# Glycemic index: overview of implications in health and disease[1–4]

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**ABSTRACT** The glycemic index concept is an extension of the fiber hypothesis, suggesting that fiber consumption reduces the rate of nutrient influx from the gut. The glycemic index has particular relevance to those chronic Western diseases associated with central obesity and insulin resistance. Early studies showed that starchy carbohydrate foods have very different effects on postprandial blood glucose and insulin responses in healthy and diabetic subjects, depending on the rate of digestion. A range of factors associated with food consumption was later shown to alter the rate of glucose absorption and subsequent glycemia and insulinemia. At this stage, systematic documentation of the differences that exist among carbohydrate foods was considered essential. The resulting glycemic index classification of foods provided a numeric physiologic classification of relevant carbohydrate foods in the prevention and treatment of diseases such as diabetes. Since then, low-glycemic-index diets have been shown to lower urinary C-peptide excretion in healthy subjects, improve glycemic control in diabetic subjects, and reduce serum lipids in hyperlipidemic subjects. Furthermore, consumption of low-glycemic-index diets has been associated with higher HDL-cholesterol concentrations and, in large cohort studies, with decreased risk of developing diabetes and cardiovascular disease. Case-control studies have also shown positive associations between dietary glycemic index and the risk of colon and breast cancers. Despite inconsistencies in the data, sufficient, positive findings have emerged to suggest that the dietary glycemic index is of potential importance in the treatment and prevention of chronic diseases. *Am J Clin Nutr* 2002;76(suppl):266S–73S.

**KEY WORDS** Glycemic index, insulin, glucose, diabetes, coronary heart disease, cancer

## INTRODUCTION

The concept of a glycemic index was developed to provide a numeric classification of carbohydrate foods on the assumption that such data would be useful in situations in which glucose tolerance is impaired. In many ways, the glycemic index concept was an extension of the dietary fiber hypothesis of Burkitt and Trowell (1), who suggested that foods that are more slowly absorbed may have metabolic benefits in relation to diabetes and to the reduction of coronary heart disease (CHD) risk. At the same time the dietary fiber hypothesis was formed, the concept of a cluster of diseases related to central adiposity and intraabdominal fat mass with attendant insulin resistance was being developed (2–5). The similarity of many of the issues that were raised after the formulation of both concepts further defined possible preventive and therapeutic roles for the glycemic index classification of foods. The necessary research in this area was greatly facilitated by the compilation of comprehensive glycemic index food tables (6).

## GLYCEMIC INDEX AND GLYCEMIC LOAD

The glycemic index is the indexing of the glycemic response of a fixed amount of available carbohydrate from a test food to the same amount of available carbohydrate from a standard food consumed by the same subject (initially, the standard "food" was glucose, but more recently it has been white bread; 7, 8). The blood glucose area after consumption of the test food was expressed as a percentage of the standard. The glycemic load, which assesses the total glycemic effect of the diet and has proved very useful in epidemiologic studies, is the product of the dietary glycemic index and total dietary carbohydrate (9–11). In general, the insulin responses, when measured, related well to glycemic responses (12, 13). It also appeared that the rate of digestion of the food was an important determinant of glycemic response (14, 15). Thus, the rate of liberation of the carbohydrate products of digestion in vitro over 3–5 h reflected the blood glucose area in vivo (14). Intrinsic and extrinsic factors that alter the rate of gastrointestinal motility, digestion and absorption, and the nature of the starch, cooking method, particle size, and the presence of fiber, fat, and proteins were all found to result in differences in the glycemic index (16, 17). The starchy staples of traditional cultures were often foods that had lower glycemic indexes, such as pasta, whole-grain pumper-

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[2] Presented at a symposium held at Experimental Biology 2001, Orlando, FL, 1 April 2001.

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*Am J Clin Nutr* 2002;76(suppl):266S–73S. Printed in USA. © 2002 American Society for Clinical Nutrition

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nickel breads, cracked wheat or barley, rice, dried peas, beans, and lentils (18, 19). It appears that the traditional use of low-glycemic-index carbohydrate foods in the diet was particularly prevalent among cultures that are now experiencing high rates of diabetes, eg, the Pima Indians and the Australian Aborigines, and where the change to high-glycemic-index foods has been a more recent phenomenon (20–22). Obviously, many other factors, such as obesity and reduced physical activity, must play major roles in increasing diabetes risk. Nevertheless, over time the desire for sweet foods, which resulted from rapid carbohydrate breakdown of starch in the mouth, may have resulted in the selection of rapidly digested (and hence high-glycemic-index foods) as cultures became more affluent (18). Thus, foods with high glycemic indexes are proposed further as a dietary factor that favors the development of chronic disease.

