

# THE ROLE OF GLYCEMIC INDEX & GLYCEMIC LOAD ON CARBOHYDRATE FOOD QUALITY: A STATUS REPORT



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# Table of Contents

Executive Summary .....	2
Introduction .....	3
Carbohydrates and Glycemic Response Measures .....	4
Table 1 .....	5
Table 2 .....	6
Table 3 .....	8
Table 4 .....	8
Table 5 .....	8
The GI Measurement Issues and Controversy .....	9
Factors Affecting the Variability of the Index .....	9
Table 6 .....	9
Table 7 .....	9
Table 8 .....	10
Table 9 .....	11
Glycemic Index in the Clinical Setting .....	12
Glycemic Index and Body Weight, Weight Loss and Satiety .....	12
GI/GL and Body Weight .....	12
Glycemic Index, Glycemic Load and Weight Loss .....	13
Glucose Release, Insulin Release and Insulin Sensitivity .....	13
Hunger, Satiety, Palatability and Satisfaction with GI/GL Diets .....	14
Glycemic Index, Glycemic Load and Prevention and Treatment of Diabetes .....	15
GI, GL and Prevention of Diabetes .....	15
Text Box 1 – Nutrition Recommendations and Interventions for Prevention of Diabetes .....	17
Glycemic Index and Loading in Treating T2DM .....	18
Text Box 2 – Nutrition Recommendations for the Management of Diabetes CHO in Diabetes Management .....	18
Glycemic Index, Glycemic Load and Gestational Diabetes .....	20
Pre-Diabetes and the Insulin Resistance Syndrome and GI/GL .....	20
Glycemic Index, Glycemic Load and Markers of Coronary Risk and Cardiovascular Disease .....	21
GI/GL, Blood Lipids and Markers of Coronary Risk .....	21
GI/GL, Stroke and Cardiovascular Disease .....	21
Glycemic Index, Glycemic Load and Cancer .....	22
Breast Cancer .....	22
Text Box 3 - Prospective Studies Which Show No Association of GI and GL with Breast Cancer .....	23
Glycemic Index, Glycemic Load and Colon Cancer Risk .....	23
Glycemic Index, Glycemic Load and Pancreatic Cancer .....	24
Glycemic Index, Glycemic Load and Other Cancers .....	24
Summary for Glycemic Index and Glycemic Load for all Cancers .....	26
Glycemic Index for Athletes .....	26
Conclusions .....	27
List of Acronyms .....	29
Glossary .....	29
References .....	32

## Executive Summary

Carbohydrate food quality has become a hot topic due to its link with glycemic response and chronic diseases. Yet, glycemic response as measured by glycemic index (GI) and glycemic load (GL) is variable. Further, there is misleading use of GI and GL due to lack of understanding regarding what is being compared and that the comparison is of 50g of available CHO (not food) and 50g of glucose. To add to this problem within and between lab variations, plant varietal differences and cooking methods produce other sources of variability. The measure is done with a single food eaten alone, but foods are not usually eaten alone, but in combination, thereby adding more variability. These sources of variability suggest that assigning numbers to individual foods would not only be difficult and too imprecise for food labeling, but also that it would fail to adequately inform the consumer. To add to the complexity, markedly different diets can have the same glycemic score.

Thus, tying either GI or GL to chronic disease endpoints is very difficult and this has been shown in a number of instances. For example, data linking GI/GL to either weight maintenance or long-term weight loss is inconsistent, despite the fact that some studies indicated that low GI or GL diets, compared those higher in GI or GL, may be weakly associated with greater satiety and reduced hunger. In terms of the risk of type 2 diabetes mellitus (T2DM), high dietary GI or GL is associated in some studies. However, the pattern is inconsistent and has confounders such as age, BMI, lifestyle and other dietary factors – especially dietary fiber. Diets low in dietary fiber are strongly associated with increased risk of T2DM and the association is amplified when diets are high in dietary GI or GL. While data exist which both support and contradict benefits of low GI/GL diets in the management of diabetes, the American Diabetes Association recommends that diabetics consuming high GI diets switch to lower GI diets to help control postprandial hyperglycemia.

Findings are inconsistent on the role of low-GI diets on risk factors for coronary heart disease (CHD) and cancer. Some studies show a small reduction in total cholesterol and markers of inflammation for hyperlipidemic subjects selecting low GI diets compared with high GI diets. The role of GI or GL in cancer risk is inconsistent and depends on the type of cancer. While case-control studies showed positive associations between GI and GL intake for a number of types of cancers, pooled cohort studies showed no consistent associations between colorectal, pancreatic, breast cancer or other cancer risks and GI or GL. Further studies are needed which improve the assignment of GI and GL to the diet along with careful choice of subjects in the cohorts.

Total carbohydrate in the diet appears to trump the GI or GL of the diet when considering fuel for exercise. For the meal prior to endurance exercise, data indicate there may be a competitive advantage to selecting low-to-moderate GI/GL foods, and limited data indicating an advantage of a higher GI/GL diet or food for replenishing glucose after exercise.

# Introduction

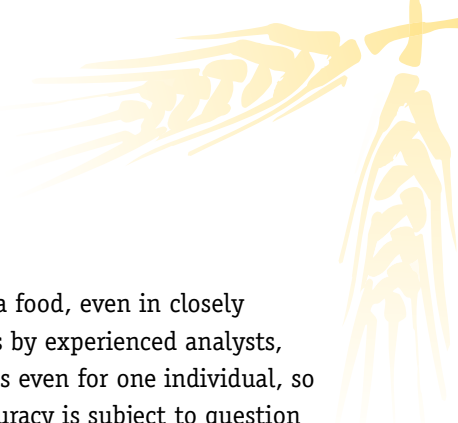
Scrutiny surrounding the quality of carbohydrate (CHO) foods has in the last decade started to approach that of fats. Large epidemiological studies have linked the glycemic response to chronic diseases by associating low glycemic index (GI) or glycemic load (GL) diets with a number of positive health impacts. These include: (1) improved glycemic control in diabetic subjects, which is associated with reduced risk of diabetes, (2) more favorable lipid profiles, which are associated with lower risk of cardiovascular disease, and (3) reduced markers of inflammation, which are associated with lower risk of metabolic syndrome, overweight and other chronic diseases. A few studies have shown associations between dietary GI/GL and the risk of colon, breast and other cancers. Despite studies that indicate associations, there are also a number of studies that fail to link GI/GL of the diet with health and disease risk.

Two major possibilities may account for the lack of consistency among studies. One has to do with potential confounding due to diet quality. The other is related to variability associated with the method of determining GI and GL in the studies.<sup>1</sup> In terms of confounding, low GI/GL diets could be linked to reduced disease risk because they are comprised of fruits, vegetables, nuts, legumes and whole grains. These inherently nutrient intense, phytochemical-rich, high fiber foods all have the capacity to lower disease risk regardless of their GI/GL.<sup>2,3</sup> On the other hand, foods and diets can have a low GI/GL if they contain low GI sweeteners such as fructose or are high in meat and fat. These widely variant diets are likely to have quite different effects. In like manner, foods with a high GI/GL could be positively associated with daily consumption of highly processed snacks, and negatively associated with consumption of nutrient-rich foods.<sup>4</sup> Thus, a high dietary GI/GL may reflect food patterns less likely to deliver disease-protecting nutrients. Thus the GI/GL of some diets may be more about what is or is not present with the CHO rather than glycemic effect of the CHO.

The determination of the GI of a food, even in closely controlled laboratory conditions by experienced analysts, creates large standard deviations even for one individual, so the measure's precision and accuracy is subject to question by many.<sup>5</sup> In like manner, determination of the dietary GI or GL from food frequency also has many potential sources of error.<sup>1</sup> This is compounded by the fact that changes in amounts of the food or combinations of foods may change the measured glycemic response.

Proponents contend that, despite the variability, using the GI/GL concept is important in making diet selections, and that GI/GL should be controlled for both treatment and prevention of chronic diseases. Detractors contend that the measure's variability makes the use of GI/GL valuable only in a laboratory setting.

Thus carbohydrate foods find themselves front-and-center in a nutritional controversy. No longer are they viewed merely as a staple or as a source of energy, but rather they have been added to a list of food components to be evaluated when deciding how much and which type to include in the diet. This review will focus on studies that have been published since the prior review (Jones, 2002) and will cover the measures of blood glucose, the variability of the measure, the relationship of GI and GL to diabetes, weight control, coronary heart disease and other chronic diseases and its role in fueling endurance sports. Also included are recommendations, regulations and current consumer understanding regarding use of GI and GL in the diet.



