

Carbohydrate awareness and diabetes

Allick G, Bisschop PH, Ackermans MT, Endert E, Meijer AJ, Kuipers F, Sauerwein HP, Romijn JA. A low-carbohydrate/high-fat diet improves glucoregulation in type 2 diabetes mellitus by reducing postabsorptive glycogenolysis. J Clin Endocrinol Metab 89 (12): 6193-6197, 2004

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The aim of this study was to examine the mechanisms by which dietary carbohydrate and fat modulate fasting glycemia. We compared the effects of an eucaloric high-carbohydrate (89% carbohydrate) and high-fat (89% fat) diet on fasting glucose metabolism and insulin sensitivity **in seven obese patients with type 2 diabetes** using stable isotopes and euglycemic hyperinsulinemic clamps. At basal insulin levels glucose concentrations were 148 +/- 11 and 123 +/- 11 mg/dl (8.2 +/- 0.6 and 6.8 +/- 0.6 mmol/liter) on the high-carbohydrate and high-fat diet, respectively ($P < 0.001$), with insulin concentrations of 12 +/- 2 and 10 +/- 1 microIU/ml (82 +/- 11 and 66 +/- 10 pmol/liter) ($P = 0.08$). **Glucose production was higher on the high-carbohydrate diet (1.88 +/- 0.06 vs. 1.55 +/- 0.05 mg/kg.min (10.44 +/- 0.33 vs. 8.61 +/- 0.28 micromol/kg.min) ($P < 0.001$) because of higher glycogenolysis.** Gluconeogenic rates were not different between the diets. During the use of hyperinsulinemic euglycemic clamps, insulin-mediated suppression of glucose production and stimulation of glucose disposal were not different between the diets. **Free fatty concentrations were suppressed by 89 and 62% ($P < 0.0001$) on the high-carbohydrate and high-fat diet, respectively.** We conclude that **short-term variations in dietary carbohydrate to fat ratios affect basal glucose metabolism in people with type 2 diabetes merely through modulation of the rate of glycogenolysis, without affecting insulin sensitivity of glucose metabolism.**

Full text: <http://jcem.endojournals.org/cgi/content/full/89/12/6193>

Arora S, McFarlane SI. Review on "Atkins Diabetes Revolution: The Groundbreaking Approach to Preventing and Controlling Type 2 Diabetes" by Mary C. Vernon and Jacqueline A. Eberstein. Nutr Metab (Lond) 91 (1): 14, 2004

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Before beginning the review of this book, we had no particular opinion about the role of low carbohydrate diets in diabetes. In order to write a fair and unbiased review, we have done a rather extensive search on the subject. **One of the most disturbing findings of our search is the amount of hostility towards low carbohydrate diets that is on the web and in the scientific literature. We found several sites that present no scientific arguments but are, rather, full of ad hominem attacks.** This was particularly disturbing in that we are in the midst of a growing epidemic of obesity and diabetes with very alarming figures and projections from all over the world. Any intervention that has the potential for helping curb this dangerous epidemic which claims thousands of lives every day should be looked at with a great deal of objectivity. **The low carbohydrate approach, in fact, is not new and was used in England more than a century ago, made popular by William Harvey [1], an ENT surgeon.** He prescribed a low carbohydrate diet for William Banting, an obese carpenter who had been having a great difficulty

losing weight. **Banting was able to lose weight and as a service, he published in 1863 a small booklet entitled Letter on Corpulence Addressed to the Public [2], the first book to be published on obesity and one which popularized low carbohydrate diets.** He has been called "**Father of low carbohydrate diets**" and was honored by his name being included in the dictionary as the verb "to bant" meaning "to diet". The low carbohydrate diet also been called a "Harvey-Banting diet" after the names of these pioneer. Since then, it has been in and out of fashion with different versions and names but with the same underlying concept, most recently popularized by the late Dr. Robert C. Atkins.

The Atkins Diabetes Revolution [3] plan is similar to the Atkins weight loss strategy: four levels of carbohydrate restriction are instituted. The induction phase restricts dieters to 20 g of carbohydrate. On the weight loss plan, this is recommended for about 2 weeks. In diabetes this is maintained until glycemic control is attained. In the latter stages, carbohydrates are added as long as weight loss or stability is maintained. **For diabetes, carbohydrates are only reintroduced if glycemic control is acceptable.** In the later phases, the Atkins Diabetes plan adds a Glycemic Ranking (AGR), derived from the glycemic index, glycemic load and net carbs. **Preference is given to whole fruits and berries and juices and dried fruits are low on the list. As in weight loss, exercise is "mandatory."**

The Atkins Diabetes Revolution book is an attempt by the authors to present the low carbohydrate diet as a preventive and treatment strategy for patients with type 2 diabetes and those with the metabolic syndrome, who are at high risk for developing diabetes and cardiovascular disease. In doing so, the book, which is very well written, and which clearly presents illustrative cases, explains very complex metabolic concept in a very easy to read and understandable format. The first nine chapters explain the different concepts involved in glucose and lipid metabolism and the interplay of the various cardiovascular risk factors that culminate in cardiovascular disease the number one killer of Americans today. Definitions of metabolic syndrome, pre-diabetes, body mass index, waist to hip ratio, central obesity and their relationship to diabetes, heart attacks and strokes, are eloquently presented with a great deal of accuracy yet in a simple format. **Most impressive were the case presentations, especially that of reactive hypoglycemia and carbohydrate craving. This response is associated with hyperinsulinemia in the pre-diabetic phase and sometimes puzzles clinicians unless they know to look for it.**

The second section of the book is devoted to an in-depth discussion of the various macro and micronutrients and their role in diabetes and obesity. Concepts such as the glycemic index and glycemic load are very well illustrated. The last section consists of meal plans and menus of low carbohydrate diet that the book is advocating.

The concept of low carbohydrate diet and glycemic control certainly has a pathophysiological merit. First, dietary carbohydrates are the principal source for the initial rise of glucose in the diabetic populations, who generally have a defect in the first phase insulin secretion that is responsible for handling the glucose load [4]. There is mounting evidence that postprandial hyperglycemia is in itself a risk factor for cardiovascular disease in the diabetic patients [5]. This evidence comes from large, well-conducted, randomized controlled trials [5,6]. Furthermore, control of postprandial hyperglycemia has been shown to provide cardiovascular benefits, and contribute to the overall decrease of hemoglobin A1c, something that has been clearly shown to reduce microvascular disease in both type 1 and type 2 diabetes [7,8]. Second, the initial blood glucose rise associated with high carbohydrate load, in the presence of absolute/relative insulin deficiency leads to significant rise in triglycerides and free fatty acids which perpetuate the cycle of insulin resistance [9,10]. So, from a metabolic stand point, low carbohydrate diet makes physiologic sense. However, in the science and practice of medicine, not everything that makes sense turns out to work the way it is supposed to. In looking at the low carbohydrate diet, we must examine the evidence from the studies that were conducted using such diets keeping in mind that weight loss by itself, is beneficial in terms of improving insulin

sensitivity and correcting the abnormalities associated with the metabolic syndrome and insulin resistance [9,10]. **Also, weight loss has much greater effect on the prevention of type 2 diabetes in pre-diabetic patients than pharmacological interventions [9].** This fact was well illustrated in the Diabetes Prevention Program, a large multicenter trial sponsored by the National Institute of Health, where pre-diabetic patients on diet and exercise program had a 58% reduction in the development of diabetes, compared to only 34% reduction with the use of metformin [11]. This landmark study had a population where women and minorities were very well represented [11]. **The fact that weight loss was associated with reduction of type 2 diabetes in high risk populations was illustrated in several other studies including examples from Finland and from China, making it evident that weight loss works for a variety of ethnic populations [12-15].**

In two recent randomized controlled trials published in the New England Journal of Medicine [16,17], the effects of low carbohydrate and low fat diets were compared in obese and diabetic patients. Both of these studies showed **a substantial decrease of triglycerides in patients on low carbohydrate diet with simultaneous increase in high-density lipoprotein (HDL) over 6 months to 1 year period. The studies did not show a change in the low-density lipoprotein (LDL) values in the low carbohydrate group compared to their baseline, while those on traditional low fat diet had a reduction in LDL levels. Patients on low carbohydrate diet, however, had substantially significant weight loss, almost double that achieved with the traditional diet, in the first 3–6 months.** At one year, there was no significant difference in weight loss between the two groups [16-18]. **Although participants on the low carbohydrate diet initially tended to have higher rate of side effects such as nausea, muscle cramps and constipation, compliance with diet was similar in both groups. In fact, more participants adhered to the low carbohydrate diet.** Although weight loss was similar after one year between groups, the effects on atherogenic dyslipidemia and glycemic control were still more favorable with a low-carbohydrate diet after adjustment for differences in weight loss.

