day) content. This has been demostrated in Type II diabetics treated by diet and sulfonylureas [1, 5, 6, 88] as well as by diet and insulin [1, 4, 5, 6, 88]. Diabetics requiring insulin or sulfonylureas prior to high-carbohydrate, high-fiber (HCF) diet therapy can reduce or eliminate them altogether in HCF diets while maintaining adequate glycemic

control [1, 4, 5, 6, 7, 33, 89, 90, 91, 92]. The distribution of energy-containing nutrients in these diets is listed in Table 3. The low fiber diets are higher in simple carbohydrate that the high-fiber diets. Since a high ratio of simple to complex carbohydrate has been shown to increase the endogenous insulin response [93], fasting blood glucose [94, 95] and postprandial blood glucose [96] in normal and diabetic human subjects, the results of HCF studies cannot be interpreted on the basis of total carbohydrate and fiber alone. Some investigators who show improved glycemic response to HCF diets do not report the ratio of simple to complex carbohydrate employed in the experimental design [97], thus further complicating the difficulty of interpretation.

Other studies have focused on the glycemic response to high-carbohydrate diets in adult and diabetic hypertriglyceridemic subjects. As early as the 1930's researchers began to associate high-carbohydrate diets with improved glucose tolerance and decreased insulin requirements in normal and diabetic subjects (reported in [6]). Diets containing 60% of the energy as carbohydrate resulted in decreased fasting plasma glucose (160 mg/dl) compared to diets where 40% of kcal were fed as carbohydrate (200 mg/dl; $P < 0.05$), while insulin usage in diabetics decreased from 51 to 48 units per day ($P < 0.01$) during the six-week study [98]. Because additional carbohydrate was incorporated as cereals and vegetables in this study, an increased level of fiber may have influenced these values. Fiber influence could be discounted however, when insulin-treated diabetics were fed equivalent amounts of dietary fiber (20 - 23 g/day) but high (70%) and low (43%) carbohydrate. Reduction in insulin dosage (20 units/day to 12 units/day) was required to avoid hypoglycemia on the high-carbohydrate diet ($P<0.01$;[7]). Neither was fiber a variable when young, normal subjects were fed sucrose at 60% and 80% daily kcal for 2 to 3 weeks,

TABLE 3

Composition of representative 2000 kcal diets[a]

| Component | Control | | High-carbohydrate, high-fiber | |
|---|---|---|---|---|
| | g | %kcal | g | %kcal |
| Protein | 98 | 20 | 95 | 19 |
| Carbohydrate | | | | |
| Total available | 215 | 43 | 360 | 72 |
| Simple | 100 | | 90 | |
| Complex | 115 | | 270 | |
| Fat | 83 | 37 | 20 | 9 |
| Total plant fiber | 31 | | 74 | |

[a] Source: reference [33]

and glucose tolerance improved compared to sucrose at 20% and 40% levels [8]. Similarly,glucose tolerance was enhanced when Brunzell fed dextrimaltose to insulin-treated diabetics for one week (reported in [97, 99]). However, glycemic response has not uniformly improved at high levels of carbohydrate intake. Hypertriglyceridemic subjects experienced impaired glucose tolerance when carbohydrate was fed at 85% of kcal [10], and postprandial glucose deteriorated in non-insulin-dependent diabetics receiving 60% of their kcal as carbohydrate [100]. Other investigators [101] found diabetic control at high levels of carbohydrate intake well-maintained, but not improved.

High levels of fiber from mixed dietary sources have improved numerous parameters of glycemic control [22, 27, 34]. Some investigations have concentrated on cereal fibers [102], others on leguminous fibers [103, 104], many on guar and pectin [20, 26, 31, 32, 35 - 37, 60, 98, 103, 105] , and a few on fruits and vegetables [30, 102]. Results of these studies have shown conclusively that fiber from different sources has different physiological actions [104] and these can be modified by the form [106] and degree of intactness [30] in which the fiber is administered. This was shown elegantly by Haber and Heaton [30] when they fed three meals, each containing 60 g carbohydrate from apples to normal volunteers: a) apple-juice (fiber-free), b) apple-puree (fiber-disrupted), and c) whole apples (fiber intact). The whole apples produced greatest satiety and the least rise in serum insulin and glucose ($P<0.05$) as opposed to fiber-free juice and fiber-disrupted puree.

Of the specific fiber sources which have been studied, most is known about guar and pectin. This is largely attributable to the work of Jenkins et al. [18, 26, 28, 31, 32, 35, 60, 103, 104, 106, 107]. Guar and pectin improve meal glucose tolerance without altering endogenous insulin secretion by normal subjects or Type II diabetics [20, 60] and reduce insulin needs by

more than 12% ($P<0.05$) in insulin-dependent diabetics as assessed by an artificial endocrine pancreas [37]. Longer term studies with guar and pectin show a large (30 - 68%) reduction in glycosuria [26, 35] with a simultaneous decrease in insulin doses [35]. In all of these studies the beneficial effects of guar and pectin have been accomplished without concurrent increase in dietary carbohydrate. Leguminous fibers have exerted similar but more pronounced effects on parameters of carbohydrate tolerance, both with [91] and without [103, 104] increasing the percentage of kilocalories from carbohydrate. Fiber from apple and carrot [30, 102] significantly improves glucose tolerance.

High (30 - 54 g/day) mixed dietary fiber, normal carbohydrate (43 - 53%) diets have shown inconsistency in normalizing glycemia. Maturity-onset diabetics seem to benefit from 30g mixed dietary fiber daily [27]. Such diets result in significantly lower mean plasma glucose and endogenous insulin values compared to isocaloric diets with equal carbohydrate. Similar results were obtained when 54 g dietary fiber and 53% carbohydrate were fed to insulin-treated diabetics for 10 days [34]. An index of mean daily glucose values decreased with fiber addition (317 to 224; $P<0.05$) as did 24-hour urine glucose excretion (17.5 to 3.1 g/day; $P<0.025$). This is significant because it is the only high-fiber, normal carbohydrate study to maintain the same ratio of simple to complex carbohydrate between high and low-fiber, equal carbohydrate diets. Other studies vary this ratio, so that results are difficult to interpret on the basis of fiber alone. In one such study [22], diabetics were fed high (33 g/day) compared to low (18 g/day) dietary fiber for six weeks. Carbohydrate was maintained at 35% of kcal but the ratio of simple to complex carbohydrate was higher on the high-fiber than low-fiber diet. No significant changes were observed in glycosylated

hemoglobin or 24-hour urinary glucose excretion, although postprandial plasma glucose was slighly reduced (14.5 to 11.6 millimoles/liter). The authors concluded that increasing fiber without increasing carbohydrate did not improve diabetic control.

Hypoglycemic effects have also been obtained when 26 g fiber from corn bran and soy hulls were added to low (3 g crude) fiber diets of 10 healthy subjects for 30 days [102]. One-hour postprandial glucose significantly decreased with both fiber sources (109 to 71 mg/dl and 113 to 78 mg/dl, respectively; $P<0.05$).

b. Fiber from wheat bran: Along with cellulose, wheat bran is the most commonly added fiber to baked goods [108], so it is natural that many studies connected with the glycemic effects of fiber will also scrutinize wheat bran. The bran of wheat comprises all the layers of the grain kernel outside the endosperm (from which flour is made). Wheat bran is neither of uniform composition nor composed entirely of fiber; both will vary with the type of wheat from which the bran is derived [44, 109]. In general, wheat bran contains between 38 and 45% neutral detergent fiber by weight [86], and is rich in cellulose, hemicelluloses and lignin [110]. Its digestibility is estimated between 36% [111] and 56% [112]; the large variation found is probably due to the particle size used in estimating digestibility, as small particles are better digested than large [55].

Wheat bran has generally been found to enhance glucose tolerance in normal individuals. When forty patients with diverticular disease were treated with 24 g bran/day for six months, oral glucose tolerance was improved at one ($P<0.002$) and one-and-one-half ($P<0.04$) hours, even though bran was not administered with the glucose load [113]. When 41 g wheat bran was given with a 50 g glucose load to normal subjects, blood glucose was significantly

lower at 30 minutes ($P<0.05$) compared to the control, and the area under the glucose tolerance curve was reduced [60]. Similarly [114], wheat bran intake at approximately 36 g/day improved glucose tolerance in normal subjects at all points on the curve greater than 30 minutes.

Reduction in glucose values is also experienced by carbohydrate-sensitive individuals. After raw bran was consumed (20 g/day; 1 month) by 38 adults with impaired glucose tolerance, areas under the tolerance curves for both glucose and insulin were significantly ($P< 0.001$) reduced [115]. Supplementation of approximately 35 g/day wheat bran, resulted in significantly ($P< 0.01$) diminished glycosuria in both stable (26 to 13 g/day) and labile (53 to 36 g/day) diabetics [116]. Blood glucose was also significantly lower in the afternoons and evenings compared to control values. In both groups, glycosylated hemoglobin was depressed with wheat bran addition, but not significantly during the 15 day evaluation period.

c. Fiber from cellulose: Unlike wheat bran, cellulose is virtually ubiquitous among members of the plant kingdom, its composition is uniform, and it is almost 100% dietary fiber. Whereas bran is a food containing carbohydrate, protein, fat, vitamins and minerals, there is no significant nutrient value to be derived from cellulose. Cotton and wood pulp are excellent sources of cellulose, which is generally purified to food-grade fiber from the latter. The versatility of cellulose lies in its absence of flavor and color, and its indistinguishable shape when added to food products as a fiber-enhancer [117]. Improvement in glucose tolerance has been experienced by carbohydrate-insensitive individuals when 15 g methylcellulose was taken with a 50 g glucose load. One hour after the glucose load, blood glucose was significantly lower compared to the control and there was a 29% reduction ($P<0.05$) in the area under the glucose tolerance curve [60].

Improvement in glucose tolerance was not observed in other normal subjects under similar conditions [114]. Streptozotocin-induced diabetic rats have experienced a significant ($P < 0.05$) reduction in fasting plasma glucose when cellulose was fed as 10% of the diet [59]. This observation has been confirmed in humans by Miranda et.al. [29], who found significantly ($P < 0.001$) lower mean plasma glucose values in insulin-dependent diabetic patients fed diets with 20 g crude fiber (predominantly as cellulose) compared with isocaloric diets containing 3 g crude fiber (120 mg/dl vs. 169 mg/dl). Serum-free insulin levels remained unchanged. Hypoglycemic reactions were more frequent on the high-fiber diet.

d. Mechanism of action: A number of mechanisms have been proposed for the hypoglycemic effects of dietary fiber and are discussed below.

Foods with a high-fiber content may delay gastric emptying, slowing carbohydrate release into the small intestine, and subsequent absorption into the blood [33, 118]. Jenkins has coined the term "lente" or "slow-release carbohydrate" to describe this phenomenon [28]. Second, the formation of intraluminal gels by soluble viscous fibers such as pectin and guar, may result in slower absorption of carbohydrate from these gels in the small intestine [33]. Studies with fibers of varying viscosities show that the rise in blood glucose is highly correlated with the viscosity of the fiber [28, 60, 107]. Another suggested mode of action involves the reduction in intestinal transit time by insoluble fibers, thereby diminishing the time for carbohydrate absorption in the small intestine [33]. Fourth, the composition of the fiber itself may affect gastric emptying. Wheat bran enhances glucose tolerance to a greater extent than cellulose [114], causing the authors to speculate that the lipid constituents of bran slow gastric emptying and the subsequent release of glucose from the small intestine into the blood.

Recently, there is evidence for a fifth mechanism. This involves an increased number of insulin receptors in response to a high-fiber diet [119], thus increasing sensitivity to available insulin. Improved glucose tolerance on fiber-enriched diets does not appear to be related to enhanced insulin secretion [5]. Last, high-fiber diets may diminish the release of gastric inhibitory polypeptide from the intestinal mucosa [6, 27, 120]; this peptide is a stimulus for insulin secretion [121]. As such, this may be one reason fiber-supplemented meals can be accompanied by decreased insulin secretion [2, 3, 35]. Thus, a number of factors may contribute to the altered glycemic and insulinopenic effects accompanying fiber-enriched diets.

2. Effect on blood lipids

Concomittant with the hyperglycemia of diabetes mellitus exist disorders of lipid metabolism [122] that may have an important role in the development of vascular damage [6, 123 - 127]. A high frequency of vascular degeneration [128 - 130] such as arteriosclerousis [125], and micro-angiopathies of the retina and kidney [131 - 134] have been reported in studies of diabetic populations. Since the blood lipid pattern and vascular lesion in diabetes may well be related to the degree of diabetic control [6, 122 - 127, 130] and since these often lead to premature death [125], the control of hyper-lipidemia as well as hyperglycemia is a major task in the management of diabetic patients. Although hypertriglyceridemia is the most common lipid abnormality observed in patients with diabetes mellitus (90% of juvenile-onset diabetics with ketoacidosis have elevated triglyceride levels [128]), serum cholesterol is usually monitored in conjunction with triglycerides [135]. Lipoprotein electrophoresis yields supplementary information about the nature of the lipid abnormality. HDL-cholesterol analysis may reveal information on the amount of

protection offered the arterial wall against degenerative vascular changes [136].

Evidence that fiber-enriched diets ameliorate elevated atherogenic lipid levels in hyperlipidemic subjects or depress lipids in normolipemic individuals will be reviewed.

a. Fiber from mixed dietary sources: Serum lipid patterns of diabetic and hyperlipidemic subjects are almost universally enhanced when high-carbohydrate (60 - 75% of kcal) is fed in combination with high (approximately 60+ g/day) dietary fiber [1, 3 - 7, 34, 38, 89 - 92, 97, 101, 137, 138]. When healthy young adults consumed 70% of kcal as carbohydrate with either low (1 g) or high (18 g) crude fiber, significant ($P < 0.05$) reductions in fasting plasma cholesterol and triglycerides were noted on fiber-enriched diets, but not with the low-fiber diet [3]. Tremendous reduction (63%) of hypertriglyceridemia was experienced by otherwise normal patients [137] subsequent to only 12 days of high-carbohydrate (70% kcal), high-fiber (35 g/1000 kcal) diet therapy (1148 mg/dl to 426 mg/dl; $P < 0.01$), thus alleviating the rise in fasting triglycerides that normally accompanies high-carbohydrate diets [2, 9]. Other investigations reveal similiar results [7, 99]. Reductions in fasting serum triglycerides tend to be related to the magnitude of initial hypertriglyceridemia [6], as normolipemic volunteers [4] do not experience such dramatic reductions (131 mg/dl to 128 mg/dl; not significant). In general, the change in fasting serum triglycerides is inversely related to the dietary change in fiber [89].

Improvement in hypercholesterolemia has been noted with high-carbohydrate, high-fiber (HCF) diets. After fifteen months or more of treatment, HCF diets show significantly ($P < 0.001$) reduced fasting serum cholesterol (194 to 146 mg/dl [1]; 206 to 141 mg/dl [7]; 206 to 147 mg/dl [4])

compared to control values established on individual "Western" diets. High (61%) carbohydrate, high (97 g/day) leguminous fiber diets [91] ($P<0.05$) reduce normal cholesterol values after six weeks compared to traditional, low (40%) carbohydrate, low (15 g/day) dietary fiber diets in Type I and Type II diabetics (186 to 159 mg/dl). Reduction was seen with LDL-cholesterol in Type II diabetics (125 to 101 mg.dl; $P<0.01$), and in Type I (116 to 99 mg/dl) although statistical significance was not achieved in the latter. However, HDL-cholesterol, a negative risk factor in heart disease, also declined in insulin-dependent diabetics (55 to 46 mg/dl; $P<0.05$). Hypolipidemic effects of HCF diets are thought to result at least partially from the replacement of total and saturated fat with carbohydrate [6, 99].

Although improvement in the lipid picture is generally achieved with HCF diets, high-carbohydrate diets without additional fiber produce different results. Fasting serum triglycerides rise when carbohydrate is fed at 65% [9] and 70% [7] of kcal compared to 43 - 45% carbohydrate (71 to 118 mg/dl and 134 to 171 mg/dl, respectively), without increasing fiber. In addition, elevations occurred in both cholesterol (238 - 276 mg/dl) and triglycerides (305 - 624 mg/dl) when carbohydrate was increased from 17% to 85% of kcal in patients with premature atherosclerosis [10]. Some studies, however, report improvement or no change in cholesterol and triglyceride values when subjects are fed high (65 - 85%) carbohydrate diets [98, 101, 138]. Scrutiny of the method of enhancement (increasing tuberous vegetables[98]; increasing wholegrain cereals [138]; method not discussed [101]) reveals that additional fiber was probably added concurrently and inadvertently as carbohydrate was increased. Although the authors discuss their findings with reference to increased carbohydrate, fiber is probably a modifying factor which should be considered when interpreting these results. It is likely,

then, that increasing carbohydrate without increasing fiber is detrimental to the lipid picture of normal and hyperlipidemic subjects.

Just as it is difficult to increase carbohydrate for extended periods of time without also adding fiber, it is difficult to increase fiber without adding carbohydrate. Studies have attempted this in order to examine fiber effects on the lipid picture of human subjects. Fiber from a variety of food sources has been studied. Stasse-Wolthuis et al.[41] fed low (12 g) and high (45 g) dietary fiber diets each with low (170 mg) and high (663 mg) cholesterol to 46 healthy volunteers such that at least two diets were consumed by each subject and each diet was of three weeks duration. During all diets, at least 50% of the fiber was derived from breads and cereals and the other half from fruits and vegetables so that fiber from multiple natural sources was consumed. Changing from low to high-fiber diets caused a significant($P < 0.01$) reduction in serum cholesterol at both high and low levels of cholesterol intake (12 mg/dl and 17 mg/dl, respectively). Triglycerides were unaffected. Unfortunately, HDL-cholesterol also declined (4.0 mg/dl; $P < 0.05$) at both cholesterol levels when subjects changed from low to high-fiber diets, then HDL-cholesterol increased to control values when changed from high to low-fiber regimens. Rivellesse [34] found HDL-cholesterol unaffected by mixed-fiber addition for 10 days in diabetics, although the atherogenic lipids were depressed (total cholesterol 214 to 185 mg/dl, $P < 0.001$; LDL-cholesterol 130 to 108 mg/dl, $P < 0.05$; VLDL-cholesterol 24 to 21 mg/dl, not significant; total triglycerides 69 to 61 mg/dl, $P < 0.05$). Thus, the general blood lipid picture improves when subjects are fed high-fiber diets from a variety of sources, although HDL-cholesterol is sometimes depressed.

Other investigators have undertaken to determine the lipemic effects

of specific types of dietary fiber. Twenty grams per day purified fibers from carrot, cabbage, guar, pectin, bran, and apple fed to healthy subjects for three weeks induced no change in fasting serum triglycerides or cholesterol, although carrot fiber significantly depressed HDL-cholesterol [18]. Others [139] found 200 g raw carrot elicited a decrease in total serum cholesterol (255 to 228 mg/dl; $P<0.05$). Serum cholesterol was also depressed (14%; $P< 0.05$) when 26 g soy hulls were added to a typical U.S. diet (44% carbohydrate, 3 g crude fiber) for one month [42]. Similar administration of corn bran, soy hulls and textured vegetable protein reduced serum triglycerides. Guar and pectin have been shown consistently to decrease serum cholesterol in human and animal studies [18, 26, 28, 35, 80, 82, 103, 140 - 142].

In general, hypolipemic effects are attributed to a number of individual naturally-occurring food fibers, with greatest hypocholesterolemic effects being linked to the more soluble fibers.

b. Fiber from wheat bran: Because wheat bran tends to bind bile acids, it has been studied extensively for hypocholesterolemic properties. In 1976, Trusswell and Kay [143] reviewed ten studies of wheat bran and its effects of blood lipids. The human subjects on these studies ranged from 19 to 89 years old and from normal to hyperlipidemic and gall-bladder patients. Duration of the studies varied from three to nineteen weeks, and bran feeding from 14 g to 57 g per day. Wheat bran induced no effect on serum cholesterol in all but one study (- 7%), or on triglycerides in but one (- 18%). These lipid changes did not appear to be related to length of study, type of subjects or amount of bran fed. Other human studies show wheat bran to have no effect on total serum cholesterol ([144] 30 g all-bran + 30 g wheat bran per day, 16 patients, 1 month; [145] 50 g wheat bran cereal, 1 month), although HDL-cholesterol was increased on the former (55 - 61 mg/dl; $P< 0.05$).

Ranhotra [65], Vahouny [146] and Chen [141] found wheat bran ineffective in lowering total serum cholesterol or triglycerides in rats, and it has not been shown to do so in monkeys (reported in [68]). Hypercholesterolemic effects (13 mg/dl; $P < 0.005$) have been noted by others ([147] 38 g wheat bran per day, 16 subjects, 5 weeks) when HDL-cholesterol remained stable, but supression of the HDL fraction was realized in at least one study of healthy young adult males (59 to 51 mg/dl; $P < 0.001$ [108]). Enhanced HDL has been found by others (56 to 61 mg/dl after 1 month, $P < 0.05$ [144]).

