Dietary Carbohydrate (Amount and Type) in the Prevention and Management of Diabetes

A statement by the American Diabetes Association

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Diabetes has long been viewed as a disorder of carbohydrate metabolism due to its hallmark feature of hyperglycemia. Indeed, hyperglycemia is the cause of the acute symptoms associated with diabetes such as polydypsia, polyuria, and polyphagia (1). The long-term complications (retinopathy, nephropathy, and neuropathy) associated with diabetes are also believed to result from chronically elevated blood glucose levels (2–6). In addition, hyperglycemia may contribute to the development of macrovascular disease, which is associated with the development of coronary artery disease, the leading cause of death in individuals with diabetes (7–9). Thus, a primary goal in the management of diabetes is the regulation of blood glucose to achieve near-normal blood glucose.

What determines the postprandial blood glucose response?

Blood glucose concentration following a meal is determined by the rate of appearance of glucose into the blood stream (absorption) and its clearance/disappearance from the circulation (10). The rate of disappearance of glucose is largely influenced by insulin secretion and its action on target tissues (11).

The component of the diet that has the greatest influence on blood glucose is carbohydrate. Other macronutrients in the diet, i.e., fat and protein, can influence the postprandial blood glucose level, however. For example, dietary fat slows glucose absorption, delaying the peak glycemic response to the ingestion of a food that contains glucose (12–14). In addition, although glucose is the primary stimulus for insulin release, protein/amino acids augment insulin release when ingested with carbohydrate, thereby increasing the clearance of glucose from the blood (15–17).

Both the quantity and the type or source of carbohydrate found in foods influence postprandial glucose level (18,19). Although most experts agree that the total carbohydrate intake from a meal or snack is a relatively reliable predictor of postprandial blood glucose (18,20–22), the impact and relative importance that the type or source of carbohydrate has on postprandial glucose level has continued to be an area of debate (23–26). Over the last two decades, investigators have attempted to define and categorize carbohydrate-containing foods based on their glycemic response or their propensity to increase blood glucose concentration (27,28). Two methods that have been investigated as potential tools for meal planning and/or assessing disease risk associated with dietary carbohydrate intake are the glycemic index and the glycemic load. The purpose of this statement is to review the available scientific data regarding the effect of the type or source of carbohydrate on the prevention and management of diabetes and to clarify the position of the American Diabetes Association on this important topic.

What is the glycemic index?

The glycemic index is a measure of the change in blood glucose following ingestion of carbohydrate-containing foods. Some foods result in a marked rise followed by a more or less rapid fall in blood glucose, whereas others produce a smaller peak along with a more gradual decline in plasma glucose (19). The specific type of carbohydrate (e.g., starch versus sucrose) present in a particular food does not always predict its effect on blood glucose (28,29).

The glycemic index is a ranking of carbohydrate exchanges according to their effect on postprandial glycemia. It is a means of quantifying the relative blood glucose response to carbohydrates in individual foods, comparing them on a weight-for-weight basis (i.e., per gram of carbohydrate). As measured/analyzed under laboratory conditions, the glycemic index is the increase in blood glucose (over the fasting level) that is observed in the 2 h following ingestion of a set amount of carbohydrate in an individual food. This value is then compared with the response to a reference food (glucose or white bread) containing an equivalent amount of carbohydrate (27).

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

What is glycemic load?

While the glycemic index provides a ranking of foods based on their blood glucose response, it does not take into account the effect of a typical amount of carbohydrate in a food portion on glycemia. In an effort to improve the reliability of predicting the glycemic response of a given diet, Salmeron et al. (30) have suggested the use of the glycemic load. As defined, the glycemic load of a particular food is the product of the glycemic index of the food and the amount of carbohydrate in a serving. By summing the glycemic load contributed by individual foods, the overall glycemic load of a meal or the whole diet can be calculated (30).

If carbohydrates increase blood glucose, why not restrict total carbohydrate intake in individuals with diabetes?