Despite the evidence from these randomized controlled trials, published in the prestigious New England Journal of Medicine, **there is a significant amount of reluctance in the scientific community to acknowledge the beneficial effects of low carbohydrate diets.** These studies, in fact, provide a striking example of this resistance. A commentary in the same issue of the New England Journal of Medicine [20] states that "In both studies, the reduction in serum triglyceride levels in subjects randomly assigned to the low-carbohydrate diet might have been anticipated as a result of their greater weight loss, although it is true that reduced carbohydrate intake is generally associated with reduced triglyceride levels" [20]. In this statement, despite the fact that low carbohydrate diet is known to reduce serum triglyceride, the authors suggest otherwise. In another statement, the authors of the commentary state that "the rise in HDL cholesterol in the subjects following the low-carbohydrate diet (a change observed only by Foster et al.) may reflect a change in HDL subfractions that occurs with increased intake of saturated fats, and this change has not been shown to be beneficial. Thus, caution is urged about over-interpretation of this observation as a beneficial result of a low-carbohydrate, high-fat diet" [20]. Again this statement illustrates the difficulty in acknowledging what a randomized controlled trial has shown. The authors suggest, without any evidence that the rise in HDL cholesterol might have been in the non-beneficial HDL subfraction. In other words, when low carbohydrate diet is shown to decrease triglycerides, a suggestion is made that it might be just secondary to weight loss and when this diet increases HDL, it is also suggested that it could be the non-beneficial HDL. Now, let us examine the evidence provided by the one year follow-up study on the same group of patients where the investigators conclude that **"Although weight loss was similar between groups, the effects on atherogenic dyslipidemia and glycemic control were still more favorable with a low-carbohydrate diet after adjustment for differences in weight loss"** [18]. This indicates that the statements made in the commentary [20], in an attempt to dismiss or downplay the beneficial effects of low carbohydrate diet were simply wrong. Furthermore, the statement made in the commentary

regarding the HDL cholesterol, not only lacks objective evidence, but also contradicts the current findings that lowering insulin level by controlled carbohydrates shift HDL production to a much more desirable, lighter HDL2subfractions [21,22].

On the other hand, the American Diabetes Association, despite recommending the traditional low fat diet, has recently reduced the recommended carbohydrate contents in the diet, perhaps reflecting a trend towards a reduced carbohydrate diet to follow [19].

Returning to the Atkins book, despite the fact that the book is very well referenced, certain statements such as "high carbohydrate diet leads to diabetes" are not well substantiated, unless of course such a diet leads to weight gain, which it may. Furthermore, **the book does not devote a sufficient amount of space discussing the side effects associated with dieting in general and low carbohydrate diet in particular. This is of concern, since it leaves the reader with the impression that the low carbohydrate diet or dieting, in general, has no negative consequences.** Nonetheless, the amount of information the book provides in a simple, yet accurate format will benefit patients with diabetes and their families as well as those who are at risk for developing diabetes and the metabolic syndrome. If, after reading this book, the reader is able to identify that he or she is at risk for diabetes and the metabolic syndrome and takes action that could potentially save his or her life the book will be a valuable contribution. Atkins Diabetes Revolution has a list price of \$25.95 and is available at Amazon.com and presumably other sites for half that price. Possibly, a shorter and still more affordable version of the book would be helpful for diabetic patients, their families and for the general reader, to help identify their risk for the disease.

As clinicians, we would not be comfortable recommending any diet without first hand experience. **The Atkins Diabetes Revolution, however, is sufficiently convincing to make us believe that some form of low carbohydrate intervention is worth investigating and should be considered by practitioners.** The highly negative un-scientific response of critics, if anything, encourages us in this direction.

Full text: <http://nutritionandmetabolism.com/content/1/1/14>

Boden G, Sargrad K, Homko C, Mozzoli M, Stein TP. Effect of a low-carbohydrate diet on appetite, blood glucose levels, and insulin resistance in obese patients with type 2 diabetes. Ann. Intern. Med. 142 (6): 403-411, 2005

Temple University School of Medicine, Philadelphia, Pennsylvania, and University of Medicine and Dentistry of New Jersey School of Osteopathic Medicine, Stratford, New Jersey.

BACKGROUND: It is not known how a low-carbohydrate, high-protein, high-fat diet causes weight loss or how it affects blood glucose levels in patients with type 2 diabetes. **OBJECTIVE:** To determine effects of a strict low-carbohydrate diet on body weight, body water, energy intake and expenditure, glycemic control, insulin sensitivity, and lipid levels in obese patients with type 2 diabetes. **DESIGN:** Inpatient comparison of 2 diets. **SETTING:** General clinical research center of a university hospital. **PATIENTS:** 10 obese patients with type 2 diabetes. **INTERVENTION:** Usual diets for 7 days followed by a low-carbohydrate diet for 14 days. **MEASUREMENTS:** Body weight, water, and composition; energy intake and expenditure; diet satisfaction; hemoglobin A1c; insulin sensitivity; 24-hour urinary ketone excretion; and plasma profiles of glucose, insulin, leptin, and ghrelin. **RESULTS:** **On the low-carbohydrate diet, mean energy intake decreased from 3111 kcal/d to 2164 kcal/d.** The mean energy deficit of 1027 kcal/d (median, 737 kcal/d) completely accounted for **the weight loss of 1.65 kg in 14 days** (median, 1.34 kg in 14 days). **Mean 24-hour plasma profiles of glucose levels normalized, mean hemoglobin A1c decreased from 7.3% to 6.8%, and insulin sensitivity improved by approximately 75%. Mean plasma triglyceride and cholesterol levels decreased** (change, -35% and -10%, respectively).

LIMITATIONS: The study was limited by the short duration, small number of participants, and lack of a strict control group. **CONCLUSION:** In a small group of obese patients with type 2 diabetes, a low-carbohydrate diet followed for 2 weeks resulted in spontaneous reduction in energy intake to a level appropriate to their height; weight loss that was completely accounted for by reduced caloric intake; much improved 24-hour blood glucose profiles, insulin sensitivity, and hemoglobin A1c; and decreased plasma triglyceride and cholesterol levels. **The long-term effects of this diet, however, remain uncertain.**

Full text: <http://www.annals.org/cgi/reprint/142/6/403>

Campbell LV, Marmot PE, Dyer JA, Borkman M, Storlien LH. The high-monounsaturated fat diet as a practical alternative for NIDDM. Diabetes Care 17(3): 177-182, 1994

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OBJECTIVE--To examine the dietary preferences of and metabolic effects in patients with non-insulin-dependent diabetes mellitus (NIDDM) of a home-prepared high-monounsaturated fat (HM) diet compared with the recommended high-carbohydrate (CHO) diet. **RESEARCH DESIGN AND METHODS--****Ten men with mild NIDDM prepared HM and high-CHO diets at home alternately and in random order for 2 weeks each with a minimum 1-week washout.** Before and after each diet, 24-h urine glucose, fasting lipids, fructosamine, and 6-h profiles of glucose, insulin, and triglycerides were measured. Dietary preferences were assessed by questionnaire. **RESULTS--**In the HM diet, patients consumed 40% of energy intake as CHO and 38% as fat (21% monounsaturated) compared with 52 and 24%, respectively, in the high-CHO diet, with equal dietary fiber content. Body weight and total energy intake were similar in both. **The HM diet resulted in significantly lower 24-h urinary glucose excretion, fasting triglyceride, and mean profile glucose levels.** The fructosamine levels, the fasting total, low-density lipoprotein, and high-density lipoprotein cholesterol, and the prandial triglyceride concentrations did not differ significantly as a result of the diets. The two diets did not differ in ratings for overall acceptance, taste, cost, ease of preparation, variety, or satiety. **CONCLUSIONS--****Prepared at home, the HM diet was, in the short-term, metabolically better in some aspects than the currently recommended diet for NIDDM. It also provided a palatable alternative.**

Full text: <http://care.diabetesjournals.org/cgi/content/full/17/3/177>

Coulston AM, Hollenbeck CB, Swislocki AL, Chen YD, Reaven GM. Deleterious metabolic effects of high-carbohydrate, sucrose-containing diets in patients with non-insulin-dependent diabetes mellitus. Am J Med 82 (2): 213-220, 1987

The effects of variations in dietary carbohydrate and fat intake on various aspects of carbohydrate and lipid metabolism were studied in patients with non-insulin-dependent diabetes mellitus (NIDDM). Two test diets were utilized, and they were consumed in random order over two 15-day periods. One diet was low in fat and high in carbohydrate, and corresponded closely to recent recommendations made by the American Diabetes Association (ADA), containing (as percent of total calories) 20 percent protein, 20 percent fat, and 60 percent carbohydrate, with 10 percent of total calories as sucrose. **The other diet contained 20 percent protein, 40 percent fat, and 40 percent carbohydrate, with sucrose accounting for 3 percent of total calories.** Although plasma fasting glucose and insulin concentrations were similar with both diets, **incremental glucose and insulin responses from 8 a.m. to 4 p.m. were higher (p less than 0.01), and mean (+/- SEM) 24-hour urine glucose excretion was significantly greater (55 +/- 16 versus 26 +/- 4 g/24 hours p**

less than 0.02) in response to the low-fat, high-carbohydrate diet. In addition, fasting and postprandial triglyceride levels were increased (p less than 0.001 and p less than 0.05, respectively) and high-density lipoprotein (HDL) cholesterol concentrations were reduced (p less than 0.02) when patients with NIDDM ate the low-fat, high-carbohydrate diet. Finally, since low-density lipoprotein (LDL) concentrations did not change with diet, the HDL/LDL cholesterol ratio fell in response to the low-fat, high-carbohydrate diet. **These results document that low-fat, high-carbohydrate diets, containing moderate amounts of sucrose, similar in composition to the recommendations of the ADA, have deleterious metabolic effects when consumed by patients with NIDDM for 15 days.** Until it can be shown that these untoward effects are evanescent, and that long-term ingestion of similar diets will result in beneficial metabolic changes, **it seems prudent to avoid the use of low-fat, high-carbohydrate diets containing moderate amounts of sucrose in patients with NIDDM.**

Full text: [http://linkinghub.elsevier.com/retrieve/pii/0002-9343\(87\)90058-1](http://linkinghub.elsevier.com/retrieve/pii/0002-9343(87)90058-1)

Coulston AM, Hollenbeck CB, Swislocki AL, Reaven GM. Persistence of hypertriglyceridemic effect of low-fat high-carbohydrate diets in NIDDM patients. Diabetes Care 12 (2): 94-101, 1989

Department of Medicine, Stanford University School of Medicine, California.