Studies conducted since the Trusswell and Kay review suggest wheat bran might exhibit hypocholesterolemic properties in some individuals. Thirty-eight patients with impaired glucose tolerance experienced significant ($P < 0.001$) reductions in serum cholesterol (234 to 212 mg/dl) and triglycerides (108 to 97 mg/dl) when 20 g wheat bran was added to their normal diet for one month. Fourteen subjects were studied for an additional two months; half discontinued wheat bran use while half continued to incorporate it into their diets. Patients who continued bran treatment maintained their metabolic improvement but the half who discontinued bran did not [115]. Similar results have been obtained by others [148, 149]. Hypocholesterolemic properties of bran have been shown after two to three weeks when ingested as part of a high-cholesterol diet by normal subjects [141,150] but not until six weeks in other studies [151]. Wicks [151] postulates this delay in the action of bran may indicate that the hypocholesterolemic action of bran is not merely a result of impeding the absorption of secondary bile acids, but rather that its action may be to reduce the formation of secondary bile acids by altering colonic microflora. Such a change would presumably take longer to occur.

A 12% decline in total plasma cholesterol (168 to 149 mg/dl; $P<0.05$

[42]), with LDL-cholesterol declining similarly (105 to 83 mg/dl; $P < 0.05$) has been noted in young adults fed 26 g hard red spring wheat bran for 30 days in addition to a normal "Western" diet. Interestingly, soft white wheat bran (American Association of Cereal Chemists (AACC), chemically defined wheat bran) did not induce this decrease in lipoprotein cholesterol fractions, although its composition is similar to the hard red spring wheat bran. At higher levels (36 g/day) AACC wheat bran fed to young adults did induce a reduction in the LDL-cholesterol fraction (59 to 51 mg/dl; $P < 0.001$ [148]). Uniformity in the action of wheat bran has not been realized between studies, even with identical wheat bran, and when strong similarities exist between subjects, amount fed, and duration of the study.

c. Fiber from cellulose: Hypocholesterolemic or hypotriglyceridemic effects attributable to cellulose are rare in the literature, except at very high levels of intake. Feeding cellulose to rats at less than 20% feed weight, generally induces no reduction in total serum cholesterol or the LDL and VLDL fractions [59, 65, 142, 146], but incorporating cellulose as 30% of the diet weight [66] produces a significant ($P < 0.05$) drop in these lipids (total cholesterol 140 to 119 mg/dl; LDL + VLDL 31 to 21 mg/dl). The lower serum cholesterol is associated with an increase in the fecal excretion of neutral steroids and bile acids. This observation has been confirmed in human studies at very high levels (100 g/day) of cellulose feeding [67]. In the latter study, adolescent girls were fed a series of three diets for 10 days each; a) control, b) control plus 4000 mg cholesterol and c) control plus 4000 mg cholesterol plus 100 g microcrystalline cellulose per day. Serum cholesterol and fecal bile acid excretion were lowest on the control diet (138 mg/dl; 79 mg/day, respectively). Cholesterol feeding markedly elevated serum cholesterol from the control (226 mg/dl), but the addition of cellulose

(diet c) brought the cholesterol closer to the control level (170 mg/dl). The hypocholesterolemic effect was accompanied by a tremendous increase in fecal bile acid excretion (147 (diet b) to 213 (diet c) mg/day). Other human studies which have evaluated the hypocholesterolemic potential of cellulose generally conclude its effect is non-existent [62, 63, and 2 studies reviewed in 64], but the maximum intake of cellulose on these diets was 16 g/day. Cellulose is probably hypocholesterolemic at very high levels of intake but does not exert significant physiologic action at lower levels commonly incorporated into test diets. Its effect on triglycerides and lipoprotein-cholesterol fractions has not been evaluated in humans at high levels of intake.

d. Mechanism of action: The major hypothesis for a mechanism of hypocholesterolemic action of the dietary fibers is that bile acids are bound by fiber in the gut and excreted in the feces rather than re-entering the enterohepatic circulation. This lowers the bile acid pool and affects the hepatic metabolism of cholesterol by diverting it into the bile pool. This makes less cholesterol available for incorporation into the various lipoprotein fractions and consequently, less is available for release into the circulation [33, 46, 152]. In addition, diets high in fiber tend to be high in carbohydrate; high-fiber high-carbohydrate diets in turn, are generally low in fat and cholesterol. Fiber may indirectly contribute to depressed lipid levels by displacing foods known to contribute to the atherogenic lipids [153].

# MATERIAL AND METHODS

## A. Patient Population and Experimental Protocol

Four young adult (18 - 26 years) non-obese human subjects (2 male, 2 female) with Type I diabetes mellitus (duration 6 - 18 years) volunteered to participate in this study. Pertinent clinical data are shown in Table 4. All expressed motivation to participate. Experimental and baseline diets were consumed for six weeks followed by a four-week "recovery" period during which each subject consumed a diet to which he/she was accustomed prior to experimentation (Figure 2). Each patient served as his own control. Informed consent was obtained (Appendix A). A detailed diet habit/food preference questionnaire (Appendix B) was completed by each subject to facilitate individualized diet planning. Diet records were maintained in booklet form throughout the study periods (Figure 3) and activity records kept for five consecutive work/school days of each study period (Figure 4). In the diet booklets, subjects also recorded weekly weights, hypoglycemic reactions and factors which may have affected insulin needs or blood sugar (Figure 5). Verbal and written directions for using the booklets were given to the subjects (Appendix C).

During the control period, subjects followed normal daily routines at home, recording the information contained in Figures 3, 4, and 5. Diet record information from control periods was used to calculate the average amount of protein, fat (total, saturated, and cholesterol), carbohydrate (total and simple), dietary fiber and kilocalories the individuals consumed at each meal and snack. Calculations were based on tables from published sources [11, 12, 83, 154 - 168]. Both high-fiber diet variations (wheat bran and cellulose) were calculated to include identical proportions of the above nutrients consumed during the control period. The exception was that 60 grams of dietary fiber were

TABLE 4.

Clinical Data for Patient Population at Beginning of Study

| Patient | Sex | Age (yrs) | Duration of Diabetes (yrs) | Height (cm) | Weight (kg) | C-peptide (pmol/L) | $HbA_1c$ %* | Diet (kcal) | Average Daily Insulin |
|---|---|---|---|---|---|---|---|---|---|
| G.C. | M | 24 | 13 | 175 | 68 | 0.3 | 8.0 | 2491 | 50 U |
| G.W. | F | 26 | 14 | 157 | 49 | 0.3 | 12.1 | 1190 | 44 U |
| S.H. | F | 23 | 6 | 163 | 64 | 0.4 | 9.6 | 1332 | 28 U |
| D.P. | M | 19 | 18 | 188 | 77 | 0.6 | 9.0 | 3276 | 70 U |
| ——— | | — | — | | | — | ——— | ——— | ——— |
| $\bar{X}$ | | 23 | 12 | | | 0.4 | 9.7 | 2072 | 48 U |

*Hemoglobin $A_1c$, Normal, non-diabetic value < 5%

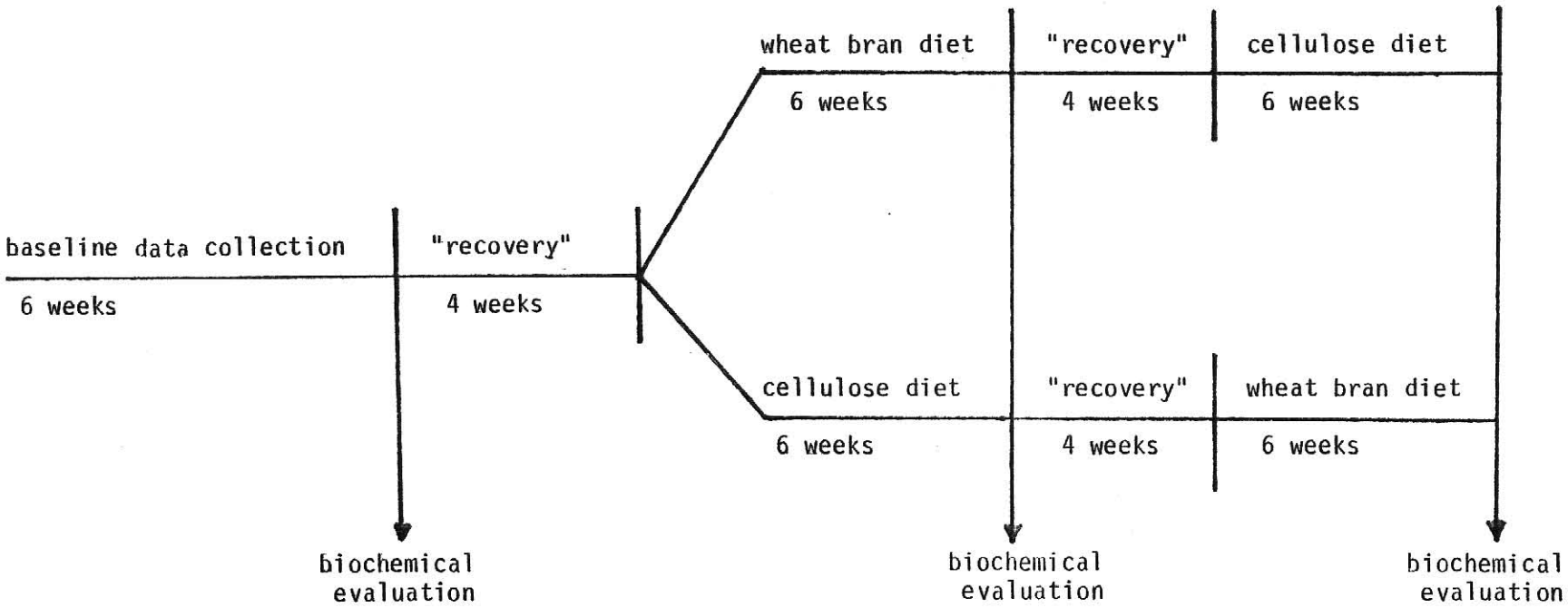


FIGURE 2. Time diagram of experimental design

Date:_____ Urine Sugar:_____

Time: _____ Ketone:_____

Method:_____ Ins:___U___ + ___U___

Time:_____ am pm First Meal

| Amount | Food | How Prepared |
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Date:_____ Urine Sugar:_____

Time:_____ Ketone:_____

Method:_____ Ins:___U___ + ___U___

Time:_____ am pm Second Meal

| Amount | Food | How Prepared |
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FIGURE 3. Example of diet-record booklet

| Time | Intensity | Activity |
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FIGURE 4. Example of activity record

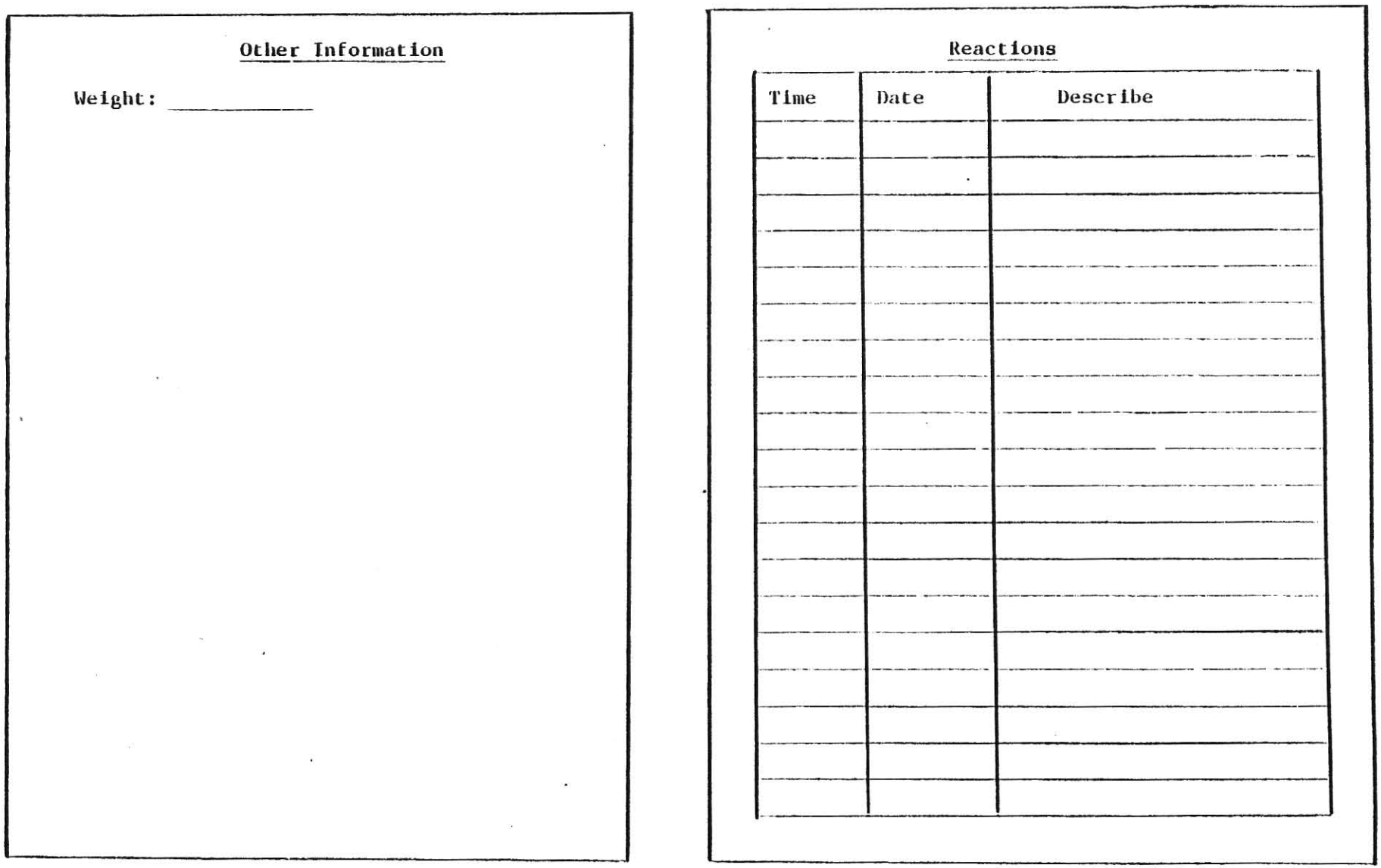


FIGURE 5. Forms for recording hypoglycemic reactions and other information pertinant to diabetic control

incorporated into both the wheat bran and cellulose diets, with 50% of the fiber being derived from hard red spring wheat bran or microcrystalline cellulose on the respective treatments. Diets were planned to allow for individual preferences and constraints.

Information on daily activities during the baseline phase was used to calculate the approximate number of kilocalories expended in one-hour periods [169]. An outline of the calculation procedure is contained in Appendix D. Individual kilocalorie expenditure was then duplicated while subjects were connected to the biostator®. (Subjects rode a stationary bicycle once an hour at 10 miles per hour for the length of time required to approximate hourly energy expenditure during the control period.) Bicycle exercise on both high-fiber treatments was identical to the control so that exercise while on the biostator would not affect insulin requirements. In addition, free-living activity information was collected during high-fiber diets to compare these average activity levels with those levels during the control diet.

Throughout the study, patients were instructed to test their urine for sugar quarter in die by the 2 drop Clinitest® method[a] approximately one-half hour before each meal and again at bedtime. If Clinitest was unreasonably inconvenient, subjects were to test their urine with Testape® [b]. Urine was checked for ketones[c] or [d] only if urine sugar exceeded 2% for three or more consecutive times. All patients had been previously instructed in self-insulin-

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® : Registered trademark

[a]Ames Division, Miles Laboratories, Inc., Elkhart, Indiana 46515

[b]Eli Lilly and Company, Indianapolis, Indiana 46285

[c]Acetest®, Ames Division, Miles Laboratories, Elkhart, Indiana 46515

[d]Keto-diastix Reagent Strips®, Ames Division, Miles Laboratories, Elkhart, Indiana 46515

ization and were told to continue such treatment throughout the entire study. All insulin doses and urine test results were recorded as described in Figure 3.

During high-fiber diets, fiber was consumed as fruits, vegetables, cereals and bread. Special breads were developed for the high-fiber diets through the joint cooperation of the American Institute of Baking and the Department of Foods and Nutrition, Kansas State University, both of Manhattan, Kansas. A wheat bran bread was developed to contain 30% of the flour weight as hard red spring wheat bran (Appendix E) and a cellulose bread formulated to contain 30% of the flour weight as microcrystalline cellulose (Appendix F)[a]. Several granola products were developed to help achieve the required amount of wheat bran into the wheat bran diet (Appendix G). Subjects selected the individual granola they most preferred and consumed this, in addition to wheat bran bread and other fibers, on the wheat bran diet. Nutritive composition of breads and granolas was calculated from published values of individual ingredients [11, 83, 154 - 157, 160, 162, 163, 288]; these values were used in high-fiber diet calculations. Chemical analysis was performed post facto (Appendix H) to compare calculated values with actual values (Tables 5, 6, and 7).

At the conclusion of the baseline and high-fiber diets, patients were hospitalizied at St. Francis Medical Center, Wichita, Kansas. Subsequent to an overnight fast, blood was drawn for cholesterol, triglycerides, lipoproteins and hemoglobin $A_1c$. Analysis was performed in the hospital laboratory by standard clinical methods. Patients then underwent 12 hours of computer-controlled insulin-glucose infusions on the Biostator II-Controller (Ames Division, Miles Laboratories), which was under United States Department of Agriculture, Food and Drug Administration field testing at the time. A research

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[a]Microcrystalline cellulose kindly donated by FMC Corporation, Philadelphia, Pennsylvania, 19103

TABLE 5

Composition of baked wheat-bran bread (per 100 g):

Calculated values[a] vs. chemically-analyzed values[b]

| Component | Calculated value (g) | Chemically-Analyzed value (g) |
|---|---|---|
| Protein | 10.6 | 11.3 |
| Carbohydrate | | |
| Total | 40.8 | 34.7[c] |
| Complex | 36.9 | 31.2[d] |
| Simple | 3.9[d] | 3.5 |
| Fat | | |
| Total | 2.5 | 1.2 |
| Saturated | 0.4 | 0.2[e] |
| Unsaturated | 2.1[d] | 1.1[e] |
| Cholesterol | --- | --- |
| Total Dietary Fiber | 6.4 | 9.6 |
| Wheat Bran | 13.1 | --- |
| Cellulose | 2.1 | 1.4 |
| Kilocalories[f] | 227 | 195 |

[a]based on nutritive composition of ingredients from published sources [11, 12, 83, 154 - 157, 160, 162, 163].

[b]Appendix C: (dry matter) * (nutritive value on 100% dry matter basis) = nutrient in bread "as fed"

[c]100 - (protein + ash + neutral detergent fiber + ether extract) = % carbohydrate on 100% dry matter basis. (carbohydrate on 100% dry matter basis) * (dry matter) = total carbohydrate in bread "as fed"

[d]by difference

[e]estimated by percentage of tatal fat in calculated values

[f][(protein + total carbohydrate) * (4)] + [(fat) * (9)] = kcal

TABLE 6

*Composition of baked cellulose bread (per 100 g)*

Calculated values[a] vs. chemically analyzed values[b]

| Component | Calculated value (g) | Chemically-analyzed value (g) |
|---|---|---|
| Protein | 8.7 | 9.5 |
| Carbohydrate | | |
| Total | 35.2 | 26.9[c] |
| Complex | 30.4 | 24.1[d] |
| Simple | 1.2[d] | 2.8 |
| Fat | | |
| Total | 2.8 | 2.0 |
| Saturated | 0.5 | 0.4[e] |
| Unsaturated | 2.3[d] | 1.7[e] |
| Cholesterol | --- | --- |
| Total Dietary Fiber | 13.3 | 19.3 |
| Cellulose | 12.4 | 12.1 |
| Kilocalories[f] | 201 | 164 |

[a]based on nutritive composition of ingredients from published sources [11, 12, 83, 154 - 157, 160, 162, 163].

