

# The Role of the Glycemic Index in the Prevention and Management of Diabetes: A Review and Discussion

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## ABSTRACT

Achieving and maintaining blood glucose (BG) levels as close to normal as possible is crucial for the prevention of long-term complications in type 1 and type 2 diabetes and requires an intensive approach to management. Nutrition is of the utmost importance in intensive diabetes management and has been described as the cornerstone of care. A major focus of the nutritional management of diabetes is the improvement of glycemic control by balancing food intake with endogenous and/or exogenous insulin levels. Several attempts have been made to control the glycemic response to food, particularly to foods rich in carbohydrate. One way to classify the glycemic response to various carbohydrate-containing foods is the glycemic index (GI).

Although the concept of the GI has made it easier to predict the glycemic response of carbohydrate-containing foods, the clinical utility of this concept continues to be questioned. However, a growing body of scientific evidence, including data from epidemiological and clinical studies, has linked low-GI diets with improved outcomes, i.e. decreased risk of development of type 2 diabetes, and improvement in metabolic control and quality of life in individuals with diabetes. Still, debate continues about how the GI can best be incorporated

## RÉSUMÉ

Atteindre et maintenir la glycémie aussi près que possible de la normale est essentiel pour prévenir les complications à long terme du diabète de type 1 et de type 2 et exige une démarche rigoureuse. L'alimentation est de la plus haute importance pour le traitement intensif du diabète et on dit qu'elle est la pierre angulaire des soins. Un des buts importants de l'alimentation en présence de diabète est d'améliorer l'équilibre glycémique en créant un équilibre entre l'apport alimentaire et les concentrations endogènes et/ou exogènes d'insuline. On a souvent tenté de contrôler la réponse de la glycémie aux aliments, surtout ceux qui sont riches en glucides. Un des moyens de classer la réponse de la glycémie à la consommation de divers aliments qui contiennent des glucides est l'indice glycémique.

Le concept d'indice glycémique permet de prévoir plus facilement la réponse glycémique aux aliments qui contiennent des glucides, mais l'utilité clinique de ce concept continue d'être mise en doute. Cependant, un nombre croissant d'observations scientifiques, y compris des données provenant d'études épidémiologiques et cliniques, indiquent qu'une alimentation faible en glucides améliore le devenir des patients, c'est-à-dire qu'elle réduit le risque de diabète de type 2 et améliore l'équilibre métabolique et la qualité de vie chez les personnes atteintes de diabète. Pourtant, le débat continue sur la façon d'incorporer l'indice glycémique à la pratique courante des professionnels de la santé. Ce résumé est une analyse documentaire qui évalue l'utilité clinique de l'indice glycémique dans le traitement du diabète par l'alimentation et donne des suggestions sur la façon de l'intégrer à la pratique courante.

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into everyday practice by healthcare professionals. This paper reviews the literature, assesses the clinical utility of the GI in the nutritional management of diabetes and provides suggestions on how to integrate it into practice.

## INTRODUCTION

The goal of the clinical management of type 1 and type 2 diabetes is to control metabolic abnormalities in order to prevent both acute (hyperglycemia, hypoglycemia) and long-term (retinopathy, nephropathy, neuropathy, cardiovascular disease [CVD]) complications without negatively affecting quality of life (1). Achieving and maintaining blood glucose (BG) levels as close to normal as possible is crucial for the prevention of long-term complications in both type 1 and type 2 diabetes; however, attaining stringent glycemic targets requires an intensive approach to management. Nutrition is of utmost importance in the intensive management of diabetes and is often described as the cornerstone of care. A major focus of nutritional management of diabetes is the improvement of glycemic control by balancing food intake with endogenous and/or exogenous insulin levels.

Several strategies to control the glycemic response to food, particularly those rich in carbohydrate, have been developed and investigated. These include carbohydrate counting, use of very low carbohydrate and starvation diets, artificial sweeteners, pharmacotherapy and inhibitors of carbohydrate absorption. One way to classify the glycemic response to various carbohydrate-containing foods is the glycemic index (GI). This term was first coined by David Jenkins and colleagues to describe the extent to which BG rises after ingestion of 50 g of available carbohydrate in a test food compared with ingestion of an equivalent amount of carbohydrate in a reference food, usually glucose or white bread (2). Although the GI has made it easier to predict the glycemic response to carbohydrate-containing foods, the clinical utility of this concept continues to be questioned (3,4). There is also concern that people living with diabetes may misapply the GI (5). Although not currently endorsed by the American Diabetes Association (ADA) (6,7), use of the GI is advocated by the World Health Organization (WHO) (8) and diabetes associations in Europe, Australia, South Africa and Canada (9). The use of the GI in practice, and the use of low-GI diets in particular, was advocated in a report prepared by the joint Food and Agriculture Organization (FAO)/WHO Expert Consultation Committee (8). The report highlights how the GI can be applied to mixed meals, or to entire diets, and favours its use in the management of individuals at high risk of developing diabetes and those with established diabetes (8,9).

In the management of type 1 and type 2 diabetes, glycemic control is assessed mainly by fasting and preprandial BG levels and by longer-term indices such as glycosylated hemoglobin (A1C) (1). However, postprandial glycemia should also be considered (10), as there is evidence suggesting

it may be an independent risk factor in the development of diabetes-related complications, including CVD (11). With respect to diet composition, both the amount and source of carbohydrate, as defined by the GI, are important factors influencing postprandial glycemia (12). Furthermore, a growing body of evidence, including data from epidemiological and clinical studies, has linked low-GI diets with improved outcomes such as a decreased risk of development of type 2 diabetes (13,14) and improvements in both metabolic control (15-23) and quality of life (23) in individuals with established diabetes. However, debate continues as to how the GI can best be incorporated into everyday practice by healthcare professionals and into the daily lives of individuals with diabetes.

This technical review defines the concept of GI, reviews the relevant research, assesses the clinical utility or usefulness of the GI in the nutritional management of diabetes, and provides suggestions for how to integrate this concept into practice based on current knowledge. All relevant GI literature (studies, reviews, meta-analyses, editorial commentaries) from 1980 to 2003 were examined.

## WHAT IS THE GI?

The term “glycemic index” describes the acute glycemic response to different types or sources of carbohydrate compared to a reference carbohydrate (glucose or white bread). Glycemic response and GI are not synonymous (24). Glycemic response to food refers to the extent to which BG rises with food ingestion. The GI was developed as a way to “standardize” the glycemic response to carbohydrate (i.e. sugars and starch) and foods rich in carbohydrate, such as grain products, fruits, vegetables and dairy products (2,25). The GI is, therefore, an index or ranking of the postprandial glycemic response to different sources of carbohydrate in comparison with a reference carbohydrate. The GI is expressed as the incremental area under the BG response curve, above baseline, over a period of 2 to 3 hours, excluding values that fall below baseline (26). The GI is a reflection of the rate of conversion of carbohydrates into glucose. With quickly converted carbohydrates (high GI) there is a rapid rise in BG and a larger insulin secretion (26). Slowly converted carbohydrates (low GI) produce lower BG concentrations and lower insulin responses (26). With low-GI carbohydrates, BG may remain slightly above fasting levels for a longer period of time compared with high-GI carbohydrates, but cause less of a “spike” in both the BG and insulin response (26). The calculation of the GI is noted in Figure 1. Figure 2 illustrates the concept of the GI by depicting the

area under the BG response curve of spaghetti (test food) compared with glucose (reference food).