# Carbohydrates and Glycemic Response Measures

The nutrition of CHOs was thought to be quite simple. Physiological effects of digestible carbohydrates were thought to be directly related to whether the CHO was classed as simple, containing one or two sugar units (a mono- or disaccharide), or complex, containing multiple sugar units (a polysaccharide). In the old paradigm, all simple sugars were assumed to enter the bloodstream quickly, and all complex CHOs, because they would need to be broken down by digestive enzymes, would enter the bloodstream slowly (Figure 1A). Despite the fact that data from the 1930s indicated that this paradigm might be in error,<sup>6</sup> it was not until the 1970s that this nutritional dogma was actively researched.<sup>7</sup> These data showed that some complex CHOs could have a glycemic response similar to simple sugars and vice versa, which yielded a new paradigm (Figure 1B). In 1981, David Jenkins and his colleagues at the University of Toronto developed a method to quantify the effect of various carbohydrates on the blood glucose response in people with diabetes. Thus, the GI concept was born.<sup>8</sup> Subsequently the GI was derived in an attempt to consider quantity of carbohydrate.

Simply stated the **Glycemic Index** measures how quickly a carbohydrate enters the bloodstream and elevates blood sugar. The actual GI measurement compares the standard blood glucose-raising effects of ingesting 50g of a standard, usually glucose, to ingesting 50g of **available CHO**<sup>i</sup> from a particular food. The measurement follows the rise and fall in blood glucose,<sup>i</sup> which is measured as the area-under-the-curve (AUC) for a 2-hour time period after ingestion of the test food or standard glucose. For each subject, the AUC for

Figure 1

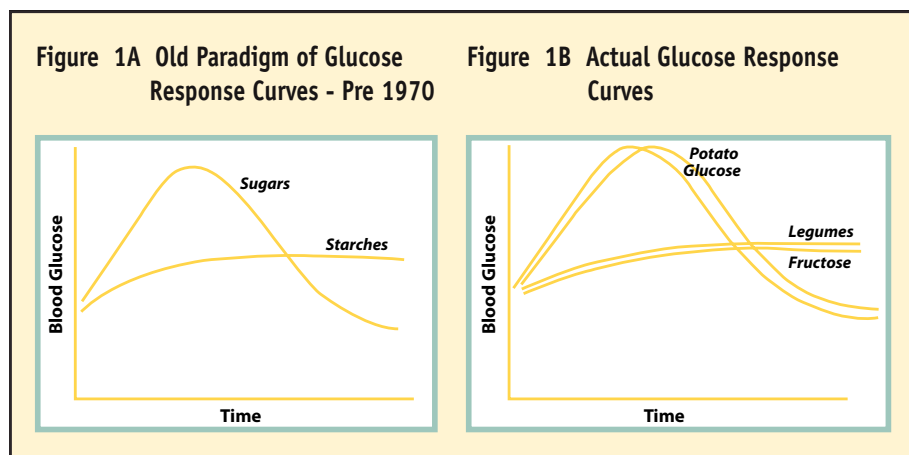
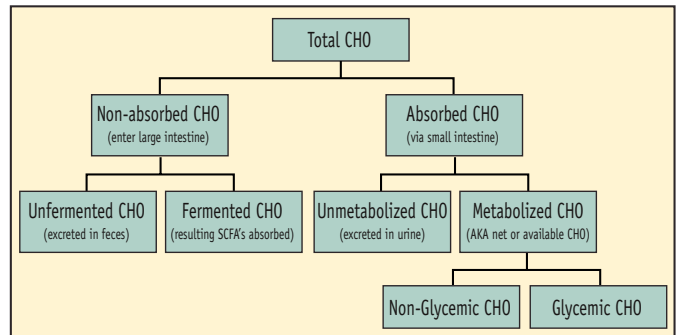


Figure 2: Carbohydrates in Digestion and Available Carbohydrate



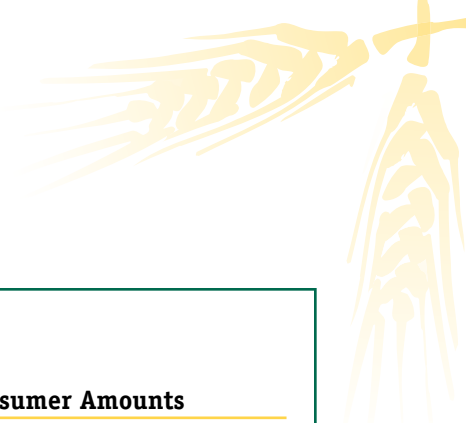
<sup>i</sup>'Available carbohydrate' is carbohydrate that is digested and absorbed in the small intestine. (schema from Steve Brooks, Health Canada)

glucose is arbitrarily assigned the value of 100. The GI is a ratio calculated by comparing the AUC observed with the feeding of the test food to the AUC with glucose.

It must be pointed out that GI compares equal amounts of **available CHO** (Figure 2) in the test food to 50g of glucose. Many diet books, popular press articles, and even some health professionals *erroneously* promote that the measure compares identical gram amounts of food, e.g., that it compares the blood glucose curves of 50g of test food to 50g of glucose.

Many fail to understand that the quantity of food needed to reach 50g of available CHO may differ dramatically. Foods that are high in water, dietary fiber and other unavailable (not broken down in the small intestine) CHO require portions much larger than 50g to deliver 50g of available CHO. Table 1 shows the GI amounts of some sample carbohydrate foods needed to reach 50g of CHO. Thus interpretation of GI numbers from the table must be done with care. For example, some following low-GI diets avoid carrots, which in original tables carried high-GI values. However, the diet authors fail to say or are unaware that nearly 7 raw carrots or 5 cups of cooked carrots are needed for 50g of available CHO (Table 1).

<sup>i</sup> Bread was introduced as a standard in order to compare CHO in food, not merely glucose in solution. Rice has been shown to be a good standard in cultures where it is the predominant staple.



**Table 1: Amount of Food to Yield 50 g of Available CHO**

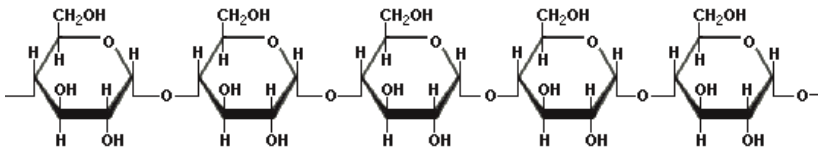
Food	Grams of food	gm of CHO	Consumer Amounts
Glucose	50	50	~ 4 Tbsp
Converted rice	61, dry	50	1/3 c dry (1 c cooked)
Russet potato	317 raw	50	1 large potato
Whole kernel corn	279	50	1 3/4 c (cooked, drained)
Enriched white bread	102	50	~ 3 slices
Carrots	896	50	~ 7 cups, shredded raw or ~ 5 cups cooked

Data from Crapo et al<sup>233</sup> and USDA Tables of Food Composition

**Figure 3 Structures of Amylose and Amylopectin**

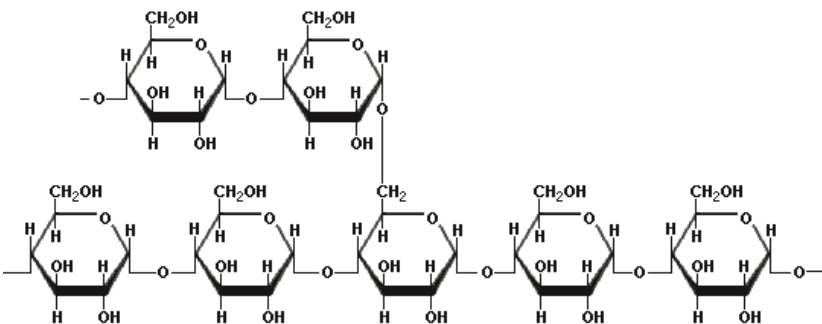
**Figure 3A Amylose**

Amylose molecules consist typically of 200 to 20,000 glucose units, which form a helix as a result of the bond angles between the glucose units.



**Figure 3B Amylopectin**

Amylopectin differs from amylose in that it is highly branched. Short chains of about 30 glucose units are attached with 1  $\alpha \rightarrow 6$  linkages approximately every twenty to thirty glucose units along the chain. Amylopectin molecules may contain up to two million glucose units.



**Figure 3C A pictogram of highly branched amylopectin**

The side branching chains are clustered together within the amylopectin molecule.



Characteristics of the food affect its GI. For example, the physical structure of a food is one crucial aspect. Dense, compact foods such as nuts, pasta, non-starchy vegetables, fruit, and legumes impede penetration of starch-digesting enzymes, the amylases. This translates into slower glucose release into the bloodstream and a lower GI. Such foods are sometimes described as slowly available glucose (SAG) starches.<sup>9,10</sup> In contrast, non-viscous or porous foods such as bread allow fast enzyme penetration. The result is a high GI due to fast digestion and quick release of glucose into the bloodstream. The foods in this category are sometimes referred to as rapidly available glucose (RAG) starches.<sup>11</sup> Table 2 gives the GI and GL for some selected foods. GIs for common foods may differ by more than 5-fold.