Although low-fat high-carbohydrate diets are recommended for patients with non-insulin-dependent diabetes mellitus (NIDDM) in an effort to reduce the risk of coronary artery disease (CAD), the results of short-term studies have shown that these diets can lead to changes in carbohydrate and lipid metabolism associated with an increased risk of CAD. This study has extended these earlier observations by determining the metabolic effects of such diets over a longer period in these patients. The comparison diets contained either 40 or 60% of the total calories as carbohydrates, with reciprocal changes in fat content from 40 to 20% consumed in random order for 6 wk in a crossover experimental design. The ratio of polyunsaturated to saturated fat and the total cholesterol intake were held constant in the two diets. **Plasma glucose and insulin concentrations were significantly (P less than .001) elevated throughout the day when patients consumed the 60% carbohydrate diet, and 24-h urinary glucose excretion more than doubled (0.8 vs. 1.8 mol/24 h). Fasting plasma total and very-low-density lipoprotein (VLDL) triglyceride (TG) concentrations increased by 30% (P less than .001) after 1 wk on the 60% carbohydrate diet, and the magnitude of carbohydrate-induced hypertriglyceridemia persisted unchanged throughout the 6-wk study period.** Total plasma cholesterol concentrations were similar after both diets. However, VLDL cholesterol (VLDL-chol) was significantly increased, whereas both low-density lipoprotein (LDL-) and high-density lipoprotein (HDL-) chol concentrations were significantly decreased after consumption of the 60% carbohydrate diet. Consequently, neither total-chol-to-HDL-chol nor LDL-chol-to-HDL-chol ratios changed. (ABSTRACT TRUNCATED AT 250 WORDS)

Full text: no full text available?

Daly ME, Paisey R, Paisey R, Millward BA, Eccles C, Williams K, Hammersley S, MacLeod KM, Gale TJ. Short-term effects of severe dietary carbohydrate-restriction advice in Type 2 diabetes - a randomized controlled trial. Diabet Med 23 (1): 15-20, 2006

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OBJECTIVE: This study sought to examine the effects of a **3-month programme of dietary advice to restrict carbohydrate intake** compared with reduced-portion, low-fat advice in **obese subjects with poorly controlled Type 2 diabetes**. **RESEARCH DESIGN AND METHODS:** **One hundred and two patients with Type 2 diabetes were recruited across three centres** and randomly allocated to receive group education and individual dietary advice. Weight, glycaemic control, lipids and blood pressure were assessed at baseline and 3 months. Dietary quality was assessed at the end of study. **RESULTS:** **Weight loss was greater in the low-carbohydrate (LC) group (-3.55 +/- 0.63, mean +/- sem) vs. -0.92 +/- 0.40 kg, P = 0.001) and cholesterol : high-density lipoprotein (HDL) ratio improved (-0.48 +/- 0.11 vs. -0.10 +/- 0.10, P = 0.01)**. However, relative saturated fat intake was greater (13.9 +/- 0.71 vs. 11.0 +/- 0.47% of dietary intake, P < 0.001), although absolute intakes were moderate. **CONCLUSIONS:** **Carbohydrate restriction was an effective method of achieving short-term weight loss compared with standard advice, but this was at the expense of an increase in relative saturated fat intake.**

Full text: <http://www.blackwell-synergy.com/doi/pdf/10.1111/j.1464-5491.2005.01760.x>

Dashti Hussein M, Mathew Thazhumpal C, Khadada Mousa, Al-Mousawi Mahdi, Talib Husain, Asfar Sami K, Behbahani Abdulla I and Al-Zaid Najji S. Beneficial effects of ketogenic diet in obese diabetic subjects. Mol Cell Biochem 10.1007/s11010-007-9448-z (on-line fast), Friday, April 20, 2007

Objective: Obesity is closely linked to the incidence of type II diabetes. It is found that effective management of body weight and changes to nutritional habits especially with regard to the carbohydrate content and glycemic index of the diet have beneficial effects in obese subjects with glucose intolerance. Previously we have shown that ketogenic diet is quite effective in reducing body weight. Furthermore, it favorably alters the cardiac risk factors even in hyperlipidemic obese subjects. In this study the effect of ketogenic diet in obese subjects with high blood glucose level is compared to those with normal blood glucose level for a period of 56 weeks.

Materials and methods: **A total of 64 healthy obese subjects with body mass index (BMI) greater than 30, having high blood glucose level and those subjects with normal blood glucose level were selected in this study.** The body weight, body mass index, blood glucose level, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, urea and creatinine were determined before and at 8, 16, 24, 48, and 56 weeks after the administration of the ketogenic diet.

Results: **The body weight, body mass index, the level of blood glucose, total cholesterol, LDL-cholesterol, triglycerides, and urea showed a significant decrease from week 1 to week 56 (P < 0.0001), whereas the level of HDL-cholesterol increased significantly (P < 0.0001).**

Interestingly these changes were more significant in subjects with high blood glucose level as compared to those with normal blood glucose level. The changes in the level of creatinine were not statistically significant.

Conclusion: This study shows the beneficial effects of ketogenic diet in obese diabetic subjects following its long-term administration. Furthermore, it demonstrates that **in addition to its therapeutic value, low carbohydrate diet is safe to use for a longer period of time in obese diabetic subjects.**

Full text: <http://www.springerlink.com/content/v720m444015q760n/fulltext.pdf>

Fuh MM, Lee MM, Jeng CY, Ma F, Chen YD, Reaven GM. Effect of low fat-high carbohydrate diets in hypertensive patients with non-insulin-dependent diabetes mellitus. Am J Hypertens 3 (7): 527-532, 1990

Department of Medicine, Tri-Service General Hospital, Taipei, Republic of China.

Effects of variations in dietary fat and carbohydrate content on various aspects of glucose, insulin, and lipoprotein metabolism were **evaluated in 11 patients with hypertension, who also had non-insulin-dependent diabetes mellitus (NIDDM)**. All of these patients were being treated with sulfonylureas, thiazides, and beta-adrenergic receptor antagonists. The comparison diets contained either 40 or 60% of total calories as carbohydrate, with reciprocal changes in fat content from 40 to 20%. The diets were consumed in a random order for 15 days in a crossover experimental design. The ratio of polyunsaturated to saturated fat and total cholesterol intake were held constant in the two diets. **Plasma glucose and insulin concentrations were significantly (P less than .001) elevated throughout the day when patients consumed the 60% carbohydrate diet. Fasting plasma total and very-low-density lipoprotein (VLDL) and triglyceride (TG) concentrations increased by 30% (P less than .001) after 15 days on the 60% carbohydrate diet.** Total plasma cholesterol concentrations were similar on both diets, as were low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol concentrations.

Full text: not available?

Gannon Mary C, Nuttall Frank Q, Saeed Asad, Jordan Kelly, and Hoover Heidi. An increase in dietary protein improves the blood glucose response in persons with type 2 diabetes. Am J Clin Nutr 78: 734–741, 2003

Background: In single-meal studies, dietary protein does not result in an increase in glucose concentrations in persons with or without type 2 diabetes, even though the resulting amino acids can be used for gluconeogenesis.

Objective: The metabolic effects of **a high-protein diet** were compared with those of the prototypical healthy (control) diet, which is currently recommended by several scientific organizations.

Design: The metabolic effects of both diets, consumed for 5 wk each (separated by a 2–5-wk washout period), **were studied in 12 subjects with untreated type 2 diabetes**. The ratio of protein to carbohydrate to fat was 30:40:30 in the high-protein diet and 15:55:30 in the control diet. The subjects remained weight-stable during the study.

Results: With the fasting glucose concentration used as a baseline from which to determine the area under the curve, **the highprotein diet resulted in a 40% decrease in the mean 24-h integrated glucose area response**. Glycated hemoglobin decreased 0.8% and 0.3% after 5 wk of the high-protein and control diets, respectively; the difference was significant ($P < 0.05$). The rate of change over time was also significantly greater after the high-protein diet than after the control diet ($P < 0.001$). **Fasting triacylglycerol was significantly lower after the high-protein diet than after the control diet.** Insulin, C-peptide, and free fatty acid concentrations were not significantly different after the 2 diets.