## CONCERN OVER UTILITY OF THE GLYCEMIC INDEX CLASSIFICATION

It is said that the glycemic index concept lacks clinical utility because differences in glycemic indexes between foods are lost once these foods are consumed in a mixed meal (23). Part of the reason for this is that when a mixed meal consists of several carbohydrate sources, the effect of the lower glycemic index component is diluted in proportion to the amount of carbohydrate from other foods. Appropriate calculation of the mixed-meal glycemic index is therefore required (8). Small amounts of fat added to the meal have also been considered to greatly alter the glycemic response. However, in studies in which 8–24 g fat was fed in mixed meals containing 38–104 g carbohydrate, the added fat had little effect on predicted glycemic response (24). Furthermore, although large deviations in the dietary macronutrient profile will occur over time, these differences by definition will also average out over time. Only in those subjects in whom there are substantial differentiations in daily macronutrient intake are changes in the dietary glycemic index likely to be obscured, and in such individuals any meaningful attempt at dietary modification is also likely to be difficult.

It is said that the glycemic index concept adds further needless complications and restrictions to the dietary management of diseases and that such factors cannot be justified by the modest gains that might accrue (25). An alternative view might be that the glycemic index is simply a tool for alerting the potential consumer to new starchy foods they may not otherwise have considered eating. Over time, the introduction of new foods will expand the range of food choices available, providing foods to be selected not only for their glycemic index, but also for their range of health advantages. A certain amount of dietary understanding is certainly required, eg, carrots with a high glycemic index are not taboo. It is realized that there are other considerations relevant to the consumption of carrots, and that the glycemic index is not significant in low-energy foods in which the ratio of other desirable factors (eg, minerals, vitamins, and fiber) to available carbohydrate is high.

## MECHANISMS OF ACTION

The hypothesized metabolic effects relate to the rate at which glucose is absorbed from the small intestine. A reduced rate of glucose absorption after the consumption of low-glycemic-index carbohydrate foods will reduce the postprandial rise in gut hormones (eg, incretins) and insulin. The prolonged absorption of carbohydrate seen over time will maintain suppression of the free fatty acids (FFA) and the counterregulatory responses, while at the same time achieving lower blood glucose concentrations (**Figure 1**). Over time, with the reduction in FFA concentrations and the rise in the respiratory quotient with tissue insulinization, glucose is withdrawn from the circulation at a faster rate. Consequently, blood glucose concentrations return toward baseline despite continued glucose absorption from the small intestine. The rise in peak postprandial blood glucose is therefore reduced together with the incremental blood glucose area above baseline. Studies in healthy men have shown this effect after a glucose solution was sipped at an even rate over 180 min as opposed to being consumed as a bolus at zero time (26). A marked economy in insulin secretion with sipping the glucose solution was also seen (**Figure 2**), together with improved glucose clearance ($K_G$) for intravenous glucose at 4 h. This was coincident with the lower serum FFA concentrations compared with those after the bolus intravenous-glucose-tolerance test. In part, this improvement, which was also seen after consumption of low-glycemic-index meals, may be the result of sustained tissue insulinization, suppression of FFA release (26, 27), and the absence of a counterregulatory endocrine response (26, 28). Other studies that used low-glycemic-index meals showed an improved second meal carbohydrate tolerance that was reminiscent of the Staub-Traugott effect (ie, in which the first meal improves the glucose tolerance of the second meal) and related the improved postprandial glycemia of the second standard meal to lower FFA concentrations (27, 29).