[b]Appendix C: (dry matter) * (nutrient value on 100% dry matter basis) = nutrient "as fed"

[c]100 - (protein + ash + neutral detergent fiber + ether extract) = carbohydrate on 100% dry matter basis. (carbohydrate on 100% dry matter basis) * (dry matter) = total carbohydrate "as fed"

[d]by difference

[e]estimated by percentage of total fat in calculated values

[f][(protein + total carbohydrate) * (4)] + [(fat) * (9)] = kcal

TABLE 7

Composition of cooked granolas (per 100 g) as fed
Calculated values[a] vs. chemically-analyzed values[b]

| Component | $DP_1G$[c] | | $DP_2G$[d] | | GC G[e] | | GW/SH G[f] | |
|---|---|---|---|---|---|---|---|---|
| | Calculated | Analyzed | Calculated | Analyzed | Calculated | Analyzed | Calculated | Analyzed |
| Protein(g) | 12.1 | 13.5 | 14.3 | 17.9 | 14.9 | 18.2 | 13.9 | 16.8 |
| Carbohydrate(g) | | | | | | | | |
| Total | 35.7 | 31.5 | 39.9 | 35.0 | 36.6 | 30.6 | 39.6 | 38.2 |
| Simple | 19.8[g] | 24.4 | 26.8[g] | 29.5 | 24.4[g] | 24.9 | 26.4[g] | 33.4 |
| Complex | 15.9 | 7.1[g] | 13.0 | 5.5[g] | 12.2 | 5.7[g] | 13.2 | 4.8[g] |
| Fat(g) | | | | | | | | |
| Total | 16.1 | 18.6 | 8.3 | 9.7 | 13.1 | 15.4 | 7.8 | 9.0 |
| Saturated | 2.4 | 3.6[h] | 0.8 | 1.8[h] | 1.2 | 2.9[h] | 0.8 | 1.7[h] |
| Unsaturated | 13.7[g] | 15.0[h] | 7.4[g] | 7.9[h] | 11.9[g] | 12.5[h] | 6.7[g] | 7.3[h] |
| Cholesterol | --- | --- | --- | --- | --- | --- | --- | --- |
| Total Dietary Fiber(g) | 15.9 | 26.7 | 19.9 | 24.6 | 18.9 | 23.4 | 20.0 | 23.7 |
| Cellulose(g) | NE[i] | 5.1 | NE[i] | 5.0 | NE[i] | 5.4 | NE[i] | 5.6 |
| Wheat Bran(g) | 34.1 | --- | 45.5 | --- | 41.2 | --- | 45.6 | --- |
| Kilocalories (kcal)[j] | 336 | 347 | 291 | 299 | 324 | 334 | 281 | 301 |

[a] based on nutritive composition of ingredients from published sources [11, 12, 83, 154 - 157, 160, 162, 163]

[b] Granolas were analyzed without raisins. Values for raisins were calculated into the analyzed values, using nutritive composition of raisins from published sources

[c] Granola consumed by DP during first three weeks of wheat bran diet

[d] Granola consumed by DP during second three weeks of wheat bran diet

[e] Granola eaten by GC throughout the wheat bran diet

[f] Granola consumed by both GW and SH throughout the wheat bran diet

[g] by difference

[h] estimated from percentage of total fat in calculated values

[i] not estimated

[j] [(protein + total carbohydrate)*(4)] + [(fat * (9)] = kcal

protocol was followed as outlined (Appendix I). Calibration of the apparatus was performed hourly after obtaining a venous blood sample and monitoring by Dextrometer Reflectance method (Ames Division, Miles Laboratories).

B. Statistical Analyses:

Statistical analyses were conducted by Dr. Arthur Dayton, Head of the Department of Statistics, Kansas State University. Two-way analysis of variance was used for unequal sample sizes, and least square means for estimating diet effects. When F-tests were significant, two-tailed T-tests were performed. Subsequent to identifying independent variables which might be physiologically-related to response variables such as insulin doses, glycosylated hemoglobin, and serum lipids, stepwise regression analysis was performed to identify which variables were significantly related to the response variables.

Statistics were performed on differences from control diet values by subtracting a control diet variable from the same variable observed on a high-fiber treatment diet. For example, if the six-week average of daily insulin doses for a patient was 50 units insulin/day during the control diet and 44 units/day during the wheat bran diet, statistical analyses for the wheat bran diet were performed on:

Wheat bran diet value - control diet value

= 44 - 50

= - 6.

This was repeated for all observations from both diet treatments to determine the difference of a treatment observation from the control, and the difference of the two treatment observations from each other.

# RESULTS

## A. Free-living

### 1. Acceptability of diets

Although high-fiber diets were individually calculated for greatest acceptability, the study participants did not think the diets would be realistic for extended periods of time. Voluminous quantities of granola cereals and vegetables were contributing factors in this assessment. Two patients experienced cramping and bloating with the high level of wheat bran; in one patient this disappeared after the first week (GW) but in the other (SH), the level of wheat bran had to be reduced from 80 to 57 g wheat bran per day before severe cramping was ameliorated. All subjects judged the breads and granola acceptable, but the quantity of granola made 100% compliance difficult on the wheat bran diet.

Consuming 30 grams of dietary fiber from cellulose did not cause the gastrointestinal upset experienced with wheat bran. This may have been related to the difference in quantity of wheat bran and cellulose which had to be consumed to obtain 30 g dietary fiber. Whereas cellulose is virtually 100% dietary fiber, the hard red spring wheat bran utilized in this study was 37.4%. In order to obtain 30g dietary fiber, 80.2 g of wheat bran had to consumed. In addition, the large particle size of wheat bran may have contributed to patient discomfort [170].

### 2. Food consumption

Average daily consumption of protein, carbohydrate, fat, cholesterol, fiber and kilocalories (kcal) on all three diets is reported in Table

8. The deviation from instructed dietary intake is reported in Appendix J. Although high-fiber diets were planned to be isocaloric with individual control diets in energy-containing nutrients and cholesterol, there were significant decreases in the actual consumption of total carbohydrate and cholesterol on the wheat bran diet and in total carbohydrate and protein on the cellulose diet. Average caloric intake and energy expenditure were not significantly different from the control, although there were large individual variations (DP on both diets, GW on the wheat bran diet).

3. Meal times

By subjective evaluation, the regularity of meal consumption times did not appear to vary greatly between diets. Subjects who consumed meals at irregular times on the high-fiber diets, also had done so on the control diet. The average time at which each meal and snack was consumed is reported in Appendix K.

4. Urine sugar index, hemoglobin $A_1c$, and hypoglycemic reactions

The average daily urine sugar index on the control diet was 1.7, it declined to 1.4 on the cellulose diet and 0.9 on the wheat bran diet. (Table 9). Although significant differences from the control were not observed with either diet (cellulose $P < 0.43$; wheat bran $P < 0.09$), stepwise regression analysis showed the decline in urine sugar index accounted for 82% of the variation in hemoglobin $A_1c$, the latter of which is a relatively new measure of diabetic control. Without exception, the urine sugar index and hemoglobin $A_1c$ changed in the same direction, but the magnitude of change was inconsistent. This is reflected in the mean values on the cellulose diet where, although the

TABLE 8

Average daily consumption of protein, carbohydrate, fat, cholesterol, fiber and kilocalories[a] and average daily kilocalorie expenditure[b] on the control and high-fiber diets: Actual values (A) and deviation from control (*D*)[c]

| | | Protein (g) | | Carbohydrate (g) | | | | Fat (g) | | | | Chol (mg) | | Dietary fiber (g) | | | | | | Kcal intake | | Energy Expenditure (Kcal) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Total | | Simple: Complex | | Total | | Saturat: Unsatur. | | | | Total | | Cellulose | | WB[d] | | | | | |
| Name | Diet | (A) | *(D)* | (A) | *(D)* | (A) | *(D)* | (A) | *(D)* | (A) | *(D)* | (A) | *(D)* | (A) | *(D)* | (A) | *(D)* | (A) | *(D)* | (A) | *(D)* | (A) | *(D)* |
| GC | Cont | 134 | | 264 | | 1.0 | | 100 | | 0.6 | | 569 | | 28 | | 7 | | 0 | | 2491 | | 2935 | |
| | Cellu[f] | 127 | *- 7* | 254 | *-10* | 1.1 | *+0.1* | 95 | *- 5* | 0.5 | *-0.1* | 506 | *- 63* | 59 | *+31* | 25 | *+18* | 0 | *0* | 2402 | *- 89* | 2835 | *-100* |
| | WB | 144 | *+10* | 261 | *- 3* | 1.1 | *+0.1* | 109 | *+ 9* | 0.5 | *-0.1* | 488 | *- 81* | 82 | *+54* | 17 | *+10* | 27 | *+27* | 2570 | *+ 79* | 2957 | *+ 22* |
| GW | Cont | 49 | | 112 | | 0.8 | | 61 | | 0.6 | | 250 | | 28 | | 9 | | 0 | | 1190 | | 2131 | |
| | Cellu | 52 | *+ 3* | 90 | *-22* | 0.6 | *-0.2* | 66 | *+ 5* | 0.4 | *-0.2* | 119 | *-131* | 53 | *+25* | 26 | *+15* | 0 | *0* | 1156 | *- 34* | 2526 | *+395* |
| | WB | 52 | *+ 3* | 113 | *+ 1* | 1.3 | *+0.5* | 48 | *-13* | 0.5 | *-0.1* | 57 | *-193* | 53 | *+25* | 14 | *+ 5* | 22 | *+22* | 1078 | *-112* | 2190 | *+ 59* |
| SH | Cont | 62 | | 153 | | 1.7 | | 55 | | 0.5 | | 214 | | 18 | | 5 | | 0 | | 1332 | | 2835 | |
| | Cellu | 64 | *+ 2* | 145 | *- 8* | 1.5 | *-0.2* | 54 | *- 1* | 0.4 | *-0.1* | 110 | *-104* | 66 | *+48* | 31 | *+26* | 0 | *0* | 1316 | *- 16* | 2980 | *+145* |
| | WB | 64 | *+ 2* | 139 | *-14* | 2.1 | *+0.4* | 55 | *0* | 0.6 | *+0.1* | 188 | *- 26* | 58 | *+40* | 12 | *+ 7* | 18 | *+18* | 1309 | *- 23* | 2719 | *-116* |
| DP | Cont | 146 | | 329 | | 1.1 | | 152 | | 0.7 | | 614 | | 22 | | 7 | | 0 | | 3276 | | 3197 | |
| | Cellu | 127 | *-19* | 287 | *-42* | 1.1 | *0* | 138 | *-14* | 0.6 | *-0.1* | 585 | *- 29* | 53 | *+31* | 23 | *+16* | 0 | *0* | 2853 | *-423* | 3171 | *- 26* |
| | WB | 146 | *0* | 284 | *-45* | 1.2 | *+0.1* | 158 | *+ 6* | 0.5 | *-0.2* | 631 | *+ 17* | 58 | *+36* | 12 | *+ 5* | 18 | *+18* | 3141 | *-135* | 3079 | *-118* |
| $\bar{X}$ | Cont | 98 | | 215 | | 1.2 | | 92 | | 0.6 | | 412 | | 24 | | 7 | | 0 | | 2072 | | 2775 | |
| | Cellu | 93 | *- 5* | 194 | *-21* | 1.1 | *-0.1* | 88 | *- 4* | 0.5 | *-0.1* | 330 | *- 82* | 58 | *+34* | 26 | *+19* | 0 | *0* | 1932 | *-140* | 2878 | *+103* |
| | $\pm$ S.E.[g] | | *3.7* | | *4.4* | | *0.1* | | *6.0* | | *0.05* | | *22.3* | | *4.7* | | *1.7* | | *1.4* | | *58.8* | | *71.9* |
| | $P <$ [h] | | *0.024* | | *0.02* | | *0.59* | | *0.58* | | *0.08* | | *0.04* | | *0.006* | | *0.002* | | *1.00* | | *0.10* | | *0.25* |
| | WB | 102 | *+ 4* | 199 | *-16* | 1.4 | *+0.2* | 93 | *+ 1* | 0.5 | *-0.1* | 341 | *- 79* | 63 | *+39* | 14 | *+ 7* | 21 | *+21* | 2024 | *- 48* | 2736 | *- 39* |
| | $\pm$ S.E.[g] | | *3.7* | | *4.4* | | *0.1* | | *6.0* | | *0.05* | | *22.3* | | *4.7* | | *1.7* | | *1.4* | | *58.8* | | *71.9* |
| | $P <$ [h] | | *0.38* | | *0.05* | | *0.12* | | *0.95* | | *0.20* | | *0.06* | | *0.004* | | *0.002* | | *0.001* | | *0.48* | | *0.64* |
| | $P <$ [i] | | *0.18* | | *0.46* | | *0.15* | | *0.66* | | *0.50* | | *0.75* | | *0.54* | | *0.02* | | *0.003* | | *0.35* | | *0.26* |

[a] average calculated from 15 consecutive days of the 42-day food records maintained by each subject on each diet. Selection of the 15 days was as follows: 5 days during which activity was recorded plus 5 days previous and 5 days following.

[b] calculated from [169]; based on an average of 3 days from the 5-day activity records. Days with highest and lowest activity were not calculated into the 3-day average.

[c] statistical analyses were performed on *D*'s (*D* = experimental diet - control diet) for each dietary component

[d] wheat bran [e] kilocalories [f] cellulose [g] standard error of the *D* means

[h] statistical probability that cellulose or wheat bran deviation mean is different from the control

[i] statistical probability that cellulose and wheat bran deviation means are different from each other

TABLE 9

Index of daily urine sugar[a] and hemoglobin $A_1c$ at conclusion of dietary treatment: actual values (A) and deviation from control (*D*)[b]

| Name | Diet | Daily Urine Sugar Index (A) | Daily Urine Sugar Index (*D*) | Hemoglobin $A_1c$ (%)[c] (A) | Hemoglobin $A_1c$ (%)[c] (*D*) |
|---|---|---|---|---|---|
| GC | Control | 1.5 | | 8.0 | |
| | Cellulose | 1.8 | *+0.3* | 9.1 | *+1.1* |
| | Wheat bran | 1.7 | *+0.2* | 9.3 | *+1.3* |
| GW | Control | 2.1 | | 12.1 | |
| | Cellulose | 2.7 | *+0.6* | 15.3 | *+3.2* |
| | Wheat bran | 0.9 | *-1.2* | 10.7 | *-1.4* |
| SH | Control | 1.5 | | 9.6 | |
| | Cellulose | 0.1 | *-1.4* | 8.7 | *-0.9* |
| | Wheat bran | 0.1 | *-1.4* | 8.1 | *-1.5* |
| DP | Control | 1.7 | | 9.0 | |
| | Cellulose | 1.1 | *-0.6* | 7.8 | *-1.2* |
| | Wheat bran | 1.0 | *-0.7* | 7.9 | *-1.1* |
| $\bar{X}$ | Control | 1.7 | | 9.7 | |
| | Cellulose | 1.4 | *-0.3* | 10.2 | *+0.5* |
| | $\pm$ *S.E.*[d] | | *0.3* | | *0.8* |
| | $P <$ [e] | | *0.43* | | *0.55* |
| | Wheat bran | 0.9 | *-0.8* | 9.0 | *-0.7* |
| | $\pm$ *S.E.*[d] | | *0.3* | | *0.8* |
| | $P <$ [e] | | *0.09* | | *0.46* |
| | $P <$ [f] | | *0.33* | | *0.36* |

[a] Index of daily urine sugar was calculated for each six-week diet as follows: numerical rankings were assigned to urine test results: with Clinitest®, N=0, tr=1, 1/2%=2, 1%=3, 2%=4, 3%=5, 5%=6. On occasions when testape® or diastix® were used, N and 1/10%=0, 1/4%=1, 1/2%=2, 2%=4. The formula was then used to calculate an index for each patient:

$$\left( \frac{\text{sN at breakfast}}{\text{T at breakfast}} + \frac{\text{sN at lunch}}{\text{T at lunch}} + \frac{\text{sN at dinner}}{\text{T at dinner}} + \frac{\text{sN at HS snack}}{\text{T at HS snack}} \right) \div 4$$

where sN = the sum of the numerical rankings for the 6-week diet period, and
T = total number of urine tests performed

[b] Statistical analyses were performed on *D*'s (*D* = experimental diet - control diet) of urine sugar index and hemoglobin $A_1c$

[c] normal, non-diabetic value < 5%

[d] standard error of the *D* means

[e] statistical probability that cellulose or wheat bran deviation mean is different from the control

[f] statistical probability that cellulose and wheat bran deviation means are different from each other

urine sugar index declined, hemoglobin $A_1c$ rose. Most of the increase in hemoglobin $A_1c$ in this case can be attributed to one subject (GW). Overall, the index of daily urine sugars is probably not a good indicator of glycemic control on this study because of the irregularity with which some patients tested their urine.

The number of hypoglycemic reactions per week is expressed in Table 10. Hypoglycemic reactions were most frequent during the wheat bran diet period, but virtually equivalent when the cellulose and control diets were consumed.

5. Daily insulin doses

The average daily insulin dose during the baseline diet was 48 units of U-100 insulin per day; it decreased to 43 units during the cellulose diet and 44 units during the wheat bran diet (Table 11). The lower insulin dosage during the wheat bran diet was accompanied by improved urine sugar index and hemoglobin $A_1c$ (Table 9). Average changes in energy intake and kilocalorie expenditure were small and probably did not influence glycemic control. The reduction in average insulin dose during the cellulose diet and the increase in mean hemoglobin $A_1c$ are largely attributable to GW who also slightly reduced her caloric intake and, according to energy records, increased her energy expenditure. This increase in energy expenditure was recorded by GW during the third week of the cellulose diet, and reflects energy expenditure for that week. However, during the last two and one-half weeks of the cellulose diet GW was very inactive and stressed (taking Ph.D. preliminary examinations). During this period she experienced marked hyperglycemia, glycosuria and ketosis, accompanied by an increased hemoglobin $A_1c$ and urine sugar index.

GC reduced his average insulin dose on both the cellulose and wheat

TABLE 10

Number of hypoglycemic reactions per week, experienced by subjects during control and high-fiber diets

| Name | Diet | | |
|---|---|---|---|
| | Control | Cellulose | Wheat Bran |
| GC | 2.0 | 1.4 | 3.2 |
| GW | 0.6 | 1.3 | 1.3 |
| SH | 2.0 | 2.2 | 2.5 |
| DP | 1.0 | 1.0 | 1.5 |
| $\bar{X}$ | 1.4 | 1.5 | 2.1 |

TABLE 11

Insulin needs and factors which influence insulin needs in free-living environment and during biostator monitoring
Actual values (A) and deviation from control (*D*)[a]

| | | Average Daily Values | | | | | | Values at Biostator Evaluation | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Total Insulin (U) | | Energy Expenditure (kcal)[b] | | Energy Intake (kcal)[c] | | Total Biostator Insulin (U)[d] | | Postprandial Biostator Insulin (U)[e] | | Weight (lb)[f] | |
| Name | Diet | A | *D* | A | *D* | A | *D* | A | *D* | A | *D* | A | *D* |
| GC | Control | 50 | | 2935 | | 2491 | | 66.0 | | 41.5 | | 150 | |
| | Cellulose | 43 | *- 7* | 2835 | *-100* | 2402 | *- 89* | 47.7 | *- 18.3* | 38.9 | *- 2.6* | 150 | *0* |
| | Wheat bran | 44 | *- 6* | 2957 | *+ 22* | 2570 | *+ 79* | 38.0 | *- 28.0* | 23.5 | *-18.0* | 152 | *+ 2* |
| GW | Control | 44 | | 2131 | | 1190 | | 33.2 | | 20.7 | | 107 | |
| | Cellulose | 27 | *-17* | 2526 | *+395* | 1156 | *- 34* | 41.6 | *+ 8.4* | 27.0 | *+ 6.3* | 112 | *+ 5* |
| | Wheat bran | 27 | *-17* | 2190 | *+ 59* | 1078 | *-112* | 23.1 | *- 10.1* | 19.2 | *- 1.5* | 110 | *+ 3* |
| SH | Control | 28 | | 2835 | | 1322 | | 39.3 | | 34.7 | | 139 | |
| | Cellulose | 31 | *+ 3* | 2980 | *+145* | 1316 | *- 16* | 55.3 | *+ 16.0* | 38.2 | *+ 3.5* | 135 | *- 4* |
| | Wheat bran | 35 | *+ 7* | 2719 | *-116* | 1309 | *- 23* | 47.2 | *+ 7.9* | 37.8 | *+ 3.1* | 135 | *- 4* |
| DP | Control | 70 | | 3197 | | 3276 | | 49.3 | | 45.6 | | 170 | |
| | Cellulose | 72 | *+ 2* | 3171 | *- 26* | 2853 | *-423* | 70.7 | *+ 21.4* | 60.9 | *+15.3* | 178 | *+ 8* |
| | Wheat bran | 71 | *+ 1* | 3079 | *-118* | 3141 | *-135* | 59.2 | *+ 9.9* | 50.7 | *+ 5.1* | 175 | *+ 5* |
| $\bar{X}$ | Control | 48 | | 2775 | | 2072 | | 47.0 | | 35.6 | | 142 | |
| | Cellulose | 43 | *- 5* | 2878 | *+103* | 1932 | *-140* | 53.8 | *+ 6.9* | 41.3 | *+ 5.6* | 144 | *+ 2* |
| | ± S.E.[g] | | *0.88* | | *71.87* | | *58.77* | | *1.6* | | *2.2* | | *0.78* |
| | P < [h] | | *0.02* | | *0.25* | | *0.10* | | *0.034* | | *0.084* | | *0.07* |
| | Wheat bran | 44 | *- 4* | 2736 | *- 38* | 2024 | *- 48* | 41.9 | *- 5.1* | 32.8 | *- 2.8* | 143 | *+ 1* |
| | ± S.E.[g] | | *0.88* | | *71.87* | | *58.77* | | *1.6* | | *2.2* | | *0.78* |
| | P < [h] | | *0.03* | | *0.64* | | *0.48* | | *0.052* | | *0.29* | | *0.16* |
| | P < [i] | | *0.50* | | *0.26* | | *0.35* | | *0.02* | | *0.07* | | *0.55* |

[a] statistical anlaysis was performed on the *D*'s (*D* = experimental diet - control diet) for each measurement [b] calculated from [169]; based on an average of 3 days from the 5-day activity records. Days with highest and lowest activity were not calculated into the 3-day average. [c] average calculated from 15 consecutive days of the 42-day food records maintained by each subject on each diet. Selection of the 15 days was as follows: 5 days during which activity was recorded plus 5 days previous and 5 days following. [d] total units of U-100 insulin infused during 12 hours of biostator monitoring. [e] units of U-100 insulin infused postprandially. For example, if 2 hours elapsed between lunch and PM snack on the control diet, 2 hours and 10 minutes elasped between them on the cellulose diet and 2 hours and 8 minutes on the wheat bran diet, the amount of insulin infused in the 2-hour interval following lunch would be used as the postprandial lunch insulin. Postprandial time intervals varied between meals and between subjects, but were constant for a given subject at a given meal on all diets. [f] actual weight on the day of biostator monitoring. [g] standard error of the *D* means. [h] statistical probability that cellulose or wheat bran diet deviation mean is diffrent from the control. [i] statistical probability that cellulose and wheat bran diet deviation means are different from each other.

bran diets but concurrent improvement in control, as assessed by hemoglobin $A_1c$ and urine sugar index, was not realized. Changes in GC's energy intake and kilocalorie expenditure were small and paralleled each other. During this period, GC experienced hyperglycemia and glycosuria after his morning meal and snack and verged on hypoglycemic reactions in the afternoon. Adjustments were made constantly to his morning and evening insulin dosages in an attempt to achieve glycemic control; this goal was never fully attained. SH and DP increased their daily insulin dosages from the control and achieved improvement in urine sugar index and hemoglobin $A_1c$ while encountering hypoglycemic reactions slightly more frequently. Increased energy expenditure and reduced calorie intake by SH and DP respectively, may have accounted for part of the reduction in urine sugar index and hemoglobin $A_1c$ and an increased number of hypoglycemic reactions.