Several other aspects of starch structure determine the rate of starch digestion, and hence the GI of a starch-containing food. First is the proportion of the two types of starch molecules, amylose and amylopectin. While both are glucose polymers, in amylose, glucose is ordered in a long, linear chain. In amylopectin,

glucose units are joined into a highly-branched, tree-like structure, resembling the liver carbohydrate glycogen. (Figures 3 A and B depict the two starch types. Figure 3C depicts the highly branched amylopectin.) Amylase acts by attaching to the end of starch chain, so it slowly peels sugar units off from the end of the long chain amylose. Thus, it steadily releases glucose into the bloodstream. For amylopectin with its many branch points, amylase attaches to the available ends and releases a number of sugar units

at once. This triggers a rapid release of the glucose and a rapid entry into the bloodstream, resulting in a high GI.

Another aspect that affects the rate of glucose digestion is whether the starch is raw (ungelatinized) or cooked with liquid (gelatinized). Ungelatinized starches such as those in the raw oatmeal used in the making of muesli, raw potato or unripe banana have low-GIs and are SAG (Figure 4).<sup>12,13</sup> Dextrinized starches (cooked with dry heat) have

**Table 2: GI and GL of Selected Carbohydrate Foods**

<b>Food</b>	<b>GI</b>	<b>amt</b> (Gms Unless Noted)	<b>GL</b>
<b>Cereals, breads and grain products</b>			
All-Bran® (Kellogg's)	38	30	8
Cornflakes (Kellogg's, UK)	93±14	30	23
mean of five studies	81±3	30	20
Bread White flour, homemade (UK)	89	30	12
mean of sixteen studies	75±2	30	11
White bread, homemade, fresh, toasted (UK)	66	30	9
mean of three studies	60	30	8
Stay Trim™, whole grain bread (Natural Ovens)	70±10	30	10
Traditional French baguette	57±9	30	10
Enriched white bread	71±9	30	10
Apple muffin, made with rolled oats and sugar	44±6	60	13
Apple muffin, made rolled oats and without sugar	48±10	60	9
Bagel, white	69	70	24
Chocolate cake made from packet mix with chocolate frosting (Betty Crocker)	38±3	111	20
<b>Rices</b>			
Basmati, white, boiled (Mahatma brand, Australia)	58±8	150	22
Brown (Canada)	66±5	150	21
Brown, steamed (USA) <sup>11,14</sup>	50	150	16
Brown rice, boiled in excess water for 25 min.	72±6	150	29
<b>Pastas</b>			
Fettucine, egg (Australia)	32±4	180	15
Fettucine, egg (Mother Earth Fine Foods)	47±6	180	2
Fusilli pasta twists, boiled 10 min. in salted water	61±9	180	29
Fusilli pasta twists, boiled in 10 min. unsalted water	54±11	180	26
Fusilli pasta twists, tricolor, boiled in 10 min. unsalted water	51±11	180	23
Fusilli pasta twists, whole wheat, dry pasta, boiled 10 min. in unsalted water	55±8	180	23
<b>Snacks</b>			
Coca Cola®, soft drink	63	8 oz	16
Popcorn, plain, cooked in microwave oven (Uncle Toby's, Australia)	89	20	10

<http://www.mendosa.com/gilists.htm>

intermediate GIs. Further, native starches from different species vary in both granule structure and composition, both of which affect the glycemic response.

The specific sugar type also impacts the GI. Glucose has a high GI (Figure 1A), and fructose has a low one (Figure 1B). Sucrose (table sugar) and high fructose corn syrup are approximately 50% glucose and 50% fructose, so their resulting GIs reflect the mix of these two monosaccharides and are – to most people’s surprise – moderate GI foods.

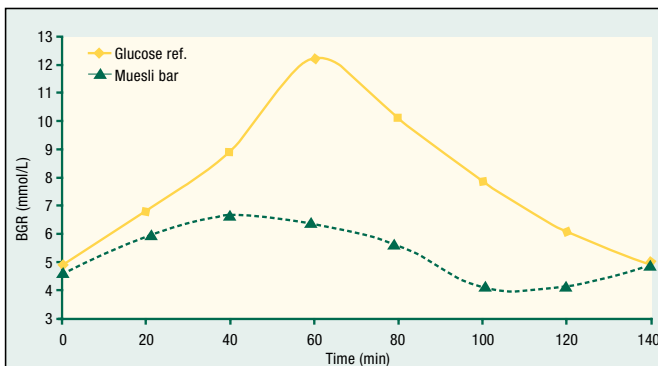
The macronutrient composition of the food also affects the GI. Fat or protein in the food can change the rate of starch digestion and absorption and lowers the GI.<sup>14</sup> Table 3 gives selected foods their GI and their fat content. Foods high in fiber, especially soluble fiber, often have a low GI. Thus most studies are unable to determine whether the effect was due to the fiber in the diet or the low GI/GL of the diet. A recent study was designed to address this issue. While the authors of this well-controlled study suggested that low GI was more important than dietary fiber, the study failed to equalize fiber intake between the low and high GI groups.<sup>15</sup> The low GI diet had 7 grams more of fiber (half the usual North American fiber intake) than the high GI diet, so while the study concluded that low GI/GL was the reason for health benefits, the question remains unresolved.

**The GL** attempts to take into account both the GI and the amount of CHO in an ordinary serving of a particular food. Thus, the GL is calculated by multiplying the GI by the number of grams of CHO in a serving of the food. Some foods with a high GI such as carrots may have a low GL. Critics of the GL measure claim that it takes an already imprecise measure, the GI, and potentially amplifies the error by multiplying it by the grams of CHO. Table 2 compares the GI and GL of selected foods.

Another measure, the **glycemic glucose equivalent** (GGE) was developed by Munro and his colleagues in New Zealand.<sup>16,17</sup> GGE combines GI, food composition and

<sup>ii</sup> The insulinemic index is an index comparing the insulin curves after the ingestion of an equal amount of carbohydrate (50 g) in a food.

**Figure 4 Blood Glucose Response Curve (BGR) of Slowly Digested Muesli Bar** (courtesy of Munro,<sup>13</sup> New Zealand, Crop Institute)



food quantity, so it comes closest to reflecting the blood glucose-elevating effect of a specific portion of food eaten. Specifically, GGE gives the theoretical weight of glucose that would induce the glycemic response equivalent to that induced by the given amount of ingested food. Table 4 compares the GI and GGE in certain foods and shows how determination of high and low is affected. The GGE has the advantage of communicating what the actual effect of eating a certain amount of food will be. Table 5 gives an example that shows that the GI of a food is unchanged no matter how much is eaten, but the GGE changes as the quantity of food increases.<sup>13</sup>

It is also important to note that any of the glycemic response measurements fail to consider insulin responses, despite assertions to the contrary in some popular diet books. **The insulinemic index**<sup>ii</sup> compares the postprandial insulin responses over a 2-hour period after the ingestion of a 240-calorie portion of food compared to a standard reference food.<sup>18</sup> Some argue that this less well-known index is more important than measures of glycemic response and should replace or at least be used with it. Insulin secretion is stimulated by a variety of dietary factors in addition to blood glucose. Even foods with little or no CHO, such as meat, eggs or milk, stimulate insulin secretion. Obviously the amount of insulin secreted can affect the glycemic response, especially in those individuals for whom the insulin sensitivity is normal.