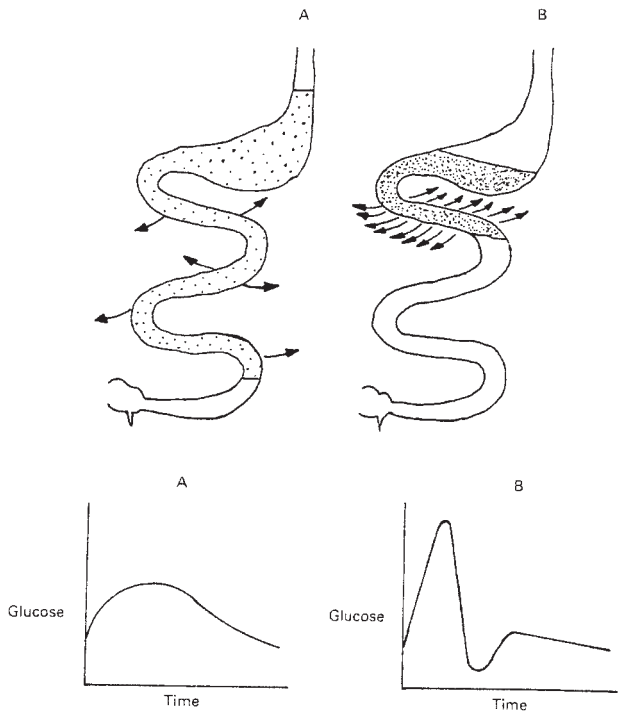


**FIGURE 1.** Hypothetical effect of feeding diets with a low (A) or high (B) glycemic index on gastrointestinal glucose absorption and postprandial blood glucose.

In addition, increased food frequency, as a model for mimicking the slow digestion of low-glycemic-index foods, has been shown to reduce glycemic and insulinemic responses over the course of a day in diabetic subjects (30, 31). In the longer term, increased food frequency has been associated with altered adi-

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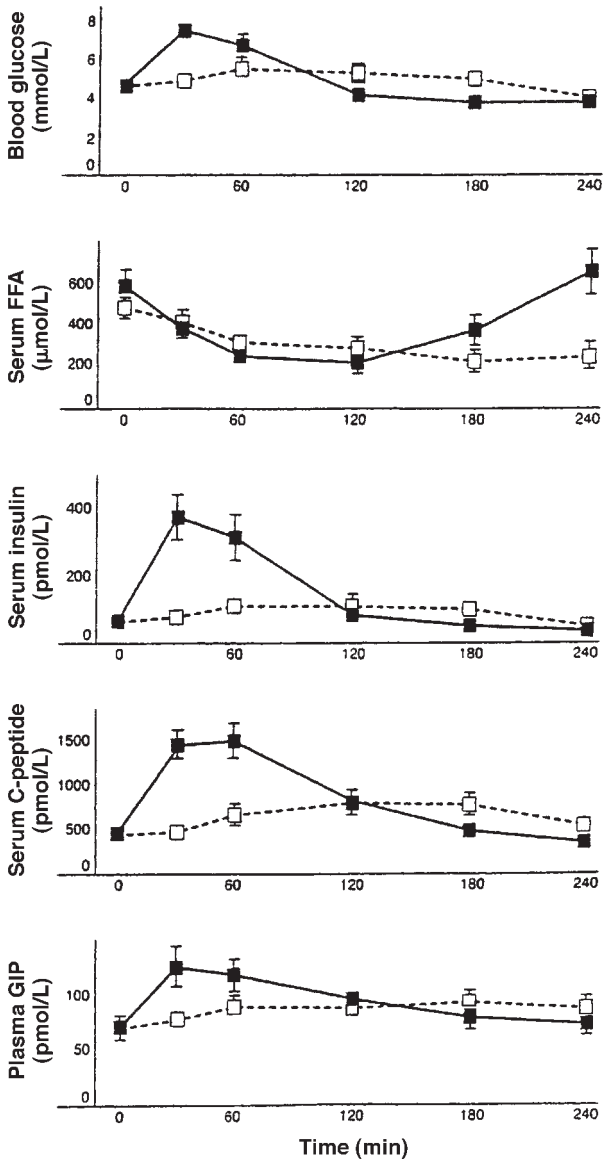


**FIGURE 2.** Mean (±SE) blood glucose, serum free fatty acids (FFA), serum insulin, serum C-peptide, and plasma gastric inhibitory polypeptide (GIP) concentrations after consuming a glucose solution (50 g in 700 mL $H_2O$) as a bolus over 5 min at time 0 (■) or after sipping the same solution over 0–3.5 h at an even rate (□).

pose tissue enzyme concentrations (32) and reduced fasting blood lipid concentrations, even though the same foods were eaten in the same amount in any given 24-h period (33–38). For reasons that are not clear, not all studies have shown these effects (39). However, spreading the nutrient load does not appear to be advantageous in terms of increased thermogenic effects that would favor weight reduction (40).