6. Weight changes during dietary regimens

Changes in weight which occurred during dietary treatments are recorded in Table 12. The three-pound weight loss experienced by GW during the cellulose diet was subsequent to ketosis in the last two and one-half weeks of this diet. SH and DP both experienced their greatest change in weight during the control diet. DP gained three pounds during the wheat bran diet. A reduction in weight was experienced by all subjects during the cellulose diet.

7. Total cholesterol, total triglycerides and lipoprotein fractions

Fasting blood lipids, drawn at the conclusion of each six-week dietary treatment, are listed in Table 13. Mean total cholesterol decreased from 198 mg/dl on the control diet to 171 ($P < 0.05$) and 174 ($P < 0.07$) mg/dl on the cellulose and wheat bran diets, respectively. The mean decrement during both diets was accompanied by an average reduction in dietary cholesterol

TABLE 12

Body weight changes in pounds, during
control, high-fiber cellulose and high-fiber wheat bran dietary evaluations

| | Diet | | |
|---|---|---|---|
| Name | Control | Cellulose | Wheat bran |
| GC | 0 | -3 | 0 |
| GW | -1 | -3 | weight not recorded |
| SH | -3 | -2 | 0 |
| DP | +5 | -3 | +3 |

TABLE 13

Fasting serum lipid values (mg/dl) at conclusion of six-week dietary treatments: Actual value (A) and deviation from control (D)[a]

| Name | Diet | Total Cholesterol (A) | Total Cholesterol (D) | Total Triglycerides (A) | Total Triglycerides (D) | HDL[b] Cholesterol (A) | HDL[b] Cholesterol (D) | LDL[c] Cholesterol (A) | LDL[c] Cholesterol (D) |
|---|---|---|---|---|---|---|---|---|---|
| GC | Control | 157 | | 60 | | 82 | | 63 | |
| | Cellulose | 128 | -29 | 36 | -24 | 35 | -47 | 57 | - 6 |
| | Wheat bran | 150 | - 7 | 62 | + 2 | 44 | -38 | 94 | +31 |
| GW | Control | 230 | | 102 | | 87 | | 123 | |
| | Cellulose | 188 | -42 | 60 | -42 | 56 | -31 | 120 | - 3 |
| | Wheat bran | 159 | -71 | 92 | -10 | 59 | -28 | 82 | -41 |
| SH | Control | 221 | | 86 | | 70 | | 134 | |
| | Cellulose | 223 | + 2 | 86 | 0 | 68 | - 2 | 138 | + 4 |
| | Wheat bran | 222 | + 1 | 62 | -24 | 77 | + 7 | 133 | - 1 |
| DP | Control | 183 | | 54 | | 32 | | 141 | |
| | Cellulose | 145 | -38 | 42 | -12 | 22 | -10 | 115 | -26 |
| | Wheat bran | 163 | -20 | 74 | +20 | 20 | -12 | 128 | -13 |
| $\overline{X}$ | Control | 198 | | 76 | | 68 | | 115 | |
| | Cellulose | 171 | -27 | 56 | -20 | 45 | -23 | 108 | - 7 |
| | $\pm$ S.E.[d] | | 8 | | 10 | | 2 | | 11 |
| | $P <$ [e] | | 0.05 | | 0.14 | | 0.002 | | 0.54 |
| | Wheat bran | 174 | -24 | 73 | - 3 | 50 | -18 | 109 | - 6 |
| | $\pm$ S.E.[d] | | 8 | | 10 | | 2 | | 11 |
| | $P <$ [e] | | 0.07 | | 0.78 | | 0.003 | | 0.63 |
| | $P <$ [f] | | 0.85 | | 0.32 | | 0.18 | | 0.92 |

a statistical analyses were performed on the D's [D = experimental diet - control diet] for each lipid component

b high-density lipoprotein

c low-density lipoprotein. calculated by $c_s - c_{HDL} - (TG/5)$, where $c_s$ = total serum cholesterol, $c_{HDL}$ = HDL-cholesterol, and TG = total serum triglycerides [171].

d standard error of the D means

e statistical probability that cellulose or wheat bran deviation mean is different from the control

f statistical probability that cellulose and wheat bran deviation means are different from each other.

and a slight decrease in the ratio of saturated to unsaturated fat consumed (Table 8). However, stepwise regression analysis revealed that 70% of the reduction in total serum cholesterol could be accounted for by the addition of fiber; dietary cholesterol did not meet the 0.15 significance level for entry into the regression model. Nevertheless, individual variations in dietary cholesterol and fat consumption were subjectively scrutinized in relation to changes in total serum cholesterol The reduction in GC's total serum cholesterol was accompanied by a reduction in dietary cholesterol on both high-fiber diets. There was a greater reduction in serum cholesterol on the cellulose diet than on the wheat bran diet, even though dietary cholesterol was higher during the cellulose diet. In GW, the opposite was observed: the more pronounced reduction in dietary cholesterol during the wheat bran diet paralleled a more pronounced reduction in total serum cholesterol. DP was the only subject who increased cholesterol consumption during the wheat bran diet and this was accompanied by reductions in total serum cholesterol, although the magnitudes of change between dietary and serum cholesterol levels were inconsistent.

There was an overall reduction in total serum triglycerides during the cellulose diet (-20 mg/dl) but virtually none on the wheat bran diet; this trend was consistent for all subjects except SH. No dietary factors that would account for reduced serum triglycerides met the 0.15 significance level for entry into the regression model. Neither changes in total dietary carbohydrate nor alterations in the simple to complex carbohydrate ratio consistently paralleled a change in total serum triglycerides. Improvement in control, as assessed by hemoglobin $A_1c$ and urine sugar index, was not accompanied consistently by reduced triglyceride levels.

All subjects except SH experienced a marked reduction in HDL-chol-

esterol levels during both high-fiber diets (-23 mg/dl, $P<0.002$ during the cellulose diet; -18 mg/dl $P<0.003$ during the wheat bran diet). The reduction in total serum cholesterol appeared to be accounted for largely by the decrement in the HDL-cholesterol fraction. HDL-cholesterol was reduced in subjects who increased (GW and SH, cellulose diet) and decreased (SH and DP, wheat bran diet) their energy expenditure, although, as noted earlier, the large increase in kilocalorie expenditure recorded by GW while consuming the cellulose diet was not representative of the whole dietary period.

With the exception of one subject, the high-fiber diets did not result in significant reductions in the LDL-cholesterol fraction. GC showed a large increase in LDL-cholesterol (63 to 94 mg/dl) which was accompanied by a marked reduction in HDL-cholesterol (84 to 44 mg/dl) for a dramatic reduction in the HDL to LDL-cholesterol ratio (1.3 to 0.5) with the wheat bran diet. In no other subject was such a pronounced change in this ratio observed. Increases in LDL-cholesterol were not related consistently to diabetic control (Table 9) either with individual study participants or when calculated as means for each diet.

Changes in serum lipids should be scrutinized in relation to changes in body weight during the dietary treatments. DP gained three pounds during the wheat bran diet but he still exhibited a reduction in all fasting serum lipids measured except total triglycerides (Table 13). The fasting serum lipids of SH appeared unaffected by a two pound weight loss during the cellulose diet but her fasting total triglycerides were markedly reduced during the wheat bran diet when her weight remained constant. Thus, a change in weight did not appear to affect her serum lipids. GC showed more marked reduction in all serum lipids on the cellulose diet when his weight decreased by three pounds, compared to the wheat bran diet when his weight remained constant.

In this study, the reduction in weight of all subjects during the cellulose diet period may be partially responsible for the reduction in all serum lipids measured following consumption of that diet. The mean reductions in total serum cholesterol and LDL-cholesterol were due to GW. Since her weight change during the wheat bran diet treatment is unknown, determining whether her reduction in serum lipids is due more to diet or to weight change is impossible.

## B. Biostator Evaluation

### 1. Energy and fiber consumption

The consumption of dietary protein, carbohydrate, fat, fiber and kilocalories during biostator monitoring is recorded in Table 14. Differences between diets in the saturated to unsaturated fat ratio and dietary cholesterol were physiologically insignificant for the purpose of monitoring changes in blood glucose and insulin needs. Slight differences in total kcal intake for individuals between diets were also physiologically insignificant. In each subject, all energy-containing nutrients and the ratio of simple to complex carbohydrate, were identical at each meal to the average amounts consumed during the free-living baseline period. Minor differences were physiologically insignificant. During the free-living phase of the high-fiber diets, subjects were to consume 60 g dietary fiber with 50% being derived from cellulose or wheat bran. During biostator monitoring, less than 60 g was consumed because the subjects were not fed an evening snack. SH's consumption of wheat bran fiber is especially low because she could not tolerate more without experiencing gastrointestinal upset. The percentage of fiber from wheat bran or cellulose consumed by the other subjects in the respective diets was not ex-

TABLE 14

Consumption of dietary protein, carbohydrate, fat, cholesterol, fiber and total kilocalories of patients during biostator monitoring

| Name | Diet | Protein (g) | Carbohydrate (g) | | Fat (g) | | Chol (mg) | Dietary Fiber (g) | | | Total kcal |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Total | Simple:Complex | Total | Saturat: Unsatur. | | Total | Cellulose | Wheat Bran | |
| GC | Cont | 126 | 234 | 0.9 | 92 | 0.4 | 552 | 26 | 10 | 0 | 2275 |
| | Cellu*(a)* | 126 | 234 | 0.9 | 92 | 0.4 | 520 | 55 | 28 | 0 | 2285 |
| | WB *(b)* | 126 | 233 | 0.9 | 93 | 0.3 | 459 | 56 | 12 | 26 | 2274 |
| GW | Control | 42 | 84 | 0.8 | 52 | 0.6 | 241 | 22 | 9 | 0 | 975 |
| | Cellu | 42 | 84 | 0.8 | 52 | 0.6 | 177 | 49 | 24 | 0 | 966 |
| | WB | 42 | 84 | 0.7 | 51 | 0.6 | 40 | 49 | 14 | 24 | 964 |
| SH | Control | 56 | 135 | 1.6 | 47 | 0.4 | 156 | 15 | 5 | 0 | 1181 |
| | Cellu | 56 | 135 | 1.6 | 47 | 0.6 | 79 | 53 | 26 | 0 | 1184 |
| | WB | 56 | 135 | 1.6 | 47 | 0.5 | 91 | 53 | 11 | 20 | 1178 |
| DP | Control | 143 | 341 | 1.2 | 142 | 0.7 | 763 | 22 | 5 | 0 | 3212 |
| | Cellu I | 143 | 341 | 1.2 | 142 | 0.6 | 664 | 58 | 29 | 0 | 3215 |
| | Cellu II | 143 | 341 | 1.2 | 143 | 0.6 | 642 | 58 | 29 | 0 | 3214 |
| | WB | 143 | 341 | 1.2 | 143 | 0.6 | 569 | 59 | 14 | 28 | 3210 |
| $\bar{X}$ | Control | 117 | 199 | 1.1 | 83 | 0.5 | 428 | 21 | 7 | 0 | 1911 |
| | Cellu | 117 | 199 | 1.1 | 83 | 0.6 | 360 | 54 | 27 | 0 | 1913 |
| | WB | 117 | 198 | 1.1 | 83 | 0.5 | 290 | 54 | 13 | 24 | 1907 |

*(a)* cellulose
*(b)* wheat bran

actly 50%, either. This reflects a discrepancy between the percentage of fiber from wheat bran or cellulose that was calculated to be in the high-fiber products, and the percentage that was subsequently found to be present by chemical analysis. Reported in Table 14 are the actual amounts of energy-containing nutrients and fiber which were consumed.

2. Insulin infusion

a. Total and postprandial: Significantly more total insulin was required to achieve normoglycemia during biostator monitoring during the cellulose diet compared to the control diet (53.8 units, cellulose; 47.0 units, control; $P < 0.024$) but the high-fiber wheat bran diet significantly reduced insulin needs during biostator monitoring (41.9 units, wheat bran; 47.0 units, control; $P < 0.052$). Identical trends were observed for postprandial insulin needs (Table 11). Three subjects demonstrated a definite increase in insulin need when the cellulose diet was consumed; only one subject (GC) required less insulin. DP was the first subject to consume the cellulose diet on the biostator and because of his unexpected increase in insulin needs compared to the control, the biostator evaluation of the cellulose diet was repeated three weeks later. Similar total insulin requirements (73.2 units during cellulose I and 68.2 units during cellulose II) and virtually identical postprandial insulin requirements (60.7 units during cellulose I and 61.0 units during cellulose II) were obtained at both evaluations.

While consuming the wheat bran diet, two subjects required more insulin than than during the control (SH and DP) while the other two required less insulin (GC and GW). But because of the huge reduction in GC's insulin needs during wheat bran feeding (-28 units total insulin; - 18 units postprandial insulin) mean insulin needs for all subjects showed a significant re-

duction. Weight changes between biostator evaluations (Table 11) were not related consistently to changes in biostator insulin needs for most subjects. The increase in DP's weight between control and high-fiber diets (+8 pounds, cellulose; + 5 pounds, wheat bran) might account for part of his increased insulin needs, but probably not for the large difference seen in total insulin usage on the biostator (+21.4 units, cellulose; + 9.9 units, wheat bran).

b. Peak postprandial blood glucose concentration and insulin infusion rate: Continuous monitoring of blood glucose concentration and the rate of insulin infusion during biostator evaluation, revealed that both the mean peak blood glucose concentration and the mean peak rate of insulin infusion after each meal were consistently lower during wheat bran feeding compared to the control diet (Table 15). The only exception was a marginal increase in the mean peak blood glucose concentration after the dinner meal. Although none of the mean differences between the control and wheat bran diets was statistically significant by itself, the trend toward lower blood glucose and insulin infusion rate was strongly evident. This trend indicates that high-fiber wheat bran feeding reduces postprandial glycemic excursions and postprandial insulin needs. Similar conclusions cannot be drawn about high-fiber cellulose feeding. Mean postprandial blood glucose and insulin-rate peaks during cellulose feeding were usually equal to or greater than those during feeding of the control, although reduced peaks were observed after breakfast. Thus, during biostator monitoring, high-fiber wheat bran feeding appeared to reduce both peak blood glucose concentration and peak insulin infusion rate compared to a normal-fiber control diet and a high-fiber cellulose diet.

c. Delay in peaks of postprandial blood glucose concentration and insulin-infusion rate: Not only were the postprandial peak concentrations of blood glucose and insulin infusion rate reduced during high-fiber wheat bran

TABLE 15

Delay in (min) and height of postprandial blood glucose (mg/dl) and insulin-rate (milliunits/min) peaks during biostator monitoring: Actual values (A) and deviation from control (D)[a]

| | | Postprandial Blood Glucose Peak | | | | | | | | | | | | Postprandial Insulin Rate Peak | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Breakfast | | | | Lunch | | | | Dinner | | | | Breakfast | | | | Lunch | | | | Dinner | | | |
| | | Time | | Conc[b] | | Time | | Conc[b] | | Time | | Conc[b] | | Time | | Rate | | Time | | Rate | | Time | | Rate | |
| Name | Diet | (A) | (D) | (A) | (D) | (A) | (D) | (A) | (D) | (A) | (D) | (A) | (D) | (A) | (D) | (A) | (D) | (A) | (D) | (A) | (D) | (A) | (D) | (A) | (D) |
| GC | Cont[a] | 40 | | 140 | | 45 | | 158 | | 35 | | 117 | | 30 | | 282 | | 35 | | 299 | | 30 | | 203 | |
| | Cellu[d] | 65 | +25 | 163 | +23 | 45 | 0 | 149 | - 9 | 35 | 0 | 162 | +45 | 45 | +15 | 231 | -51 | 45 | +10 | 300 | + 1 | 30 | 0 | 276 | + 73 |
| | WB[e] | * | | * | | 45 | 0 | 117 | -41 | 60 | +25 | 110 | - 7 | * | | * | | 45 | +10 | 171 | -128 | 60 | +30 | 47 | -156 |
| GW | Cont | 80 | | 142 | | 10 | | 159 | | 35 | | 122 | | * | | * | | 40 | | 162 | | 20 | | 69 | |
| | Cellu | 60 | -20 | 106 | -36 | 85 | +75 | 146 | -13 | 95 | +60 | 160 | +38 | 40 | | 61 | | 65 | +25 | 203 | + 41 | 60 | +40 | 221 | +152 |
| | WB | 65 | -15 | 166 | +24 | 60 | +50 | 103 | -56 | 65 | +30 | 111 | -11 | 40 | | 291 | | 80 | +40 | 53 | -109 | 60 | +40 | 80 | + 11 |
| SH | Cont | 30 | | 199 | | 40 | | 143 | | 40 | | 143 | | 20 | | 300 | | 25 | | 276 | | 30 | | 300 | |
| | Cellu | 55 | +25 | 180 | -19 | 70 | +30 | 167 | +24 | 30 | -10 | 137 | - 6 | 40 | +20 | 300 | 0 | 60 | +35 | 254 | - 22 | 25 | - 5 | 150 | -150 |
| | WB | 55 | +25 | 139 | -60 | 50 | +10 | 161 | +18 | 50 | +10 | 171 | +28 | 45 | +25 | 209 | -91 | 40 | +15 | 300 | + 24 | 45 | +15 | 300 | 0 |
| DP | Cont | 40 | | 194 | | 35 | | 148 | | 45 | | 177 | | 20 | | 300 | | 35 | | 262 | | 15 | | 241 | |
| | CelluI[f] | 40 | 0 | 211 | +17 | 35 | 0 | 123 | -25 | 40 | - 5 | 164 | -13 | 25 | + 5 | 312 | +12 | 30 | - 5 | 248 | - 14 | 35 | +20 | 312 | +71 |
| | CelluII[g] | 45 | + 5 | 185 | - 9 | 40 | + 5 | 173 | +25 | 35 | -10 | 181 | + 4 | 30 | +10 | 300 | 0 | 30 | - 5 | 297 | + 35 | 30 | +15 | 169 | +22 |
| | WB | 40 | 0 | 166 | -28 | 45 | +10 | 133 | -15 | 55 | +10 | 175 | - 2 | 30 | +10 | 294 | - 6 | 40 | + 5 | 214 | - 48 | 40 | +25 | 313 | +22 |
| $\bar{X}$ | Cont | 48 | | 169 | | 33 | | 152 | | 39 | | 140 | | 23 | | 294 | | 34 | | 250 | | 24 | | 203 | |
| | Cellu | 56 | + 8 | 164 | - 5 | 59 | +26 | 152 | 0 | 49 | +10 | 157 | +17 | 37 | +14 | 275 | -19 | 50 | +16 | 256 | + 6 | 37 | +14 | 222 | +10 |
| | ± S.E.[h] | | 1.4 | | 16.0 | | 4.7 | | 9.4 | | 7.3 | | 12.2 | | 1.4 | | 15.8 | | 4.4 | | 26.2 | | 3.9 | | 56 |
| | P < [i] | | 0.01 | | 0.78 | | 0.006 | | 0.98 | | 0.24 | | 0.25 | | 0.01 | | 0.36 | | 0.03 | | 0.82 | | 0.03 | | 0.87 |
| | WB | 57 | + 9 | 157 | -12 | 51 | +18 | 128 | -24 | 58 | +19 | 142 | + 2 | 38 | +18 | 265 | -65 | 52 | +18 | 185 | -65 | 51 | +28 | 185 | -18 |
| | ± S.E.[h] | | 2.0 | | 22.2 | | 5.1 | | 10.2 | | 7.9 | | 13.3 | | 2.2 | | 24.6 | | 4.8 | | 28.4 | | 4.2 | | 60 |
| | P < [i] | | 0.03 | | 0.63 | | 0.03 | | 0.09 | | 0.08 | | 0.89 | | 0.02 | | 0.12 | | 0.03 | | 0.09 | | 0.003 | | 0.78 |
| | P < [j] | | 0.85 | | 0.81 | | 0.31 | | 0.17 | | 0.46 | | 0.47 | | 0.29 | | 0.25 | | 0.79 | | 0.14 | | 0.07 | | 0.75 |

[a] statistical anlayse were performed on D's (D = experimental diet - control diet) for each A value; Least-squared analysis was used and least-squared means adjusted for subject differences

[b] concentration (mg/dl) [c] control [d] cellulose [e] wheat bran [f] first biostator evaluation of cellulose diet [g] second biostator evaluation of cellulose diet

[h] standard error of the D means [i] statistical probability that cellulose or wheat bran deviation mean is different from the control

[j] statistical probability that cellulose and wheat bran deviation mean are different from each other

* postprandial peak difficult to determine because of extreme hypoglycemia or hyperglycemia at the beginning of breakfast consumption

feeding, but the mean time at which these peaks occured was delayed significantly in comparison to the control diet (Table 15). Almost without exception, the delay in blood glucose and insulin infusion rate peaks, was observed in all subjects at all meals. This seems to indicate that the appearance of postprandial glucose in the blood, and the need for insulin, is delayed when high levels of fiber from wheat bran or cellulose are fed with meals.