Blood glucose is increased in individuals with diabetes in both the fed and fasted state. This abnormal metabolic response is due to insufficient insulin secretion, insulin resistance, or a combination of both. Although dietary carbohydrate increases postprandial glucose levels, avoiding carbohydrate entirely will not return blood glucose levels to the normal range. Additionally, dietary carbohydrate is an important component of a healthy diet. For example, glucose is the primary fuel used by the brain and central nervous system, and foods that contain carbohydrate are important sources of many nutrients, including water-soluble vitamins and minerals as well as fiber (31). Given the above, low-carbohydrate diets are not recommended in the management of diabetes. Recently, the National Academy of Sciences–Food and Nutrition Board recommended that diets provide 45–65% of calories from carbohydrate, with a minimum intake of 130 g carbohydrate/day for adults (31).

What determines the glycemic effect of a carbohydrate-containing food?

Both the amount (grams) of carbohydrate as well as the type of carbohydrate in a food will influence its effect on blood glucose level. The specific type of carbohydrate (e.g., starch versus sucrose) present in a particular food does not always accurately predict its effect on blood glucose (28,29). For example, sugars such as sucrose and fructose have a lower glycemic response/glycemic index despite their shorter chain length (32–36). In fact, a variety of factors intrinsic to a given food can influence its impact on blood glucose. These include the physical form of the food (i.e., juice versus whole fruit, mashed potato versus whole potato), ripeness, degree of processing, type of starch (i.e., amylose versus amylopectin), style of preparation (e.g., cooking method and time, amount of heat or moisture used), and the specific type (e.g., fettucine versus macaroni) or variety (e.g., long grain versus white) of the food (26). Extrinsic variables such as the coingestion of protein and fat, prior food intake, fasting or preprandial glucose level, and degree of insulin resistance will also alter the effect of a specific carbohydrate-containing food on blood glucose concentration (19,26,28).

Which has a greater influence on blood glucose, the type of carbohydrate or the total amount of carbohydrate?

Both the amount (27,37) and the source (27,38) of carbohydrate are important determinants of postprandial glucose. The relative effects of each have been recently studied. Brand-Miller et al. (in response to a letter from Mendosa [39]) reported that they analyzed the relative impact of the glycemic index and total carbohydrate content of individual foods on glycemic load (the product of glycemic index and total grams of carbohydrate) using linear regression analysis. Carbohydrate content (total grams) alone explained 68% of the variation in glycemic load, while the glycemic index of the food explained 49%. When total carbohydrate and glycemic index were both included in the regression analysis, the glycemic index accounted for 32% of the variation.

Wolever and Bolognesi (21,22) tested the hypothesis that both the type and amount of carbohydrate influence glycemic response in normal subjects. Their findings demonstrated that the amount of carbohydrate ingested (whether in a single food or as part of a meal) accounted for 57–65% of the variability in glucose response, while the glycemic index of the carbohydrate explained a similar amount (60%) of the variance (21,22). Together, the amount and the glycemic index of carbohydrate accounted for ~90% of the total variability in blood glucose response, indicating the cumulative effect of both factors on postprandial blood glucose concentration.

Wolever and Mehling (40) examined the long-term effect of varying the type or amount of dietary carbohydrate on postprandial plasma glucose, insulin, and lipid levels in 34 subjects with impaired glucose tolerance. After 4 months, mean plasma glucose concentrations over 8 h were lowered by the same amount on both the low-carbohydrate, high–monounsaturated fat and the high-carbohydrate, low–glycemic index diets when compared with values in subjects on the high-carbohydrate, high–glycemic index diet. Thus, in patients with impaired glucose tolerance, reducing the glycemic index of the diet for 4 months reduced postprandial plasma glucose by the same amount as reducing carbohydrate intake.

What are some of the issues regarding the glycemic index?

1) The glycemic index takes only the type of carbohydrate into account, ignoring the total amount of carbohydrate in a typical serving, although both the type and amount of carbohydrate influence the postprandial glycemic and insulin response of a given food as typically consumed (18,22,26).

By definition, the glycemic index is a ranking of foods according to their effect on postprandial glycemia. It compares equal quantities of carbohydrate and provides a measure of carbohydrate quality but not quantity. Thus, the glycemic index provides information about how carbohydrate-containing foods affect blood glucose following ingestion of a single food in addition to that obtained from knowledge about the total amount of carbohydrate. As such, the index is not intended to be used in isolation, but rather can and should be used in conjunction with other food and nutrition strategies (e.g., total amount of carbohydrate, modification of dietary fat intake, portion control).