## EFFECTS IN HEALTH AND DISEASE

In healthy young men, low-glycemic-index diets have minimal effects in the short term (**Table 1**; 41, 42). In one euglycemic hyperinsulinemic clamp study, glucose disposal was impaired after 3 wk of a low-glycemic-index diet at high, but not low, insulin infusion rates (42). However, in another study of healthy men, 24-h urinary C-peptide output was found to be reduced with low-glycemic-index diets (41). In addition, LDL-cholesterol concentrations were reduced with the low-glycemic-index diet as was the serum C-peptide response to a standard breakfast after 2 wk. Nevertheless, there were higher blood glucose concentrations at 45 and 60 min that were associated with the lower C-peptide response. This apparent impairment in glucose tolerance may have been related to gut adaptive responses with less incretin secretion because the intravenous glucose tolerance test was similar in both treatments (41). On the other hand, middle-aged, insulin-resistant women, many of whom had already suffered a myocardial infarction, showed improved insulin sensitivity after an insulin tolerance test (43). In studies of persons with type 1 and 2 diabetes, most studies (10 of 14) (Table 1; 44–57) showed improvement in glycated proteins, and in one study, plasminogen activator inhibitor 1 concentrations were also reduced (54). These effects occurred despite large variations in the glycemic index difference between the test and control treatments, the short duration of many studies, and the limited numbers of subjects in others. However, in an assessment of the effects of monounsaturated fat compared with high-carbohydrate diets and low- compared with high-glycemic-index diets in patients with diabetes, the effects of both interventions on glycated proteins were comparable (**Figure 3**; 59). After consuming a low-glycemic-index diet for 1 mo, patients with hyperlipidemia showed reduced LDL-cholesterol and triacylglycerol concentrations (in those with higher triacylglycerol concentrations), despite no significant difference in body weight (58). These data are not definitive but suggest a potential therapeutic utility of the glycemic index concept.

## EPIDEMIOLOGIC INSIGHTS

Two studies (one that used the third National Health and Nutrition Examination Survey database and the other a British study) showed a negative relation between glycemic index and HDL cholesterol, suggesting that low-glycemic-index diets may preserve HDL cholesterol and thus have a potentially positive effect in reducing CHD risk (**Table 2**; 65, 66). In relation to CHD, the Nurses' Health Study showed a negative relation between fatal and nonfatal myocardial infarctions and glycemic index, as well as glycemic load (11). Of particular interest was the observation that there was no association of dietary glycemic index with CHD in persons with a body mass index (in $kg/m^2$) $<23$, suggesting that the effect of dietary glycemic index may be increasingly important in those with a greater degree of insulin resistance (Table 2). On the other hand, no significant association of glycemic index or glycemic load and CHD was seen in older men in the Zutphen study (67). The relatively small number of subjects in this study ($<1500$) and their age at the start of the study (65–84 y) may be part of the explanation: large numbers of the original cohort had already died or were excluded because of diabetes or CHD (Table 2). The population left was therefore preselected and may have been less vulnerable to environmental factors.

In relation to diabetes outcome, both the Nurses' Health Study (9) and the Health Professionals Studies (10) showed an inverse relation between glycemic index and the risk of developing diabetes by using a validated food-frequency questionnaire. In the case of the Health Professionals Study, both the association and

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**TABLE 1**
Controlled studies of the effects of low-glycemic-index (GI) diets on carbohydrate and lipid metabolism in healthy, diabetic, and hyperlipidemic subjects[1]