# DISCUSSION

## A. Free-living

### 1. Acceptability of diets

Three out of four study participants believed their diabetes was more difficult to control while consuming the high-fiber diets than it had been during control periods. Problems with both hyper- and hypoglycemia were cited. The difficulty in controlling glycemic excursions may be related to the stricter dietary guidelines with which the subjects complied during high-fiber periods. Although study subjects had been selected on the basis of their past good record of diet compliance, during the baseline period large variations (up to 100%) in almost all subjects were observed in day-to-day kilocalorie intake and distribution of energy-containing nutrients. This observation has been confirmed by others whose subjects were also a group of highly-motivated individuals [172]. The large variation in energy intake may actually be one means of maintaining diabetic control, especially in relation to a large variation in energy expenditure. In the present study during high-fiber diet periods, the subjects were expected to eat the same number of kilocalories at every meal and snack and they could not use kilocalorie variation to help maintain glycemic control. This left them with only one realistic alternative: to adjust their insulin dosage. Thus, on the high-fiber diets one of the means they had used previously to maintain diabetic control was no longer available, glycemic control was more difficult, and this probably affected overall acceptability of the diets.

Another factor affecting acceptability of the high-fiber wheat bran diet was the gastrointestinal side effects experienced by some of the study participants. Three of the subjects reported feeling "bloated" and

experienced increased flatus. Both are common with high-fiber diets [18], and the social implications connected with flatus did not enhance acceptability of the high-fiber diets. All the subjects reported an increased frequency, number, and urgency of stool defication during the wheat bran diet; changes in stool habits were less pronounced when cellulose was the primary fiber source. These observations are in agreement with those of Eastwood and Mitchell [173] who reported that wheat bran has a greater capacity to increase stool weight than cellulose. This property is probably related to the greater water-holding capacity which wheat bran possesses (3 g water/g fiber [174]) compared to cellulose (0.4 g water/g fiber [44]).

2. Diet Compliance

Individual deviations in consumption between the control and high-fiber diet periods (Table 8) generally paralleled the deviations in consumption during high-fiber diets (Appendix J). Two exceptions to that tendency were observed. First, the actual consumption of total fiber, fiber from cellulose, and fiber from wheat bran were higher during high-fiber diets than during the baseline diet (as expected), but the consumption of fiber and its components was less than the amounts instructed. The second exception concerned GW's consumption of all energy-containing nutrients. GW's physician had recommended a 1400 kcal diet for her shortly after she had completed the baseline period. During baseline feeding GW had consumed approximately 1200 kcal per day. Since it would have been unethical to ignore her physician's advice when planning her high-fiber diets, her diet prescription was increased to 1400 kcal and all of the energy-containing nutrients were increased in proportion to the percentage of kcal they had provided during baseline data collection. During high-fiber feeding, GW's actual consumption of energy-

containing nutrients closely paralleled her control diet even though her diet instruction was to increase these.

In general, diet compliance was fairly good considering the long-term nature of the study and the strict diets to which subjects were asked to adhere. There was large day-to-day variation in the energy-containing nutrient consumption during high-fiber feeding, but when averaged over 15 day periods, overall food consumption was similar. However, mean dietary cholesterol consumption was reduced during high-fiber feeding compared to baseline amounts and compared to amounts they were instructed to eat.

3. Measures of glycemic control

The direction of changes in the daily urine sugar index of all subjects paralleled the direction of changes in hemoglobin $A_1c$. This observation is in agreement with that of Monnier et al. [116] with wheat bran feeding. However, in the present study, mean urine sugar index declined during high-fiber cellulose feeding while hemoglobin $A_1c$ increased. Most of this increase can be attributed to GW, who experienced very poor glycemic control (due to stressful Ph.D. preliminary examinations) during the two and one-half weeks antecedent to hemoglobin $A_1c$ measurement. Poor control is reflected by a small increase in her urine-sugar index and a large increase in hemoglobin $A_1c$. But hemoglobin $A_1c$ increased more dramatically than expected because it previously was thought to be a measure of long-term (120 days) glycemic control and relatively unresponsive to short-term fluctuations in blood glucose [176]. More recently, however, Goldstein et al. [177] have suggested hemoglobin $A_1c$ might exist as two chromatographically-indistinguishable fractions. They hypothesize a major fraction exists which is unresponsive to acute changes in blood glucose but that there is also a minor fraction which may reflect short-

term fluctuations in blood glucose. This may explain the large increase in hemoglobin $A_1c$ observed with GW during the cellulose diet, even though control, as assessed by glycosuria, was maintained until the last two and one-half weeks of this diet regimen.

The increase in GC's hemoglobin $A_1c$ is probably reflective of a decline in diabetic control over the six-week periods of both high-fiber diets, despite relatively good diet compliance. This is difficult to explain since he was amongst the most highly-motivated of the subjects. The problem of hyperglycemia after breakfast and hypoglycemia in the afternoons was recorded by GC during baseline data collection, but the situation worsened during high-fiber feeding. Part of the problem may have been due to a mean reduction in GC's total insulin dosage during both high-fiber diets compared to his baseline doses (-7 units/day, cellulose diet; -6 units/day, wheat bran diet). The decrement in glycemic control may have been due to his reduction of the insulin dose more than was optimal for him. However, when hemoglobin $A_1c$ was averaged for all subjects, it was depressed with fiber addition from wheat bran, and the reduction approached statistical significance ($P<0.09$). This is in agreement with Monnier's observation that when high-fiber is fed, predominantly from wheat bran, glycemic control is improved [116].

4. Daily insulin doses

Although a mean reduction in daily insulin doses was observed, there was large individual variation, with most of the mean reduction being accounted for by GW (- 17 units insulin/day). GW was able to reduce her insulin dose while improving glycemic control (Table 9) during consumption of the wheat bran diet. A reduction in kilocalorie consumption (- 112 kcal/

day) and an increase in energy expenditure (+ 59 kcal/day) may have accounted for part of the 40% reduction in insulin needs, but the elevated fiber most likely played a strong supporting role [34]. GC also reduced his average insulin dose but experienced deterioration in glycemic control; the decline in control is probably due less to fiber addition than to a reduction in the insulin dose. DP made no significant change in his daily insulin dosages but did realize improvement in glycemic control (Table 9) on both fiber diets. This raises the question: what changes in glycemic control would have been observed with GC had daily insulin doses not been reduced? SH also experienced improvement in glycemic control although she increased her insulin dosage during cellulose feeding by 25% over the control period. Consequently, improvement in SH's hemoglobin $A_1c$ and glycosuria cannot be attributed solely to enhanced fiber intake.

In general, the mean decrements in glycosuria and glycosylated hemoglobin with concommitant increases in the number of hypoglycemic reactions which were observed in the present study are indicative of improved glycemic control. They are also in good agreement with the same parameters measured by Monnier et al. [116] with wheat bran (35 g/day) feeding. However, his group found no change in the mean daily insulin needs of their subjects. Unfortunately, they do not report individual changes in insulin needs, so it is difficult to determine if the large variation in GW's insulin needs from baseline is typical of other subjects.

## B. Biostator Evaluation: Insulin Infusion

Reduction in insulin needs during high-fiber feeding has been documented in insulin-dependent diabetics monitored on the artificial endo-

crine pancreas. Pectin decreased postprandial insulin needs by 35% [178] and guar reduced 24-hour insulin delivery by 23% [37]. Since postprandial insulin needs account for up to 60% of total daily insulin requirements [178], postprandial insulin infusion is a good indicator of fiber's efficacy in reducing the body's demand for insulin in Type I diabetic subjects. In the present study, addition of fiber to the diet in the form of wheat bran reduced mean postprandial insulin needs by 8% ($P$ 0.29) and mean 12-hour insulin delivery by 11% ($P < 0.06$; Table 11), although there was considerable variation between subjects. Although reduction in total and postprandial insulin infusion was not observed in all subjects during wheat bran feeding, there was striking consistency among all subjects (except SH) in a lowering of the peak blood glucose following meals and the peak rate of postprandial insulin infusion (Table 15). Since blood glucose concentration dictates insulin infusion rate, the reduction of both peaks would be expected to parallel each other, as was observed. The reduction in postprandial blood glucose concentration has been widely reported by others with high-fiber feeding from various sources [20, 21, 26, 27, 118] and from wheat bran [116].

In addition to an overall reduction in the peak postprandial blood glucose and insulin infusion rates during wheat bran feeding, there was a marked delay in the time at which these peaks occurred and the delay was observed for all subjects. Others have found that absorption of glucose from carbohydrate is delayed when high-fiber foods are fed [25] and suggest this is due either to delayed gastric emptying and/or to incomplete absorption of carbohydrate from foods high in fiber. Kay et al. [52] believe glucose absorption from the small intestine and into the blood is delayed with addition of fiber to meals and that this delay not only reduces postprandial

fluctuations in blood glucose, but also is responsible for the flattened glucose tolerance and insulin response curves observed by others [31, 32]. Thus, a number of plausible mechanisms for the delay in postprandial blood glucose and insulin-rate peaks have been proposed, but the present study was not designed to determine which is(are) correct.

The present study did show a delay in postprandial blood glucose and insulin-infusion rate peaks with both wheat bran and cellulose fiber and that the peak blood glucose and insulin-infusion rates were reduced with wheat bran feeding, compared to the control. Puzzling, however, was the observation that cellulose fiber failed to reduce peak blood glucose and insulin-infusion rate consistently and that the height of these peaks was greater with cellulose than with wheat bran. The answer may lie in conclusions drawn by Jenkins in his studies with guar and pectin. Consistently, he has shown that gel-forming, soluable fibers such as guar and pectin are capable of delaying the absorption of available carbohydrate into the blood [107]. Recently, Aro [25] has compared guar and pectin with wheat bran in this respect and showed guar and pectin were more effective in delaying the absorption of available carbohydrate than was "cellulose-containing fiber such as ...(wheat) bran". Similarly, others [105] have shown a commercial fiber mixture containing cellulose, hemicellulose, lignin and pectin was less effective than pectin in inhibiting the postprandial blood glucose rise in insulin-dependent diabetics. Furthermore, Jenkins [60] has compared guar with cellulose and wheat bran and found guar was the most effective of the three in reducing the postprandial rise in blood glucose and insulin, that bran was intermediate, and cellulose was virtually ineffective in comparison to the other two. He found the reduction in mean peak rise of blood glucose concentration for each substance was highly correlated (r=0.926;

$P < 0.01$) with viscosity. Insoluble fibers such as cellulose do not contribute to viscosity. In the present study, wheat bran contained approximately 9% insoluble cellulose and 4% insoluble lignin (wet weight; Appendix H). The remaining fiber (25% of wet weight) would be partially soluble fibers [44, 110, 116] that contribute to viscosity. This may explain why cellulose was less effective than wheat bran in reducing the overall mean peak rise in blood glucose and insulin rate. However, it is still unclear as to why postprandial and total insulin infusion had to be increased during the cellulose diet compared to the control in order to maintain normoglycemia.

The significant reductions in total serum cholesterol with both wheat bran and cellulose addition are in general disagreement with the literature. Most human studies have not shown wheat bran or cellulose to be hypocholesterolemic.

Cellulose may be mildly hypocholesterolemic at very high levels of intake. The only study which has shown cellulose to lower serum cholesterol, incorporated 100 g/day of cellulose into the diet [67]. Studies which showed cellulose ineffective in lowering cholesterol used a maximum of 16 g cellulose per day [62 - 64]. In the present study a level intermediate (30 g/day) to those reported in the literature was used. The cellulose was added to the diets along with soluble fibers for a total of 60 g dietary fiber. The soluble fibers are known for their hypocholesterolemic properties and are much more effective in this regard than in cellulose [142]. In addition, consumption of dietary cholesterol decreased during the cellulose diet; this may have accounted also for part of the reduction in serum cholesterol, even though stepwise regression analysis did not show the reduction in dietary cholesterol to be signif-

icant enough to account for the decline in serum cholesterol. The decline in mean serum cholesterol observed during the high-fiber cellulose diet may be a result of these three factors acting in concert: 1) addition to the diet of soluable fibers, known to possess hypocholesterolemic properties, 2) reduction in dietary cholesterol consumption, and 3) a very mild cholesterol-lowering effect exerted by the cellulose fiber.

The reduction in total serum cholesterol observed subsequent to wheat bran feeding may be accounted for by similar factors. At the very high levels of wheat bran intake (48 - 72 g/day) such as was consumed during this study, the soluble fibers in wheat bran may have been responsible for some of the decline in total serum cholesterol. But at much lower levels usually consumed in human studies (12 - 38 g/day [80, 144, 147]) the soluble fiber from wheat bran may be physiologically insignificant, unless ingested as part of a high-cholesterol diet [141, 150, 151]. This helps to explain the inconsistency in hypocholesterolemic effects reported by others and would explain why soluble pectin generally exerts a greater cholesterol-lowering capacity [18, 26, 28, 35, 63, 80, 82, 103, 140] than wheat bran [80, 143, 147].

The significant reduction in HDL-cholesterol during both high-fiber treatments is of concern because of the protective effect this lipoprotein is thought to exert against the development of cardiovascular disease. Others also have found a reduction in HDL-cholesterol with wheat bran [148] and cellulose [38, 142] feeding, as well as fiber from mixed sources [41], but the observation is not consistent [59, 144, 145]. A reduction in total serum cholesterol is not advantageous if accompanied by a reduction in HDL-cholesterol, especially in a group of diabetic individuals who are already at greater risk for developing heart disease than the normal population.

Insignificant changes in fasting serum triglycerides with high-fiber diets have been reported in normal subjects [41] although Pivelesse [34] demonstrated high-fiber diets reduced fasting triglycerides in diabetic patients when fiber addition improved their glycemic control. In the present study there was no correlation between fasting total triglycerides, and improvement in hemoglobin $A_1c$ or urine sugar index.

# SUMMARY AND CONCLUSIONS

The present study was conducted to investigate the effects of high-fiber diets on parameters of glycemic control in four young-adult, insulin-dependent diabetic subjects. Subjects participated in a six-week period of baseline data collection during which food intake, urine sugar test results, daily insulin-dosages, time and number of hypoglycemic reactions, a five-day activity record and weekly body weight were recorded. Following the baseline period the subjects consumed two high-fiber diets, for six weeks each,separated by four-week "recovery" periods. The high-fiber (60 g dietary fiber/day) diets provided 50% of the fiber from either cellulose or wheat bran, and 50% from fruits, vegetables and legumes. The high-fiber diets were planned individually for each subject and were formulated to provide identical amounts of protein, fat, carbohydrate, and cholesterol, and identical ratios of saturated to unsaturated fat, and simple to complex carbohydrate as was consumed by the individual during the baseline period. At the conclusion of each six-week dietary treatment, subjects were hospitalized for a 12-hour metabolic profile. During this time, insulin needs and serum glucose were monitored continuously by an extracorporeal artificial endocrine pancreas (biostator), and blood was drawn for fasting serum lipids and hemoglobin $A_1c$ analyses.

Overall adherence to both high-fiber diets was good, considering the difficult conditions imposed by the study. Eighty grams of wheat bran per day caused gastrointestinal upsets initially in some subjects and had to be reduced for one person. No adverse effects were observed with cellulose feeding.

Daily insulin dosages were significantly ($P < 0.03$) reduced during both high-fiber diets and this corresponded with a reduction (improvement) in the daily urine sugar index and an increase in the number of hypoglycemic reactions per week. The wheat bran diet was more effective in improving both the latter parameters of glycemic control (urine sugar index: control = 1.7, cellulose = 1.4, wheat bran = 0.9; hypoglycemic reactions per week: control = 1.4, cellulose = 1.5, wheat bran = 2.1). Hemoglobin $A_1c$ was depressed with wheat bran addition, but increased with cellulose. Most of the increase in hemoglobin $A_1c$ during cellulose feeding was due to one subject exposed to very stressful conditions so the decline in her glycemic control at this time was not thought to be diet-related.

All serum lipids measured were depressed with high-fiber feeding, although the reductions were not significant for total triglycerides or the LDL-cholesterol fraction. Cellulose feeding was more effective in reducing total serum cholesterol than wheat bran feeding, but the amount of fiber actually consumed from wheat bran on the wheat bran diet was less than the fiber from cellulose on the cellulose diet. Part of the reduction in total serum cholesterol during both high-fiber diets may have resulted from the increase in the consumption of soluable fibers which are known to be generally hypocholesterolemic. The increase in consumption of soluable fibers was unavoidable with this study design. In addition, less dietary cholesterol was consumed during both high-fiber diets in comparison to the control diet.

HDL-cholesterol was the most significantly depressed ($P < 0.003$) of the lipids measured. This is not beneficial in a group of subjects whose risk for cardiovascular disease is already higher than the normal

population because of their diabetes.

Insulin needs during biostator monitoring were significantly ($P < 0.02$) increased during cellulose feeding compared to baseline values. The increase in insulin needs, as assessed by the biostator, is difficult to reconcile with the fact that mean daily insulin doses were reduced during free-living consumption of the cellulose diet while overall glycemic control was improved. Information obtained about changes in insulin needs was expected to be similar between daily-life and biostator monitoring, since the biostator is commonly used to determine insulin needs in diabetic subjects.

Reductions were observed in the peak concentration to which postprandial blood glucose concentration rose during the wheat bran feeding and the peak rate at which postprandial insulin was infused. Cellulose feeding produced no change, or changes in the opposite direction. However, the times at which peak blood glucose and insulin rates occurred, following a meal, was delayed significantly with both fiber diets compared to the control.

Based on the results of the present investigation, the following conclusions have been made. High-fiber feeding, predominantly as wheat bran, generally induces improvement in glycemic control and reduction in insulin needs of young adult, insulin-dependent diabetic subjects. High fiber fed primarily as cellulose is inconsistent in improving glycemic control and insulin requirements in the same subjects. Hypocholesterolemic effects observed during wheat bran and cellulose feeding in this study may have been due to one, or a combinations of three factors: 1) addition to the diet of soluble fibers 2) reduction in dietary cholesterol consumption, and 3) a mild cholesterol-lowering effect exerted by fiber from cellulose or wheat bran.

Juvenile-onset diabetic patients may benefit from high-fiber diets, with fiber predominantly as cellulose or wheat bran, but the improvement in serum lipids is not as great as reported by others when high-carbohydrate is consumed in conjunction with high-fiber.