2) The glycemic index for any particular food item is highly variable.

The glycemic response to a particular food is subject to significant variation, both within individuals and between individuals (intraindividual coefficient of variation 23–54%) (26,41–43). This variability, however, is similar to that seen for the oral glucose tolerance test (42,43). When the glycemic response is expressed as a percentage of an individual's response to a standardized food (i.e., 50 g white bread or glucose), the between-individual variation is reduced to ~10% (27,44,45).

Variation in individual glycemic response may also reflect differences in the physical and chemical characteristics of specific foods, as well as differences in methodology. For example, the type of blood sample (capillary or venous), the experimental time period, and the portion of food all influence the glycemic index of a given food. Recently, findings from a collaborative study demonstrated that similar glycemic index values can be obtained when methodology is standardized (45), although some foods continue to show wide variation in response secondary to botanical differences (46).

3) As defined, the glycemic index only measures the response to an individual food consumed in isolation. What is perhaps more relevant, however, is the ability of the index to predict blood glucose concentration when the food is part of a meal.

In general, the glycemic response to mixed meals can be predicted with some accuracy by summing up the glycemic index of the component foods (43,47–52), although not all studies have found a direct relationship between calculated and measured glycemic index of mixed meals (53–55).

4) The glycemic index does not predict postprandial blood glucose response as accurately in individuals with diabetes as it does in healthy persons.

Although the glycemic response following carbohydrate ingestion is higher in individuals with diabetes, the relative response to foods and mixed meals that vary in glycemic index is similar in individuals with diabetes and healthy subjects (44,48,52,55–57).

What studies have examined the effectiveness of the glycemic index on overall blood glucose control?

There have been several randomized trials that have examined the efficacy of diets consisting of low glycemic foods to control glycemia. The results have been mixed, with some showing (58–64) and others not showing (65–67) significant improvement. In part, this may be due to the fact that many of the studies have involved small numbers of subjects, been of relatively short duration, and shown only a modest effect. Significant variation in study design, subject characteristics, and diet composition also makes summative conclusions regarding the effectiveness of low glycemic diets on blood glucose control more challenging.

In an attempt to clarify the issue of the effect of low–glycemic index diets in the management of type 1 and type 2 diabetes, Brand-Miller et al. (68) recently conducted a meta-analysis of available studies on this topic. Their findings indicate that implementing a low–glycemic index diet lowered A1C values by 0.43% when compared with a high–glycemic index diet. The findings were similar in both type 1 and type 2 diabetes.

The findings of the meta-analysis are also consistent with the results of the EURODIAB study, a cross-sectional study involving nearly 3,000 subjects with type 1 diabetes in 31 clinics throughout Europe, in which the glycemic index of self-selected diets was positively and independently related to A1C level (69).

What studies have examined the utility of the glycemic load?

The glycemic load has been primarily used in epidemiological studies to examine the effect of diet on the risk of developing chronic diseases such as diabetes, heart disease, and cancer. Although the findings from epidemiological studies indicate a possible relationship between the propensity of the diet to raise blood glucose and the development of diabetes, they do not demonstrate cause and effect. There remains a need to demonstrate a direct relationship between the calculated glycemic load of a food or meal with a proportional change in postprandial blood glucose and/or the secretion of insulin (i.e., a physiological basis). Additionally, to determine the clinical utility of glycemic load, longer-term trials in which high–glycemic load diets are compared with low–glycemic load diets and outcomes related to long-term glucose control (i.e., A1C) and lipids are measured will be required.

Recently, Brand-Miller et al. (41) published data that examined the relationship between glycemic load, blood glucose level, and insulin response following ingestion of individual foods. Stepwise increases in glycemic load for a range of foods produced proportional increases in blood glucose and insulin. In addition, the investigators demonstrated that portions of different foods with the same glycemic load produced similar glycemic responses. Although the study was small and only examined healthy, normal-weight individuals, its findings demonstrate that calculated glycemic load can predict the blood glucose response to individual foods across a range of portion sizes. These are important findings in establishing a physiological basis for glycemic load; however, it will be necessary to examine the effect of the glycemic load of a mixed meal on postprandial glucose and insulin levels, as well as the effects on daylong glucose and insulin levels.