**Table 3: GI and Fat Content of Some Foods**

Food	GI <sup>a</sup>	Fat <sup>b</sup>
Dates	100	0
Carrots	92	0
Rice milk	87	2 <sup>c</sup>
Rice crackers/cakes	77-80	1
Whole wheat bread	75	1
Watermelon	72	0
Mars Bar	65	9
Oatmeal	58	2
Potato chips	56	10
Pound cake	54	6
Snickers	40	14 <sup>c</sup>
Chocolate cake & chocolate frosting	38	11
Lentils	32	0
Fructose	15	0

Data from <sup>a</sup><http://www.mendosa.com/gilists.htm>

<sup>b</sup><http://www.nal.usda.gov/fnic/foodcomp/cgi-bin/list> unless otherwise noted

<sup>c</sup><http://caloriecount.about.com/calories>

**Table 4: Low GI Foods May be High GGE Foods**

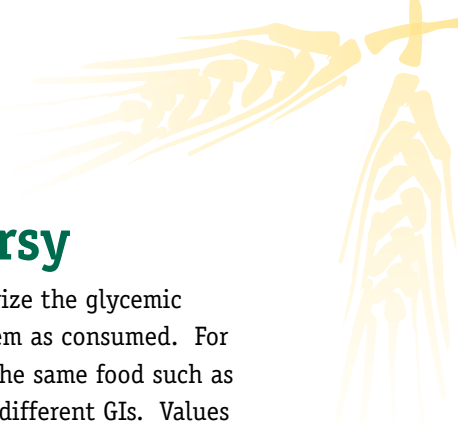
Classification of Low, Med or High	Food	GI value for the Food	Food	GGE/sv for the Food
Low GI <55 Low GGE/sv <10	Muesli	43	Rutabaga	4
	Sponge cake	46	Pumpkin, boiled	6.6
	Spaghetti	41	Cookie/raisins	6.6
			Watermelon	7.8
Medium GI 55-70 Medium GGE/sv 10-20			Broad beans	11.5
			Spaghetti	12.1
High GI >70 High GGE > 20/sv	Broad beans	79	Muesli	25.1
	Pumpkin, boiled	75	Sponge cake	24.6
	Cookie/raisins	77		
	Rutabaga	72		
	Watermelon	72		

Adapted from Munro, New Zealand Crop Institute<sup>13</sup>

**Table 5: A Comparison of GGE and GI for Muesli Bars at Serving Amount Changes**

Muesli bars eaten	GGE of Bars Eaten	GI of Bars Eaten
1	18	49
2	36	49
3	54	49
6	108	49

Munro et al ref.<sup>13</sup>



# The GI Measurement Issues and Controversy

The GI measurement itself creates controversy for several reasons. First, there is concern about both the measure’s wide variability both within and among subjects (Table 6).<sup>19,20</sup> Glycemic responses vary from day-to-day even in the same subject. Further, there is the high degree of variability both within and among subjects, even when the analysis is conducted in laboratories experienced with the procedure.<sup>19</sup> Despite rigid protocols where subjects eat identical amounts of the same food the day before the test meal, day-to-day variation is very high. For example, triplicate analysis of the GI values for white bread compared to the 50 g glucose standard in 23 adult subjects showed that there were marked differences on different days for the same subject. The coefficient of variation was 17.8% for inter-individual values, while the intra-individual variation was 42.8%.<sup>20</sup> These data show that the day-to-day variation in the same subject is often greater than variation among subjects. Some suggest that repeated baseline measures could be used to lower variability. Others suggest that the variability calls into question the measurement’s value for use in a clinical setting.<sup>21</sup>

Second, methodological protocols have raised questions. The use of only the first 2-hour portion of the curve to follow blood glucose excursion rather than the entire curve is a source of debate.<sup>22</sup> The method of blood draw is another.<sup>23</sup>

Third, variability caused by differences in the food itself can be as great as those caused by differences in the eater. For many foods the values in the GI tables often do not reflect the many sources of variability

and, thus, may poorly characterize the glycemic response of a particular food item as consumed. For example, different varieties of the same food such as rice or potatoes have markedly different GIs. Values for selected US potato varieties cooked by different methods are found in Table 7. The same food eaten at different stages of maturity or processed or cooked by varying techniques and for varying times, or stored under differing conditions can also have widely varying GIs. How the food is eaten, its preparation, and storage can affect the GI. This will be discussed in detail in a subsequent section.

## Factors Affecting the Variability of the Index

Factors associated with the act and timing of eating the food can affect the glycemic response. These include the degree of mastication, quantity of food ingested at any one time, the time period of eating and frequency of eating<sup>24</sup>, the accompanying foods and even foods eaten at prior meals. For instance, inclusion of legumes or barley in the evening alters the glycemic response at breakfast and low GI foods at breakfast lowers the GI of a CHO food at lunch. This glycemic effect of foods at a subsequent meal has been labeled the *lente* CHO effect.<sup>25,26,27</sup> The precise mechanism differs based on the time interval between meals. The lowered glycemic response at lunch is thought to be due to a reduced concentration of free fatty acids in the blood stream with the low GI breakfast. The decreased glycemic response caused by low GI foods eaten the night before is thought to be due to colonic fermentation of resistant starch or dietary fiber to produce short-chained fatty acids (SCFAs). SCFAs are reabsorbed by the liver and modulate the blood glucose response.<sup>28</sup>

**Table 6: Glycemic Index and Standard Deviations from Interlab**

	<b>GI ± std dev</b>
White bread	72.5 ± 35.8
Instant mashed potatoes	84.5 ± 32.7
Long grain rice	71.1 ± 38.2
White spaghetti	46.9 ± 26.7
Barley	34.7 ± 24.7

**Table 7: GI of Selected US\* Potatoes and Cooking Methods**

<b>Potato type and cooking method</b>	<b>GI</b>
Boiled red potatoes	89
Boiled red potatoes eaten cold	56
Roasted California white potatoes	72
Baked US Russet potatoes	77
French fries	75
Instant mashed potatoes	88

Fernandez et al. JADA. 2005; 105:557-62

\*Data on European varieties and cooking methods show even greater range than shown on this chart.<sup>234</sup>

**Table 8: Amylose and Amylopectin Content of Common Starches**

Starch	Amylose %	Amylopectin %
Corn, wheat starch	24- 25	75-76
Waxy corn starch	<1	99
High amylose corn starch	70	30
Root starches, potato and tapioca	17-20	80-83

Eliasson, AC. Carbohydrates in Food., 2nd edit, 2006. CRC Press: Boca Raton.

The chemical makeup of the starch, e.g. the proportion of the two starch moieties, amylose and amylopectin, is affected by the both the species and variety. (Table 8 gives some amylose and amylopectin contents of a sampling of foods.) Foods either naturally high in amylose or those bred or modified to increase amylose have a low glycemic response.<sup>29</sup> For example, long grain basmati rice, which is naturally high in amylose, results in lower blood glucose and insulin concentrations than most regular or short grain rices.<sup>30</sup> Similarly GI of potato varieties differ (Table 7). Waxy potatoes have GIs in the moderate range; while the GI for starchy potatoes is high.<sup>31</sup>

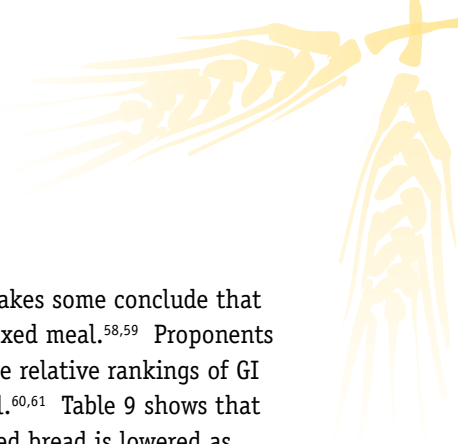
The GI of the same potato variety cooked, cooled, processed, or stored in different ways varies. Warm boiled potatoes have a different GI than those which are baked or mashed. Cooling a boiled potato gives a lower GI (Table 7) than the same potato eaten hot.<sup>32</sup> This is due to the crystallization of the starch molecules upon cooling. The crystallized starch molecule, like the ungelatinized one, is less available to the amylase and therefore has a lower GI. French fries have a lower GI than boiled potatoes, due in part to the fat content. However, studies where an equivalent amount of fat was added to boiled potatoes failed to lower the GI to the value observed in the fries. Apparently, both fat and the frying process lower the GI of french fries.<sup>33</sup>

Canning and precooking prior to vacuum-packaging raise the GI slightly over that seen with a typical home-prepared (boiled) product.<sup>34,35</sup> Further, the GI is raised more when the pasta or legume is cooked in excess liquid as for soup than in preparations that use less liquid, as in preparing a legume side dish (Table 2).

Not all processing raises the GI. Parboiling rice prior to removal of the bran to make converted rice yields rice with a somewhat lower GI than regular rice.<sup>36</sup> Different shaped pastas also differ in their GI (Table 2). Surprisingly, the GI was not related to amount of cooking or to surface area.<sup>37</sup>

Milling, particle size, grain type and intactness, processing handling and fiber type all affect the GI. Finely milled particles of many, but not all, grains have higher GIs than intact or larger particles.<sup>38,39</sup> Whole kernels may trap much of the starch as resistant starch (type I), which is not available to the enzymes.<sup>40</sup> However, this is not always the case. No change in GI was observed with microparticulation in the processing of white whole wheat to make Ultragrain™<sup>41</sup> or with grains containing significant levels of soluble fiber such as barley or oats.<sup>42</sup> Instantizing of starches to make instant cereals, rice or puddings, where only added liquid is required, markedly raises the GI.<sup>43</sup> Puffing grains to make puffed cereals or popping to make popped corn opens the structure and thus makes amylase more easily accessible. This, in turn, raises the GI. Thus, the GI of whole grains is dependent on many aspects including the degree of milling, puffing, extrusion or other processing or storage, and the type of grain and other grain components.<sup>44,45</sup> Toasting, freezing or defrosting, or toasting following freezing and defrosting all lower the GI.<sup>46</sup> Since these procedures promote starch crystal formation, the starch structure becomes more similar to the one in the native grain, decreasing the GI.