Conclusion: **A high-protein diet lowers blood glucose postprandially in persons with type 2 diabetes and improves overall glucose control. However, longer-term studies are necessary to determine the total magnitude of response, possible adverse effects, and the long-term acceptability of the diet.**

Full text: <http://www.ajcn.org/cgi/reprint/78/4/734.pdf>

Gannon MC, Nuttall FQ. Effect of a high-protein, low-carbohydrate diet on blood glucose control in people with type 2 diabetes. Diabetes 53 (9): 2375-2382, 2004

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There has been interest in the effect of various types and amounts of dietary carbohydrates and proteins on blood glucose. On the basis of our previous data, **we designed a high-protein/low-carbohydrate, weight-maintaining, nonketogenic diet**. Its effect on glucose control in people with untreated type 2 diabetes was determined. We refer to this as a low-biologically-available-glucose (LoBAG) diet. **Eight men were studied** using a randomized 5-week crossover design with a 5-week washout period. The carbohydrate:protein:fat ratio of the control diet was 55:15:30. The test diet ratio was 20:30:50. Plasma and urinary beta-hydroxybutyrate were similar on both diets. **The mean 24-h integrated serum glucose at the end of the control and LoBAG diets was 198 and 126 mg/dl, respectively. The percentage of glycohemoglobin was 9.8 +/- 0.5 and 7.6 +/- 0.3, respectively. It was still decreasing at the end of the LoBAG diet.** Thus, the final calculated glycohemoglobin was estimated to be approximately 6.3-5.4%. **Serum insulin was decreased, and plasma glucagon was increased. Serum cholesterol was unchanged.** Thus, a LoBAG diet ingested for 5 weeks dramatically reduced the circulating glucose concentration in people with untreated type 2 diabetes. **Potentially, this could be a patient-empowering way to ameliorate hyperglycemia without pharmacological intervention. The long-term effects of such a diet remain to be determined.**

Full text: <http://diabetes.diabetesjournals.org/cgi/content/full/53/9/2375>

Gannon MC, Nuttall FQ. Control of blood glucose in type 2 diabetes without weight loss by modification of diet composition. Nutr Metab (Lond) 233: 16, 2006

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BACKGROUND: Over the past several years our research group has taken a systematic, comprehensive approach to determining the effects on body function (hormonal and non-hormonal) of varying the amounts and types of proteins, carbohydrates and fats in the diet. We have been particularly interested in the dietary management of type 2 diabetes. Our objective has been to develop a diet for people with type 2 diabetes that does not require weight loss, oral agents, or insulin, but that still controls the blood glucose concentration. **Our overall goal is to enable the person with type 2 diabetes to control their blood glucose by adjustment in the composition rather than the amount of food in their diet.** **METHODS:** This paper is a brief summary and review of our recent diet-related research, and the rationale used in the development of diets that potentially are useful in the treatment of diabetes. **RESULTS:** We determined that, **of the carbohydrates present in the diet, absorbed glucose is largely responsible for the food-induced increase in blood glucose concentration.** We also determined that **dietary protein increases insulin secretion and lowers blood glucose. Fat does not significantly affect blood glucose, but can affect insulin secretion and modify the absorption of carbohydrates.** Based on these data, **we tested the efficacy of diets with various protein:carbohydrate:fat ratios for 5 weeks on blood glucose control in people with untreated type 2 diabetes.** The results were compared to those obtained in the same subjects after 5 weeks on a control diet with a protein:carbohydrate:fat ratio of 15:55:30. A 30:40:30 ratio diet resulted in a moderate but significant decrease in 24-hour integrated glucose area and % total glycohemoglobin (%tGHb). **A 30:20:50 ratio diet resulted in a 38% decrease in 24-hour glucose area, a reduction in fasting glucose to near normal and a decrease in %tGHb from 9.8% to 7.6%. The response to a 30:30:40 ratio diet was similar.**

CONCLUSION: Altering the diet composition could be a patient-empowering method of improving the hyperglycemia of type 2 diabetes without weight loss or pharmacologic intervention.

Full text: <http://nutritionandmetabolism.com/content/3/1/16>

Garg A, Grundy SM, Koffler M. Effect of high carbohydrate intake on hyperglycemia, islet function, and plasma lipoproteins in NIDDM. Diabetes Care 15 (11): 1572-1580, 1992

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OBJECTIVE--To study effects of high carbohydrate intake on hyperglycemia, islet functions, and plasma lipoproteins in patients with NIDDM. **RESEARCH DESIGN AND METHODS--**An attempt was made to induce hyperglycemia in 10 men with NIDDM by feeding them an isocaloric high-carbohydrate diet (65% of energy as simple carbohydrates [31% as glucose] and 20% as fat) for 28 days in a metabolic ward. Response to the high-carbohydrate diet was compared with that of feeding a diet rich in monounsaturated fat (45% of energy as fat [31% as monounsaturated fat] and 38% as carbohydrates) for 28 days in a cross-over manner. Islet functions were assessed by evaluating plasma glucose, insulin, C-peptide and glucagon responses to standard meal tolerance tests on days 0, 14, 21, and 28 of each dietary period. Fasting plasma lipoproteins were determined during the last week of each dietary period. **RESULTS--**The high-carbohydrate diet caused significant but modest accentuation of hyperglycemia, particularly in patients with moderately severe diabetes mellitus, whereas no change was observed with the high-monounsaturated fatty-acid diet. Accentuation of hyperglycemia was accompanied by an increase in plasma glucagon levels, but no significant change in insulin and C-peptide responses. In 1 patient, feeding the high-carbohydrate diet for 68 days produced marked hyperglycemia and caused definite suppression of insulin and C-peptide responses along with an increase in glucagon levels. **Compared with the high-monounsaturated fat diet, the high-carbohydrate diet also raised plasma triglyceride and VLDL cholesterol concentrations.** **CONCLUSIONS--**High-carbohydrate diets may cause accentuation of hyperglycemia and a rise in plasma glucagon levels in NIDDM patients. **High-carbohydrate diets also adversely affect lipoproteins and therefore may not be desirable in all NIDDM patients.**

Full text: <http://care.diabetesjournals.org/cgi/content/full/15/11/1572>

Garg A, Grundy SM, Unger RH. Comparison of effects of high and low carbohydrate diets on plasma lipoproteins and insulin sensitivity in patients with mild NIDDM. Diabetes 41 (10): 1278-1285, 1992

Veterans Affairs Medical Center, University of Texas Southwestern Medical Center, Dallas 75235-9052.

Previous studies indicate that diets rich in digestible carbohydrates improve glucose tolerance in nondiabetic individuals, but may worsen glycemic control in NIDDM patients with moderately severe hyperglycemia. The effects of such high-carbohydrate diets on glucose metabolism in patients with mild NIDDM have not been studied adequately. **This study compares responses to an isocaloric high-carbohydrate diet (60% of total energy from carbohydrates) and a low-carbohydrate diet (35% of total energy from carbohydrates) in 8 men with mild NIDDM. Both diets were low in saturated fatty acids, whereas the low-carbohydrate diet was rich in monounsaturated fatty acids. The two diets were matched for dietary fiber content (25 g/day).**

All patients were randomly assigned to receive first one and then the other diet, each for a period of 21 days, in a metabolic ward. **Compared with the low-carbohydrate diet, the high-carbohydrate diet caused a 27.5% increase in plasma triglycerides and a similar increase in VLDL-cholesterol levels; it also reduced levels of HDL cholesterol by 11%.** Plasma glucose and insulin responses to identical standard breakfast meals were studied on days 4 and 21 of each period, and these did not differ significantly between the two diets. At the end of each period, a euglycemic hyperinsulinemic glucose clamp study with simultaneous infusion of [3-3H]glucose revealed no significant changes in hepatic insulin sensitivity; and peripheral insulin-mediated glucose disposal remained unchanged (14.7 +/- 1.4 vs. 16.5 +/- 2.3 microM.kg-1.min-1 on the high-carbohydrate and low-carbohydrate diets, respectively).(ABSTRACT TRUNCATED AT 250 WORDS)

Full text: <http://diabetes.diabetesjournals.org/cgi/content/full/41/10/1278>

Garg A, Bantle JP, Henry RR, Coulston AM, Griver KA, Raatz SK, Brinkley L, Chen YD, Grundy SM, Huet BA et al Center for Human Nutrition, University of Texas Southwestern Medical Center at Dallas 75235-9052. Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus. JAMA Vol. 271 No. 18, May 11, 1994