Does a diet with a high glycemic index or load lead to diabetes?

Epidemiological studies form the basis for the hypothesis that a diet with a high glycemic load or glycemic index leads to type 2 diabetes. Findings from the Nurses' Health Study demonstrated a positive association between dietary glycemic index and risk of type 2 diabetes; the relative risk was 1.37 when the highest quintile of glycemic index was compared with the lowest. Similarly, the glycemic load was positively associated with the development of type 2 diabetes (relative risk 1.47) in women (70). More recently, a follow-up study of the participants in the Nurses' Health Study confirmed the association between glycemic load and risk of type 2 diabetes (71). In men (Health Professionals' Follow-Up Study), however, neither glycemic load nor glycemic index were associated with diabetes risk, except when adjusted for cereal fiber intake (30). Finally, in the Iowa Women's Health Study, no significant relationship between glycemic index or glycemic load and the development of type 2 diabetes was observed (72). Thus, although some studies have observed an association between glycemic index or glycemic load and type 2 diabetes, this relationship has been equivocal or absent in others.

The inconsistency of findings from epidemiological studies may result from the difficulty in predicting glycemic index (and consequently glycemic load) precisely from the dietary assessment tools (food frequency questionnaires) currently in use. Food frequency questionnaires employed to assess dietary intake were not designed to measure glycemic index per se, and data validating their reliability in this regard are limited.

Of note, there is little evidence that total carbohydrate intake is associated with the development of type 2 diabetes

(30,70,73,74). Rather, a stronger association has been observed between total fat and saturated fat intake and type 2 diabetes (75,76), although not all findings are in agreement (30). Additionally, two prospective cohort studies have shown no risk of diabetes from consuming increased amounts of sugar (74,77), and in one study, a negative association was observed between sucrose intake and diabetes risk (72). Intakes of both whole grains (72,78) and dietary fiber (in particular, cereal fiber) are associated with lower risk of type 2 diabetes (30,70–72).

At this time, there is insufficient information to determine whether there is a relationship between glycemic index or glycemic load of diets and the development of diabetes. Prospective randomized trials will be necessary to confirm the relationship between the type of carbohydrate and the development of diabetes. The relative importance of the glycemic index or load of the diet to the development of obesity will also need to be considered, as excess body fat is the single most important determinant of type 2 diabetes (71). In addition, the findings of the Diabetes Prevention Program, conducted in the U.S., and the Finnish Diabetes Prevention Study clearly demonstrate that moderate weight loss markedly reduces the development of type 2 diabetes in individuals with impaired glucose tolerance (79,80).

Summary

- Regulation of blood glucose to achieve near-normal levels is a primary goal in the management of diabetes, and, thus, dietary techniques that limit hyperglycemia following a meal are likely important in limiting the complications of diabetes.
- Low-carbohydrate diets are not recommended in the management of diabetes. Although dietary carbohydrate is the major contributor to postprandial glucose concentration, it is an important source of energy, water-soluble vitamins and minerals, and fiber. Thus, in agreement with the National Academy of Sciences–Food and Nutrition Board, a recommended range of carbohydrate intake is 45–65% of total calories. In addition, because the brain and central nervous system have an absolute requirement for glucose as an energy source, restricting total carbohydrate to <130 g/day is not recommended.
- Both the amount (grams) of carbohydrate as well as the type of carbohydrate in a food influence blood glucose level. The total amount of carbohydrate consumed is a strong predictor of glycemic response, and, thus, monitoring total grams of carbohydrate, whether by use of exchanges or carbohydrate counting, remains a key strategy in achieving glycemic control.
- A recent analysis of the randomized controlled trials that have examined the efficacy of the glycemic index on overall blood glucose control indicates that the use of this technique can provide an additional benefit over that observed when total carbohydrate is considered alone.
- Although this statement has focused primarily on the role of carbohydrate in the diet, the importance of achieving/maintaining a healthy body weight (particularly in type 2 diabetes) in the management of diabetes should not be ignored. Moderate weight loss in overweight/obese individuals with type 2 diabetes results in improved control of hyperglycemia as well as in a reduction in risk factors for cardiovascular disease.
- Because much of the risk of developing type 2 diabetes is attributable to obesity, maintenance of a healthy body weight is strongly recommended as a means of preventing this disease. The relationship between glycemic index and glycemic load and the development of type 2 diabetes remains unclear at this time.