Aspects of bread-making also affect GI. Partial dough proofing, as used in the traditional process of making a bagel, results in a lower volume, denser product that decreases the GI. The denser product probably impedes the accessibility of the amylase, so the starch yields its



glucose more slowly.<sup>47</sup> Formation of acid in the sourdough process or the addition of acid either in preparation or to the dipping oil for bread prior to eating (or acid addition to rice or potatoes in the preparation of sushi or potato salad) lowers the GI.<sup>48,49,50,51</sup> Acids may inhibit amylase by moving it away from its pH optimum.

The inclusion of other foods such as nuts or peanuts drops the GI of a food or a meal by as much as half. The change in the GI by adding nuts or acid has contributed to an important debate about the usefulness of the GI concept for consumers eating mixed meals. The GI of a food is always measured individually. However, humans mostly eat foods in combination. Data show that the GI of carbohydrate foods is lowered by other foods. For example, toppings such as cheese, chili con carne, baked beans or tuna added to baked potatoes, cooked pasta and toast lowered the GI of these foods.<sup>52</sup>

Simultaneous ingestion of other foods or food components changes the GI by several different mechanisms. Protein and dairy ingested with CHO reduces the GI of some foods, in part because protein ingestion increases the insulin response, which in turn increases the clearance of sugar from the bloodstream.<sup>53,54,55,56</sup> Ingestion of fat with CHO has little affect on insulin, but it slows gastric emptying. In addition, it slows the penetration of the amylase into the food matrix and inhibits the enzymes, thereby blunting the glycemic response.<sup>57</sup> Thus, ice cream, candy bars and iced chocolate cake all have high fat contents and fairly low GI values (Table 3). The wide range of GI values in the

presence of other components makes some conclude that the index loses its utility in a mixed meal.<sup>58,59</sup> Proponents for the GI concept report that the relative rankings of GI remain the same in a mixed meal.<sup>60,61</sup> Table 9 shows that the GI of rice and Chinese steamed bread is lowered as other foods mix with the meal.

The mixing of foods together has been a major area of controversy for the GI. Despite an analysis showing that total CHO and GI explained approximately 90 percent of the variability in glucose and insulin response irrespective of calories, protein, or fat in a meal, a recent review called into question the utility of GI and GL to adequately reflect glycemic response to food, when used in the context of a usual diet.<sup>62</sup>

Thus, the GI measure itself is quite variable with its variability dependent not only on the properties of the food and its handling, but also on the subjects eating it. Despite the variability, there have been many studies to assess whether application of the GI/GL concept can provide dietary advantages in many different settings including: 1) helping curb hunger, thus making it a useful tool for weight loss and weight maintenance, 2) regulating blood sugar and improvement in the body's sensitivity to insulin, especially in people with insulin resistance and diabetes; 3) lowering of blood lipids in people who have diabetes and those non-diabetics who have elevated blood lipids; and 4) helping determine the correct fuel before and after exercise. Each of these issues will be addressed in the following sections of the paper.

**Table 9: Glycemic Index Changes of Carbohydrate Staples with the Addition of Other Meal Items**

Food	Glycemic Index
Rice	83.2 ± 3.1
Rice and stir-fry pork	72.0 ± 14.0
Rice and stir-fry pork and celery	57.1 ± 11.2
Rice and stir-fry garlic sprout	57.9 ± 7.8
Rice and stir-fry garlic sprout and eggs	62.8 ± 16.7
Steamed bread	80.1 ± 22.5
Steamed bread and butter	68.0 ± 16.3
Steamed bread and beef	49.4 ± 22.8

Reference: Abstract of Cui H, Yang Y, Bian L, He M. [Effect of food composition of mixed food on glycemic index] [Article in Chinese] Wei Sheng Yan Jiu. 1999 Nov;28(6):356-8. (PMID: 12016989)

## Glycemic Index in the Clinical Setting

Inconsistent findings from all types of studies plague the controversy over the effects of GI/GL on the risk of certain chronic diseases. Some proponents of the GI/GL concept blame the high-GI/GL of the average US diet for obesity and a number of chronic diseases. They advocate low GI/GL to decrease disease risk.<sup>63,45</sup> Others say the data are too variable and call for measurements with more consistency.<sup>21</sup> Proponents on either side of the debate have data to support their position.

Low-GI/GL proponents have metabolic studies that show high-GI diets stimulate *de novo* lipogenesis and result in increased size of adipocytes, while low GI diets did not.<sup>64,65</sup> Low-GI diets have been shown to lower postprandial glucose, insulin and glucagon and serum fatty acid levels, to improve lipid profiles, to increase insulin sensitivity and to reduce markers of inflammation and to change other biomarkers so that they may significantly affect the risk

of obesity, diabetes, and cardiovascular disease. Therefore, advocates suggest that modulating the glycemic response by lowering dietary GI or GL of the diet is clinically useful. One recent meta-analysis supports this position.<sup>66</sup>

Yet some health professionals question the effectiveness of such a treatment and the selection of a treatment modality that is based primarily on associational data.<sup>67</sup> Concern has been expressed both about the independence and strength of the associations as well as inconsistent outcomes observed in interventions, which employed low GI or GL as a food selection tools.

The next section will look at findings that both support and fail to support the use of GI and GL to modulate specific conditions or diseases. The findings will be discussed with respect to strength of the evidence and possible confounders.

## Glycemic Index and Body Weight, Weight Loss and Satiety

### GI/GL and Body Weight

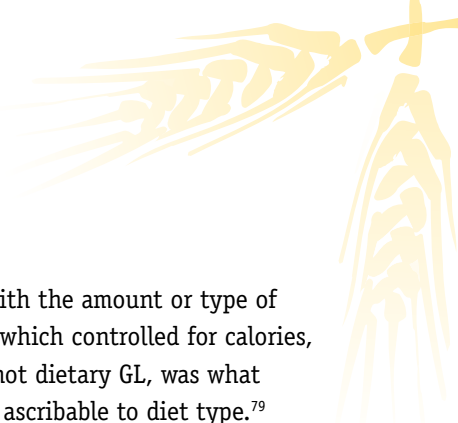
Diet crazes popular a few years ago suggested that diets with high GI/GL cause elevated body weights. Some epidemiological studies also seemed to support this idea. A review focusing on the prevention of weight gain in adult life suggested that *ad libitum* consumption of diets low in fat and high in protein and complex CHOs helped prevent weight gain,<sup>68</sup> and that selection of CHOs with a low GI might enhance this strategy. In another review of many large population studies, associations between GI and BMI were inconsistent. This review concluded by saying that “there is so far no evidence that low-GI foods facilitate weight control.”<sup>69</sup> One analysis actually showed that diets with higher GLs were associated with lower BMIs.<sup>70</sup>

The inconsistency among studies suggests many possibilities. First, there is a possibility that the data accurately reflect the situation (e.g. GI and GL do not affect body weight). It is however possible that some aspect of the method mask a relationship between GI/GL and body weight. One possible cause of error in the data is underreporting of food intake. Studies indicate that this

occurs more frequently among overweight individuals in a sample.<sup>71</sup> One study reanalyzed data to try to account for this error and did show a relationship between high GI intake and body weight.<sup>72</sup> Another cause of error can occur when assigning GI/GL to the diet from food frequency or other food intake data.<sup>1,73</sup>

Inadequate cohort segmentation can also mask a significant effect that is occurring in one population group. This was the case in one study of older adults. With both genders together, dietary GI and GL were unrelated to changes in body weight, percentage body fat, and waist circumference.<sup>74</sup> However, looking at the 191 women alone showed that GI – but not GL – was related to various measures of overweight, especially in sedentary women.

Cultural dietary patterns and age, as well as gender, may also be a source of variation. In overweight Latino youth (10-17 years old, n=120), neither GI nor GL were associated with any measure of adiposity.<sup>75</sup> Similarly, in a Danish study of 16-year-old youth (n=364) and children under 10 years of age (n=485), skinfold assessment of fatness was not



related to GI or GL for any of the 10-year-olds or 16-year-old girls, but there was association in Danish boys.<sup>76</sup>

In summary, the weight of the evidence indicates that dietary GI and GL are not related to body weight, although this appears to be inconsistent across populations and within specific subgroups. The differences may be due to genetic characteristics of the population, methodological considerations, or cultural and dietary differences. For example, diets with low GI or GL may be lower in calories and higher in protein and may be higher in fruits, vegetables, whole grains, and fiber and thus may have a better overall nutrient profile. All of these have been shown in prior research to help with body weight maintenance. On the other hand, some low GI or GL diets may be higher in fructose, meat and saturated fat. Thus GI and GL measures can give the same glycemic score to diets with vastly different nutritional properties making the determination of their relationship to weight maintenance, or any other chronic disease endpoint difficult.