The methodology of establishing the GI requires that, after an overnight fast, individuals consume in random order 50 g of available carbohydrate (excluding fibre [8,27]) of a test or reference food and consume a similar quantity of carbohydrate in a test or reference food after an overnight fast on an alternate day (28). BG levels are measured every 15 to 30 min over a period of 2 to 3 hours. The reference food (white bread or glucose) is assigned a value of 100, against which test foods are compared. To reduce variability, the reference food should be repeated at least 3 times by each subject (27,28). The mean or average GI obtained from approximately 10 individuals is used as the GI rating for a particular food (29). To simplify interpretation, the GI is often divided into 3 categories: high (>70), medium (55 to 70) and low (<55). The numbers refer to percentages in comparison with the reference food. It should be noted that the GI values based on a glucose standard are lower than those based on the white bread standard, but the relative ranking remains the same. If needed, it is possible to convert from one to the other using a factor of 1.4 (100/70), since white bread has a GI of 70 when compared to glucose (27), i.e. the area under the BG response curve produced by white bread is 70% of that produced by an equivalent amount of carbohydrate when consumed as glucose. Some researchers prefer to use white bread instead of glucose as the reference food, because it is more typical of what humans eat. However, others prefer to use glucose, as it is standardized, unlike white bread. A recent multi-laboratory study confirmed that although white bread can be used as the reference food, glucose is a more logical choice for international use (27).

## FACTORS INFLUENCING THE GI RATING

Factors that influence the rate of conversion of carbohydrates into glucose and, in turn, influence whether a food will have a low- or high-GI rating are summarized in Table 1 and include physical state of starch, sugar content, acidity and fibre content.

The physical state of starch appears to have the greatest influence on the GI rating. Degree of starch gelatinization, physical form (e.g. raw or cooked, whole or ground) and the amylose to amylopectin ratio are the main physical factors influencing the GI rating of starchy foods. The extent of starch breakdown during cooking and processing can greatly affect GI. For example, the GI of potatoes increases when they are mashed vs. whole (30), and whole kidney beans have

a much lower GI than ground kidney beans (31). By contrast, other foods such as carrots are relatively unaffected by cooking (5). As a rule, preservation of the initial food structure and less processing is associated with a lower GI. As well, a study of 25 fibre-containing foods (32) indicated that total fibre content, including uronic acids found primarily in insoluble fibre, is more important than soluble fibre content in predicting GI. Legumes are particularly high in uronic acid, which may explain why legumes tend to have a low GI. Foods with a high content of fructose, sucrose and galactose, which are found predominantly in fruits, candy, soft drinks and milk products, also tend to have a lower GI than foods with a high starch or glucose content.

## AREAS OF CONTROVERSY

Since its development, the GI has engendered much debate. Areas of controversy include its application in mixed meals, its effectiveness as a clinical tool and its use in clinical practice.

### Application in mixed meals

Much of the controversy surrounding the clinical utility of the GI pertains to its application to mixed meals. In mixed meals, typical servings may not reflect portions used for GI testing, and the presence of other dietary components, specifically fat and protein, may negate any differences in GI observed when individual foods are consumed alone (3,33).

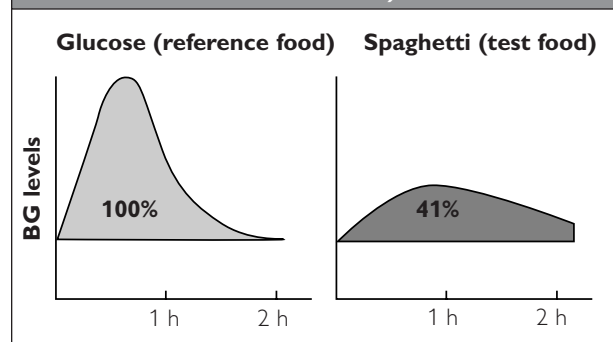
Some investigators have found that the GI of some foods can predict glycemic and insulin response when applied to mixed meals in individuals with and without diabetes (34-38), while others have found the opposite (39-42). This discrepancy in findings may be related to differences in populations studied, length of study and methodology, particularly methods used for calculating the glycemic response, e.g. some

**Figure 1. Calculation of the GI**

$$\text{GI} = \frac{\text{Incremental BG area of 50-g test carbohydrate}}{\text{Incremental BG area of 50-g reference carbohydrate}} \times 100$$

BG = blood glucose  
GI = glycemic index

**Figure 2. Measuring the GI of food (adapted from reference 35)**



The effect of food on BG levels is calculated using the AUC (shaded area). The AUC of the test food is compared with the same area after the reference food (usually 50 g of pure glucose or a 50-g carbohydrate portion of white bread).

AUC = area under the curve  
BG = blood glucose  
GI = glycemic index

investigators (39-42) used different methods for calculating glycemic response than those originally proposed and recommended (8,26,27). It was recently recommended that investigators adopt consistent methodology (27), as studies that used the recommended methods (34-38) have demonstrated that the GI can be applied to mixed meals.

It is possible to estimate the GI of an entire meal. The GI of a mixed meal (i.e. the meal GI) can be calculated by establishing the percentage of carbohydrate contributed by each serving of carbohydrate food in the meal and by knowing the GI assigned to each food (Table 2). All GI studies to date, especially those that pertain to low-GI and high-GI meals and diets, are based on the meal GI calculation. The GI concept has therefore been extended to typical meals and even to entire diets by calculating the GI of an entire day as the mean GI of each meal (13,14).

Another concept that takes into account both the amount of carbohydrate (grams) in a typical serving of a mixed meal and the GI rating is glycemic load (grams of carbohydrate x GI) (13,14). The concept of glycemic load may also have important health implications (13,14,43). The glycemic load of a meal can be reduced either by reducing the amount of carbohydrate and/or selecting foods that have a lower GI (44). Further research is needed to validate the clinical implications and clinical utility of the concept of glycemic load.

#### *Fat and protein content of a meal*

Fat and protein both affect glycemic response and this response is dependent on the absence or presence of diabetes and on the type of diabetes. Since protein is a potent stimulator of both insulin and glucagon, the effect of protein in

individuals without diabetes and those with type 2 diabetes is to maintain or reduce postprandial glycemic levels (45,46). As individuals with type 1 diabetes have no endogenous insulin, the effect of protein is to stimulate glucagon and thus increase glycemic levels (47). The resultant glycemic level therefore depends on the supply and pharmacokinetics of exogenous insulin. However, the effect of protein on glycemic response is delayed for several hours and does not appear to significantly affect immediate postprandial glycemia and, hence, fast-acting insulin needs (47).