References

1. Beisswenger PJ: Type 1 diabetes. In *Medical Management of Diabetes Mellitus*. Leahy JL, Clark NG, Cefalu WT, Eds. New York, Marcel Dekker, 2000, p. 95–114
2. The Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 329:977–986, 1993
3. The Diabetes Control and Complications Trial Research Group: The relationship of glycemic exposure (HbA_{1c}) to the risk of development and progression of retinopathy in the Diabetes Control and Complications Trial. *Diabetes* 44:968–983, 1995
4. UK Prospective Diabetes Study (UKPDS) Group: Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 352:837–853, 1998
5. UK Prospective Diabetes Study (UKPDS) Group: Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet* 352:854–865, 1998
6. American Diabetes Association: Implications of the U.K. Prospective Diabetes Study (Position Statement). *Diabetes Care* 21:2180–2184, 1998
7. Grundy SM, Benjamin IJ, Burke GL, Chait A, Eckel RH, Howard BV, Mitch W, Smith SC, Jr, Sowers JR: Diabetes and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. *Circulation* 100:1134–1146, 1999
8. Sowers JR, Epstein M, Frohlich ED: Diabetes, hypertension, and cardiovascular disease: an update. *Hypertension* 37:1053–1059, 2001
9. Haffner SM: Management of dyslipidemia in adults with diabetes. *Diabetes Care* 21:160–178, 1998
10. Schenk S, Davidson CJ, Zderic TW, Byerley LO, Coyle EF: Different glycemic indexes of breakfast cereals are not due to glucose entry into blood but to glucose removal by tissue. *Am J Clin Nutr* 78:742–748, 2003
11. DeFronzo RA, Ferrannini E: Influence of plasma glucose and insulin concentration on plasma glucose clearance in man. *Diabetes* 31:683–688, 1982
12. Collier G, O'Dea K: The effect of coingestion of fat on the glucose, insulin, and gastric inhibitory polypeptide responses to carbohydrate and protein. *Am J Clin Nutr* 37:941–944, 1983
13. Collier G, McLean A, O'Dea K: Effect of co-ingestion of fat on the metabolic responses to slowly and rapidly absorbed carbohydrates. *Diabetologia* 26:50–54, 1984
14. Nuttall FQ, Gannon MC: Plasma glucose and insulin response to macronutrients in nondiabetic and NIDDM subjects. *Diabetes Care* 14:824–838, 1991
15. Floyd JC Jr, Fajans SS, Pek S, Thiffault CA, Knopf RF, Conn JW: Synergistic effect of essential amino acids and glucose upon insulin secretion in man. *Diabetes* 19:109–115, 1970
16. Nuttall FQ, Mooradian AD, Gannon MC, Billington C, Krezowski P: Effect of protein ingestion on the glucose and insulin response to a standardized oral glucose load. *Diabetes Care* 7:465–470, 1984
17. van Loon LJ, Saris WH, Verhagen H, Wagenmakers AJ: Plasma insulin responses after ingestion of different amino acid or protein mixtures with carbohy-