### **Glycemic Index, Glycemic Load and Weight Loss**

Many popular weight loss regimens advocate low or no CHO diets as a strategy. Others advocate the inclusion of CHOs if the CHO is low GI or the diet low GL. Data from well-controlled studies show greater weight loss for subjects eating a low GI or GL diet, in the short term (less than 6 months). When these short-term weight loss studies were analyzed as part of a Cochrane review, the results showed that low GI/GL diets enabled a small (~1 kg), but statistically significant, greater weight loss than other types of weight loss diets.<sup>77</sup> While the increased average weight loss is not of great practical importance, the real advantage for those eating a low GI/GL diet was that weight loss was accompanied by a greater decrease in total and LDL cholesterol than seen with other diets. (This will be discussed further in the section that addresses GI/GL, coronary disease and blood lipids.) However, the weight loss advantage of low GI/GL was not sustained after 6 months.

Some contend that low GI/GL diets promote weight loss because they severely restrict food choice and promote satiety. The net result is fewer calories being ingested. One study with 22 obese subjects did not bear this out. It showed that the GI of the diet had no measurable impact on

hunger, satiety, or satisfaction with the amount or type of food provided.<sup>78</sup> Another study, which controlled for calories, showed that calorie restriction, not dietary GL, was what mattered in terms of weight loss ascribable to diet type.<sup>79</sup>

In general, there is a lack of controlled studies showing the effectiveness of low GI or low CHO diets for long-term weight loss and maintenance. The studies that do exist suggest that the ability to adhere to a diet made the difference. In a one-year-long randomized trial (n= 160), those who stayed on the assigned diet for the whole year – no matter which diet – lost weight.<sup>80,81</sup> There was not a statistically significant difference in the amount of weight loss among the diets. Diets, such as the Ornish or Atkins, which differed most from mainstream diets, had greater drop-out rates. A two-year study showed that a modified low CHO diet or a Mediterranean diet resulted in greater weight loss than a low fat diet (4.7 or 4.4 kg vs. 2.9 kg, respectively).<sup>82</sup> These diets were less restrictive than the extremely low GI, low CHO Atkins diet.

In conclusion, the promise of greater weight loss offered in popular low CHO diet books fails to materialize. When compared to a low fat diet, a slightly (~1 kg) greater weight loss occurs in the first 6 months but the effectiveness for long-term use still needs to be documented.

### **Glucose Release, Insulin Release and Insulin Sensitivity**

Proponents of the theory that low GI/GL diets help with weight loss suggest that high GI/GL diets raise blood glucose and result in insulin release. This, in turn, is said to increase hunger and adversely affect satiety. Yet physiological studies frequently show that blood glucose concentration has little effect on satiety or hunger. In fact, data on ingested sugars shows that glucose in the duodenum suppressed hunger, increased fullness and satiety ratings, reduced energy intake and increased insulin responses.<sup>83</sup> One study supports the theory that GL/GI can influence hunger ratings. In this study a high GI beverage consumed with a meal causes higher hunger ratings before the next meal than when an equivalent volume of the high GI beverage is consumed throughout the day. In the latter case, the high GI beverage consumed in small frequent doses would have a low GL and a yield a more steady blood glucose, which appeared to result in lower hunger responses.<sup>84</sup>

Low GI/GL diets are also purported to lower insulin release, which in turn, is said to decrease hunger or affect caloric intake. However, the findings supporting this are mixed. For example, in a study of 38 overweight French subjects where the GI of the diet was lowered by changing from regular starch to resistant starch, there was no change in insulin sensitivity. However, there was a trend towards reduced hunger and a significantly greater weight loss in the low GI starch group.<sup>85</sup> Insulin sensitivity improved in another small study of adult women (n=7). Substituting 60% of their high GI CHO calories with low GI CHO not only increased insulin sensitivity 20%, but also average glucose and insulin levels dropped approximately 40%, and caloric requirements increased by 11%. Fat oxidation supplied much more of the energy at rest on the low GI diet than the high GI one.<sup>86</sup> Thus the latter study suggests that a low GI diet might be advantageous for weight and caloric intake.

However, not all studies show an advantage for a low GI diet or an effect on insulin. For example, 22 overweight individuals, eating either low GI, high GI, or high-fat hypocaloric diets for 12 weeks, had the same increase in insulin sensitivity and the same weight loss.<sup>78</sup> In another study with 34 overweight adults, dietary GI caused no significant differences in first-phase acute insulin release or mean percentage change in insulin sensitivity. The high GI group showed a mean percentage change in insulin sensitivity of 26 and in the low GI of 24.<sup>87</sup> Nearly identical results occurred in overweight Latino youth.<sup>75</sup>

Thus some studies show an effect of insulin on hunger and satiety, depending on subject characteristics, but others do not. Differences in food used may also account for differences observed. In other cases the effect appeared to be due to specific foods being fed. For example, barley – a very low GI food – did not cause diminished appetite in 14 healthy, normal weight adults when compared to the same diet formulated with a higher GI food such as wheat.<sup>88</sup> Despite barley's 32% lower glycemic and insulinemic responses as well as higher satiety index,<sup>89</sup> food intake for the remainder of the day after the wheat meal was 23% less than after the barley meal. Thus, under this experimental condition, the lowered glycemic and insulinemic response did not translate into lower caloric ingestion.

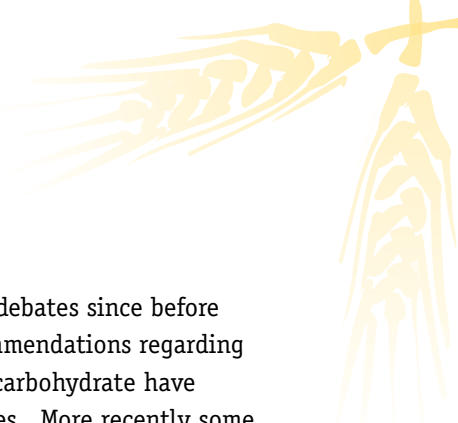
Data from animal studies<sup>90</sup> suggest that low GI or GL diets impact weight and adipose distribution because of metabolic changes that influence fat synthesizing enzymes, metabolism, and deposition. Human data suggest that high GI diets and low fiber diets favor formation of chylomicrons,<sup>92</sup> and low GI diets favor fat oxidation in the overweight women.<sup>86</sup> However, in overweight Latino youth, no effect of dietary GI was seen on fat deposition. In these subjects the degree of adiposity was affected by amount of sucrose in the diet, and not by dietary GI.<sup>75</sup>

Low GI diets created by using intact, whole grains instead of refined grains caused gene down-regulation of certain fat-metabolizing genes in subcutaneous adipose tissue. However, it is difficult to determine if the effects are due to components of various grain types such as rye or barley versus wheat, or to the dietary fiber content or lower GI seen in some intact grains.<sup>93</sup>

### Hunger, Satiety, Palatability and Satisfaction with GI/GL Diets

Satiety and the ability to control food intake is thought to be one of many important aspects in controlling overeating and obesity. An early review of short-term studies indicated that consumption of low GI CHOs may delay the return of hunger and reduce subsequent energy intake relative to consumption of higher GI CHOs.<sup>94</sup> Two studies showed that low GI diets decreased hunger ratings, but only one showed weight loss. A study using the WeightWatchers® POINTS program was compared with the same program using a low GI modification. Ratings of hunger – especially in the afternoon – as well as desire to eat were consistently lower for those eating the low GL modification.<sup>95</sup> However, after 12 weeks, there was no difference in weight loss or other measures. Nonetheless, the authors suggested that the subjective benefits of lower hunger and lower desire to eat may affect adherence to the diet over the long term. In overweight French subjects, the lower GI diet for 5 weeks, compared to those on the high GI diets, not only decreased hunger ratings before lunch and dinner, but also translated into slightly greater weight loss.<sup>85</sup> A study of 8- to 11-year-old children showed a non-significant trend towards consumption of fewer calories with less eaten at lunch after a low- versus high-GI, isocaloric breakfast.<sup>96</sup>

Like other studies with GI/GL, there is not concordance



among studies. A year-long study with 34 healthy overweight U.S. adults eating calorie-restricted diets found that the GI or GL of the diet had no effect on weight loss, hunger or satiety.<sup>79</sup>

In summary, there may be a weak trend towards greater satiety and reduced hunger with a low GI or GL diet, but the difference in satiety fails to translate into changes in caloric intake. Methodology issues with respect to the best way to measure satiety and impact on overall caloric intake could be one reason for inconsistency among studies. Satiety can be examined through perceived hunger, feelings of fullness, and subsequent intake at various intervals after eating, just to name a few. Adding to the difficulty is that satiety is a function of many food attributes and GI might be among them. Diets, which deliver adequate nutrition, may reduce the desire to eat. Many low GI/GL diets are rich in fruits, vegetables, and whole grains, foods rich in nutrients and low in calories. In addition, these foods tend to have high volume per calorie<sup>97</sup> and offer fermentable dietary fiber, resistant starch, and slowly available CHO, all of which have been shown to offer satiation and are associated with reduced body weight.<sup>98, 99</sup>

Food palatability is another aspect that affects satiety. Humans and rats alike will seek energy dense foods or over-consume highly palatable foods.<sup>101</sup> A recent study showed that people on a 'diet' craved foods which delivered a high energy density and fat content and were low in protein and fiber, regardless of whether the diet had a high or low GL.<sup>102</sup> Further, the ability to compensate for calories is compromised by foods high in sugar and fat.<sup>103</sup> Since these foods may have high GI/GL, energy density and palatability, their lack of impact on caloric intake or satiety might be erroneously attributed to high GI when it should be attributed to palatability or energy density.