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# APPENDIX

APPENDIX A

Effect of dietary fiber on insulin requirements and serum lipids

In juvenile-onset diabetes mellitus

INFORMED CONSENT

I,_____, have volunteered to participate in a study designed to evaluate the effectiveness of dietary manipulations on glucose and lipid metabolism. I have been asked to complete the study which will conclude by June 1981, but I should feel free to withdraw at any time. I understand that I may refuse to undergo any of the testing procedures without prejudice.

Participation will require the following:

A. Physical measurements:

(1) body weight -- taken initially and on a weekly basis during the experimental trials

(2) body height -- taken initially

B. Maintaining records of:

(1) the foods that I eat, and the times that I eat them

(2) the amount of my insulin dose(s) and time of dose(s)

(3) my activity level (5 days on each diet)

(4) urine test results - % sugar at each test

C. Answering questionaires pertaining to:

(1) my food preferences, habits and patterns -- initially

(2) my typical activity level & range of activities -- initially

(3) typical daily insulin dose(s) and time of dose(s) -- initially, and as part of the daily record - keeping format.

D. Testing of diets planned to meet my nutritional needs and food preferences as much as possible, given the limitations imposed by the study design:

(1) testing a 3-day cycle of each planned experimental diet.

(2) tasting the experimental breads and related experimental recipes which will be used to increase the amount of fiber in the diets I will be consuming

(3) I understand the purpose of the testing-tasting procedures is to familiarize myself with the diets & breads and to allow for changes to be made to improve acceptability of the diets before the study begins.

E. Consuming the two experimental diets, each for six weeks duration on a 3-day cycle, followed by a 3-6-week "rest" period in which I will be able to eat my regular diet.

F. Three 14-hour periods of Biostator II continuous glucose monitoring. This will require my hospitalization at St. Francis Medical Center. No personal expense will be incurred from this hospitalization.

The possible hazzards to me during this study are outlined as follows:

(1). Hypoglycemic reactions: I will be requested to carry small amounts of simple carbohydrates with me at all times.

(2) The Biostator

a. Blood loss: This will be little (if any) more than that incurred by frequent sampling need. Matched blood will be available should the need arise.

b. Venipuncture: Catheters will be inserted in one or both arms and may cause pain, irritation or infection. These hazards will be carefully monitored and appropriate action taken should it become necessary.

c. Heparinization: The heparin solution is a low concentration and large volumes would be needed to pose any threat to me. Although a machine malfunction with a large infusion of heparin is possible, it has not been reported in extensive testing. Coagulation will be monitored and counteracted with protamine, if needed.

d. Machine malfunction: Possible areas of malfunction are: 1) improper glucose readouts, 2) improper interpretation by the computer, 3) with improper insulin or glucose infusion. The Biostator has been extensively tested, however, and is almost fail-safe. Nevertheless, the dangers to me of these malfunctions are: 1) insufficient insulin or glucose infusion to properly control the blood glucose level with 2) continuing hyperglycemia. Since both of these possibilities pose a serious threat to me periodic venous blood sampling will be performed through another vein, or capillary blood will be obtained by fingerstick and glucose levels monitored in the laboratory or by Dextrometer Reflectance method at the bedside.

Clinical judgement will at all times be used so as not to endanger my life or health. All precautions, both clinical and biochemical, will be taken to ensure my welfare.

The Biostator contains built-in alarms to signal machine malfunctions, clots in the line, a blood sugar below 40 mg/100ml or a change of blood sugar value greater than 20 mg/100 ml in one minute.

I understand that my name and any study results connected with my name will remain confidential. I will have an opportunity at the end of the study to find out the conclusions. The generalities of the study have been explained to my satisfaction at this time, but I will feel free to ask questions regarding this study at anytime.

I understand that I am not likely to receive immediate personal benefit from the study. However, the use of high fiber, high carbohydrate diet regimens has allowed certain diabetics to reduce the exogenous insulin dose required to maintain satisfactory blood glucose levels, and it is possible this may be the case with me.

I have read and understand the above statement. I hereby voluntarily consent to participate.

Date_____ Signature_____

Witness_____

_____

Parent or legal representative on Participant's behalf if participant is less than 21 years of age or not legally competent

I have explained the above to the participants (or parent or guardian) on the date stated on this Informed Consent.

_____ _____

Witness Investigator

_____

Date

UNIVERSITY OF KANSAS SCHOOL OF MEDICINE -
WICHITA FACULTY, P.A.

1001 NORTH MINNEAPOLIS
WICHITA, KANSAS 67214
(316) 268-8228

BIOSTATOR
DATA REPORT FORM C

## CONSENT FOR PARTICIPATION IN RESEARCH ACTIVITIES

Participant:..... Date of study:.....

1. I hereby authorize Doctors ....., ....., ....., and such assistants as may work under their supervision to perform upon me the following procedures in connection with a research project:
   The use of a system that continuously measures blood glucose and possibly infuses insulin and/or glucose to control the blood glucose level. This investigational instrument has been developed to temporarily perform some of the functions of the human pancreas.
2. I am informed of possible benefits to myself or others associated with the procedure described above. These are:
   I understand that use of this instrument may help to better define a management regimen appropriate for my condition. This information could possibly help others.
3. I am informed of certain hazards and discomforts which might be associated with the procedures described above. These are:
   Catheters (plastic tubes) will be inserted in one or both arms and may cause pain, irritation or infection. These hazards will be carefully looked for and treated before they become severe. I may get hypoglycemia (low blood sugar) which can cause nervousness, sweating, light headedness or sleepiness but glucose will be given if these are severe.

4. I am informed that the following alternative procedures are available that would be advantageous to me:

   If I have poorly controlled diabetes this may be controlled with routine medical care in this hospital without use of this investigational instrument although this instrument is intended to provide better control of my diabetes for short periods.

5. I understand that the investigator is willing to answer any inquiries I may have concerning the procedures herein described. All the inquiries I have at this time have been answered.

6. I understand that I am free to withdraw my consent and to discontinue participation in the project or activity at any time. I also understand that I may ask a question or state a concern to the Chairman of the Institutional Review Committee, and that the investigator will, on request, tell me how to reach the Committee Chairman.

7. I understand that all reasonable efforts will be made to keep my identity confidential by being given a code number for identification whenever possible. My personal physician and/or the Food & Drug Administration may review my records at any time in the future and I have not surrendered my rights to good, prudent medical and nursing care. Information from my medical record will be made available to other scientists while keeping my personal identity confidential whenever possible.

8. I understand that The University of Kansas College of Health Sciences and affiliated hospitals do not maintain a policy of medical treatment or compensation for physical injuries incurred as a result of participating in biomedical or behavioral research.

9. I have read and understand the above, and I hereby consent to performance of the above procedures upon me.

.....

Participant

Date:.....

.....

Parent or legal representative on Participant's behalf if participant is less than 21 years of age or not legally competent.

I have explained the above to the participant (or parent or guardian) on the date stated on this Consent for Participation.

.....

Witness

.....

Investigator

Date:.....

APPENDIX B

Diet Habit/Food Preference Questionnaire

1. Will you be willing to eat 3 to 5 oz. of a granola-type product each day, while on the experimental diets? ___yes ____no
(It may be necessary that at least 3 oz. of this be eaten each day).

2. Will you be willing to eat 4 to 8 slices of high-fiber bread or its equivalent each day, while on the experimental diets? ____yes ____no
(It may be that at least 4 slices of high-fiber bread be eaten daily).
Will you be willing to eat at least 1 oz. of a 100% wheat bran product of your choice each day? ____yes ____no

   Please explain how you think you may feel about this_____

   _____

   _____

   _____

3. Do you often eat away from home?____yes ____no

   a. If yes, when? (Mark "B" for bring own, "P" for purchase it)

   | | | |
   |---|---|---|
   | __ breakfast | __ times per week OR | __ times per month |
   | __ a.m. snack | __ times per week OR | __ times per month |
   | __ lunch | __ times per week OR | __ times per month |
   | __ afternoon snack | __ times per week OR | __ times per month |
   | __ supper | __ times per week OR | __ times per month |
   | __ evening snack | __ times per week OR | __ times per month |

   b. If you purchase the food you eat away from home, specify the type of food and the meal or snack for which it is purchased:

   | Meal/Snack | Type of food purchased while eating away from home |
   |---|---|
   | breakfast | _____ |
   | a.m. snack | _____ |
   | lunch | _____ |
   | afternoon snack | _____ |
   | supper | _____ |
   | evening snack | _____ |

   c. Where do you usually eat your meal(s) or snack(s) away from home - bought or purchased?

   | Meal or Snack | Where eaten |
   |---|---|
   | _____ | _____ |
   | _____ | _____ |
   | _____ | _____ |
   | _____ | _____ |

4. Do you consider yourself to have a good appetite?_____

5. What time of the day are you most hungry?
__morning
__midmorning
__noon
__afternoon
__evening
__bedtime

6. Do you drink fruit juice? ____yes ____no

   a. What kinds do you like?_____

   _____

7. Do you eat fruit? ____yes ____no

   a. What kinds do you like?_____

   _____

   b. At what time(s) do you prefer to eat fruit?
   __morning
   __midmorning
   __noon
   __afternoon
   __evening
   __bedtime
   __no preference

8. Do you eat cheese? ____yes ____no

   a. If yes, what kind(s) do you eat?_____

   b. How often do you eat cheese?_____

9. Do you eat breakfast-type cereals? ____yes ____no

   If yes, circle the kinds you like.

   100% bran raisin bran all bran corn flakes bran buds farina

   whole oats wheat flake cereal shredded wheat granola others

   (please specify) _____

   _____

   What is (are) you favorite(s) 100% wheat bran products?_____

   _____

10. Do you eat eggs? ____yes ____no

   a. If yes, how do you like them prepared?
   __fried
   __scrambled
   __poached
   __other (Please specify) _____

   _____

11. Do you drink milk? ____yes ____no

a. If yes, when?
__morning
__noon
__evening
__snacks (specify)_____

b. What kind?
__skim
__2%
__whole
__other (explain) _____

C. How many cups per day?_____

12. Circle where you use milk: in cooking on cereal in coffee

13. Do you eat meat or meat exchanges for your noon meal? ____yes ____no

a. If yes, what kind(s)? _____

_____

b. How do you like to eat it?
__on sandwich
__in salad
__other (explain) _____

14. Do you eat meat for your evening meal? ____yes ____no

a. If yes, what kind(s)? _____

_____

b. How do you eat it?
__simply cooked, few sauces or gravies
__usually with sauces or gravies
__in casseroles
__other (please explain) _____

_____

15. How often do you eat:

a. beef? __times per day OR __times per week OR __times per month
b. pork? __times per day OR __times per week OR __times per month
c. veal? __times per day OR __times per week OR __times per month
d. fish? __times per day OR __times per week OR __times per month
e. poultry? __times per day OR __times per week OR __times per month
i) How do you eat poultry?
__with the skin
__without the skin
ii) Would you eat poultry without the skin, if requested to do so for a 6-week experimental period of time? ____yes ____no

16. Do you eat potatoes? ____yes ____no

a. If yes, how often? _____

B. How do you eat them?

__boiled _____
__baked _____
__mashed _____
__fried _____
__potato chips _____

Use the space after each method of preparation to indicate any accompaniments you may eat with the potatoes e.g. butter, margarine, sour cream, catsup, dip, etc.

17. Do you eat cooked vegetables other than potatoes? ____yes ____no
List your favorite kinds and how you like them prepared

| | Vegetable | How Prepared |
|---|---|---|
| a. | | |
| b. | | |
| c. | | |
| d. | | |
| e. | | |
| f. | | |
| g. | | |
| h. | | |
| i. | | |
| j. | | |
| k. | | |
| l. | | |
| m. | | |
| n. | | |
| o. | | |
| p. | | |

Use other side of this sheet, if necessary.

18. Do you eat raw vegetables, including salads? ____yes ____no

Please include the kinds of raw vegetables you like, how you like them prepared, and with what other food(s) you like to eat them, (see examples below). This information will help us to prepare your individual menu with the measurements that will be easiest for you to use when preparing your meals.

| EXAMPLE: | Kind of raw vegetable | How prepared | Foods associated with it |
|---|---|---|---|
| | carrot | sticks | plain, or in salad with lettuce |
| | carrot | shredded | with raisins |
| | tomato | slices | topped with cottage cheese |
| | cabbage | ground | in cole slaw |

| | Kind of raw vegetable | How prepared | Foods associated with it |
|---|---|---|---|
| a. | | | |
| b. | | | |
| c. | | | |
| d. | | | |

Continued on next page

18. (Continued)

| Kind of raw vegetable | How prepared | Foods associated with it |
|---|---|---|
| e. | | |
| f. | | |
| g. | | |
| h. | | |
| i. | | |
| j. | | |
| k. | | |
| l. | | |
| m. | | |
| n. | | |
| o. | | |
| p. | | |
| q. | | |
| r. | | |
| s. | | |
| t. | | |
| u. | | |
| v. | | |
| w. | | |
| x. | | |
| y. | | |
| z. | | |

19. How frequently do you eat:

a. macaroni? _____

b. spaghetti? _____

c. rice? _____

d. noodles? _____

e. bread? _____
About how many slices of bread do you eat per day? _____

20. Circle the foods that you eat. Indicate what you like to put on them.

| Food | What you put on it |
|---|---|
| a. White bread | |
| b. whole wheat bread | |
| c. high fiber bread | |
| d. rolls | |
| e. biscuits | |
| f. pancakes | |
| g. crackers (specify kind) | |
| _____ | |
| _____ | |

21. Do you eat any of the following prepared with artificial sweetener? (Circle appropriate foods.)

milk puddings custard ice cream

22. Circle the foods that you have eaten within the past month.

candy pie sweet roll cake cookie sugar

22. (continued)

a. How often do you normally eat this (these)?

_____times/week OR times/month

b. If any were "dietetic" please specify the specific name of the product(s)_____

_____

23. Do you eat snacks between meals? ____yes ____no If yes, when?

__morning
__afternoon
__evening

24. How much coffee do you drink in a day? _____
What do you put in it? _____
Would you be willing to limit coffee consumption to 3 cups per day?
____ yes ____ no

25. How much tea do you drink in a day? _____
What do you put in it? _____

26. How many soft drinks do you drink in a week? ____ diet ____ regular
What percent of these are cola-type beverages? _____
How often do you drink beer? _____
About how much beer do you drink each time? _____
What kind of beer do you drink?_____
How often do you drink other alcoholic beverages? _____
What kind of alcoholic beverage & how much of each kind would you drink each time? _____
Would you be willing to forego all alcoholic beverages for a 6-week period of time? ____ yes ____ no (Abstinence is requested, but not required to participate in the study).

27. Do you eat soup? ____ yes ____ no

a. If yes, what kinds are your favorites? _____

_____

b. Are these home-made or purchased? _____

28. Do you eat stews? ____ yes ____ no

If yes, what kinds are your favorites? _____

_____

29. Do you eat casseroles? ____ yes ____ no

a. If yes, what kinds are your favorites? _____

_____

b. Please include recipes, if you like. They would be helpful, particularly if the casserole is not a common one.

30. Do you use dressing on salads? ____ yes ____no

a. How much do you use? (Please be as specific as you can) _____

b. What kinds of dressing do you most frequently use? _____

_____

31. Do you salt foods in cooking? ____ yes ____ no At the table? ____ yes ____ no

32. Do you season your vegetables with

__bacon?
__butter?
__margarine?

33. Do you use non-meat sources of protein such as
__pinto beans?
__navy beans?
__peanut butter?
__dried beans?
__other? (Please specify) _____

a. Are any of these eaten in place of meat? ____ yes ____ no

b. If yes, which one(s)? _____

How often? _____

34. What kind of margarine do you use? (brand name) _____

35. Do you use oil in cooking? ____ yes ____ no If yes, what kind? _____

36. How often do you do each of the following?
a. Cook own meals _____ c. eat in restaurants _____
b. carry sack lunch _____ d. cooking done for you _____

37. Check those which you like to eat:

__Mexican foods?
__Spanish foods?
__Chinese foods?
__Italian foods?
__Kosher foods?

38. Do you have trouble eating or chewing foods ____ yes ____no
If yes, please explain. _____

_____

39. What are some of your favorite foods?

a. _____ j. _____
b. _____ k. _____
c. _____ l. _____
d. _____ m. _____
e. _____ n. _____
f. _____ o. _____
g. _____ p. _____
h. _____ q. _____
i. _____ r. _____

40. Are there any foods you will not eat?

a. _____ h. _____
b. _____ i. _____
c. _____ j. _____
d. _____ k. _____
e. _____ l. _____
f. _____ m. _____
g. _____ n. _____

41. Weight.

a. How much do you weigh? _____

b. How much would Dr. Guthrie like you to weigh? _____

c. How much would YOU like to weigh? _____

d. Has your weight changed within the past six months? ____ yes ____ no

i) How many pounds were gained? _____
ii) How many pounds were lost? _____

42. Exercise

a. In addition to necessary daily walking, etc., do you exercise? ____ no ____ yes

b. If yes, what type of exercise? (complete the following table as in the example)

| Type of exercise | Amount of time | Daily | Weekly |
|---|---|---|---|
| eg. X jog | 10 minutes | X | |
| X swim | 1/2 hour | | X |
| ___jog | _____ | _____ | _____ |
| ___walk | _____ | _____ | _____ |
| ___bicycle | _____ | _____ | _____ |
| ___run fast | _____ | _____ | _____ |
| ___bowl | _____ | _____ | _____ |
| ___swim | _____ | _____ | _____ |
| ___calisthenics | _____ | _____ | _____ |
| ___other (specify) | _____ | _____ | _____ |
| ___ | _____ | _____ | _____ |

C. Is your occupation physically active?

___very (specify) _____
___moderately (specify) _____
___sedentary (desk job) _____

43. What is your occupation? _____

44. Check any of the following which you are currently taking at home:

___ vitamin or mineral supplements (specify product, brand, and amount)

_____

___ other nutritional supplements (e.g. protein, etc.) Specify product, brand, and amount. _____

___ medication other than insulin. Specify type, dose, and reason. __

_____

45. Insulin

a. What kind(s) of insulin do you take? _____

b. What is (are) the average dose(s)? _____

c. How much do(es) your average dose(s) vary? _____

_____

d. At what time(s) do you take your insulin? _____

e. When was the last time you had an insulin reaction? _____

How frequent are insulin reactions with you? _____

f. When was the last time you had a hyperglycemic reaction? _____

How frequent are these with you? _____

g. How close to the same time each day do you:

i) take your insulin? _____

ii) eat your meals? _____

h. Are you accustomed to recording your insulin dose and/or time of dose?

____ yes ____ no

46. Urine testing

a. How often do you test your urine? _____

b. What method do you normally use to test your urine? _____

c. Do you regularly record your urine test results? _____

d. Do you have any experience with the 2 gtt clinitest method? ____ no ____ yes

47. Have you ever recorded food intake on a regular basis? ____ yes ____ no
If yes, for how long? _____

48. With what kind of a diet do you currently work?

___exchanges
___calorie points
___carbohydrate points
___combination of the above (specify) _____
___other (specify) _____

48a. Where do you live?

____dormitory
____fraternity
____sorority
____with parents
____alone
____with roomate
____with husband and/or children (circle appropriate)

48b. Please include your address below:

_____
_____

49. If you work with any type of diet or combination of diets in question #46, please specify the number and type of exchanges or points for each meal and snack, as you normally eat them. PLEASE BE VERY SPECIFIC.

50. Write the types of foods you choose for your usual meals and snacks OR write what you have eaten within the past 24 hours IF it was a fairly typical day.

DON'T FORGET TO INCLUDE ITEMS SUCH AS SUGAR, CREAM, MILK, BUTTER, DRESSINGS, ETC.

| | Kind of food | How prepared | How much |
|---|---|---|---|
| First meal<br>time:_____<br>place:_____<br>_____ | | | |
| Snack<br>time:_____<br>place:_____ | | | |
| Second meal<br>time:_____<br>place:_____<br>_____ | | | |
| Snack<br>time:_____<br>place:_____ | | | |
| Third meal<br>time:_____<br>place:_____<br>_____ | | | |
| Snack<br>time:_____<br>place:_____ | | | |

51. Many of the following foods are relatively high in dietary fiber. Others are necessary to maintain a well-balanced diet or to add interest and palatability to meals and snacks. According to the scale below, please rate your preference for the foods which follow. PLEASE CONSIDER ALL FOODS ONLY IN VIEW OF A SIX-WEEK EXPERIMENTAL DIET PERIOD.

Scale:

A. Like it well and could eat daily, if necessary
B. Like it all right and could eat it at least once every two or three days, if necessary.
C. Neither like, nor dislike, but wouldn't mind eating fairly often, if necessary.
D. Mildly dislike. Would prefer not to eat it, but would if diet could not be worked out any other way.
E. Would not eat it.
F. Have never eaten it.

Begin rating foods on the following page.