drate. *Am J Clin Nutr* 72:96–105, 2000
18. Franz MJ, Bantle JP, Beebe CA, Brunzell JD, Chiasson JL, Garg A, Holzmeister LA, Hoogwerf B, Mayer-Davis E, Mooradian AD, Purnell JQ, Wheeler M: Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. *Diabetes Care* 25:148–198, 2002
19. Institute of Medicine: *Dietary Reference Intakes: Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC, National Academies Press, 2002
20. Gannon MC, Nuttall FQ, Westphal SA, Fang S, Ercan-Fang N: Acute metabolic response to high-carbohydrate, high-starch meals compared with moderate-carbohydrate, low-starch meals in subjects with type 2 diabetes. *Diabetes Care* 21:1619–1626, 1998
21. Wolever TM, Bolognesi C: Source and amount of carbohydrate affect postprandial glucose and insulin in normal subjects. *J Nutr* 126:2798–2806, 1996
22. Wolever TM, Bolognesi C: Prediction of glucose and insulin responses of normal subjects after consuming mixed meals varying in energy, protein, fat, carbohydrate and glycemic index. *J Nutr* 126: 2807–2812, 1996
23. Franz MJ: The glycemic index: not the most effective nutrition therapy intervention. *Diabetes Care* 26:2466–2468, 2003
24. Ludwig DS: The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *JAMA* 287:2414–2423, 2002
25. Jenkins DJ, Kendall CW, Augustin LS, Franceschi S, Hamidi M, Marchie A, Jenkins AL, Axelsen M: Glycemic index: overview of implications in health and disease. *Am J Clin Nutr* 76:266S–273S, 2002
26. Pi-Sunyer FX: Glycemic index and disease. *Am J Clin Nutr* 76:290S–298S, 2002
27. Jenkins DJ, Wolever TM, Taylor RH, Barker H, Fielden H, Baldwin JM, Bowling AC, Newman HC, Jenkins AL, Goff DV: Glycemic index of foods: a physiological basis for carbohydrate exchange. *Am J Clin Nutr* 34:362–366, 1981
28. Foster-Powell K, Miller JB: International tables of glycemic index. *Am J Clin Nutr* 62:871S–890S, 1995
29. Wolever TM, Nguyen PM, Chiasson JL, Hunt JA, Josse RG, Palmason C, Rodger NW, Ross SA, Ryan EA, Tan MH: Determinants of diet glycemic index calculated retrospectively from diet records of 342 individuals with non-insulin-dependent diabetes mellitus. *Am J Clin Nutr* 59: 1265–1269, 1994
30. Salmeron J, Ascherio A, Rimm EB, Colditz GA, Spiegelman D, Jenkins DJ, Stampfer MJ, Wing AL, Willett WC: Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care* 20:545–550, 1997
31. Institute of Medicine of the National Academies: *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients)*. Washington, DC, National Academy Press, 2002
32. Bantle JP, Laine DC, Castle GW, Thomas JW, Hoogwerf BJ, Goetz FC: Postprandial glucose and insulin responses to meals containing different carbohydrates in normal and diabetic subjects. *N Engl J Med* 309:7–12, 1983
33. Bantle JP, Laine DC, Thomas JW: Metabolic effects of dietary fructose and sucrose in types I and II diabetic subjects. *JAMA* 256:3241–3246, 1986
34. Bantle JP, Swanson JE, Thomas W, Laine DC: Metabolic effects of dietary fructose in diabetic subjects. *Diabetes Care* 15: 1468–1476, 1992
35. Bantle JP, Swanson JE, Thomas W, Laine DC: Metabolic effects of dietary sucrose in type II diabetic subjects. *Diabetes Care* 16: 1301–1305, 1993
36. Miller JB, Pang E, Broomhead L: The glycaemic index of foods containing sugars: comparison of foods with naturally-occurring v. added sugars. *Br J Nutr* 73:613–623, 1995
37. Gannon MC, Nuttall FQ, Westphal SA, Neil BJ, Seaquist ER: Effects of dose of ingested glucose on plasma metabolite and hormone responses in type II diabetic subjects. *Diabetes Care* 12:544–552, 1989