OBJECTIVE--To study effects of variation in carbohydrate content of diet on glycemia and plasma lipoproteins in patients with non-insulin-dependent diabetes mellitus (NIDDM). DESIGN--A four-center randomized crossover trial. SETTING--Outpatient and inpatient evaluation in metabolic units. PATIENTS--**Forty-two NIDDM patients receiving glipizide therapy.** INTERVENTIONS--A high-carbohydrate diet containing 55% of the total energy as carbohydrates and 30% as fats was compared with a high-monounsaturated-fat diet containing 40% carbohydrates and 45% fats. The amounts of saturated fats, polyunsaturated fats, cholesterol, sucrose, and protein were similar. The study diets, prepared in metabolic kitchens, were provided as the sole nutrients to subjects for 6 weeks each. To assess longer-term effects, a subgroup of 21 patients continued the diet they received second for an additional 8 weeks. MAIN OUTCOME MEASURES--Fasting plasma glucose, insulin, lipoproteins, and glycosylated hemoglobin concentrations. Twenty-four-hour profiles of glucose, insulin, and triglyceride levels. RESULTS--The site of study as well as the diet order did not affect the results. Compared with the high-monounsaturated-fat diet, the high-carbohydrate diet increased fasting plasma triglyceride levels and very low-density lipoprotein cholesterol levels by 24% ($P < .0001$) and 23% ($P = .0001$), respectively, and increased daylong plasma triglyceride, glucose, and insulin values by 10% ($P = .03$), 12% ($P < .0001$), and 9% ($P = .02$), respectively. Plasma total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol levels remained unchanged. The effects of both diets on plasma glucose, insulin, and triglyceride levels persisted for 14 weeks. CONCLUSIONS--**In NIDDM patients, high-carbohydrate diets compared with high-monounsaturated-fat diets caused persistent deterioration of glycemic control and accentuation of hyperinsulinemia, as well as increased plasma triglyceride and very-low-density lipoprotein cholesterol levels, which may not be desirable.**

Full text: <http://jama.ama-assn.org/cgi/content/full/271/18/1421>

Gutierrez M, Akhavan M, Jovanovic L, Peterson CM. Utility of a short-term 25% carbohydrate diet on improving glycemic control in type 2 diabetes mellitus. J Am Coll Nutr 17 (6): 595-600, 1998

Sansum Medical Research Foundation, Santa Barbara, California 93105, USA.

OBJECTIVE: To determine if introduction of a low carbohydrate diet might be a useful option for type 2 diabetic patients who do not achieve glucose target levels despite conventional treatment. **METHODS:** Subjects with type 2 diabetes, either treated with diet alone (n=9) or second generation sulfonylurea agents (n= 19), which were discontinued, were placed on a diet based on ideal body weight and comprised of 25% carbohydrate. After a mean of 8 weeks, they were then switched to a calorically equivalent diet, but composed of 55% carbohydrate. **RESULTS: Compared to baseline diet, after 8 weeks of a 25% diet, subjects showed significantly improved glycemia as evidenced by fasting blood glucose values (p<0.005) and hemoglobin A1c levels (p<0.05).** Those previously treated with oral hypoglycemic agents showed, in addition, a significant decrease in weight and diastolic blood pressure despite the discontinuation of the oral agent. When then placed on a 55% carbohydrate diet, the hemoglobin A1c rose significantly over the ensuing next 12 weeks (p<0.05). **CONCLUSION: A low carbohydrate, calorically-restricted diet has beneficial short-term effects in subjects with type 2 who have failed either diet or sulfonylurea therapy and may obviate the necessity for insulin. Our study also affirms the need for reassessing the role of diet whenever type 2 diabetic patients manifests hyperglycemia, despite conventional oral treatment or diet management.**

Full text: <http://www.jacn.org/cgi/content/full/17/6/595>

Hays JH, Gorman RT, Shakir KM. Results of use of metformin and replacement of starch with saturated fat in diets of patients with type 2 diabetes. Endocr Pract 8 (3): 177-183, 2002

Christiana Care Health Services, Inc., Cardiology Research, Newark, Delaware 19718, USA.,

OBJECTIVE: To improve glycemic control by substituting saturated fat for starch, to identify any adverse effect on lipids masked by the extensive use of metformin and lipid-lowering drugs, and to attempt to separate dietary effects from effects of multiple drugs. **METHODS:** We undertook a retrospective review of medical records of patients who completed 1 year of follow-up after dietary prescription. **The study subjects included 151 patients in the diet group (whose dietary instructions included high saturated fat but starch avoidance) and 132 historical control subjects (who were allowed unlimited monounsaturated fat but had restriction of starch in their diets).** **RESULTS:** Hemoglobin A1c (HbA1c) levels improved in both study groups (-1.4 +/- 0.2% [P<0.001]; 95% confidence interval [CI], -1.9 to -0.9). Use of metformin was associated with a decrease in HbA1c (-0.12 +/- 0.003%/mo [P<0.001]; 95% CI, -0.17 to -0.07). The diet group had an additional decrease of -0.7 +/- 0.2% (P<0.001; 95% CI, -1.1 to -0.3). **Weight increase was associated with the use of insulin** (+0.3 +/- 0.07 kg/mo [P<0.001]; 95% CI, 0.2 to 0.5), sulfonylurea (+0.18 +/- 0.06 kg/mo [P<0.01]; 95% CI, 0.05 to 0.30), and troglitazone (+0.7 +/- 0.2 kg/mo [P<0.005]; 95% CI, 0.3 to 1.2). Although not statistically significant, metformin therapy showed a trend for weight loss (-0.14 +/- 0.08 kg/mo; P = 0.07). **An additional weight loss was noted in the diet group** (-2.65 +/- 0.62 kg [P<0.001]; 95% CI, -3.87 to -1.44). Hydroxymethylglutaryl-coenzyme A reductase inhibitor use was associated with reduced total cholesterol level (-1.7 +/- 0.6 mg/dL per month [P<0.005]; 95% CI, -2.9 to -0.5). The diet group had an additional decrease of -13.0 +/- 4.5 mg/dL (P<0.001; 95% CI, -21.9 to -4.1). No significant effect of the diet on triglyceride, low-density lipoprotein, or high-density lipoprotein levels was detected. **CONCLUSION: Addition of saturated fat and removal of starch from a high-monounsaturated fat and starch-restricted diet improved glycemic control and were associated with weight loss without detectable adverse effects on serum lipids.**

Full text:

[http://aace.metapress.com/app/home/contribution.asp?referrer=parent&backto=issue,1,11;journal,40,83;linkingpublicationresults,1:300404,1;](http://aace.metapress.com/app/home/contribution.asp?referrer=parent&backto=issue,1,11;journal,40,83;linkingpublicationresults,1:300404,1)

Heine RJ, Diamant M, Mbanya JC, Nathan DM. Management of hyperglycaemia in type 2 diabetes: the end of recurrent failure? BMJ 333 (7580): 1200-1204, 2006

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The epidemic of type 2 diabetes imposes an enormous and growing burden on health care worldwide. The number of people with type 2 diabetes around the world is estimated to rise from 151 million in 2000 to 300 million by 2025. **The recognition that strict glycaemic control can reduce microvascular complications has made the effective treatment of hyperglycaemia a priority.** Recently, the diabetes control and complications trial reported that intensive therapy aimed at normoglycaemia has beneficial effects on cardiovascular disease in type 1 diabetes. **In type 2 diabetes, epidemiological data from the UK prospective diabetes study suggest that lowering glycaemia will reduce the risk of cardiovascular disease.** The treatment of hyperglycaemia in type 2 diabetes is complex; combinations of glucose lowering drugs are often needed to achieve and maintain blood glucose at target values. The development of new classes of drugs to lower blood glucose has increased the treatment options.

Full text: <http://www.bmj.com/cgi/content/full/333/7580/1200>

Low CC, Grossman EB, Gumbiner B. Potentiation of effects of weight loss by monounsaturated fatty acids in obese NIDDM patients. Diabetes 45 (5): 569-575, 1996

Department of Medicine, University of Rochester, NY 14620, USA.

Although moderate weight loss improves glycemic control in obese NIDDM patients, quite often it is not normalized. To determine whether the response to weight loss can be improved by altering the macronutrient composition of hypocaloric diets, **17 obese NIDDM patients were studied** at 1) baseline, 2) after dieting for 6 weeks on a formula diet enriched in either monounsaturated fatty acids (MUFAs, n = 9) or carbohydrates (CHOs, n = 8) at a 50% caloric deficit, and 3) after 4 weeks of postdiet refeeding on the respective formulas with caloric intake titrated to achieve weight maintenance. Fasting, 24-h, and oral glucose tolerance test (OGTT) blood glucose, plasma insulin, and C-peptide levels were measured. All prediet parameters were similar between groups. After dieting, although weight loss was similar between groups, **the fasting glucose level decreased significantly more in the MUFA group (-4.6 +/- 0.7 mmol/l) than in the CHO group (-2.4 +/- 1.0 mmol/l; P < 0.05).** Twenty-four-hour glycemia decreased in both groups after dieting, but the MUFA group had a greater decrease than the CHO group (P < 0.05, analysis of variance [ANOVA]). **Although decreases in fasting glycemia were maintained in both groups after refeeding, postprandial glycemia deteriorated after refeeding with the CHO- but not the MUFA-enriched formula (P < 0.05).** After dieting and refeeding, fasting C-peptide increased 204 +/- 47 pmol/l in the MUFA group, but the CHO group remained at prediet levels (P < 0.05). Twenty-four-hour C-peptide levels were similar between groups after dieting and refeeding, despite the lower glycemia and CHO content of the MUFA formula. However, when equal amounts of CHO were consumed during the OGTT, the MUFA group had significantly higher C-peptide levels after both dieting and refeeding (P < 0.05). Fasting, 24-h, and OGTT insulin levels were similar between groups throughout the study. These results indicate that **macronutrient composition is an**

important determinant of the glycemic response to weight-loss therapy in obese NIDDM patients. Based on the C-peptide response during the OGTT, increased CHO-induced insulin secretion is one possible mechanism by which this occurs.