| Subjects | Duration | Change in dietary GI[2] | Change in glycated proteins | Type of glycated proteins | Change in blood lipids | Comments | First author, year, and reference |
|---|---|---|---|---|---|---|---|
| | *wk* | | % | | % | | |
| Healthy men aged 33 y (*n* = 6) | 2 | −41 | −7[3,4] | Fructosamine | −15 TC[3,5] | −32% urinary C-peptide excretion,[3,5] −12% 24-h creatine clearance[3,5] | Jenkins, 1987 (41) |
| Young men aged 24 y (*n* = 7) | 3 | −24 | NA | NR | NR | Euglycemic hyperinsulinemic clamp showed no difference at low plasma insulin but was reduced with low-GI diets at high plasma insulin | Kiens, 1996 (42) |
| Insulin-resistant, middle-aged women (post MI) (*n* = 28) | 3 | −18 | NA | NR | No lipid changes | With short insulin-tolerance test, in vivo insulin sensitivity improved after low-GI diet | Frost, 1998 (43) |
| Diabetic | | | | | | | |
| Type 1, aged 12 y (*n* = 7 M) | 6 | −12 | −19[3,4] | Fructosamine | −14 TC[3,4] | Reduced postprandial glucose response to a standard meal (90–180 mm) after low-GI diet | Collier, 1988 (44) |
| Type 1, aged 44 y (*n* = 4 M, 4 F) | 3 | −14 | −18[3,4] | Fructosamine | −5.8 TG[3,4] | −8.9% phospholipids,[3,4] – 6.1% in daily insulin needs with low-GI diet[3,4] | Fontvieille, 1988 (45) |
| Type 1 (*n* = 7 M, 2 F) | 2 | −27 | −6.5[5] | Fructosamine | NR | Fasting blood glucose 23% lower with low-GI diet compared with control; no changes in insulin therapy | Lafrance, 1998 (46) |
| Type 1, aged 28 y (*n* = 54) | 24 | −20 | −5.5[5] | Hb $A_{1c}$ | — | Study design allowed for 35-g difference in fiber content between diets; −8.6 mmol/L daily blood glucose and less hypoglycemic events with low-GI diet | Giacco, 2000 (47) |
| Type 1, aged 8–13 y (*n* = 53 M, 51 F) | 52 | −1.2 | −6.5[3,5] | Hb $A_{1c}$ | NR | −31% hyperglycemic events with low-GI diet; no changes in insulin therapy | Gilbertson, 2001 (48) |
| Type 2, aged 65 y (*n* = 2 M, 6 F) | 2 | −23 | −6.6[3,4] | Hb $A_{1c}$ | −5.8 TC[3,4] | −30% fasting blood glucose with low-GI diet (−8% NS with control)[3,4] | Jenkins, 1988 (49) |
| Type 2, aged 62 y (*n* = 10 M, 6 F) | 12 | −14 | −11[3,4] | Hb $A_{1c}$ | — | −75% 24-h urinary glucose output,[3,5] used pasta and legumes to reduce GI | Brand, 1991 (50) |
| Type 2, overweight (BMI = 32), aged 63 y (*n* = 3 M, 3 F) | 6 | −28 | −8[3,5] | Fructosamine | −6.8 TC[3,5] | −22.4% TG for 5 subjects with TG < 2.2 mmol/L[3,5] | Wolever, 1992 (51) |
| Type 2, aged 67 y (*n* = 7 M, 8 F) | 2 | −27 | −3.4[3,5] | Fructosamine | −7[3,5] TC | −30% 24-h urinary C-peptide,[3,5] −29% postbreakfast blood glucose,[3,5] TG rose with control (*P* = −0.027) and fell with low-GI diet but the 2-wk treatment difference was NS | Wolever, 1992 (52) |
| Type 2, BMI = 29, aged 56 y (*n* = 20 M, 6 F) | 12 | −5 | −16[3,4] | Fructosamine | −12.3 TC[3,4] −26 TG[3,4] | −21% fasting blood glucose in low-GI group[3,4] | Frost, 1994 (53) |
| Type 2, BMI = 25.3, aged 65 y (*n* = 15 M, 5 F) | 3 | −31 | −5.9[3,4] | Hb $A_{1c}$ | −5 TC[3,5] −8 LDL-C[3,5] | −31% 9-h blood glucose profile,[3,5] −53% PA1-1[3,5]; diet used same foods and relied on grinding (fine particle size) to raise GI | Järvi, 1999 (54) |
| Type 2, BMI = 30.4, aged 57.4 y (*n* = 14 M, 7 F) | 4 | −20 | −1.8[5] | Fructosamine | +6 HDL[3,5] | Fasting plasma glucose 8% lower with low- compared with high-GI diet (NS); diets did not contain legumes or pasta | Luscombe, 1999 (55) |
| Type 1 (*n* = 10 M, 2 F) and type 2 (*n* = 2 M, 4 F), BMI = 24.8, aged 47.2 y | 5 | −26 | −13[3,5] | Fructosamine | −20 TG[3,5] | −11% fasting blood glucose,[3,5] −13% mean daily blood glucose[3,5]; beans and pasta, rye bread, and fruit used to lower GI; balanced for total and soluble fiber | Fontvieille, 1992 (56) |
| Type 1, BMI = 21, aged 26 y (*n* = 12); type 2, BMI = 30, aged 59 y (*n* = 12) | 4 | −5 | −3[5] | Hb $A_{1c}$ | No lipid differences | No postprandial blood glucose differences found between high- and low-GI diets; rice, potatoes, pasta, carrots, and beetroot used in the high-GI diet; legumes used in the low-GI diet | Calle-Pascual, 1988 (57) |
| Hyperlipidemic subjects, BMI = 24, aged 47.5–57 y (*n* = 30) | 4 | −17 | −1.3 (*n* = 6)[5] | Fructosamine | When TG >2.0 mmol/L (*n* = 24); −8.8 TC,[3,5] −19.3 TG,[3,5] −9.1 LDL-C[3,5] | Changes in weight loss and fat intake did not explain the lipid effects; GI was lowered with pumpernickel bread, bulgur, pasta, barley, and legumes; 5% reduction in 24-h urinary C-peptide (*n* = 10) (NS) | Jenkins, 1987 (58) |

[1] Hb $A_{1c}$, glycated hemoglobin; MI, myocardial infarction; NR, not reported; PAI-1, plasminogen activator inhibitor 1; TC, total cholesterol; TG, triacylglycerol. BMI is in kg/m$^2$.
[2] The reference food was white bread.
[3] $P < 0.05$.
[4] Difference from baseline after treatment (within low-GI treatment).
[5] Endpoint difference (between treatments).