38. Brand JC, Nicholson PL, Thorburn AW, Truswell AS: Food processing and the glycemic index. *Am J Clin Nutr* 42:1192–1196, 1985
39. Mendosa R: Glycemic load values. *Am J Clin Nutr* 77:994–995, 2003
40. Wolever TM, Mehling C: Long-term effect of varying the source or amount of dietary carbohydrate on postprandial plasma glucose, insulin, triacylglycerol, and free fatty acid concentrations in subjects with impaired glucose tolerance. *Am J Clin Nutr* 77:612–621, 2003
41. Brand-Miller JC, Thomas M, Swan V, Ahmad ZI, Petocz P, Colagiuri S: Physiological validation of the concept of glycemic load in lean young adults. *J Nutr* 133: 2728–2732, 2003
42. Frost G, Dornhorst A: The relevance of the glycaemic index to our understanding of dietary carbohydrates. *Diabet Med* 17: 336–345, 2000
43. Wolever TM, Nuttall FQ, Lee R, Wong GS, Josse RG, Csima A, Jenkins DJ: Prediction of the relative blood glucose response of mixed meals using the white bread glycemic index. *Diabetes Care* 8: 418–428, 1985
44. Jenkins DJ, Wolever TM, Jenkins AL, Thorne MJ, Lee R, Kalmusky J, Reichert R, Wong GS: The glycaemic index of foods tested in diabetic patients: a new basis for carbohydrate exchange favouring the use of legumes. *Diabetologia* 24:257–264, 1983
45. Wolever TM, Vorster HH, Bjorck I, Brand-Miller J, Brighenti F, Mann JI, Ramdath DD, Granfeldt Y, Holt S, Perry TL, Venter C, Xiaomei W: Determination of the glycaemic index of foods: interlaboratory study. *Eur J Clin Nutr* 57:475–482, 2003
46. Foster-Powell K, Holt SH, Brand-Miller JC: International table of glycemic index and glycemic load values: 2002. *Am J Clin Nutr* 76:5–56, 2002
47. Wolever TM, Jenkins DJ: The use of the glycemic index in predicting the blood glucose response to mixed meals. *Am J Clin Nutr* 43:167–172, 1986
48. Wolever TM, Jenkins DJ, Vuksan V, Josse RG, Wong GS, Jenkins AL: Glycemic index of foods in individual subjects. *Diabetes Care* 13:126–132, 1990
49. Collier GR, Wolever TM, Wong GS, Josse RG: Prediction of glycemic response to mixed meals in noninsulin-dependent diabetic subjects. *Am J Clin Nutr* 44:349–352, 1986
50. Chew I, Brand JC, Thorburn AW, Truswell AS: Application of glycemic index to mixed meals. *Am J Clin Nutr* 47:53–56, 1988
51. Gulliford MC, Bicknell EJ, Scarpello JH: Differential effect of protein and fat ingestion on blood glucose responses to high- and low-glycemic-index carbohydrates in noninsulin-dependent diabetic subjects. *Am J Clin Nutr* 50:773–777, 1989
52. Indar-Brown K, Noreberg C, Madar Z: Glycemic and insulinemic responses after ingestion of ethnic foods by NIDDM and healthy subjects. *Am J Clin Nutr* 55:89–95, 1992
53. Coulston AM, Hollenbeck CB, Liu GC, Williams RA, Starich GH, Mazzaferri EL, Reaven GM: Effect of source of dietary carbohydrate on plasma glucose, insulin, and gastric inhibitory polypeptide responses to test meals in subjects with non-insulin-dependent diabetes mellitus. *Am J Clin Nutr* 40:965–970, 1984
54. Hollenbeck CB, Coulston AM, Reaven GM: Glycemic effects of carbohydrates: a different perspective. *Diabetes Care* 9: 641–647, 1986
55. Laine DC, Thomas W, Levitt MD, Bantle JP: Comparison of predictive capabilities of diabetic exchange lists and glycemic index of foods. *Diabetes Care* 10:387–394, 1987
56. Coulston AM, Hollenbeck CB, Swislocki AL, Reaven GM: Effect of source of dietary carbohydrate on plasma glucose and insulin responses to mixed meals in subjects