Full text: <http://diabetes.diabetesjournals.org/cgi/content/full/45/5/569>

Martin WF, Armstrong LE, Rodriguez NR. Dietary protein intake and renal function. Nutr Metab (Lond) 202: 25, 2005

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Recent trends in weight loss diets have led to a substantial increase in protein intake by individuals. As a result, the safety of habitually consuming dietary protein in excess of recommended intakes has been questioned. In particular, **there is concern that high protein intake may promote renal damage by chronically increasing glomerular pressure and hyperfiltration.** There is, however, a serious question as to whether there is significant evidence to support this relationship in healthy individuals. In fact, some studies suggest that hyperfiltration, the purported mechanism for renal damage, is a normal adaptative mechanism that occurs in response to several physiological conditions. **This paper reviews the available evidence that increased dietary protein intake is a health concern in terms of the potential to initiate or promote renal disease.** While protein restriction may be appropriate for treatment of existing kidney disease, **we find no significant evidence for a detrimental effect of high protein intakes on kidney function in healthy persons after centuries of a high protein Western diet.**

Full text: <http://www.nutritionandmetabolism.com/content/2/1/25>

Nuttall FQ, Gannon MC. Metabolic response of people with type 2 diabetes to a high protein diet. Nutr Metab (Lond) 131 (1): 6, 2004

Metabolic Research Laboratory, Endocrine, Metabolism & Nutrition Section, Minneapolis VA Medical Center, Minneapolis, USA. nutta001@umn.edu.

BACKGROUND: One of the major interests in our laboratory has been to develop a scientific framework for dietary advice for patients with diabetes. Knowledge regarding the metabolic consequences and potential effects on health of protein in people with type 2 diabetes has been a particular interest. RESULTS: We recently have completed a study in which dietary protein was increased from 15% to 30% of total food energy. **The carbohydrate content was decreased from 55% to 40%, i.e. dietary protein replaced part of the carbohydrate.** This resulted in a **significant decrease in total glycohemoglobin, a decrease in postprandial glucose concentrations and a modest increase in insulin concentration.** Renal function was unchanged. Currently we also are determining the metabolic response to a diet in which the carbohydrate content is further decreased to 20% of total food energy. The %tGHb decrease was even more dramatic than with the 40% carbohydrate diet. CONCLUSION: From these data we conclude that increasing the protein content of the diet at the expense of carbohydrate can reduce the 24-hour integrated plasma glucose concentration, at least over a 5-week period of time. The reduction was similar to that of oral agents. Renal function was not affected significantly. **Thus, increasing the protein content of the diet with a corresponding decrease in the carbohydrate content potentially is a patient empowering way of reducing the hyperglycemia present with type 2 diabetes mellitus, independent of the use of pharmaceutical agents.**

Full text: <http://nutritionandmetabolism.com/content/1/1/6>

Parillo M, Giacco R, Ciardullo AV, Rivellese AA, Riccardi G. Does a high-carbohydrate diet have different effects in NIDDM patients treated with diet alone or hypoglycemic drugs? Diabetes Care 19 (5): 498-500, 1996

Institute of Internal Medicine and Metabolic Diseases, Medical School, University of Naples Federico II, Italy.

OBJECTIVE--To compare the effects of a high-carbohydrate diet on blood glucose and plasma lipids in NIDDM patients with either mild or severe glucose intolerance. **RESEARCH DESIGN AND METHODS**--A crossover design with a 15-day intervention diet was used. **Eighteen patients** were separated into two groups on the basis of hypoglycemic treatment (diet, n = 9, or diet plus glibenclamide, n = 9) and were assigned to a 15-day treatment with a high-carbohydrate/low-fiber diet containing 60% energy from carbohydrate and 20% from fat **or a low-carbohydrate/low-fiber diet with 40% energy from carbohydrate and 40% from fat** and then crossed over to the other diet for 15 more days. **RESULTS**—**The high-carbohydrate diet produced a significant increase in postprandial blood glucose in patients on glibenclamide (13.6 +/- 1.4 vs. 11.0 +/- 1.8 mmol/l, P < 0.002, while no difference was recorded in the group on diet alone (9.7 +/- vs. 8.9 +/- 0.6 mmol/l).** Postprandial insulin levels were significantly higher after the high-carbohydrate diet in the group on diet alone (248 +/- 32 vs. 192 +/- 28 pmol/l, P < 0.01), while no significant differences were observed in the other group (226 +/- 19 vs. 202 +/- 24 pmol/l) The high-carbohydrate diet also induced a significant increase in fasting plasma triglyceride concentrations in both groups (1.36 +/- 0.2 vs. 1.12 +/- 0.2 mmol/l, P < 0.05 and 1.4 +/- 0.3 vs. 1.1 +/- 0.1 mmol/l, P < 0.05). No differences were observed in fasting plasma cholesterol and HDL. **CONCLUSIONS**--**The effects of the high-carbohydrate diet on blood glucose control in NIDDM patients differ according to severity of glucose intolerance.**

Full text: <http://care.diabetesjournals.org/cgi/content/full/19/5/498>

Rasmussen OW, Thomsen C, Hansen KW, Vesterlund M, Winther E, Hermansen K. Effects on blood pressure, glucose, and lipid levels of a high-monounsaturated fat diet compared with a high-carbohydrate diet in NIDDM subjects. Diabetes Care 16(12): 1565-1571, 1993

Medical Department M, Aarhus Community Hospital, Denmark.

OBJECTIVE--To compare the influence on blood pressure, glucose, and lipid levels of a diet rich in monounsaturated fatty acids with an isocaloric, high-carbohydrate diet **in 15 NIDDM subjects.** **RESEARCH DESIGN AND METHODS**—A crossover design with diet interventions and wash-out periods of 3 wk was applied. The patients were randomly assigned to a 3-wk treatment with a high-carbohydrate diet containing 50% of energy as carbohydrate and 30% of energy as fat (10% of energy as monounsaturated fatty acids) **or an isocaloric diet with 30% of energy as carbohydrate and 50% of energy as fat (30% of energy as monounsaturated fatty acids).** On the last day of the two diets, 24-h ambulatory blood pressure was measured and day profiles of glucose, hormones, and lipids were performed to a test menu rich in carbohydrates. **RESULTS**--**The diet rich in monounsaturated fat reduced daytime systolic (131 +/- 3 vs. 137 +/- 3 mmHg, P < 0.04) and 24-h systolic blood pressure (126 +/- 8 vs. 130 +/- 10 mmHg, P < 0.03) as well as daytime diastolic (78 +/- 2 vs. 84 +/- 2 mmHg, P < 0.02) and diurnal diastolic blood pressure (75 +/- 6 vs. 78 +/- 5 mmHg, P < 0.03) as compared with the high-carbohydrate diet.** Evidence of

lowered blood glucose levels on the high-monounsaturated diet compared with the high-carbohydrate diet were found with lower fasting blood glucose (6.1 +/- 0.3 vs. 6.8 +/- 0.5 mM, P < 0.05), lower average blood glucose levels (7.4 +/- 0.5 vs. 8.2 +/- 0.6 mM, P < 0.04), and peak blood glucose responses (9.9 +/- 0.6 vs. 11.3 +/- 0.7 mM, P < 0.02). The two diets had the same impact on lipid levels. **CONCLUSIONS--A diet rich in monounsaturated fat has beneficial effects on blood pressure and glucose metabolism, whereas no adverse effects on lipid composition in NIDDM subjects is detected.**

Full text: <http://care.diabetesjournals.org/cgi/content/full/16/12/1565>

Samaha FF, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, Williams T, Williams M, Gracely EJ, Stern L. A low-carbohydrate as compared with a low-fat diet in severe obesity. NEJM 348 (21): 2074-2081, 2003

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BACKGROUND: The effects of a carbohydrate-restricted diet on weight loss and risk factors for atherosclerosis have been incompletely assessed. **METHODS:** We randomly assigned **132 severely obese subjects (including 77 blacks and 23 women) with a mean body-mass index of 43 and a high prevalence of diabetes (39 percent) or the metabolic syndrome (43 percent) to a carbohydrate-restricted (low-carbohydrate) diet or a calorie- and fat-restricted (low-fat) diet.** **RESULTS:** Seventy-nine subjects completed the six-month study. An analysis including all subjects, with the last observation carried forward for those who dropped out, showed that **subjects on the low-carbohydrate diet lost more weight than those on the low-fat diet (mean [±SD], -5.8±8.6 kg vs. -1.9±4.2 kg; P=0.002) and had greater decreases in triglyceride levels (mean, -20±43 percent vs. -4±31 percent; P=0.001), irrespective of the use or nonuse of hypoglycemic or lipid-lowering medications.** Insulin sensitivity, measured only in subjects without diabetes, also improved more among subjects on the low-carbohydrate diet (6±9 percent vs. -3±8 percent, P=0.01). The amount of weight lost (P<0.001) and assignment to the low-carbohydrate diet (P=0.01) were independent predictors of improvement in triglyceride levels and insulin sensitivity. **CONCLUSIONS: Severely obese subjects with a high prevalence of diabetes or the metabolic syndrome lost more weight during six months on a carbohydrate-restricted diet than on a calorie- and fat-restricted diet, with a relative improvement in insulin sensitivity and triglyceride levels, even after adjustment for the amount of weight lost.** This finding should be interpreted with caution, given the small magnitude of overall and between-group differences in weight loss in these markedly obese subjects and the short duration of the study. Future studies evaluating long-term cardiovascular outcomes are needed before a carbohydrate-restricted diet can be endorsed.