## MILK AND DAIRY PRODUCTS

| | A | B | C | D | E | F |
|---|---|---|---|---|---|---|
| skim milk | | | | | | |
| 2% milk | | | | | | |
| whole milk | | | | | | |
| American processed cheese | | | | | | |
| cheddar cheese | | | | | | |
| creamed cottage cheese | | | | | | |
| low-fat cottage cheese | | | | | | |
| low-fat mozarella cheese | | | | | | |
| low-fat ricotta cheese | | | | | | |
| Cheez-ola (low cholesterol cheese) | | | | | | |
| Count-down (low fat cheese) | | | | | | |
| eggs | | | | | | |
| egg substitute (eg. egg beaters) | | | | | | |
| Morning Star Farms -sausage patties or links | | | | | | |

## MEAT, POULTRY AND FISH

| | | | | | | |
|---|---|---|---|---|---|---|
| beef, lean | | | | | | |
| beef, medium fat | | | | | | |
| lamb | | | | | | |
| pork, lean | | | | | | |
| ham, lean | | | | | | |
| veal | | | | | | |
| chicken, light meat | | | | | | |
| chicken, dark meat | | | | | | |
| turkey, light meat | | | | | | |
| turkey, dark meat | | | | | | |
| cod | | | | | | |
| salmon | | | | | | |
| tuna, in water (not oil) | | | | | | |
| sardines | | | | | | |

## BREADS, CEREALS, AND STARCHY VEGETABLES

| | A | B | C | D | E | F |
|---|---|---|---|---|---|---|
| white beans | | | | | | |
| kidney beans | | | | | | |
| pinto beans | | | | | | |
| brown beans | | | | | | |
| lima beans | | | | | | |
| 100% bran cereal | | | | | | |
| whole wheat bread | | | | | | |
| high-fiber bread | | | | | | |
| corn | | | | | | |
| corn grits | | | | | | |
| corn flakes | | | | | | |
| graham crackers | | | | | | |
| farina | | | | | | |
| egg noodles | | | | | | |
| oatmeal | | | | | | |
| peas | | | | | | |
| popcorn (no oil) | | | | | | |
| potatoes | | | | | | |
| brown rice | | | | | | |
| white rice | | | | | | |
| dinner roll | | | | | | |
| rye wafers | | | | | | |
| spaghetti | | | | | | |
| winter squash | | | | | | |
| summer squash | | | | | | |
| sweet potatoes | | | | | | |
| wheat flake cereal | | | | | | |
| shredded wheat | | | | | | |
| baked beans | | | | | | |
| granola-type products | | | | | | |

| FRUITS | A | B | C | D | E | F |
|---|---|---|---|---|---|---|
| apples | | | | | | |
| apricots | | | | | | |
| banana | | | | | | |
| blackberries | | | | | | |
| cherries | | | | | | |
| grapefruit | | | | | | |
| grapes | | | | | | |
| cantalope | | | | | | |
| honey-dew melon | | | | | | |
| orange | | | | | | |
| peach | | | | | | |
| pear | | | | | | |
| pineapple | | | | | | |
| plums | | | | | | |
| strawberries | | | | | | |
| tangerine | | | | | | |
| rhubarb | | | | | | |
| rasins | | | | | | |
| FAT-CONTAINING FOODS : In evaluating the following, consider their use in cooking or as accompaniments. | | | | | | |
| margarine -tub | | | | | | |
| -bar | | | | | | |
| -liquid | | | | | | |
| corn oil | | | | | | |
| cottonseed oil | | | | | | |
| peanut oil | | | | | | |
| safflower oil | | | | | | |
| soybean oil | | | | | | |
| peanut butter | | | | | | |
| almonds | | | | | | |
| peanuts | | | | | | |
| pecans | | | | | | |

Vegetables

Please note how you prefer to eat your vegetables by marking R for RAW and C for COOKED. for example, if you love raw carrots but absolutely detest them cooked, mark

| | A | B | C | D | E | F |
|---|---|---|---|---|---|---|
| CARROTS | R | | | | C | |

or, if you like cabbage fairly well either raw or cooked, but wouldn't want to eat either every day, mark

| | A | B | C | D | E | F |
|---|---|---|---|---|---|---|
| CABBAGE | | | R/C | | | |

| | A | B | C | D | E | F |
|---|---|---|---|---|---|---|
| ASPARAGUS | | | | | | |
| BEAN SPROUTS | | | | | | |
| GREEN BEANS | | | | | | |
| BEETS | | | | | | |
| BROCCOLI | | | | | | |
| BRUSSEL SPROUTS | | | | | | |
| CABBAGE | | | | | | |
| CARROTS | | | | | | |
| CAULIFLOWER | | | | | | |
| CELERY | | | | | | |
| CUCEMBER | | | | | | |
| EGGPLANT | | | | | | |
| KALE GREENS | | | | | | |
| LETTUCE | | | | | | |
| ONIONS | | | | | | |
| PARSNIPS | | | | | | |
| RADISHES | | | | | | |
| SUMMER SQUASH | | | | | | |
| TOMATOES | | | | | | |
| TURNIPS | | | | | | |
| ZUCCHINI | | | | | | |
| RUTABAGA | | | | | | |

Is there anything additional you feel we should know? If so, please include it here.

APPENDIX C

## DIET RECORD INFORMATION

Date:

1. If you are a daytime person, you need only write this in when you start a new book. Just make sure the date is correct.
2. If you frequently work at night and are switching between nighttime and daytime activity, please include the date at all meals. This is particularly important for "graveyard-shift" workers.

Time: This should be to the nearest 5 minutes of giving yourself insulin.

Method:

This refers to the method of urine testing. Indicate whether the method was clinitest or testape.

Urine Sugar:

Indicate this as "+" or "%", whichever the colored paper has coded to indicate urine sugar.

Acetone:

This test need only be performed if your urine sugar has been greater than 2% for 3or more consecutive times.

Insulin:

The ___U___ + ___U___ should be completed similar to the following example:

12 U NPH + 10 U Reg

Time:

Next to each meal label ie FIRST MEAL, SNACK, SECOND MEAL, etc., there
***** **** ***** ****** ****
is a blank to be filled in for "Time". This should be the time you BEGIN consumption of that meal or snack.

Time: Met: Sugar: Acetone:

At the bottom of each page labled THIRD MEAL you will see the above words.
**********
"Met:" stands for "method" and again, this refers to the method of urine testing.
"Time:" should indicate the time urinalysis was performed and this should be the last possible thing you do before you go to bed.

Other Information:

This heading appears on the second last page of all the booklets. This is where you should record things which might affect blood sugar and for which there was not room in the format on the previous pages. Examples of such things include:

1. medications:
   a. Are you currently taking a medication?
   b. Have you discontinued a medication you have been taking for a long time?
   c. Include over-the-counter preparations as well as prescription medications.
   d. Be sure to indicate the NAME of the medication and manufacturer.
2. General Health
   a. Were you sick?
   b. Were you bedfast?
3. Anything else you can think of that may have some effect on your system, i.e. wide variation of your mood, etc.

Reactions:

You will find a reaction table on the last page of your booklets. Please use it in the event you should have a reaction. Use it also if you feel a reaction coming on but are able to take the correct precautions before anything actually happens. This will help us to see a change in insulin requirements or other needs which you might have.

Describe what happened and why you think it may have happened.

MEAL AND SNACK TABLES

Amount:

1. Use whatever measure is the most convenient at the time, however,
2. WHENEVER POSSIBLE, WEIGH YOUR FOODS ON THE SCALE PROVIDED. This will help our data collection in two ways:
   a. The more accurate your records, the more accurate our data, and the more relevant the information we can extract from the data.
   b. It helps you to become more proficient in estimating food weights so that when you are in a position in which it is impossible or highly impractical to weigh your foods, we can still have a relatively good estimate of your food consumption.
3. If it is easier to measure the volume than the weight, MEASURE THE VOLUME. The important thing is TO MEASURE. e.g. 3/4 cup macaroni hamburger tomato casserole, 1 c. milk, 2 oz beef patty.
4. If you are unable to weigh or measure, estimate the weight or measure. If you aren't confident with this, estimate the dimensions of the food.

Food:

1. Identify the food. If it is relatively unalterable such as a raw apple or pear, no further qualification is necessary in this column. If it is a casserole, please describe the main ingredients. If it is a food that comes in a variety of forms such as skim, 2%, or whole milk, indicate the type. THIS IS VERY IMPORTANT.

How Prepared:

Indicate if the food was raw, fried, baked, boiled, steamed, etc. Don't forget to include hidden calorie items, such as "green beans cooked in fat."

WEIGHING YOURSELF: GUIDELINES

As you start each week of the diets, it will be necessary to weigh yourself so that we can ensure a constant weight. Please follow these guidelines so that we can obtain the greatest possible consistency with your home scale.

1. Weigh first thing in the morning AFTER going to the bathroom and BEFORE eating or drinking anything, including water.
   a. If you eat or drink something before weighing, weigh yourself by following these guidlines on the next day.
2. Weigh yourself either naked or in your underwear, but BE CONSISTENT.
3. ZERO THE SCALE BEFORE WEIGHING.

APPENDIX D

Method of calculation of hourly energy expenditure

NAME:_____ DATE:_____ BIOSTATOR DIET:_____

Factor: kg body weight / 1000 * 5 = _____ kg * 5 / 1000 = _____

| Time to Time | | Activity | ml $O_2$/kg/min * factor = kcal/min * min = kcal | | | | |
|---|---|---|---|---|---|---|---|
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APPENDIX E

Wheat bran bread formula

| Ingredient | % Flour Weight |
|---|---|
| Hard red spring & winter wheat blend bread flour[a] | 100.00 |
| Water | 112.18 |
| Hard red spring wheat bran[b] | 30.00 |
| Vital wheat gluten[c] | 10.00 |
| Sucrose | 10.00 |
| Compressed yeast[d] | 4.00 |
| All-purpose shortening[e] | 3.00 |
| Sodium chloride | 2.50 |
| Bromate-type yeast food[f] | 0.60 |
| Sodium-stearoyl-2-lactylate | 0.50 |
| Calcium propionate | 0.40 |
| Asorbic acid (in solution) | 100 ppm |
| Potassium bromate (in solution) | 75 ppm |
| Azodicarbonamide (in solution) | 20 ppm |

[a]Kansas Diamond Bleached Wheat Patent Bread Flour (protein = 11.5%), Dixie Portland Flour Mills, Inc., Memphis, TN 38101

[b]Department of Grain Science, KSU, Manhattan, KS 66506

[c]Paniplus D (254) Vital Wheat Gluten, Olathe, KS 66061

[d]Red Star Compressed Yeast, Universal Foods Corporation, Milwalkee, WI 53201

[e]ADM All-Purpose Shortening; Archer Daniels Midland Co., Decatur, IL 62525

[f]C.M. Yeast Food, ITT Paniplus, Olathe, KS 66061

Method of wheat bran bread preparation

1. Fifty percent of the wheat bran was soaked in 14.89 percent of the total water for one hour.

2. With the exception of salt and the remaining bran, all dough ingredients were mixed in an 80 quart aluminum bowl with appropriate aluminum dough hook in an institutional mixer[a] for one minute at speed one, one minute at speed two and three minutes at speed three until development of good gluten film.

3. With mixer at speed one, salt was sprinkled on dough and mixed for a total of one minute.

4. The bran-water mixture was then added to the dough and mixed at speed one until incorporated.

5. With mixer at speed one, dry bran was sprinkled onto dough until it was worked into the dough surface, then mixed at speed two until just incorporated into dough.

6. Dough was placed in fermentation cabinet for 45 minutes (88° F wet bulb, 86° F dry bulb).

7. Dough was then scaled to 22 3/4 ounces, rounded and benched 20 minutes.

8. Dough was molded[b] and placed in one-pound silicon-coated bread pans, then proofed (100° F dry bulb, 95° F wet bulb) to template height (Figure 6A).

9. Bread was baked at 425° F for 35 minutes in a rotary oven, cooled, sliced, and double bagged[c].

---

[a]Hobart Corporation, M-802, Troy, OH 45373

[b]Pressure plate 3.5; Top roll 3.0; Bottom roll 1.7
Acme Rol-Sheeter, Model No. 88; D.R. McClain and Son, Pico Rivera, CA

[c]Bread was first placed on 1 1/2 mil plastic bread bag and tie, then 4 mil plastic bread bag and tied.

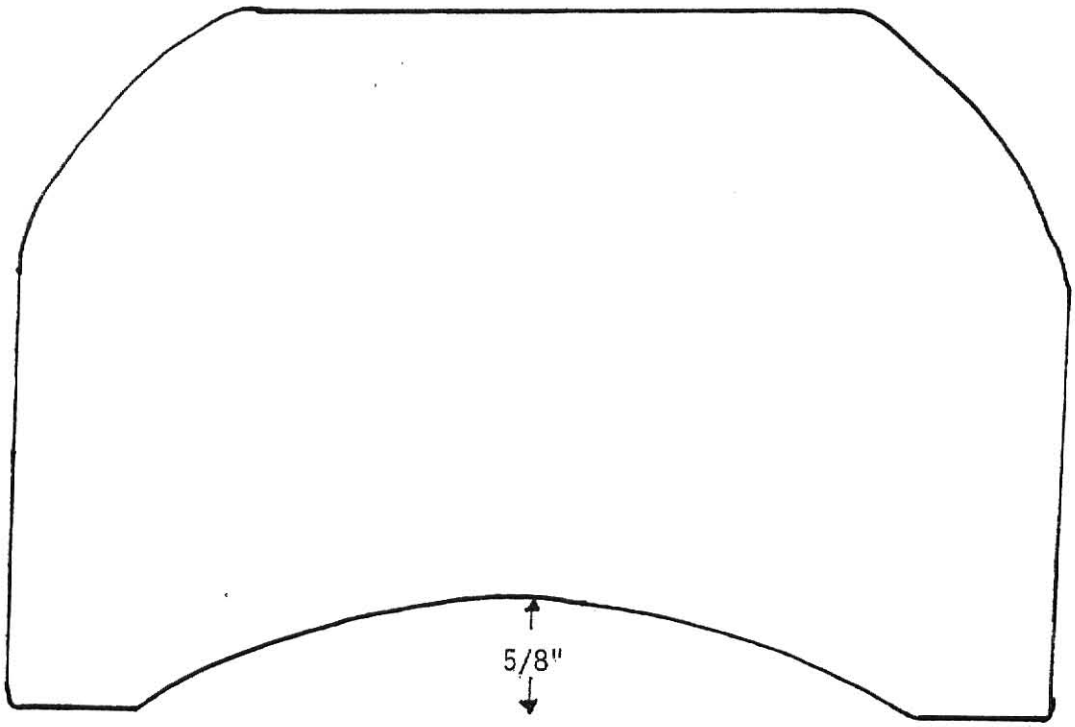


FIGURE 6A. Template used for proofing wheat bran bread [life-size]

## APPENDIX F

### Cellulose bread formula

| Stage | Ingredient | % Flour | Weight |
|---|---|---|---|
| Sponge | Hard red spring & winter wheat blend bread flour[a] | | 60.00 |
| | Bromate-type yeast food[b] | | 0.60 |
| | Compressed yeast[c] | | 0.40 |
| | Water | | 36.00 |
| Dough | Hard red spring & winter wheat blend bread flour[a] | | 40.00 |
| | Vital wheat gluten[d] | | 10.00 |
| | Sucrose (granulated) | | 10.00 |
| | Non-fat dry milk | | 6.00 |
| | All-purpose shortening[e] | | 5.00 |
| | Bread sours | | 0.50 |
| | Sodium-stearoyl-2-lactylate | | 0.50 |
| | Calcium propionate | | 0.40 |
| | Potassium bromate (in solution) | | 75 ppm |
| | Azodicarbonamide (in solution) | | 20 ppm |
| | Ascorbic acid (in solution) | | 150 ppm |
| | Sodium choloride (in solution) | | 3.29 |
| | Total dough water | | 91.03 |
| | Microcrystalline cellulose[f] | | 30.00 |

[a]Kansas Diamond Bleached Wheat Patent Bread Flour (protein = 11.5%); Dixie-Portland Flour Mills, Inc., Memphis, TN 38101

[b]C.M. Yeast Food, ITT Paniplus, Olathe, KS 66061

[c]Red Star Compressed Yeast, Universal Foods Corporation, Milwalkee, WI 53201

[d]Paniplus D (254) Vital Wheat Gluten, Olathe, KS 66061

[e]ADM All-Purpose Shortening; Arther Daniels Midland Co., Decatur, IL 62525

[f]Avicel - pH type 101; FMC Corporation, Philadelphia, PA 19103

Method of cellulose bread preparation

1. Sponge ingredients were mixed in an 80 quart aluminum bowl with appropriate aluminum dough hook in an institutional mixer[a] for two minutes at speed one and two minutes at speed two.
2. The sponge was fermented in a fermentation cabinet for two and one-half hours (88° F dry bulb, 86° F wet bulb).
3. At the end of sponge fermentation, all dough ingredients (except cellulose, 64.8% of the salt and 70.3% of the water) were mixed in same mixer and equipment for one minute at speed one. The sponge was immediately added and mixed with the dough for 30 seconds at speed one, 30 seconds at speed two, and then on speed three until gluten development had occured (9 - 10 minutes).
4. The remaining salt, dissolved in the remaining water, was then added to the dough, along with the cellulose. With the mixer on speed one, mixing was initiated with the bowl in "down" position until water was sufficiently absorbed. The mixing bowl was then raised to "up" position and mixing continued at speed two until cellulose was evenly dispersed.
5. The dough was then covered with plastic and rested in fermentation cabinet for ten minutes.
6. Dough was scaled to 29 1/2 ounces, rounded and benched ten minutes. Dough was then punched down, molded in rol-sheeter[b], and placed in silicon-lined bread pans[c] and placed in proof box (100° F on dry bulb, 95° F on wet bulb) to proof until template height (Figure 7A).
7. Bread was baked in a rotary oven at 400° F for 42 minutes, cooled, sliced and double-bagged[d], and frozen at 0° F until needed.

---

[a]Hobart Corporation, Model M-802, Troy, OH 45373

[b]Pressure plate = 4.0; Top role = 3.0; Bottom role = 2.0
Acme Rol-Sheeter, Model # 88; D.R. M[c]Clain and Son, Pico Rivera, CA

[c]4x tin plate, green color, silicon glazed bread pan, 22 ox. capacity

[d]Bread was first placed on 1 1/2 mil plastic bread bag and tie, then 4 mil plastic bread bag and tied.

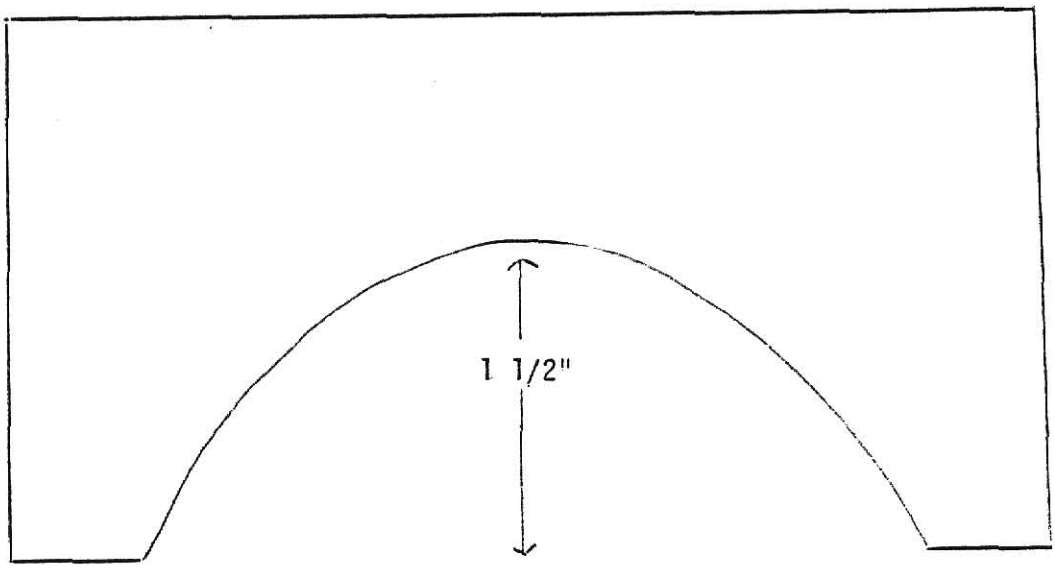


FIGURE 7A. Template used for proofing of cellulose bread [life-size]

## APPENDIX G

Granola recipes and method of preparation

| Ingredient | Amount (g) | | | |
|---|---|---|---|---|
| | $DP_1G$[a] | $DP_2G$[b] | GC G[c] | GW/SH G[d] |
| Egg white | 2632 | 1152 | 3008 | 3008 |
| Banana (EP)[e] | 2820 | 1152 | 3008 | 3008 |
| Wheat Bran | 3290 | 1260 | 3290 | 3290 |
| Crisco Shortening | 940 | -- | -- | -- |
| Whole Wheat Flour | 940 | -- | -- | -- |
| Cinnamon | 28 | 11 | 28 | 28 |
| Sesame Seeds | -- | -- | 846 | 846 |
| Brown Sugar Twin | 188 | 72 | 188 | 188 |
| Slivered Almonds | 940 | 360 | 940 | -- |
| Raisins | 1880 | 720 | 1880 | 1880 |

[a]Granola eaten by DP during first three weeks of wheat bran diet.