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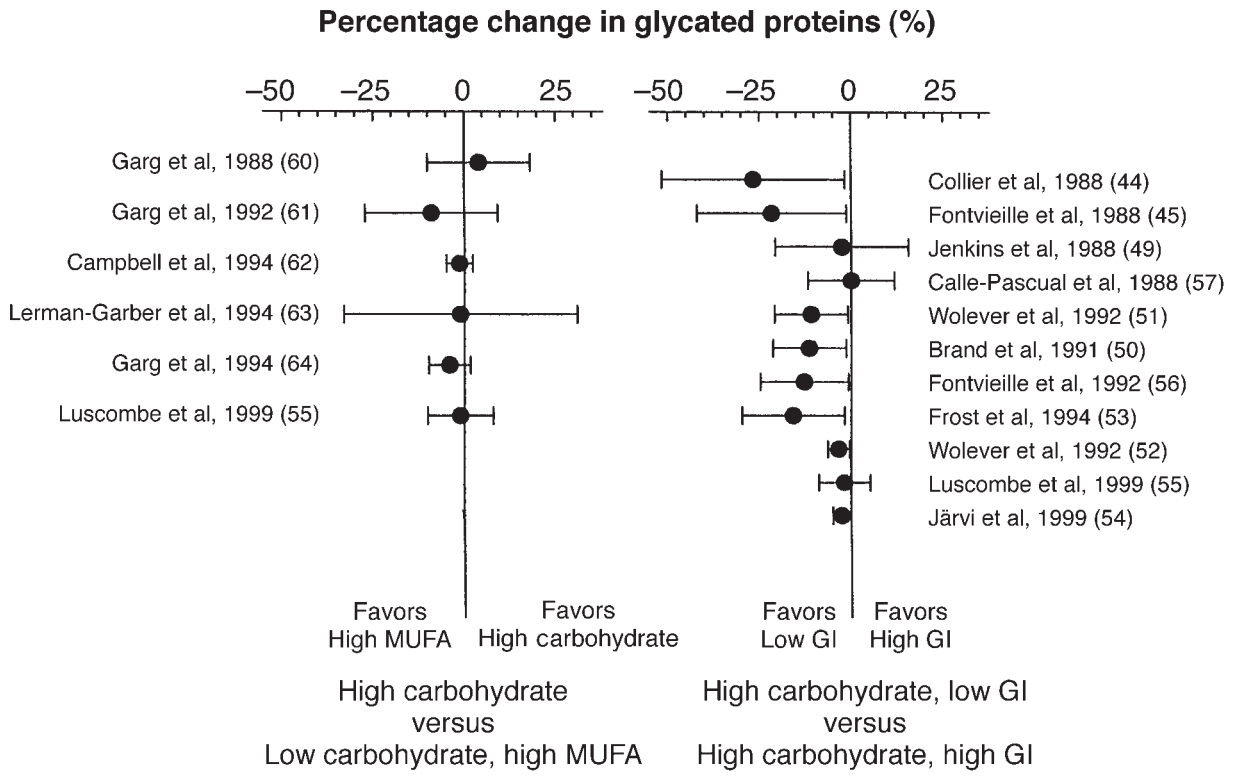


**FIGURE 3.** Mean (±SD) difference from the control diet in glycated proteins (hemoglobin $A_{1c}$ or serum fructosamine) in diabetic subjects consuming either low-glycemic-index (GI) or high-monounsaturated–fatty acid (MUFA) diets. The vertical line indicates no effect. Adapted from reference 59.

the trend became significant only after adjustment for fiber intake (10). The Iowa Women's Health Study, although it also showed a negative association between cereal fiber intake and the risk of diabetes, showed no significant association between glycemic index or load and diabetes incidence (69). This discrepancy may relate to the frequency of application of the food-frequency questionnaire during the study, the glycemic index database used, and the age range of the subjects studied. Older cohorts selected as free of disease at the outset of a study may already have excluded a significant proportion of vulnerable subjects. In this respect, the Iowa Women's Health Study subjects were generally older than the subjects in the Nurses' Health Study (Table 2).