Although fat does not have a direct impact on glycemic response, it may influence glycemic response indirectly by delaying gastric emptying, and, thus, carbohydrate absorption, and by altering insulin sensitivity (12). However, evidence suggests that, although fat may delay the glycemic response to carbohydrate (47-49), the impact is clinically insignificant, especially with respect to quantities of fat typically consumed per meal (47-49). In contrast, the types of fat consumed may affect insulin sensitivity and, thus, glycemic response (12). In their recent review of the evidence regarding the role of types of fat and carbohydrate on risk of development of type 2 diabetes, Hu and colleagues point out that recent evidence is suggestive of the role of specific types of fat rather than total fat in the development of type 2 diabetes (12). It appears that polyunsaturated fat and possibly long-chain n-3 fatty acids could be protective, whereas a higher intake of saturated fat and trans fat could adversely affect glucose metabolism and insulin resistance (12). They also point out that the type of carbohydrate, classified according to GI, is also very important in this regard, and conclude that in addition to total energy balance, dietary recommendations to prevent and manage

**Table 1. Factors that influence the GI rating of a food (adapted from reference 35)**

<b>Factor</b>	<b>Mechanism</b>	<b>Examples of foods</b>
Degree of starch gelatinization	The less gelatinized (swollen) the starch, the slower the rate of digestion.	Spaghetti, oatmeal
Physical form of food	The fibrous coat around beans and seeds and intact plant cell walls acts as a barrier; slowing down access of enzymes to starch inside.	Pumpernickel and whole grain bread, legumes, pasta cooked al dente
Amylose to amylopectin ratio	The more amylose a food contains, the slower its rate of starch digestion.	Basmati rice, legumes, cornstarch
Fibre	Viscous, soluble fibres increase the viscosity of the intestinal contents and slow down the interaction between the starch and the enzymes.  Finely milled whole grain flours have fast rates of digestion and absorption because the fibre is not viscous.	Rolled oats, beans, lentils, apples  White bread, some breakfast cereals
Sugar (sucrose)	The digestion of sugar (sucrose), which is composed of glucose and fructose, produces only half as many glucose molecules as the same amount of starch. The presence of sucrose also restricts gelatinization of the starch molecule by binding to water during manufacturing.	Some cookies, some breakfast cereals
Acidity	Acids in food slow down gastric emptying.	Oranges, sourdough bread

diabetes should focus more on the quality of both fat and carbohydrate in the diet rather than on quantity alone (12).

### Glycemic index vs. fibre content

Some critics of the GI believe that any impact of GI is actually due to the fibre content of the food. Although there is a relationship between the dietary fibre content and the GI rating of a food (32), this relationship is modest, accounting for only 21% of the variability of the GI rating (32). However, the importance of dietary fibre in the prevention and management of diabetes must still be considered, especially in light of recent epidemiological and clinical evidence (13,14,22,50,51). Three recent epidemiological studies have found a significant protective effect of cereal fibre intake (13,14,50), especially when coupled with a low-GI intake (13,14). The benefits of a high-fibre diet, therefore, appear to be additive in the context of a low-GI intake. With respect to management of diabetes, a recent study in adults with type 2 diabetes demonstrated that a high dietary fibre intake (50-g total as: 25-g insoluble and 25-g soluble fibre) compared with a moderate intake (24-g) total, resulted in significant improvements in glycemic control and plasma lipid concentrations (51). Similarly, a recent randomized, controlled clinical trial (22) in adults with type 1 diabetes found improvement in A1C levels and a lower incidence of hypoglycemia (<3.0 mmol/L) with consumption of low-GI/high-fibre foods compared with high-GI/low-fibre foods.

The evidence seems to indicate that low-GI rankings and high dietary fibre are independent, protective factors in the etiology of type 2 diabetes. Furthermore, added benefits may be realized in prevention of type 2 diabetes and in the management of type 1 and type 2 diabetes if these 2 factors are used together (13,14,22).

### Variability of glycemic response

Another area of controversy pertains to the observed variability of glycemic response both within and between individuals. Wolever has argued that although subjects may respond differently to carbohydrate foods from day to day, between-subject variability is generally small (26,27). However, there is a significant difference between subjects when comparing those without diabetes and those with type 1 and type 2 diabetes.

For example, individuals with type 2 diabetes show the least within-subject variability in glycemic response, followed by subjects without diabetes and, lastly, by those with type 1 diabetes (34,52). There is also variability in the GI ranking of the same foods tested by different researchers (29). This could reflect both regional food composition and methodological differences such as choice of reference food, especially if white bread is used, as it is more difficult to standardize than glucose. However, a recent multi-laboratory study undertaken to estimate the magnitude of variation in GI ratings among experienced laboratories did not find a significant difference in the mean GI rating of 5 different foods (27).

Despite the variability of response between individuals and the potential influence of other dietary components such as fat, protein and fibre, the overall ranking of GI is preserved. That is, a low-GI food will tend to raise BG to a lesser extent than a high-GI food under equivalent macronutrient conditions (17-21,31,53-55).

### Method of calculation of glycemic response

The GI, as originally developed, is based on the *incremental area of the BG response curve above baseline*. Therefore, any BG values that fall below baseline are not considered in the calculation (26). However, some investigators have used different methods than that originally proposed. Bantle and Nuttall's groups use a method whereby the area beneath the fasting level is subtracted from the area above the fasting level to give a "net incremental area" (26). Reavan's group includes the "total area under the curve" (i.e. above and below baseline) (26). These methodological differences may explain some of the discrepancies among studies, especially those led by the aforementioned investigators, which include studies that support the position that the GI has no clinical utility, especially in the context of a mixed meal (39-42).

### Effectiveness of GI and international consensus

The ADA does not currently endorse the GI for the nutritional management of diabetes (6,7,9). The ADA contends that although low-GI foods may reduce postprandial BG levels, there is insufficient evidence of long-term benefit (e.g. improvement in A1C and lipid levels) to recommend the use of low-GI diets for individuals with type 1 and type 2 diabetes

<b>Meal (quantity)</b>	<b>Carbohydrate (g)</b>	<b>% of carbohydrate of total meal</b>	<b>GI</b>	<b>Contribution to meal GI (% of carbohydrate x GI)</b>
Orange juice (125 mL)	13	23	46	11
Kellogg's Corn Flakes® (30 g)	24	43	84	36
Milk (125 mL)	6	11	27	3
White toast (1 slice)	13	23	70	16
TOTAL	56	100	–	66

GI = glycemic index

(4,6,7,56). Furthermore, it is believed that the GI would likely complicate meal planning and would be difficult for individuals with diabetes to implement in their daily lives (4). However, some studies, including a recent meta-analysis, do show benefits of low-GI diets beyond reduction of postprandial BG, including improvements in A1C, lipid levels and quality of life (15-23,57,58). Moreover, studies have demonstrated that individuals with diabetes can integrate the GI concept into their diet, find it simple and easy to use (59-61), and are not misapplying it (62). As well, studies have demonstrated an association between low-GI diets and reduction of risk for the development of type 2 diabetes (13,14).

Research based on the GI concept has largely focused on the role of low-GI diets in the prevention of type 2 diabetes, management of type 1 and type 2 diabetes, CVD risk management, and obesity and weight regulation.

## GI IN THE PREVENTION AND MANAGEMENT OF DIABETES

Postprandial glucose is a key factor in the etiology of type 2 diabetes and its complications, and is emerging as an important predictor of morbidity and mortality (10,63). Data from the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study demonstrated that an increase of 1.0 mmol/L in postprandial BG resulted in a 7% increase in total mortality over a 5- to 10-year period (63). Postprandial BG levels >7.0 mmol/L have been shown to directly reduce flow-mediated vasodilation and removal of very low-density lipoprotein from circulation (64). Therefore, strategies that aim to reduce postprandial hyperglycemia, such as low-GI foods (65), or pharmacologic approaches such as use of acarbose (66) may have profound benefits in preventing diabetes and its complications.

### GI in the prevention of type 2 diabetes

An important test of the clinical usefulness of the GI concept is whether it predicts long-term disease risk, especially the incidence of type 2 diabetes (12).