[b]Granola eaten by DP during second three weeks of wheat bran diet.

[c]Granola eaten by GC throughout wheat bran diet.

[d]Granola consumed by both GW and SH throughout wheat bran diet.

[e]edible portion

## Method of preparation of granola

The following general method was employed in the preparation of all the granolas. Although the method includes all possible ingredients, they were not all added in any given recipe.

1. Preheat rotary oven to 300° F.
2. With wire whip, whip egg white in mixing bowl until smooth peaks are formed.
3. With wire whip, in separate bowl, whip banana until lumps disappear.
4. In large mixing bowl with paddle, thoroughly mix Crisco shortening, whole wheat flour, and wheat bran.
5. Add to large mixing bowl: whipped egg white, whipped banana, cinnamon, sesame seed, brown sugar twin, and slivered almonds. Mix thoroughly.
6. Label and weigh baking trays. Place granola on baking trays and weigh again. Bake in rotary oven until thoroughly dry to touch.
7. Cool. Weigh each tray with granola.
8. Calculate percent ingredient loss, percent moisture loss, and grams wheat bran/100 g cooked granola. These calculations are used to figure grams of uncooked raisins which should be added to the granolas for each meal and snack.

## APPENDIX H

Fibers and energy-containing nutrients contained in wheat bran and cellulose breads, wheat bran granola and wheat bran on 100% dry matter basis

| Food | DM[b] | %NDF[c] | %ADF[d] | %Lignin[e] | %Cell[f] | DM[b] | %Ash | mg/g N[g] | %Prot[h] | %EE[i] | %WSC[j] | %T CHO[k] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CB[l] | .59788 | 32.313 | 20.556 | 0.605 | 20.309 | .59741 | 3.358 | 25.473 | 15.921 | 3.374 | 4.657 | 45.034 |
| WB B[m] | .59152 | 16.164 | 3.094 | 1.123 | 2.401 | .58886 | 3.756 | 30.616 | 19.135 | 2.067 | 5.946 | 58.878 |
| $DP_1G$[n] | .97448 | 32.810 | 10.963 | 5.145 | 6.130 | .97493 | 4.202 | 27.200 | 17.000 | 24.171 | 10.573 | 21.817 |
| $DP_2G$[o] | .95401 | 32.635 | 11.346 | 5.017 | 6.496 | .95379 | 5.123 | 39.699 | 24.812 | 13.854 | 15.786 | 23.576 |
| GC G[p] | .95854 | 29.916 | 12.257 | 5.172 | 7.167 | .95731 | 5.384 | 39.161 | 24.476 | 21.095 | 11.277 | 19.129 |
| GW/SH G[q] | .97153 | 31.122 | 11.970 | 4.25[o] | 7.56[o] | .96102 | 5.566 | 37.465 | 23.416 | 12.857 | 20.292 | 27.039 |
| WB[r] | .87952 | 42.509 | 14.384 | 4.595 | 10.159 | .85855 | 7.633 | 31.786 | 19.866 | 3.863 | 6.343 | 26.129 |

[a]Analysis performed by Analytical Laboratory, Animal Science Department, Weber Hall, Kansas State University, Manhattan, KS. [b]Dry matter [AOAC 13th ed., 1980; 14.003]. [c]Neutral detergent fiber [Forage Fiber Analysis. Agriculture Handbook No. 379, December, 1970]. [d]Acid detergent fiber [ibid]. [e]Lignin [ibid]. [f]Cellulose [ibid]. [g]Milligrams per gram nitrogen [AOAC, 13th ed., 1980; 2.057]. [h]% protein = mg/g N * 6.25 [i]Ether extract [ibid, 7.056] [j]Water-solu carbohydrate [McDonald, p., Henderson, A.R.: J. Sci. Fd. Agric. 15: 395 - 398, 1964]. [k]Total carbohydrate = 100 - (NDF + ash + rotein + ether extract) [l]Cellulose bread [m]Wheat bran bread [n]Granola eaten by DP during first three weeks of wheat bran diet. [o]Granola eaten by DP during second three weeks of wheat bran diet. [p]Granola eaten by GC throughout wheat bran diet. [q]Granola consumed by both GW and SH throughout wheat bran diet. [r]Wheat bran

APPENDIX I

Research Protocol

## Background

Several sources have now developed mechanical devices for closed loop monitoring and control of the blood glucose. Such devices were originally developed with the goal of an implantable artificial B-cell for continuous use. Such a system still eludes researchers, but the work has led to the development of extracorporal closed loop systems capable of: a) continuous glucose monitoring for periods up to 72 hours; b) the integration of the blood glucose values by computer; and c) computer controlled insulin-glucose infusions for the control of the blood glucose level.

Continuous glucose monitors-controllers (CGM-C) have been used extensively in Diabetes Research Centers on normal and diabetic patients and the computer algorhythms have been well worked out. The instruments have great practical significance for clinical medicine but have not yet been field tested on actual patients in a hospital setting. The FDA has requested field testing prior to marketing of the CGM-C units. One such unit developed by the Ames Company, a division of Miles Laboratories in Elkhart, Indiana, is ready for such field testing. This instrument, called a Biostator II-Controller, has been tested and refined repeatedly in various Diabetes Centers around the country for over five (5) years. The continuous glucose monitor portion of the Biostator II has been approved by the FDA and is currently being marketed as a single instrument.

The controller portion of the instrument still requires field testing, and will be field tested in three (3) centers around the country. We have been asked by Miles Laboratories to be one of these three centers for field testing of the Controller. Miles will supply a Controller (consisting of a continuous glucose monitor, computer, and insulin-infusion pump). The company has prepared a protocol to be followed. The essence of this protocol (without the numbers) is presented below.

### Purpose of the Research

To field test the Miles Biostator Continuous Glucose Monitor-Controller under actual field conditions in diabetic patients to determine the ability to practice to control diabetics, and attain and maintain normoglycemia.

### Methodology

A. Patient population

1. Children over the age of ten years (10 years) and adults with diabetes mellitus with hyperglycemia.

2. Pregnant diabetics during labor and delivery

3. Diabetics during surgery.

The diabetics with hyperglycemia will include patients in diabetic ketoacidosis (DKA) -- both newly diagnosed patients and old diabetic patients with DKA for whatever reason, and patients with uncontrolled hyperglycemia who need re-regulation.

B. Management

We have considerable experience with the management of diabetic patients with the above problems including the use of continuous insulin infusion in DKA, labor and delivery, and surgery. Data on over one hundred patients so managed are available for comparison controls for the machine-controlled group.

During this protocol all patients with the above conditions and above ten (10) years of age (so that proper consent can be obtained) will be controlled with the Biostator. A double lumen catheter is inserted into a peripheral vein. A small amount of heparin is infused through one lumen to maintain anticoagulation of the line. Heparin does not infuse into the patient. Blood is drawn continuously through another lumen by a pump inside the Biostator. Blood is drawn at a rate of 2cc/hour. The blood then passes into the machine where the blood glucose is determined by the glucose oxidase method and the values printed out on hard copy and on a readout on a display. The lag time is 90 seconds from arm to readout.

Glucose values are then automatically fed by the machine to a computer which is programmed to control a second pump which can infuse insulin and/or glucose through a second indwelling catheter. The computer can be programmed to control the blood glucose at a present value, to respond to rate of change in the blood glucose, or to maintain a present infusion rate for insulin and/or glucose irrespective of the glood glucose level.

Advantages of the Machine

Continuous insulin infusion is now an accepted method of controlling blood glucose during DKA, hyperglycemia, labor and delivery and during surgery. It is performed, however, usually by an open loop system (i.e., there is no computer control and blood samples need to be withdrawn at periodic intervals to monitor response). The continuous insulin infusion technique has, however, been proven to be a safe and effective method for controlling hyperglycemia.

A closed loop system incorporating automatic glucose control via

continuous glucose monitoring and variable infusion rates controlled by the blood glucose level would greatly simplify the continuous insulin infusion method and facilitate glucose control without the inherent danger of overshoot hypoglycemia seen with the open loop system. We feel the system will be particularly useful during labor and delivery and during long surgical procedures where hypoglycemia is difficult to detect and where frequent blood sampling is difficult. A closed loop system should then have great practical usefulness in the field and should be commercially available.

Disadvantages and Dangers to the Patient

The Biostator has been extensively tested over a five-year period in ten Diabetes Centers and found to be safe and effective in diabetics under controlled conditions in a clinical research center. There is every reason to believe it will perform as well under field conditions, but since that is the purpose of this experiment that fact is not known for sure. We feel the machine has been sufficiently tested by diabetes experts to pose no hazards to sick patients. Possible hazards are as follows:

1. Blood loss

   The blood loss by continuous monitoring will be little (if anymore) than that incurred by frequent sampling need with open loop systems.

2. Venipuncture

   These individuals will be sick patients in need of insulin therapy and would have venipuncture in any event.

3. Heparinization

   The amount of heparin infused to keep the line open is no more than needed to keep a heparin lock open and should pose no threat to the patient. Indeed the heparin does not enter the patient at all. A machine malfunction with a large infusion of heparin is possible but has not been reported in extensive testing. Coagulation will be monitored and the heparin counteracted with protamine if needed. The heparin solution is in a low concentration, i.e., 5000 units in 100 cc of NaCl, and large volumes would be needed to cause any difficulty.

4. Machine malfunction

   The Biostator has been so extensively tested and refined that it is almost fail safe, but of course no machine is completely so. Possible areas of malfunction are: a) improper glucose value readouts, b) improper interpretation by the computer, c) with improper insulin or glucose infusion. The dangers of these malfunctions are: a) insufficient insulin or glucose

infusion to properly control the blood glucose level with continuing hyperglycemia and/or DKA, b) over insulinization with hypoglycemia. Both of these possibilities pose a serious threat to the patient so that they must be watched for. This will be done by periodic venous blood sampling through another vein or by finger stick (capillary blood) to monitor blood glucose levels in the chemistry labotatory or by Dextrostix-Eyetone Reflectance meter at the bedside. Clinical judgement will at all times be used so as not to danger the life or health of any patient. All precautions, both clinical and biochemical will be taken to insure the patients' welfare. Informed consent will in all cases be obtained and the dangers explained to patients and/or parents or other responsible individuals in the case of comatose individuals. The Biostator contains built-in alarms to signal machine malfunctions, clots in the line, a blood sugar below 40 mg/dl or a change of blood sugar value greater than 20 mg/dl in one minute.

We feel that the machine (Biostator Monitor and Glucose Controller) has been thoroughly tested and is now, in effect, a commercial instrument which offers tremendous advantages in the management of hyperglycemia with few dangers.

Field testing can be carried out in our institutions which will provide the data needed for FDA approval and commercial availability. We ask approval of this protocol by Human Experimentation so that the protocol can be instituted in August, 1979.

## APPENDIX J

Average daily instruction for protein, carbohydrate, fat, cholesterol, fiber and kilocalories on the high-fiber diets[a]: instructed (I) and deviation from instruction (*D*)[b]

| Name | Diet | Protein (g) | | Carbohydrate (g) | | | | Fat (g) | | | | Chol. (mg) | | Dietary Fiber (g) | | | | | | Kcal[d] intake | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Total | | Simple : Complex | | Total | | Saturat : Unsatur. | | | | Total | | Cellulose | | WB[a] | | | |
| | | (I) | *(D)* | (I) | *(D)* | (I) | *(D)* | (I) | *(D)* | (I) | *(D)* | (I) | *(D)* | (I) | *(D)* | (I) | *(D)* | (I) | *(D)* | (I) | *(D)* |
| GC | Cellu[e] | 134 | *- 7* | 260 | *- 6* | 1.1 | *0* | 99 | *- 5* | 0.6 | *-0.1* | 552 | *-46* | 70 | *-11* | 31 | *- 6* | 0 | *0* | 2449 | *-47* |
| | WB | 140 | *+ 4* | 250 | *+10* | 1.2 | *-0.1* | 103 | *+ 6* | 0.5 | *0* | 568 | *-80* | 80 | *+ 2* | 15 | *+ 2* | 77 | *- 4* | 2457 | *+113* |
| GW | Cellu | 60 | *- 8* | 125 | *-35* | 1.0 | *-0.4* | 71 | *- 5* | 0.6 | *-0.2* | 197 | *-78* | 69 | *-16* | 33 | *- 7* | 0 | *- 7* | 1357 | *-201* |
| | WB | 56 | *- 4* | 134 | *-22* | 0.8 | *+0.5* | 72 | *-24* | 0.6 | *-0.1* | 251 | *-200* | 65 | *-12* | 15 | *- 1* | 79 | *-18* | 1424 | *-346* |
| SH | Cellu | 64 | *- 1* | 145 | *0* | 1.8 | *-0.3* | 54 | *0* | 0.4 | *0* | 201 | *-91* | 69 | *- 3* | 32 | *- 1* | 0 | *0* | 1313 | *+ 3* |
| | WB | 63 | *+ 1* | 157 | *-18* | 2.1 | *0* | 56 | *- 1* | 0.6 | *0* | 180 | *+ 8* | 62 | *- 4* | 15 | *- 3* | 61 | *-12* | 1366 | *- 57* |
| DP | Cellu | 146 | *-19* | 318 | *-31* | 1.2 | *-0.1* | 154 | *-16* | 0.7 | *-0.1* | 637 | *-52* | 70 | *-17* | 32 | *- 9* | 0 | *0* | 3182 | *-329* |
| | WB | 150 | *- 4* | 314 | *-30* | 1.2 | *0* | 153 | *+ 5* | 0.6 | *-0.1* | 584 | *+47* | 86 | *-29* | 16 | *- 4* | 79 | *-30* | 3198 | *- 57* |
| $\bar{X}$ | Cellu | | *- 9* | | *-18* | | *-0.2* | | *- 6* | | *-0.1* | | *-67* | | *-12* | | *- 6* | | *0* | | *-144* |
| | $\pm$ S.E.[f] | | *2.2* | | *5.4* | | *0.15* | | *6.2* | | *0* | | *38* | | *3.6* | | *1.5* | | *3.8* | | *68* |
| | $P <$ [g] | | *0.03* | | *0.5* | | *0.29* | | *0.38* | | *0.02* | | *0.18* | | *0.5* | | *0.03* | | *1.0* | | *0.13* |
| | WB | | *-0.5* | | *-14* | | *+0.1* | | *-4* | | *-0.1* | | *-56* | | *-11* | | *- 1* | | *-16* | | *- 87* |
| | $\pm$ S.E.[f] | | *2.2* | | *5.4* | | *0.15* | | *6.2* | | *0* | | *38* | | *3.6* | | *1.5* | | *3.8* | | *68* |
| | $P <$ [g] | | *0.85* | | *0.07* | | *0.56* | | *0.61* | | *0.09* | | *0.24* | | *0.6* | | *0.43* | | *0.02* | | *0.30* |
| | $P <$ [h] | | *0.8* | | *0.71* | | *0.26* | | *0.78* | | *0.18* | | *0.86* | | *0.85* | | *0.13* | | *0.06* | | *0.60* |

[a] average calculated from 15 consecutive days of the 42-day food records maintained by each subject on each diet. Selection of the 15 days was as follows: 5 days during which activity was recorded plus 5 days previous and 5 days following.
[b] statistical analyses were performed on *D*'s. (*D* = consumed - instructed) for each dietary component.
[c] wheat bran [d] kilocalories [e] cellulose
[f] standard error of the *D* means
[g] statistical probability that cellulose or wheat bran deviation mean is different from the control
[h] statistical probability that cellulose and wheat bran deviation means are different from each other.

Appendix K

Average time ± S.E.M.[a] at which meals and snacks were consumed by subjects in a free-living environment on control diets, cellulose and wheat bran diets[b]

| | | Meal Time (hour : minute) ± S.E.M. (minutes) | | | | | |
|---|---|---|---|---|---|---|---|
| Name | Diet | Breakfast | AM snack | Lunch | PM snack | Dinner | HS snack |
| GC | Control | 8:08± 8 | 10:45± 6 | 12:40± 9 | 16:04± 9 | 18:11± 7 | 22:30±17 |
| | Cellulose | 7:17±15 | 11:50±10 | 12:53±10 | 16:20±10 | 19:14±10 | 22:59±10 |
| | Wheat bran | 7:38±10 | 10:44± 5 | 12:24± 5 | 15:43± 6 | 18:24± 7 | 22:38± 8 |
| GW | Control | 7:42±13 | 9:54±10 | 12:30± 6 | 16:10±13 | 18:11± 5 | 20:44±22 |
| | Cellulose | 7:13±21 | 9:42±20 | 11:59± 7 | 16:39±16 | 18:06± 8 | 20:41±34 |
| | Wheat bran[c] | | | | | | |
| SH | Control | 6:33± 8 | 9:40± 6 | 11:46± 4 | 15:19± 6 | 18:27± 4 | 21:10± 4 |
| | Cellulose | 6:37± 8 | 9:25± 7 | 11:49± 5 | 15:36± 6 | 18:05±25 | 21:27± 3 |
| | Wheat bran | 6:36±12 | 9:21± 8 | 11:45± 6 | 15:57± 7 | 18:16± 3 | 21:15± 6 |
| DP | Control | 8:18±13 | d | 11:58± 8 | 15:07±28 | 17:43± 5 | 21:43±27 |
| | Cellulose | 8:02± 3 | d | 11:26± 5 | 15:23±18 | 17:33± 3 | 21:24±16 |
| | Wheat bran | 8:07± 6 | d | 11:35± 7 | 15:33±15 | 17:36± 5 | 21:18±11 |

[a] standard error of the mean

[b] averaged over 6 week period for all diets

[c] meal times not recorded

[d] AM snack not consumed by DP

# EFFECT OF DIETARY FIBER ON INSULIN REQUIREMENTS AND SERUM LIPIDS IN JUVENILE-ONSET DIABETES MELLITUS

by

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AN ABSTRACT OF A MASTER'S THESIS

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ABSTRACT

Four young adult (18 - 26 years) non-obese human subjects (2 male, 2 female) with Type I diabetes mellitus volunteered to consume a series of three diets: baseline (normal daily intake), wheat bran (normal daily intake plus 80 g wheat bran per day) and cellulose (normal daily intake plus 30 g cellulose per day). Wheat bran and cellulose diets were both
tain 60 g dietary fiber with 50% of the dietary fiber from wheat bran or cellulose, respectively and to be equivalent to baseline diets in protein, carbohydrate, fat cholesterol and the ratios of simple to complex carbohydrate and saturated to unsaturated fat. Each patient served as his own control. Diets were of six weeks duration, separated by four-week "recovery" periods. At the conclusion of each diet, subjects were hospitalized to undergo 12 hours of computer-controlled, insulin-glucose infusions (Biostator, Ames Co.) Dietary intake during hospitalization was equivalent to normal daily intake (baseline) and normal daily intake plus the respective fiber (high-fiber). Significant reductions were seen in fasting serum cholesterol for both high-fiber diets (baseline 198 mg/dl; wheat bran 171; cellulose 174. Triglycerides during the wheat bran diet were reduced, but not significantly (baseline 76 mg/dl; wheat bran 56 mg/dl); cellulose feeding did not change fasting serum triglycerides (73 mg/dl). High-density lipoproteins were significantly reduced with both types of fiber feeding (baseline 68 mg/dl; cellulose 48; wheat bran 50; $P < 0.003$). Mean daily insulin doses decreased ($P < 0.03$) in response to fiber addition (baseline 48 units; wheat bran 44; cellulose 43); mean biostator insulin requirements decreased with wheat bran (baseline 47 units; wheat bran 42; $P < 0.02$) but not with cellulose (54 units). The discrepancy between free-living and biostator insulin requirements is difficult

to explain since the biostator is often used to determine free-living insulin requirements. Both high-fiber wheat bran and high-fiber cellulose diets exerted hypocholesterolemic effects but a least part of the cholesterol-lowering observed may have been due to an increased consumption of soluable fibers. Juvenile-onset diabetic subjects may benefit from high-fiber diets, with fiber predominantly as cellulose or wheat bran, but the improvement in serum lipids is not as great as reported by others high-carbohydrate is consumed in conjunction with high-fiber. In addition, high-fiber feeding predominantly as wheat bran, generally induces improvement in glycemic control and reduction in insulin needs of young adult Type I diabetic subjects. High fiber fed predominantly as cellulose is inconsistent in improving glycemic control and insulin requirements in the same subjects.