The psychological impact of diets on the dieter may also be important. Many low GI/GL diets encourage eating of unlimited amounts of certain types of food. Not feeling restricted about all food categories may have a freeing effect and may help people stay on a diet.<sup>104</sup>

### **Glycemic Index, Glycemic Load and Prevention and Treatment of Diabetes**

The role of diet, especially CHOs, in both treating and

preventing diabetes has fueled debates since before the discovery of insulin. Recommendations regarding the optimal amount of fat and carbohydrate have varied markedly over the decades. More recently some have focused not only on the amount of each of the macronutrients, but also on the glycemic response and the role of GI and GL.

Despite over 30 years of data, there is still controversy on the role of GI and GL in the diet for preventing or treating both type 1 and type 2 diabetes.<sup>105</sup> This will be discussed in the following section of this review.

### **GI, GL and Prevention of Diabetes**

Some, but not all, early epidemiological studies associated high GI/GL diets with the development of type 2 diabetes mellitus (T2DM). Data from both the Physicians' Health Study (n ~ 42,000 male health professionals)<sup>107</sup> and the Nurses' Health Study<sup>108</sup> (n ~ 84,000 female nurses) showed that those in the quintile ingesting high GL diets versus those in the quintile ingesting low GL diets had a significantly increased risk of T2DM. Diets with both a high GL and low cereal fiber showed especially elevated diabetes risk. However, this was not shown in all studies. For example, the Iowa Women's Health Study<sup>109</sup> with ~36,000 post-menopausal women showed no such association.

Newer studies exhibit the same inconclusive pattern. A recent review and several studies provide support for an association. A systematic review combining 37 prospective cohort studies showed that those ingesting the highest dietary GI or GL, compared to the lowest, had an adjusted relative risk for T2DM of 1.40 for GI and 1.27 for GL.<sup>66</sup> Similarly those in the top 10% for GL, compared to the lowest 10%, had an increased risk of T2DM (RR: 2.47) in the 20-year follow-up study of 85,059 women in the Nurses' Health Study I and II.<sup>110</sup> CHO intake and consumption of short-grain rice (a high GI food) was measured in a cohort of 64,227 Chinese middle-aged women. The relative risk of developing T2DM for the highest quintile compared to the lowest quintile was 1.21 for GI and 1.34 for GL.<sup>111</sup>

However, a similar number of studies showed no association between GI or GL and the risk of T2DM. In the UK Whitehall II study with 70% men and 30% women (n=

7321), high-dietary GI was not associated with increased risk of diabetes. In fact, high GL was actually associated with **decreased** risk.<sup>112</sup> Those eating a diet in the highest tertile of GL had a hazard ratio (HR) for T2DM of 0.70 compared to the lowest tertile. In the Health, Aging and Body Composition prospective cohort study of 70-80 year olds (n = 2,248)<sup>113</sup> there was no association between dietary GI or GL and the risk of developing T2DM. In a representative sample of 2000 older Australians followed for 10 years, neither GI nor GL were involved in the risk of developing T2DM. Only vegetable fiber was independently associated with reduced risk of T2DM.<sup>114</sup> However, in a secondary analysis using a subset of the cohort under 70 years of age, a high-GI CHO diet was linked to increased risk of T2DM.

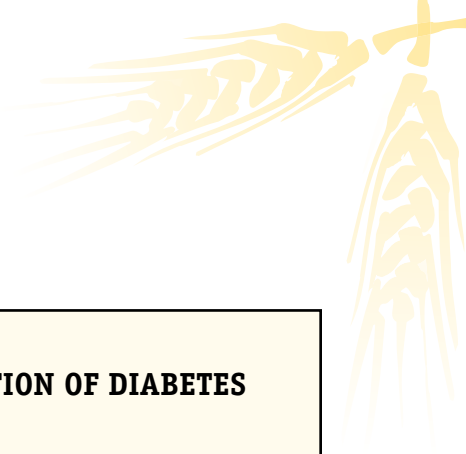
Body weight appeared to have an impact on the association between dietary GI or GL and the risk for T2DM, but the effect was not consistent across studies. For example in a prospective study of 36,787 Australian men and women aged 40-69 years, the risk of T2DM was increased (OR 1.37) for those in the highest quartile of white bread intake or dietary GI compared with the lowest. However, these relationships failed to remain significant after adjustment for BMI and waist-to-hip ratio. Conversely, in an 8-year study following 59,000 U.S. black women, the association between GI and GL and risk of diabetes mellitus became more robust when BMI was considered. Specifically, the incident risk ratios (IRR) associating dietary GI and the risk of developing T2DM was 1.23. (Note, the IRR between the intake of cereal fiber and T2DM was inversely associated, 0.82. For those with normal weight (BMI < 25.0), IRRs increased when the diets were both high in GI and low in cereal fiber.<sup>115</sup> Yet another outcome was observed in overweight Chinese subjects (BMI > 25.0). In this cohort, increasing the GL of the diet increased the risk of T2DM.<sup>116</sup>

Only a few intervention studies have looked at preventing T2DM by altering dietary GI. In one study, those at high risk for the T2DM were instructed to make a number of lifestyle modifications. These included participation in regular exercise and the selection of low GI foods as part of a high-CHO, low-fat, high-fiber diet. This multi-pronged intervention decreased T2DM risk by over 40%.<sup>117</sup>

While this study provides encouraging results suggesting that T2DM can be delayed by the right combination of modalities, it fails to provide conclusive evidence regarding the role of low GI or GL diets in diabetes. It is not known if each of the lifestyle modifications has an impact on T2DM prevention in its own right, or if there is synergy related to a number of lifestyle modifications.

In summary, GI and GL and the risk of T2DM are associated in some studies. However, there are many confounders and variables. The association is affected in some studies by age, BMI and other lifestyle and dietary factors. There appears to be strong evidence that diets low in dietary fiber are also associated with increased risk of T2DM. Some data suggest that the risks of T2DM are even greater when diets are both low in dietary fiber and high in dietary GI or GL.<sup>118</sup> However, since foods naturally low in GI/GL are often high in fiber and other important nutrients, the GI or GL of the food or diet may simply flag a dietary choice that helps reduce risk of T2DM, but is not necessarily related to the glycemic response. This idea was the thesis of a recent review,<sup>119</sup> which concluded that eating a diet rich in whole grain cereals and vegetables and low in refined grains, sucrose and fructose is beneficial in the prevention of diabetes. Further, the authors suggested that the effects might not be due to GI but rather to magnesium, fiber, physical structure and other microconstituents of nutritious foods (as opposed to foods that are formulated to be low in GI by altering fat levels, sweetener type, etc.) This review points out the fact that a positive association is merely that – an association. It does not mean causality.<sup>120</sup>

Recommendations from the American Diabetes Association (ADA) to prevent T2DM are presented in Text Box 1. Low GI and GL foods are recommended because they generally are nutritious foods. The following quote characterizes the ADA's thinking on GI and GL in terms of diabetes prevention. "In relation to GI/GL and prevention of T2DM (*type 2 diabetes mellitus*) there is insufficient information from observational studies to determine whether a positive association exists or not. Only randomized controlled clinical intervention studies will be able to provide the final answer."<sup>121</sup>



**Text Box 1:**

**NUTRITION RECOMMENDATIONS AND INTERVENTIONS FOR THE PREVENTION OF DIABETES (PRIMARY PREVENTION) American Diabetes Association 2008<sup>122</sup>**