Data from 2 large epidemiological studies (13,14) indicate that a high dietary GI intake is positively associated with a high risk of developing type 2 diabetes, even after adjusting for age, body mass index (BMI), smoking status, physical activity, family history, alcohol consumption, and cereal fibre, total energy and total amount of carbohydrate consumed (13,14). However, an epidemiological study involving older women did not find an association between GI and development of self-reported type 2 diabetes (50). One of the criticisms of the latter study (50) is that, in addition to relying on self-reported information regarding the development of type 2 diabetes, it also included an elderly cohort, potentially introducing a selection bias (65).

As a direct relationship of cause and effect cannot be established from the observational designs of these epidemiological studies, evidence from randomized, controlled trials

is warranted. The recent results of such a study (66), utilizing acarbose, a pharmacologic agent that slows carbohydrate absorption and has been compared with low-GI foods (65), is promising in this regard. However, large, long-term, randomized, controlled trials on the impact of low-GI diets vs. high-GI diets on the development of type 2 diabetes are needed to provide more definitive answers.

### GI in the management of type 1 and type 2 diabetes

#### *Type 2 diabetes*

When the GI of a meal was lowered while maintaining both the total macronutrient and fibre composition consistent, a significant reduction in postprandial glycemia and insulinemia was observed in adults with type 2 diabetes (19-21, 31,54,55,60). One study found no difference in A1C and pre- and postprandial glycaemic levels between low- and high-GI meals (67).

#### *Type 1 diabetes*

Research since the late 1980s has also documented improved serum fructosamine and A1C levels in type 1 diabetes with low-GI diets (15,17,18,22,23,57). Two studies found no difference in A1C levels and insulin requirements between low- and high-GI meals in adults with type 1 diabetes (67,68). In a recent cross-sectional study, a positive association was observed between a low-GI diet and a lower A1C concentration, independent of fibre intake, based on data collected from 3-day food records from 2810 men and women with type 1 diabetes (57). A recent randomized, controlled clinical trial (22) also found improved A1C, including a lower incidence of hypoglycemia (<3.0 mmol/L) in adults with type 1 diabetes with consumption of low-GI/high-fibre foods compared with high-GI/low-fibre foods. Another recent randomized, controlled clinical trial found a significant improvement in A1C as well as quality of life in children with type 1 diabetes who received nutrition education emphasizing low-GI food choices compared with standard nutrition advice involving carbohydrate exchanges (23).

A recent meta-analysis of randomized controlled trials of low-GI diets in the management of type 1 and type 2 diabetes concluded that choosing low-GI in place of high-GI foods has a small but clinically significant effect on medium-term glycaemic control as assessed by fructosamine or A1C levels (58). Therefore, the preponderance of the evidence does show a positive effect of low-GI vs. high-GI diets in the management of both type 1 and type 2 diabetes. However, as the majority of these findings have been in the context of conventional insulin therapy (1 to 2 injections/day), further research on high-GI vs. low-GI diets under conditions of intensive insulin therapy (3 or more injections/day or insulin pump therapy) and the use of insulin analogues is needed. As well, given the day-to-day variability in glycaemic response, noted particularly in individuals with type 1 diabetes (34), further research of the efficacy of the GI concept in this population is warranted.

Aside from dietary composition, other factors that may influence glycemic response and must be considered in the context of diabetes management include preprandial glycemia (69,70), medication type and dose, timing of medication consumption, exercise and level of stress. The fact that there are so many variables that affect glycemic control does not invalidate the GI concept as a way to standardize the impact of carbohydrates on glycemic control.

## **ROLE OF THE GI IN CVD AND RISK MANAGEMENT**

### **Blood lipids**

Control of lipid levels is also paramount in the management of diabetes. Since the late 1980s, studies have also shown improved serum lipids in both type 1 and type 2 diabetes with low-GI vs. high-GI diets (16-21,53,54,71,72). Wolever and colleagues found a reduction of 7% in total serum cholesterol in adults with type 2 diabetes following consumption of a low-GI diet compared to a high-GI diet (54). In a recent randomized, controlled study of adults with type 2 diabetes, Jarvi and colleagues (21) found a reduction in low-density lipoprotein cholesterol (LDL-C) and a marked reduction of the CVD risk factor plasminogen activator inhibitor (PAI) -1 following consumption of a low-GI compared with a high-GI diet. However, a decrease in high-density lipoprotein cholesterol (HDL-C) was also noted in this study (21). In contrast, Buyken and colleagues observed higher concentrations of HDL-C in European adults with type 1 diabetes consuming low-GI vs. high-GI diets (57). This discrepancy in control of HDL-C may be related to differences in study design (i.e. cross-sectional vs. randomized study design) or perhaps to true differences between individuals with type 1 vs. type 2 diabetes. Further research is therefore required to clarify this observation. An inverse relationship was noted between GI and HDL-C in a cross-sectional study of adults in England, in which GI was the only dietary variable associated with HDL-C concentrations (73). Similarly, in looking at food frequency questionnaires and HDL-C concentrations of 13 907 American adults (males and females) participating in the National Health and Nutrition Examination Survey III (NHANES III) study, Ford and Liu (74) found that a high dietary GI and high glycemic load were associated with a lower concentration of plasma HDL-C. A high dietary glycemic load was also found to increase the risk of coronary heart disease, independent of traditional coronary artery disease risk factors in American women (75).

### **Other CVD risk factors**

Liu and colleagues also found that a high dietary glycemic load was also positively associated with high-sensitivity C-reactive protein in middle-aged women, especially in those who were overweight (BMI >25 kg/m<sup>2</sup>) (76). Short-term intervention studies have also found lower day-long insulin levels in healthy lean and obese individuals following the consumption of a low-GI compared to a high-GI diet of equivalent macronutrient composition (77,78).

As both chronic hyperinsulinemia and postprandial hyperglycemia are important risk factors for CVD (11), short-term studies suggest that use of low-GI diets may prove beneficial in the prevention of CVD (79,80).

## **THE ROLE OF GI IN OBESITY AND WEIGHT MANAGEMENT**

Weight loss can help lower blood pressure (BP), BG levels and serum triglycerides (TG), as well as increase HDL-C levels and improve insulin sensitivity (81). Furthermore, recent evidence has indicated that weight reduction of as little as 5 to 7% of initial weight, achieved through intensive lifestyle changes, can decrease the risk of development of type 2 diabetes in high-risk individuals (i.e. those with impaired glucose tolerance) (82-84).

Although no long-term clinical trials have examined the effects of GI on body weight regulation, there are numerous animal studies and short-term clinical trials that have demonstrated that consumption of low-GI foods results in greater weight loss than consumption of high-GI foods of equivalent macronutrient composition (85). Furthermore, it has been postulated that high-GI foods may play a critical role in the etiology of obesity and the metabolic syndrome (86). The GI concept has been associated with satiety and the possible prevention of obesity (87), which may be related to the higher satiety that is associated with slowly digested carbohydrates (88-90). The extended presence of food in the gut has been shown to stimulate satiety-signalling receptors (91) and may be 1 of the mechanisms by which low-GI foods exert their effect on suppression of hunger (90). In a recent randomized study involving 10 healthy subjects, Liljeberg and colleagues found that higher satiety was achieved with a barley breakfast that had a low GI, was high in resistant starch and high in dietary fibre (92). Another study indicated prolonged satiety after consumption of a low-GI meal vs. a moderately high-GI meal in obese adolescents (93). In addition, weight loss has been achieved when low-GI diets were consumed (91). In a recent randomized trial involving 11 overweight men fed either a low-GI or high-GI isocaloric diet for 5 weeks, the low-GI diet resulted in a mean reduction in total fat mass of 0.5 kg (94). Although low-GI foods are associated with prolonged satiety, high-GI but not low-GI foods have been shown to suppress hunger in the short term according to a recent study (95). Therefore, it has been suggested that there may be a role for both high-GI and low-GI foods with respect to weight regulation (90). However, more studies are needed to extend these findings.