with NIDDM. *Diabetes Care* 10:395–400, 1987
57. Wolever TM, Jenkins DJ, Josse RG, Wong GS, Lee R: The glycemic index: similarity of values derived in insulin-dependent and non-insulin-dependent diabetic patients. *J Am Coll Nutr* 6:295–305, 1987
58. Wolever TM, Jenkins DJ, Vuksan V, Jenkins AL, Wong GS, Josse RG: Beneficial effect of low-glycemic index diet in overweight NIDDM subjects. *Diabetes Care* 15:562–564, 1992
59. Brand JC, Colagiuri S, Crossman S, Allen A, Roberts DC, Truswell AS: Low-glycemic index foods improve long-term glycemic control in NIDDM. *Diabetes Care* 14:95–101, 1991
60. Fontvieille AM, Rizkalla SW, Penfornis A, Acosta M, Bornet FR, Slama G: The use of low glycaemic index foods improves metabolic control of diabetic patients over five weeks. *Diabet Med* 9:444–450, 1992
61. Frost G, Wilding J, Beecham J: Dietary advice based on the glycaemic index improves dietary profile and metabolic control in type 2 diabetic patients. *Diabet Med* 11:397–401, 1994
62. Jarvi AE, Karlstrom BE, Granfeldt YE, Bjorck IE, Asp NG, Vessby BO: Improved glycemic control and lipid profile and normalized fibrinolytic activity on a low-glycemic index diet in type 2 diabetic patients. *Diabetes Care* 22:10–18, 1999
63. Giacco R, Parillo M, Rivellese AA, Lasorella G, Giacco A, D'Episcopo L, Riccardi G: Long-term dietary treatment with increased amounts of fiber-rich low-glycemic index natural foods improves blood glucose control and reduces the number of hypoglycemic events in type 1 diabetic patients. *Diabetes Care* 23:1461–1466, 2000
64. Gilbertson HR, Brand-Miller JC, Thorburn AW, Evans S, Chondros P, Werther GA: The effect of flexible low glycemic index dietary advice versus measured carbohydrate exchange diets on glycemic control in children with type 1 diabetes. *Diabetes Care* 24:1137–1143, 2001
65. Lafrance L, Rabasa-Lhoret R, Poisson D, Ducros F, Chiasson JL: Effects of different glycaemic index foods and dietary fibre intake on glycaemic control in type 1 diabetic patients on intensive insulin therapy. *Diabet Med* 15:972–978, 1998
66. Luscombe ND, Noakes M, Clifton PM: Diets high and low in glycemic index versus high monounsaturated fat diets: effects on glucose and lipid metabolism in NIDDM. *Eur J Clin Nutr* 53:473–478, 1999
67. Heilbronn LK, Noakes M, Clifton PM: The effect of high- and low-glycemic index energy restricted diets on plasma lipid and glucose profiles in type 2 diabetic subjects with varying glycemic control. *J Am Coll Nutr* 21:120–127, 2002
68. Brand-Miller J, Hayne S, Petocz P, Colagiuri S: Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. *Diabetes Care* 26:2261–2267, 2003
69. Buyken AE, Toeller M, Heitkamp G, Karamanos B, Rottiers R, Muggeo M, Fuller JH: Glycemic index in the diet of European outpatients with type 1 diabetes: relations to glycated hemoglobin and serum lipids. *Am J Clin Nutr* 73:574–581, 2001
70. Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC: Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *JAMA* 277:472–477, 1997
71. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC: Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med* 345:790–797, 2001
72. Meyer KA, Kushi LH, Jacobs DR Jr, Slavin J, Sellers TA, Folsom AR: Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. *Am J Clin Nutr* 71:921–930, 2000
73. Lundgren H, Bengtsson C, Blohme G, Isaksson B, Lapidus L, Lenner RA, Saaek A, Winther E: Dietary habits and incidence of noninsulin-dependent diabetes mellitus in a population study of women in Gothenburg, Sweden. *Am J Clin Nutr* 49:708–712, 1989
74. Colditz GA, Manson JE, Stampfer MJ, Rosner B, Willett WC, Speizer FE: Diet and risk of clinical diabetes in women. *Am J Clin Nutr* 55:1018–1023, 1992
75. Marshall JA, Hamman RF, Baxter J: High-fat, low-carbohydrate diet and the etiology of non-insulin-dependent diabetes mellitus: the San Luis Valley Diabetes Study. *Am J Epidemiol* 134:590–603, 1991
76. Tsunehara CH, Leonetti DL, Fujimoto WY: Diet of second-generation Japanese-American men with and without non-insulin-dependent diabetes. *Am J Clin Nutr* 52:731–738, 1990
77. Janket SJ, Manson JE, Sesso H, Buring JE, Liu S: A prospective study of sugar intake and risk of type 2 diabetes in women. *Diabetes Care* 26:1008–1015, 2003
78. Fung TT, Hu FB, Pereira MA, Liu S, Stampfer MJ, Colditz GA, Willett WC: Whole-grain intake and the risk of type 2 diabetes: a prospective study in men. *Am J Clin Nutr* 76:535–540, 2002
79. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 346:393–403, 2002
80. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, Keinanen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M: Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 344:1343–1350, 2001