The glycemic index may have relevance to cancer prevention. In addition, insulin resistance and insulin-like growth factors have been implicated in the so-called diet-related cancers: colon, breast, and prostate (73, 74). Preliminary data support this association for colon cancer (75). A case-control study showed a direct association between dietary glycemic index and colon cancer risk. A sedentary lifestyle in conjunction with a high-glycemic-index diet increased risk relative to a sedentary lifestyle with a low dietary glycemic index or relative to an active lifestyle with a high dietary glycemic index (76). An Italian case-control study reported that the dietary glycemic index was related to colorectal cancer risk, ie, the higher the glycemic index, the greater the risk of colorectal cancer (71). The same relation of glycemic index and disease was also shown for breast cancer (72). Prostate and ovarian cancers, among other forms of cancer, may be influenced by the dietary glycemic index. In these cases, insulin resistance and insulin-like growth factors have also been implicated (72, 77). Therefore, the greater part of the epidemiologic literature provides additional support for a role of dietary glycemic index in disease.

## NEWER ASPECTS OF GLYCEMIC INDEX RESEARCH

There is considerable interest in the relations between insulin resistance, the generation of reactive oxygen species, tissue damage, and the liberation of proinflammatory cytokines and acute phase proteins, the latter appearing to be powerful markers of chronic diseases, notably CHD (78). The dietary glycemic index may play a role in this sequence of events.

Studies have shown that the postprandial rise in glucose is consistent with depression of serum antioxidants, including lycopene and vitamin E (79, 80). Presumably, the higher the glycemia, the greater the postprandial depression of serum antioxidants (80). Finally, supplementing subjects' diets with the antioxidant vitamin E has been shown to improve glycemic control (81). Studies such as these suggest a possible beneficial role for low-glycemic-index diets by reducing oxidative damage.

It has been suggested that obesity is related to glycemic index or glycemic load (28, 82, 83). Studies on altering glycemic index and load have indicated that the lower the glycemic index and load of the first meal, the less food is consumed in the subsequent meal (28). Longer-term studies are required to define the relevance of these interesting findings.

Finally, more studies are required to assess the relation of glycemic index to chronic diseases, including cancer, CHD, and

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**TABLE 2**

Cross-sectional and cohort studies of the relation of glycemic index (GI) to the risk of cardiovascular disease, diabetes, and cancer and its association with HDL and glycated hemoglobin (Hb $A_{1c}$)[1]