It has been reported that both normal weight and overweight individuals exhibit predicted glycemic responses to foods with different GI ratings (96-98). However, most of the studies that show a role for the use of the GI concept in weight management have been conducted in subjects without diabetes and have been of short duration. Therefore, more long-term research is required to examine the role of GI in

weight management, particularly in individuals with diabetes. Furthermore, obesity results from multi-factorial causes, such as genetics, lack of physical activity and over consumption of energy. Excessive hunger is only 1 cause of overeating. In the absence of conclusive evidence, debate continues regarding the merits of low-GI diets in the prevention and management of obesity (99,100).

## **POSTULATED MECHANISMS OF THE GI IN THE DEVELOPMENT OF DIABETES, CVD AND OBESITY**

Some of the postulated mechanisms related to the role of GI in the development of type 2 diabetes, CVD and obesity are outlined in a recent article (101). With respect to development of diabetes, dietary GI alters risk for type 2 diabetes, independent of weight change, via effects on hyperinsulinemia, insulin resistance (101), demand on beta cells and beta cell function (101,102).

With respect to altering the risk of CVD, GI has effects on both postprandial hyperglycemia and postprandial insulinemia, both of which are independent risk factors for CVD, as well as effects on traditional CVD risk factors (LDL-C, HDL-C and TG) and emerging CVD risk factors such as PAI-1 and high-sensitivity C-reactive protein. Postprandial hyperglycemia increases CVD risk by increasing oxidative stress, which, in turn, has negative consequences on BP, blood clot formation and endothelial function. Blood insulin levels, which have been shown to be up to 2-fold higher after macronutrient-controlled high-GI vs. low-GI mixed meals, have independent effects on BP, serum lipids, coagulation factors and endothelial function (101). The postulated relationship between GI and the development of obesity involves the reactive hypoglycemia, resulting from hyperinsulinemia that has been demonstrated after consumption of high-GI carbohydrates (101). The insulin-induced hypoglycemia appears to provoke prolonged hyperphagia that persists well after restoration of normal glycemia (101). As well, hyperinsulinemia can lead to insulin resistance that, in turn, can lead to the development of the metabolic syndrome (86,103).

Although the mechanisms outlined are supported by both experimental and clinical research findings, the proposed models of the role of GI in the development of type 2 diabetes, CVD and obesity are hypothetical. Research is, therefore, required to clarify these mechanisms in the etiology of these conditions.

## **PRACTICAL ISSUES AND APPLICATION**

### **Is the GI too complex a concept to teach?**

Some educators believe that the GI is too complicated to teach (5,55,56). However, Brand-Miller and colleagues have integrated the concept into practice (59,61) and have also demonstrated benefits in both metabolic control and quality of life in individuals with diabetes (23,60). As it is not feasible to expect patients to calculate the GI of their meal or diet, application of the GI concept must involve use of exchange lists and/or food

lists and simple advice as has been successfully accomplished by Frost (60) and Brand-Miller and colleagues (23,104). The development of educational tools focusing on the GI, and continuing education for healthcare professionals regarding the GI concept, will ensure successful implementation of the GI concept in clinical practice.

### **Does using the GI limit food choice?**

Some critics of the GI concept fear that focusing on low-GI foods may limit food choice and possibly have a negative impact on the nutritional adequacy of the diet (6). In addition, not all foods have an assigned GI value and this can be an obstacle for the day-to-day use of the GI concept (105). However, recent interest in the GI has led to an increase in the number of foods that have been tested and assigned GI values (currently over 1000 foods, including Canadian foods) (106). As is the case with nutrients, the GI is subject to regional differences in food composition. Therefore, use of GI values that are country specific is critical for both research and application of the GI concept. Although the new international table of GI values is quite extensive, it is clear that more testing is urgently needed, especially of Canadian foods (106).

Traditional food patterns in many cultures typically include more low-GI foods than the Western diet (107,108). Adopting these food patterns provides a chance to learn about new and interesting foods to add to a meal plan. However, Brand-Miller and Foster-Powell recognize that there is a challenge for the food industry in producing new and palatable low-GI foods, as many people are resistant to accepting typical low-GI foods (104).

### **Is the GI ready for practice?**

Regardless of the philosophical and practical concerns previously mentioned, the GI concept is well accepted and utilized in countries such as Australia and New Zealand (59,61). Clinicians report that people with diabetes who are taught the GI concept find it simple, easy to use and helpful (59,61). Patients report that they find the advice about the GI concept simple and positive (60) and are not misapplying the concept (62). In fact, nutrition education involving the GI concept has been shown to be more successful than standard nutrition education in adults with newly diagnosed type 2 diabetes (60) and in children with type 1 diabetes (23). Frost and colleagues assessed the impact of nutrition education using the GI concept against standard nutrition advice in a randomized, controlled trial of 51 newly diagnosed adults with type 2 diabetes (60). Their results showed that when people received nutrition education focusing on low-GI foods, in addition to achieving a lower mean dietary GI intake, they also had a lower fat intake and a higher carbohydrate intake (60). A more recent randomized, controlled clinical trial also demonstrated that simple advice based on low-GI foods significantly improved A1C and quality of life in free-living children with type 1 diabetes compared with traditional advice based on carbohydrate exchanges (23).

## Implementing the GI

The GI concept is not meant to replace, but rather to supplement existing nutritional strategies, although it can be used on its own in accordance with the needs of the patient.

It is not necessary for patients to choose only low-GI foods (104), e.g. replacing half of high-GI carbohydrate with low-GI choices will lower the whole diet GI by about 15 units, which is more than sufficient to result in clinically significant improvements in glycemic control in people with diabetes (104). This increases the flexibility of the diet and allows staple foods such as potatoes and white bread, which have a high GI but are still nutritious, to be included in the diet. Other suggestions include selecting at least 1 low-GI carbohydrate choice per meal or basing at least 2 meals daily on low-GI foods (104). Also, substituting low-GI in place of high-GI breads and breakfast cereals may have the most practical impact in the Western diet (104). Another way to convey the GI concept is to present high-carbohydrate, low-fat foods in terms of “good” choices and “better” choices, making this distinction on the basis of both nutrient composition and GI (104).

Legumes have been found to be useful in lowering the GI of the diet (109). Therefore, suggesting ways to include legumes in recipes can help patients lower the total GI of their diets. As most fruits, vegetables and milk products generally have a low-GI rating and provide many essential nutrients, a variety of foods from these food groups should be encouraged as part of a healthy diet, with an emphasis on low-fat choices. As the majority of high-GI foods are found in grain products or in starchy food, this food group should be the main focus of education regarding the GI concept (104).