Full text: <http://content.nejm.org/cgi/content/full/348/21/2074>

Shah Meena, Adams-Huet Beverley, Grundy Scott M, Garg Abhimanyu. Effect of a high-carbohydrate vs a high-cis-monounsaturated fat diet on lipid and lipoproteins in individuals with and without type 2 diabetes. Nutrition Research 24 969–979, 2004

It is not known whether the extent of the improvement in lipids and lipoproteins on a high-cismonounsaturated (high-mono) diet compared with a high-carbohydrate (high-carb) diet is different in patients with type 2 diabetes mellitus (T2DM) and nondiabetic subjects. The aim of this

study is **to compare the effect of a high-mono and a high-carb diet on lipids and lipoproteins in patients with T2DM and nondiabetic subjects.**

Ten healthy nondiabetic men, 8 men with T2DM on dietary therapy alone, and 10 men with T2DM requiring insulin therapy were fed an isoenergetic high-carb diet (60% energy as carbohydrate and 25% as fat) and a high-mono diet (50% energy as fat and 35% as carbohydrate) for 2 to 4 weeks in a randomized, crossover fashion. Dietary fiber, simple carbohydrates, and cholesterol were held constant across diets.

The lipid and lipoprotein responses to these diets were compared in nondiabetic and T2DM subjects by repeated measures analysis of variance model. **Patients with T2DM had 2.2 to 2.3 times greater reductions in plasma triacylglycerol, very low-density lipoprotein (VLDL) cholesterol, and total cholesterol/high-density lipoprotein cholesterol ratio (TC/HDL) on the high-mono diet compared with the high-carb diet than the nondiabetic subjects (P = .02-.04).** The reductions in triacylglycerol and VLDL cholesterol were 2.7 times greater (P = .009-.02) in T2DM subjects with high plasma triacylglycerol concentrations (≥ 2.26 mmol/L) but only 1.4 to 2.0 times greater (P = .16-.52) in T2DM patients with low triacylglycerol concentrations (< 2.26 mmol/L) compared with nondiabetic subjects who all had low triacylglycerol concentrations (< 2.26 mmol/L). **Patients with T2DM experienced greater decreases in plasma triacylglycerol, VLDL cholesterol, and TC/HDL on a high-mono diet compared with a high-carb diet than nondiabetic subjects.** The extents of the improvements were likely related to plasma triacylglycerol concentrations in patients with T2DM.

Full text: http://www.freewebs.com/stopped_our_statins/Diet%20-%20High%20Carb%20VS%20High%20Fat.pdf

Vernon Mary C., Mavropoulos John, Transue Melissa, Yancy Jr. William S, Westman Eric C. Clinical Experience of a Carbohydrate-Restricted Diet: Effect on Diabetes Mellitus, Metabolic Syndrome and Related Disorders 1 (3): 233-237, 2003

No abstract available

Full text: <http://www.liebertonline.com/doi/pdfplus/10.1089/154041903322716714>

Vesti-Nielsen J, Jönsson E, Nilsson AK. Lasting improvement of hyperglycaemia and bodyweight: low-carbohydrate diet in type 2 diabetes. A brief report. Ups J Med Sci 110 (2): 179-183, 2005

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In two groups of obese patients with type 2 diabetes the effects of 2 different diet compositions were tested with regard to glycaemic control and bodyweight. A group of **16 obese patients with type 2 diabetes was advised on a low-carbohydrate diet, 1800 kcal for men and 1600 kcal for women, distributed as 20% carbohydrates, 30% protein and 50% fat.** Fifteen obese diabetes patients on a high-carbohydrate diet were control group. Their diet, 1600-1800 kcal for men and 1400-1600 kcal for women, consisted of approximately 60% carbohydrates, 15% protein and 25% fat. Positive effects on the glucose levels were seen very soon. **After 6 months a marked reduction in bodyweight of patients in the low-carbohydrate diet group was observed, and this remained one year later. After 6 months the mean changes in the low-carbohydrate group and the control group respectively were (+/-SD): fasting blood glucose (f-BG): -3.4 +/- 2.9 and -0.6 +/- 2.9 mmol/l; HbA1c: -1.4 +/- 1.1% and -0.6 +/- 1.4%; Body Weight: -11.4 +/- 4 kg and -1.8 +/- 3.8 kg; BMI: -4.1 +/- 1.3 kg/m² and -0.7 +/- 1.3 kg/m².** Large changes in blood glucose

levels were seen immediately. **A low-carbohydrate diet is an effective tool in the treatment of obese patients with type 2 diabetes.**

Full text: http://www.diva-portal.org/diva/getDocument?urn_nbn_se_pub_diva-182-2_fulltext.pdf

Vesti Nielsen J, Westerlund P, Bygren P. A low-carbohydrate diet may prevent end-stage renal failure in type 2 diabetes. A case report. Nutr Metab (Lond) 143: 23, 2006

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ABSTRACT: An obese patient with type 2 diabetes whose diet was changed from the recommended high-carbohydrate, low-fat type to a low-carbohydrate diet showed a significant reduction in bodyweight, improved glycemic control and a reversal of a six year long decline of renal function. The reversal of the renal function was likely caused by both **improved glycemic control and elimination of the patient's obesity.** Insulin treatment in type 2 diabetes patients usually leads to weight increase which may cause further injury to the kidney. Although other unknown metabolic mechanisms cannot be excluded, it is likely that the obesity caused by the combination of high-carbohydrate diet and insulin in this case contributed to the patient's deteriorating kidney function. In such patients, where control of bodyweight and hyperglycemia is vital, a trial with a low-carbohydrate diet may be appropriate to avoid the risk of adding obesity-associated renal failure to already failing kidneys.

Full text: <http://www.nutritionandmetabolism.com/content/3/1/23>

Vesti Nielsen Jørgen and Joensson Eva. Low-carbohydrate diet in type 2 diabetes. Stable improvement of bodyweight and glycemic control during 22 months follow-up. Nutrition & Metabolism 3:22 doi:10.1186/1743-7075-3-222006 (on-line fast), Published 14 June, 2006

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Background: Low-carbohydrate diets in the management of obese patients with type 2 diabetes seem intuitively attractive due to their potent antihyperglycemic effect. We previously reported that a 20 % carbohydrate diet was significantly superior to a 55–60 % carbohydrate diet with regard to bodyweight and glycemic control in 2 non-randomised groups of obese diabetes patients observed closely over 6 months. The effect beyond 6 months of reduced carbohydrate has not been previously reported. The objective of the present study, therefore, was to determine to what degree the changes among the 16 patients in the low-carbohydrate diet group at 6-months were preserved or changed 22 months after start, even without close follow-up. In addition, we report that, after the 6 month observation period, two thirds of the patients in the high-carbohydrate changed their diet. This group also showed improvement in bodyweight and glycemic control.

Method: Retrospective follow-up of previously studied subjects on a low carbohydrate diet.

Results: The mean bodyweight at the start of the initial study was 100.6 ± 14.7 kg. At six months it was 89.2 ± 14.3 kg. **From 6 to 22 months, mean bodyweight had increased by 2.7 ± 4.2 kg to an average of 92.0 ± 14.0 kg.** Seven of the 16 patients (44%) retained the same bodyweight from 6 to 22 months or reduced it further; all but one had lower weight at 22 months than at the beginning. **Initial mean HbA1c was 8.0 ± 1.5 %. After 6 and 12 months it was 6.6 ± 1.0 % and 7.0 ± 1.3 %, respectively. At 22 months, it was still 6.9 ± 1.1 %.**

Conclusion: Advice on a 20 % carbohydrate diet with some caloric restriction to obese patients with type 2 diabetes has lasting effect on bodyweight and glycemic control.