| Subjects | Study type | Duration | Difference in GI | Main effect | Comments | First author, year, and reference |
|---|---|---|---|---|---|---|
| HDL | | | | | | |
| NHANES III 20-y survey, BMI = 26.5 ($n$ = 6825 M, 7052 F) | Cross-sectional survey, FFQ | NR | Quintiles, GI ≤75 to ≥88 | For HDL with increasing quintile of GI 1.38–1.27, $P$ for trend < 0.001 | HDL effect in men and women with both high (>25) and low BMI (<25), after age adjustment | Ford, 2001 (65) |
| British Adults (1986–1987 survey) aged 16–64 y ($\bar{x}$ = 39.9 y) ($n$ = 699 M, 721 F) | Cross-sectional survey, 7-d DH | NR | Quintiles, mean GI: 86 | $P$ for trend (univariate analysis) for HDL (negative) < 0.001 | HDL related to total carbohydrate and starch $P$ < 0.001 (negative); 93 subjects excluded from analysis because DH and estimated energy needs discrepant by ≥1000 kcal (4187 kJ) | Frost, 1999 (66) |
| CHD | | | | | | |
| US Nurses' Health Study, aged 38–63 y, BMI = 25 ($n$ = 75 521) | Cohort, FFQ | 10 y | Quintiles, 72–80 (by GL) | CHD risk; GL, $P$ for trend < 0.0001; GI, $P$ for trend < 0.008; multivariate analysis | The relative risk of CHD was seen to increase with GL when BMI > 23 | Liu, 2000 (11) |
| Elderly Dutch men (Zutphen Study) aged 65–84 y in 1955, BMI = 25.5 (555 of 1088 men still alive from original survey plus 711 new men of same age) | Cohort and cross-sectional dietary recall at interview | 10 y (1985–1995) | Quintiles, 74–85 | CHD risk, no GI association | Earlier analysis of Zutphen data show disease-diet relations (1993–1995) but none reported in current assessment | van Dam, 2000 (67) |
| Hb $A_{1c}$ | | | | | | |
| Type 1 diabetic subjects aged 33 y (51% M), BMI = 26.7 ($n$ = 2810) | Survey, 3-d DH | NR | Quartiles, GI: 74.9–88.55 | Hb $A_{1c}$: 6.05–6.66 for quartile of GI 1–4, $P$ for trend = 0.0001 | For HDL (negative) and TG (positive), $P$ for trend in biovariate model = 0001 and 0.01, respectively | Buyken, 2001 (68) |
| Diabetes | | | | | | |
| Nurses' Health Study, aged 40–65 y ($n$ = 65 173 F) | Cohort FFQ | 6 y | Quintiles, GI: 64–79 | Diabetes RR: 1.37 (1.09, 1.71) for 5th quintile of GI, 1.47 (1.16, 1.86) for 5th quintile of GL | $P$ for trend = 0.005 after adjustment for load for diabetes for GI fiber ($P$ = 0.04 unadjusted for fiber); $P$ for trend = 0.003 for diabetes and GL after adjustment for cereal fiber | Salmeron, 1997 (9) |
| Health Professionals Study, aged 40–75 y ($n$ = 42 759 M) | Cohort FFQ | 6 y | Quintiles, GI: 65–79 | Diabetes RR: 1.37 (1.02, 1.83) for 5th quintile of GI after fiber adjustment | GI: $P$ for trend = 0.03 after adjustment for fiber; no significance for load; for high glycemic level and low cereal fiber, the RR for diabetes was 2.17 (1.04, 4.54) | Salmeron, 1997 (10) |
| Older women aged 55–69 y ($n$ = 35 988) | Cohort FFQ | 6 y | Quintiles, GI: <58 to >80 | Diabetes RR for GI in 3rd quintile: 1.22 (1.02, 1.47) but negative $P$ for trend; no effect for GL | RR of diabetes increased and then decreased with increasing quintiles of GI | Meyer, 2000 (69) |
| Cancer | | | | | | |
| US colon cancer patients ($n$ = 1099 M, 894 F) and controls ($n$ = 1290 M, 1120 F) | Case-control FFQ | 1991–1994 | NR | Colorectal cancer risk for GI in 5th quintile: 1.37 for M (1.04, 1.82), and 1.34 for F (1.00, 1.81) (after multiple adjustments, eg, age, BMI, physical activity, NSAIDs, and fiber) | Being sedentary plus a high GI resulted in a higher risk than being active plus a high GI or sedentary plus a low GI; the daily average GI was calculated differently from other epidemiologic studies; GL was not calculated | Slattery, 1997 (70) |
| Italian colorectal cancer patients ($n$ = 1125 M, 828 F) and hospital controls ($n$ = 2073 M, 208 F); BMI = 26 (mean of middle tertile) | Case-control FFQ | 1992–1996 | Quintiles (upper limit), GI: 70.7–79.6 (4th quintile) | Colorectal cancer risk for GI in 5th quintile: 1.7 (1.4, 2.0), $P$ for trend <0.001 (after multiple adjustments, eg, age, sex, physical activity, alcohol, and fiber) | Similar findings for GL | Franceschi, 2001 (71) |
| Italian breast cancer patients ($n$ = 2569) and hospital controls ($n$ = 2588) | Case-control FFQ | 1991–1994 | Quintiles (upper limit), GI: 69.6–78.9 (4th quintile) | Breast cancer risk for GI in 5th quintile: 1.4 (1.1, 1.6), $P$ for trend <0.01 (after multiple adjustments, eg, age, physical activity, alcohol, fiber, and parity) | Similar findings for GL | Augustin, 2001 (72) |

[1]CHD, coronary heart disease; DH, diet history; FFQ, food-frequency questionnaire; GL, glycemic load; NHANES III, third National Health and Nutrition Examination Survey; NSAIDS, nonsteroidal antiinflammatory drugs; RR, relative risk; NR, not reported.

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diabetes. In addition, large-scale intervention studies are underway and more are required to define the theraputive utility of the glycemic index concept.

## CONCLUSION

The dietary glycemic index concept suggests a possible role for the rate of carbohydrate digestion in the prevention and treatment of chronic disease, including those diseases that have been highlighted in the dietary fiber hypothesis and are now associated with insulin resistance. This concept is no longer novel; pharmacologic approaches to slowing carbohydrate absorption, notably the use of α-glycoside hydrolase inhibitors, are now accepted in the management of diabetes.

We thank Thomas Wolever for his help and provision of Figure 3.

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