Portion management is fundamental to nutrition therapy for diabetes (56). Overindulging in a meal consisting of low-GI foods will likely elevate BG levels. Therefore, patients should recognize that serving sizes must still be monitored, even when making low-GI choices. As well, food choices must still be based on current nutrition recommendations and nutrition guidelines for healthy eating. Teaching the GI concept should, therefore, be in keeping with these recommendations and guidelines. Since the term “glycemic index” or “GI” may be too technical for most patients, it is suggested that terms such as “small rise” and “large rise” in BG be used (110). Ultimately, the healthcare professional, along with the patient, will determine which nutritional strategy or strategies will be of benefit.

People with diabetes who are taking medication, especially those who are using newer agents and regimens, should be encouraged to measure their BG levels more frequently and be alert for the possible need to modify their treatment regimen when replacing high-GI foods with low-GI foods in their diet.

## CONCLUSIONS

Despite the fact that there is no unanimous consensus regarding practical application of the GI concept in the nutritional management of diabetes, there is a growing interest in the

use of the GI concept around the world. Criticisms about the clinical utility of the GI concept are scientific, philosophical, and educational. These arguments include the applicability of the GI in mixed meals, the variability of glycemic response within and between individuals, the perceived complexity of the GI concept, the fear that this concept may limit food choices and may be misapplied by patients and the challenge of using it in an educational context and in everyday life.

When the GI concept is applied in research and clinical settings, positive health benefits have been identified for people both with and without diabetes. These include reduction in the risk of developing type 2 diabetes and improvements in metabolic factors associated with long-term complications of type 1 and type 2 diabetes such as reduction of postprandial glycemia and insulinemia, improved glycemic control, improved lipid profile, and improvements in emerging CVD risk factors. Research also appears to indicate a role for the GI concept in the prevention and management of obesity.

The GI is sometimes viewed as a complex concept, largely because of misconceptions regarding its application in mixed meals and likely due to confusion between the terms “glycemic response” and “glycemic index.” It is important to note that the GI refers to the glycemic response to carbohydrates only, and has not been extended to proteins or fats or foods rich in protein and/or fat. Although protein and fat have been shown to mediate glycemic response, their impact on immediate postprandial glycemia remains to be clarified. Furthermore, current evidence suggests that carbohydrates are the main determinants of immediate postprandial glycemic control, with the type of carbohydrate being a very important factor in this regard. With respect to carbohydrates, it is now clear that not all carbohydrates are created equally with respect to their impact on postprandial glycemia and on other metabolic parameters. Furthermore, as there is increasing evidence regarding the potential health benefits of low-GI diets, it is important to integrate this concept into practice in as clear a manner as possible. To this end, education will be required for healthcare professionals to ensure successful integration of this concept into practice. The food industry will also have a vital role to play by increasing testing of carbohydrate foods.

With respect to the prevention and management of diabetes, the bulk of the research seems to indicate a positive role for low-GI diets. However, more long-term and applied research is needed to fully understand how people integrate the GI concept in their day-to-day lives and to determine whether positive metabolic changes can be maintained. More long-term research with respect to the role of low-GI diets in the prevention and management of CVD and obesity is also needed.

As awareness of the GI continues to grow, healthcare professionals must understand the GI to be able to provide sound advice to consumers, particularly to people with diabetes, who may have an interest in the topic.

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## REFERENCES

- Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes*. 2003; 27(suppl 2):1-152.
- Jenkins DJA, Wolever TMS, Jenkins AL, et al. The glycaemic response to carbohydrate foods. *Lancet*. 1984;2:388-391.
- Hollenbeck CB, Coulston AM. The clinical utility of the glycemic index and its application to mixed meals. *Can J Physiol Pharmacol*. 1991;69:100-107.
- Franz MJ. Carbohydrate and diabetes: is the source or the amount of more importance? *Curr Diab Rep*. 2001;1:177-186.
- Beebe C. Diets with a low glycemic index: not ready for practice yet! *Nutr Today*. 1999;34:82-86.
- Franz MJ, Horton ES, Bantle JP, et al. Nutrition principles for the management of diabetes and related complications. *Diabetes Care*. 1994;17:490-518.
- Franz MJ, Bantle JP, Beebe CA, et al. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. *Diabetes Care*. 2002;25:148-198.
- Food and Agriculture Organization of the United Nations/World Health Organization. Carbohydrates in human nutrition. Report of a Joint FAO/WHO expert consultation. *FAO Food Nutr Pap*. 1998;66:1-140.
- Nantel G. Glycemic carbohydrate: an international perspective. *Nutr Rev*. 2003;61:S34-S39.
- American Diabetes Association. Postprandial blood glucose. *Diabetes Care*. 2001;24:775-778.
- Coutinho M, Gerstein HC, Wang Y, et al. The relationship between glucose and incident cardiovascular events: a meta-regression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care*. 1999; 22:233-240.
- Hu FB, Van Dam RM, Liu S. Diet and risk of type II diabetes: the role of types of fat and carbohydrate. *Diabetologia*. 2001;44:805-817.
- Salmeron J, Ascherio A, Rimm E, et al. Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care*. 1997;20: 545-550.
- Salmeron J, Manson JE, Stampfer MJ, et al. Dietary fiber, glycemic load and risk of non-insulin-dependent diabetes mellitus in women. *JAMA*. 1997;277:472-477.
- Jenkins DJA, Wolever TMS, Collier GR, et al. The metabolic effects of a low glycemic index diet. *Am J Clin Nutr*. 1987;46:968-975.
- Jenkins DJA, Wolever TMS, Kalmusky J, et al. Low glycemic index diet in hyperlipidemia: use of traditional starchy foods. *Am J Clin Nutr*. 1987;46:66-71.
- Collier GR, Giudici S, Kalmusky J, et al. Low glycemic index starchy foods improve glucose control and lower serum cholesterol in diabetic children. *Diabetes Nutr Metab*. 1988; 1:11-19.
- Fontvieille AM, Acosta M, Rizkalla SW, et al. A moderate switch from high to low glycemic-index foods for 3 weeks improves the metabolic control of type 1 (IDDM) diabetic subjects. *Diabetes Nutr Metab*. 1988;1:139-143.
- Brand JC, Colagiuri S, Crossman S, et al. Low glycemic index foods improve long term glycemic control in NIDDM. *Diabetes Care*. 1991;14:95-101.
- Wolever TMS, Jenkins DJ, Vuksan V, et al. Beneficial effect of a low glycemic index in type 2 diabetes. *Diabet Med*. 1992;9:451-458.
- Jarvi AE, Karlstrom BE, Granfeldt YE, et al. Improved glycemic control and lipid profile and normalized fibrinolytic activity on a low-glycemic index diet in type 2 diabetic patients. *Diabetes Care*. 1999;22:10-18.
- Giacco R, Parillo M, Rivelles AA, et al. 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*. 2000;23:1461-1466.
- Gilbertson HR, Brand-Miller JC, Thorburn AW, et al. 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*. 2001;24:1137-1143.
- Wolever TM. Glycemic index versus glycemic response [letter]. *Diabetes Care*. 1992;15:1436-1437.
- Jenkins DJ, Wolever TM, Taylor RH, et al. Glycemic index of foods: a physiological basis for carbohydrate exchange. *Am J Clin Nutr*. 1981;34:362-366.
- Wolever TM. The glycemic index. *World Rev Nutr Diet*. 1990;62:120-185.
- Wolever TM, Vorster HH, Björck I, et al. Determination of the glycaemic index of foods: interlaboratory study. *Eur J Clin Nutr*. 2003;57:475-482.
- Wolever TM, Jenkins DJ, Jenkins AL, et al. The glycemic index: methodology and clinical implication. *Am J Clin Nutr*. 1991;54:846-854.
- Wolever TMS, Brand-Miller J, Foster-Powell K, et al. *The Glucose Revolution*. New York, NY: Marlowe & Company; 1999.
- Wolever TMS, Relle LK, Jenkins AL, et al. Glycemic index of 102 complex carbohydrate foods in patients with diabetes. *Nutr Res*. 1994;14:651-669.
- Jarvi AE, Karlstrom BE, Granfeldt YE, et al. The influence of food structure on postprandial metabolism in patients with non-insulin-dependant diabetes mellitus. *Am J Clin Nutr*. 1995;61:837-842.
- Wolever TMS. Relationship between dietary fiber content and composition in foods and the glycemic index. *Am J Clin Nutr*. 1990;51:72-75.
- Hollenbeck CB, Coulston AM, Reaven GM. Glycemic effects of carbohydrates: a different perspective. *Diabetes Care*. 1986;9:641-647.
- Wolever T, Nuttall F, Lee R, et al. Prediction of the relative blood glucose response of mixed meals using the white bread glycemic index. *Diabetes Care*. 1985;8:418-428.
- Collier GR, Wolever TMS, Wong GS, et al. Prediction of glycemic response to mixed meals in non-insulin dependent diabetic subjects. *Am J Clin Nutr*. 1986;44:349-352.
- Chew I, Brand JC, Thorburn AW, et al. Application of glycemic index to mixed meals. *Am J Clin Nutr*. 1988;47:53-56.