Full text: <http://www.nutritionandmetabolism.com/content/3/1/22>

Volek JS, Feinman RD. Carbohydrate restriction improves the features of Metabolic Syndrome. Metabolic Syndrome may be defined by the response to carbohydrate restriction. Nutr Metab (Lond) 162: 31, 2005

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ABSTRACT : Metabolic Syndrome (MetS) represents a constellation of markers that indicates a predisposition to diabetes, cardiovascular disease and other pathologic states. The definition and treatment are a matter of current debate and there is not general agreement on a precise definition or, to some extent, whether the designation provides more information than the individual components. We consider here five indicators that are central to most definitions and we provide evidence from the literature that these are precisely the symptoms that respond to reduction in dietary carbohydrate (CHO). **Carbohydrate restriction is one of several strategies for reducing body mass but even in the absence of weight loss or in comparison with low fat alternatives, CHO restriction is effective at ameliorating high fasting glucose and insulin, high plasma triglycerides (TAG), low HDL and high blood pressure.** In addition, low fat, high CHO diets have long been known to raise TAG, lower HDL and, in the absence of weight loss, may worsen glycemic control. Thus, whereas there are numerous strategies for weight loss, **a patient with high BMI and high TAG is likely to benefit most from a regimen that reduces CHO intake.** Reviewing the literature, **benefits of CHO restriction are seen in normal or overweight individuals, in normal patients who meet the criteria for MetS or in patients with frank diabetes.** Moreover, in low fat studies that ameliorate LDL and total cholesterol, controls may do better on the symptoms of MetS. On this basis, we feel that MetS is a meaningful, useful phenomenon and may, in fact, be operationally defined as the set of markers that responds to CHO restriction. Insofar as this is an accurate characterization it is likely the result of the effect of dietary CHO on insulin metabolism. Glucose is the major insulin secretagogue and insulin resistance has been tied to the hyperinsulinemic state or the effect of such a state on lipid metabolism. The conclusion is probably not surprising but has not been explicitly stated before. **The known effects of CHO-induced hypertriglyceridemia, the HDL-lowering effect of low fat, high CHO interventions and the obvious improvement in glucose and insulin from CHO restriction should have made this evident.** In addition, recent studies suggest that a subset of MetS, the ratio of TAG/HDL, is a good marker for insulin resistance and risk of CVD, and this indicator is reliably reduced by CHO restriction and exacerbated by high CHO intake. **Inability to make this connection in the past has probably been due to the fact that individual responses have been studied in isolation as well as to the emphasis of traditional therapeutic approaches on low fat rather than low CHO.** We emphasize that MetS is not a disease but a collection of markers. **Individual physicians must decide whether high LDL, or other risk factors are more important than the features of MetS in any individual case but if MetS is to be considered it should be recognized that reducing CHO will bring improvement.** Response of symptoms to CHO restriction might thus provide a new experimental criterion for MetS in the face of on-going controversy about a useful definition. As a guide to future research, the idea that control of insulin metabolism by CHO intake is, to a first approximation, the underlying mechanism in MetS is a testable hypothesis.

Full text: <http://nutritionandmetabolism.com/content/2/1/31>

Volek JS, Forsythe CE. The case for not restricting saturated fat on a low carbohydrate diet. Nutr Metab (Lond) 312: 21, 2005

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Comment. We would like to compliment Drs. Arora and McFarlane on their timely review of low carbohydrate diets in diabetes management [1]. **Undeniably, the prescription of low-fat, high-carbohydrate diets to treat diabetes has to be questioned and the power of carbohydrate restriction seriously considered.** The article dispels common myths and provides a convincing argument for successful use of carbohydrate restriction in treating diabetes. One point stressed by Arora and McFarlane was that mono and polyunsaturated fat should be emphasized over saturated fat as a way to achieve caloric balance on a carbohydrate-restricted diet. **We contend that the recommendation to intentionally restrict saturated fat is unwarranted and only serves to contribute to the misleading rhetoric surrounding the health effects of saturated fat. We believe restriction of saturated fat is not warranted on a low-carbohydrate diet because of our work showing favorable responses in clinical risk factors for diabetes and cardiovascular disease in low-carbohydrate diets that were rich in saturated fat [2].** In addition, German & Dillard [3] have reviewed several experimental studies of the effects of saturated fats and the results are found to be variable and there is a general failure to meet the kind of unambiguous predictions that would justify the recommendation to reduce saturated fat in the population [3]. **Other critical reviews of the evidence [4] have questioned whether public health recommendations for reducing saturated fat intake [5] are appropriate.**

The critical issues are:

- 1. The atherogenic potential of saturated fats varies greatly depending on chain length and whether it is present alone or added in foods. Stearic acid (C18) is a major saturated fat found in beef, chicken, and pork and has repeatedly been shown not to raise LDL cholesterol levels [6]. Even palmitic acid (C16), the most abundant saturated fatty acid in the diet, does not raise LDL cholesterol in the presence of adequate linoleic acid [7].**
- 2. The effect of saturated fat cannot be assumed to be independent of specific dietary conditions. In particular, hypocaloric or low total fat diets may show different results than deduced from epidemiology.** A recent report [8] showed that for a woman on a relatively low fat diet, a greater saturated fat intake was associated with a reduced progression of coronary atherosclerosis. An editorial described this as "an American paradox [9].
- 3. Evaluation of the overall health effects of saturated fat requires consideration of markers in addition to LDL-cholesterol. Isocaloric replacement of carbohydrate with any type of fat results in decreased triglycerides and increased HDL-cholesterol, the effect on HDL-cholesterol being greater for saturated fat compared to unsaturated fat [10]. Reductions in saturated fat also adversely affect HDL subpopulations by decreasing larger HDL2-cholesterol concentrations [11], whereas increases in saturated fat increase this antiatherogenic fraction [12,13].** Furthermore, very low-carbohydrate diets rich in saturated fat increase LDL size and conversion from a high-risk pattern B to a lower risk pattern A phenotype [2].
- 4. Finally, there is the concern that recommendations to limit saturated fat would lead to their replacement with carbohydrate, which can have undesirable effects (increased triglycerides with decreased HDL cholesterol) [10].**

For these reasons, we believe that the recommendation to restrict saturated fat in favor of unsaturated fat on a low-carbohydrate diet is unnecessary and may even diminish some of the beneficial physiological effects associated with carbohydrate restriction. At the very least, the food restriction required to reduce saturated fat will compromise the palatability of the diet and ultimately the acceptance of the approach to diabetes management recommended by Arora and McFarlane [1].

Full text: <http://nutritionandmetabolism.com/content/2/1/21>

Westman Eric C, Yancy Jr. William S, Haub Mark D, Volek Jeff S. Insulin Resistance from a Low Carbohydrate, High Fat Diet Perspective. Metabolic Syndrome and Related Disorders 3 (1): 14-18, 2005

No abstract available.

Full text: <http://www.liebertonline.com/doi/pdfplus/10.1089/met.2005.3.14?cookieSet=1>

Yancy Jr. William S, Vernon Mary C, Westman Eric C. A Pilot Trial of a Low-Carbohydrate, Ketogenic Diet in Patients with Type 2 Diabetes. Metabolic Syndrome and Related Disorders 1 (3): 239-243, 2003

No abstract available.

Full text: <http://www.liebertonline.com/doi/pdfplus/10.1089/154041903322716723>

Yancy WS, Foy M, Chalecki AM, Vernon MC, Westman EC. A low-carbohydrate, ketogenic diet to treat type 2 diabetes. Nutr Metab (Lond) 12:34, 2005

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ABSTRACT : BACKGROUND : The low-carbohydrate, ketogenic diet (LCKD) may be effective for improving glycemia and reducing medications in patients with type 2 diabetes. METHODS : From an outpatient clinic, we recruited 28 overweight participants with type 2 diabetes for a 16-week single-arm pilot diet intervention trial. We provided LCKD counseling, with an initial goal of <20 g carbohydrate/day, while reducing diabetes medication dosages at diet initiation. Participants returned every other week for measurements, counseling, and further medication adjustment. The primary outcome was hemoglobin A1c. RESULTS : Twenty-one of the 28 participants who were enrolled completed the study. Twenty participants were men; 13 were White, 8 were African-American. The mean [± SD] age was 56.0 ± 7.9 years and BMI was 42.2 ± 5.8 kg/m². Hemoglobin A1c decreased by 16% from 7.5 ± 1.4% to 6.3 ± 1.0% (p < 0.001) from baseline to week 16. Diabetes medications were discontinued in 7 participants, reduced in 10 participants, and unchanged in 4 participants. The mean body weight decreased by 6.6% from 131.4 ± 18.3 kg to 122.7 ± 18.9 kg (p < 0.001). In linear regression analyses, weight change at 16 weeks did not predict change in hemoglobin A1c. Fasting serum triglyceride decreased 42% from 2.69 ± 2.87 mmol/L to 1.57 ± 1.38 mmol/L (p = 0.001) while other serum lipid measurements did not change significantly. CONCLUSION : The LCKD improved glycemic control in patients with type 2 diabetes such that diabetes medications were discontinued or reduced in most participants. Because the LCKD can be very effective at lowering blood glucose,

patients on diabetes medication who use this diet should be under close medical supervision or capable of adjusting their medication.

Full text: <http://nutritionandmetabolism.com/content/2/1/34>