37. Wolever TM, Jenkins DJ, Vuksan V, et al. Glycemic index of foods in individual subjects. *Diabetes Care*. 1990;13:126-132.
38. 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*. 1996;126:2807-2812.
39. Nuttall FQ, Mooradian AD, DeMarais R, et al. The glycemic index of different meals approximately isocaloric and similar in protein, carbohydrate and fat content as calculated using the ADA exchange lists. *Diabetes Care*. 1983;6:432-435.
40. Coulston AM, Hollenbeck CB, Liu GC, et al. Effect of source of dietary carbohydrate on plasma glucose, insulin, and gastric inhibitory polypeptide responses to test meals in subjects with noninsulin-dependent diabetes mellitus. *Am J Clin Nutr*. 1984;40:965-970.
41. Laine DC, Thomas W, Levitt MD, et al. Comparison of predictive capabilities of diabetic exchange lists and glycemic index of foods. *Diabetes Care*. 1987;19:387-394.
42. Hollenbeck CB, Coulston AM, Reaven AM. Comparison of plasma glucose and insulin responses to mixed meals of high, intermediate, and low glycemic potential. *Diabetes Care*. 1988;11:323-329.
43. Willet W, Manson J, Liu S. Glycemic index, glycemic load, and risk of type 2 diabetes. *Am J Clin Nutr*. 2002;76(suppl):274S-280S.
44. Wolever TMS, 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*. 2003;77:612-621.
45. Krezowski PA, Nuttall FQ, Gannon MC, et al. The effect of protein ingestion on the metabolic response to oral glucose in normal individuals. *Am J Clin Nutr*. 1986;4:847-856.
46. Gannon MC, Nuttall FQ, Neil BJ, et al. The insulin and glucose responses to meals of glucose plus various proteins in type II diabetic subjects. *Metabolism*. 1988;37:1081-1088.
47. Peters AL, Davidson MB. Protein and fat effects on glucose response and insulin requirements in subjects with insulin-dependent diabetes mellitus. *Am J Clin Nutr*. 1993;58:555-560.
48. Gray RO, Butler PC, Beers TR, et al. Comparison of the ability of bread versus bread plus meat to treat and prevent subsequent hypoglycemia in patients with insulin-dependent diabetes mellitus. *J Clin Endocrinol Metab*. 1996;81:1508-1511.
49. Owen B, Wolever TMS. Effect of fat on glycemic responses in normal subjects: a dose-response study. *Nutr Res*. 2003;23:1341-1347.
50. Meyer KA, Kushi LH, Jacobs DR, et al. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. *Am J Clin Nutr*. 2000;71:921-930.
51. Chandalia M, Garg A, Lutjohann D, et al. Beneficial effects of high fibre intake in patients with type 2 diabetes mellitus. *N Engl J Med*. 2000;342:1392-1398.
52. Jenkins DJ, Wolever T, Wong G, et al. Glycemic responses to foods: possible differences between insulin-dependent and non-insulin-dependent diabetics. *Am J Clin Nutr*. 1984;40:971-981.
53. Fontvieille AM, Rizkalla SW, Penformis A, et al. The use of low glycemic index foods improves metabolic control of diabetic patients over five weeks. *Diabet Med*. 1992;9:440-460.
54. Wolever TMS, Jenkins DJA, Vuksan V, et al. Beneficial effect of a low-glycemic index diet in overweight NIDDM subjects. *Diabetes Care*. 1992;15:562-564.
55. Rendell M. Dietary treatment of diabetes mellitus. *N Engl J Med*. 2000;342:1440-1441.
56. Franz MJ. In defense of the American Diabetes Association's recommendations of the glycemic index. *Nutr Today*. 1999;34:78-81.
57. Buyken AE, Toeller M, Heitkamp G, et al. Glycemic index in the diet of European outpatients with type 1 diabetes: relations to glycated hemoglobin and serum lipids. *Am J Clin Nutr*. 2001;73:574-581.
58. Brand-Miller J, Hayne S, Petocz P, et al. Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. *Am J Clin Nutr*. 2003;26:2261-2267.
59. Brand-Miller J. The importance of glycemic index in diabetes. *Am J Clin Nutr*. 1994;59(suppl):747S-752S.
60. Frost G, Wilding J, Beecham J. Dietary advice based on the glycemic index improves dietary profile and metabolic control in type 2 diabetic patients. *Diabet Med*. 1994;11:397-401.
61. Brand-Miller JB, Colagiuri S, Foster-Powell K. The glycemic index is easy and works in practice. *Diabetes Care*. 1997;20:1628-1629.
62. Gilbertson HR, Thorburn AW, Brand-Miller JC, et al. Effect of low-glycemic-index dietary advice on dietary quality and food choice in children with type 1 diabetes. *Am J Clin Nutr*. 2003;77:83-90.
63. The DECODE Study Group. Glucose tolerance and mortality: comparison of WHO and American Diabetes Association diagnostic criteria. *Lancet*. 1999;354:617-621.
64. Hanefeld M, Koehler C, Henkel E, et al. Post-challenge hyperglycaemia relates more strongly than fasting hyperglycemia with carotid intima-media thickness: the RIAD Study. *Diabet Med*. 2000;17:835-840.
65. Augustin LS, Franceschi S, Jenkins DJA, et al. Glycemic index in chronic disease: a review. *Eur J Clin Nutr*. 2002;56:1049-1071.
66. Chiasson JL, Josse RG, Gomis R, et al. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomized trial. *Lancet*. 2002;359:2072-2076.
67. Calle-Pascual AL, Gomez V, Leon F, et al. Foods with a low glycemic index do not improve glycemic control of both type 1 and type 2 diabetic patients after 1 month of therapy. *Diabetes Metab*. 1988;14:629-633.
68. Lafrance L, Rabasa-Lhoret R, Poisson D, et al. The effects of different glycemic index foods and dietary fibre on glycemic control in type 1 diabetic patients on intensive insulin therapy. *Diabet Med*. 1998;15:972-978.
69. Fraser R, Horowitz M, Maddox A, et al. Hyperglycemia slows gastric emptying in type 1 diabetes mellitus. *Diabetologia*. 1990;33:675-680.
70. Schvartz E, Palmer M, Aman J, et al. Hypoglycemia increases the gastric emptying rate in healthy subjects. *Diabetes Care*. 1995;18:674-676.
71. Jenkins DJA, Wolever TMS, Kalmusky J, et al. Low glycemic index carbohydrate foods in the management of hyperlipidemia. *Am J Clin Nutr*. 1985;45:604-617.
72. Jenkins DJA, Wolever TMS, Buckley G, et al. Low glycemic-index starchy foods in the diabetic diet. *Am J Clin Nutr*. 1988;48:248-254.
73. Frost G, Leeds AA, Dore CJ, Madeiros S, et al. Glycaemic index as a determinant of serum HDL-cholesterol concentration. *Lancet*. 1999;353:1045-1048.
74. Ford ES, Liu S. Glycemic index and serum high-density

- lipoprotein cholesterol concentration among US adults. *Arch Int Med.* 2001;161:572-576.
75. Liu S, Willett WC, Stampfer MJ, et al. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J Clin Nutr.* 2000;71:1455-1461.
76. Liu S, Manson JE, Buring JE, et al. Relation between a diet with a high glycemic load and plasma concentrations of high-sensitivity C-reactive protein in middle-aged women. *Am J Clin Nutr.* 2002;75:492-498.
77. Kiens B, Richter EA. Types of carbohydrate in an ordinary diet affect insulin action and muscle substrate in humans. *Am J Clin Nutr.* 1996;63:47-53.
78. Percheron C, Colette C, Avignon A, et al. Metabolic responses to high carbohydrate breakfasts in obese patients with impaired glucose tolerance: comparison of meals containing dairy products and fruits versus bread. *Nutr Res.* 1997;17:797-806.
79. Sacks FM, Katan M. Randomized clinical trials on the effects of dietary fat and carbohydrate on plasma lipoproteins and cardiovascular disease. *Am J Med.* 2002;113(suppl 9B):13S-24S.
80. Hung T, Sievenpiper JL, Marchie A, et al. Fat versus carbohydrate in insulin resistance, obesity, diabetes and cardiovascular disease. *Curr Opin Clin Nutr Metab Care.* 2003;6:165-176.
81. Rippe JM, Crossley S, Ringer R. Obesity as a chronic disease: modern medical and lifestyle management. *J Am Diet Assoc.* 1998;98(10 suppl 2):S9-S15.
82. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care.* 1997;20:537-544.
83. Tuomihito K, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med.* 2001;344:1343-1350.
84. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med.* 2002;346:393-403.
85. Brand-Miller JC, Holt SA, Pawlak DB, et al. Glycemic index and obesity. *Am J Clin Nutr.* 2002;76 (suppl):281S-285S.
86. Kopp W. High-insulinogenic nutrition—an etiologic factor for obesity and the metabolic syndrome? *Metabolism.* 2003;52:840-844.
87. Björck I, Grandfeldt Y, Liljeberg H, et al. Food properties affecting the digestion and absorption of carbohydrates. *Am J Clin Nutr.* 1994;59(suppl):699S-705S.
88. Holt S, Brand JC, Soveney C, et al. Relationship of satiety to postprandial glycaemic, insulin and cholecystokinin responses. *Appetite.* 1992;18:129-141.
89. Holt SHA, Brand-Miller J. Particle size, satiety and the glycaemic response. *Eur J Clin Nutr.* 1994;48:496-502.
90. Anderson GH, Woodend D. Effect of glycemic carbohydrates on short-term satiety and food intake. *Nutr Rev.* 2003;61: S17-S26.
91. Slabber M, Barnard HC, Kuyl JM, et al. Effects of a low-insulin-response, energy restricted diet on weight loss and plasma insulin concentration in hyperinsulinemic obese females. *Am J Clin Nutr.* 1994;60:48-53.
92. Liljeberg HG, Akerberg AK, Björck IM. Effect of the glycemic index and content of indigestible carbohydrates of cereal-based breakfast meals on glucose tolerance at lunch in healthy subjects. *Am J Clin Nutr.* 1999;69:647-655.
93. Ball SD, Keller KR, Moyer-Mileur LJ, et al. Prolongation of satiety after low versus moderately high glycemic index meals in obese adolescents. *Pediatrics.* 2003;111:488-494.
94. Bouché C, Rizkalla SW, Luo J, et al. Five-week, low-glycemic index diet decreased total fat mass and improves plasma lipid profile in moderately overweight nondiabetic men. *Diabetes Care.* 2002;25:822-828.
95. Anderson GH, La Catherine N, Woodend DM, et al. Inverse association between the effect of carbohydrates on blood glucose and subsequent short-term food intake in young men. *Am J Clin Nutr.* 2002;76:1023-1030.
96. Ludwig DS, Majzoub JA, Al-Zahrani A, et al. High glycemic index foods, overeating, and obesity. *Pediatrics.* 1999;103:E26.
97. Rodin J, Reed D, Jamner L. Metabolic effects of fructose and glucose: implications for food intake. *Am J Clin Nutr.* 1988;47:683-689.
98. Rodin J. Effects of pure sugar vs. mixed starch fructose loads on food intake. *Appetite.* 1991;17:213-219.
99. Pawlak DB, Ebbeling CB, Ludwig DS. Should obese patients be counseled to follow a low-glycaemic index diet? Yes. *Obesity Rev.* 2002;3:235-244.
100. Raban A. Should obese patients be counselled to follow a low-glycaemic index diet? No. *Obesity Rev.* 2002;3:245-256.
101. Ludwig DS. The glycemic index: physiological mechanisms relating to obesity, diabetes and cardiovascular disease. *JAMA.* 2002;287:2414-2423.
102. Wolever TM, Mehling C. High-carbohydrate–low glycaemic index dietary advice improves glucose disposition index in subjects with impaired glucose tolerance. *Brit J Nutr.* 2002;87:477-482.
103. Minehara K, Tappy L. Dietary and lifestyle interventions in the management of the metabolic syndrome: present status and future perspective. *Eur J Clin Nutr.* 2002;56:1-6.
104. Brand-Miller JC, Foster-Powell K. Diets with a low glycemic index: from theory to practice. *Nutr Today.* 1999;34:64-72.
105. Trout D, Behall KM. Prediction of glycemic index among high-sugar, low-starch foods. *Int J Food Sci Nutr.* 1999;50: 135-144.
106. Foster-Powell K, Holt SHA, Brand-Miller JC. International tables of glycemic index and glycemic load values: 2002. *Am J Clin Nutr.* 2002;76:5-56.
107. Jenkins DD, Jenkins AL. Glycemic index and diabetes: sucrose, traditional diets and clinical utility [editorial]. *J Am Coll Nutr.* 1994;13:541-543.
108. Jenkins JA, Jenkins AL. Nutrition principles and diabetes. A role for “lente carbohydrate”? *Diabetes Care.* 1995;18: 1491-1498.
109. Trout DL, Behall KM, Osilesi O. Prediction of glycemic index for starchy foods. *Am J Clin Nutr.* 1993;58:873-878.
110. Katanas H. Diets with a low glycemic index are ready for practice. *Nutr Today.* 1999;34:87-88.