(with the evidence-based review grade level)\*

- Among individuals at high risk for developing type 2 diabetes, structured programs that emphasize lifestyle changes that include moderate weight loss (7% body weight) and regular physical activity (150 min/week), with dietary strategies including reduced calories and reduced intake of dietary fat, can reduce the risk for developing diabetes and are therefore recommended. (Level A)
- Individuals at high risk for T2DM should be encouraged to achieve the U.S. Department of Agriculture (USDA) recommendation for dietary fiber (14 g fiber/1,000 kcal) and foods containing whole grains (one-half of grain intake). (Level B)
- There is not sufficient, consistent information to conclude that low-GI diets reduce the risk for diabetes. Nevertheless, low-GI foods that are rich in fiber and other important nutrients are to be encouraged. (Level E)
- Observational studies report that moderate alcohol intake may reduce the risk for diabetes, but the data do not support recommending alcohol consumption to individuals at risk of diabetes. (Level B)
- No nutrition recommendation can be made for preventing type 1 diabetes. (Level E)
- Although there are insufficient data at present to warrant any specific recommendations for prevention of type 2 diabetes in youth, it is reasonable to apply approaches demonstrated to be effective in adults, as long as nutritional needs for normal growth and development are maintained. (Level E)

\* Level A: Good scientific evidence suggests that the benefits of using the advice outweigh the potential risks.  
Level B: At least fair scientific evidence suggests that the benefits of using the clinical advice outweigh the potential risks.  
Level C: At least fair scientific evidence suggests that there are benefits provided by the advice, but the balance between benefits and risks are too close for making general recommendations.  
Level D: At least fair scientific evidence suggests that the risks of the clinical advice outweigh potential benefits.  
Level E: Scientific evidence is lacking, of poor quality, or conflicting, such that the risk versus benefit balance cannot be assessed.

## Glycemic Index and Load in Treating T2DM

The role of diet and GI or GL in treating T2DM is no less controversial than its role in preventing it, despite early suggestions that such dietary modifications might

be useful for maintaining glycemic control. The 2008 recommendations of the ADA regarding the use of low GI or GL are shown along with its other recommendations about CHOs in Text Box 2.

### Text Box 2:

#### **NUTRITION RECOMMENDATIONS FOR THE MANAGEMENT OF DIABETES CHO IN DIABETES MANAGEMENT**

(with the evidence-based review grade level)\* See Text Box 1.

##### **Recommendations:**

- A dietary pattern that includes CHO from fruits, vegetables, whole grains, legumes, and low-fat milk is encouraged for good health. (Level B)
- Monitoring CHO, whether by CHO counting, exchanges, or experienced-based estimation remains a key strategy in achieving glycemic control. (Level A)
- **The use of GI and load may provide a modest additional benefit over that observed when total CHO is considered alone. (Level B)**
- Sucrose-containing foods can be substituted for other CHOs in the meal plan or, if added to the meal plan, covered with insulin or other glucose-lowering medications. Care should be taken to avoid excess energy intake. (Level A)
- As for the general population, people with diabetes are encouraged to consume a variety of fiber-containing foods. However, evidence is lacking to recommend a higher fiber intake for people with diabetes than for the population as a whole. (Level B)

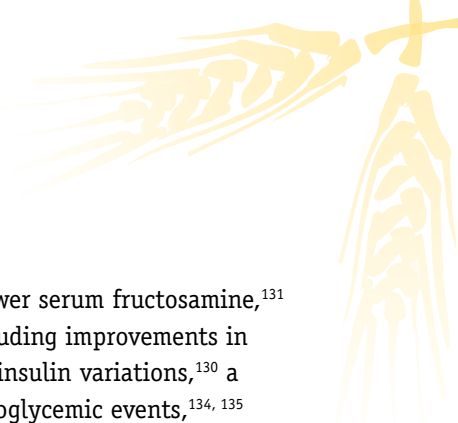
Sugar alcohols and nonnutritive sweeteners are safe when consumed within the daily intake levels established by the Food and Drug Administration (FDA). (Level A)

These ADA recommendations suggest that there may be modest benefits of lowering the GL of the diet. In terms of strength of the evidence, recommendations to use the low GI or GL in diet therapy received a grade of “B” meaning that evidence supporting this is less strong than for some of the other recommendations. One reason cited for the B grade, is that studies supporting the use of GI/GL are of short duration and have few subjects.

To address the concerns, a meta-analysis was done to ‘raise the evidence grade’ and provide more support for use of GI or GL in planning of diets. The analysis surveyed 14 studies (including 385 subjects) that met rigorous inclusion criteria. They used as their endpoint the most important marker of blood sugar control over time, glycosylated hemoglobin - referred to as HbA(1c). HbA(1c) is used as a surrogate to assess overall glycosylation of tissue throughout the body. Tissues that are glycosylated fail

to function properly so that is why this measure is so important. The analysis showed that low-GI diets reduced HbA(1c) by 0.43% points more than high-GI diets.<sup>123</sup> Taking both HbA(1c) and fructosamine data together, the authors concluded that glycated proteins were reduced an average of 7.4% more on the low-GI diet than on the high-GI diet. Thus, the findings of this review point to the potential promise of using low GI or GL to help with food selection of both type 1 and type 2 diabetics. Other authors were quick to present counter arguments stating that there is no particular benefit to using the GI or GL to select CHOs over other methods of CHO counting such as the food exchange system in the treatment of tightly controlled type I diabetes.<sup>124</sup>

The controversy is representative of the literature, which have studies that both support and fail to support a low GI/GL diet for improved HbA(1c). In a small US study using



subjects with both type 1 or type 2 diabetes, counseling to lower the GI of the diet did cause dietary changes which resulted in a lower dietary GI and a 19% reduction in HbA(1c). In addition, those in this study decreased BMI by 8% (mean loss of 17 pounds).<sup>125</sup> However in a larger randomized control study, the Canadian Trial of Carbohydrates in Diabetes with 167 type 2 diabetics, low GI, compared with a low CHO diet or a high GI diet, had no impact on HbA(1c). However, there were other positive effects of a low GI diet. Blood glucose excursions after an oral glucose challenge were lower than with the other two diets, perhaps due to changed insulin sensitivity or insulin secretion (or improvements in both). Diastolic blood pressure and high-sensitivity C-reactive protein (hs-CRP), a marker of inflammation seen in diabetics, was 30% lower when subjects followed the low-GI diet than when they ate the other diets.<sup>126</sup> This controlled study may indicate that a low GI diet may prove to be advantageous, perhaps not through consistently better HbA(1c), but through lower markers of inflammation, reduced circulating plasma lipid levels, including triglyceride and a change in the morphology and function of adipocytes. Data from diabetics fitted with insulin pumps suggest a positive role of low GI or GL. Type 1 diabetics eating low versus high GI meals had lower daytime mean blood glucose excursions with low GI meals.<sup>127</sup>

Influence of diet on genes may be one way dietary GL could have an impact. Down-regulation of genes affecting adiponectin production was seen with a high GI diet in a large cohort of rural and urban Asian Indians. Lower levels of adiponectin contribute to insulin resistance and diabetes. Also elevated were genes controlling the fatty acid-binding protein, which are associated with increased risk for hypertriglyceridemia.<sup>128</sup>

In summary, data exist which both support and do not support benefits of low GI/GL diets in the management of diabetes. The ADA Recommendations for the Management of Diabetes (Text Box 2) noted the slightly improved HbA(1c), so they recommended that diabetics consuming a high-GI diet switch to a lower GI diet as one more strategy that might be of modest benefit in controlling postprandial hyperglycemia. Many diabetics already have modified their diet to be high in fruits and vegetables and other high fiber, low GI options so their diets tend to be low to moderate GI.<sup>129, 130</sup> The key may be that GI/GL diets may offer

benefits for diabetics beyond lower serum fructosamine,<sup>131</sup> and glycated proteins,<sup>132, 133</sup> including improvements in postprandial blood glucose and insulin variations,<sup>130</sup> a reduction in the number of hypoglycemic events,<sup>134, 135</sup> improved insulin sensitivity and lipid profile,<sup>136</sup> altered gene expression and reduced inflammation.<sup>137</sup>

Despite these advantages, full endorsement of GI/GL as a strategy for diabetic diets has some hurdles. First, not all are convinced that it offers any advantage over tested dietary regimens such as the exchange system. Second, the classification of foods as low, medium or high is both arbitrary and imprecise because of the methodological problems cited in an earlier section. Third, a low GI diet can be achieved using an array of foods high in fiber, nuts, fruits and vegetables, or by using foods that do not increase fiber and nutrients. Fourth, many clinicians state that the low GI/GL diet is very complicated to explain to consumers.

One study suggests that the latter concern may not be critical.<sup>138</sup> An Australian study with 104 parent-child pairs showed that children with type 1 diabetes who followed the low-GI diet instructions had significantly lower HbA(1c) levels than those seen in the same children where the families used the traditional CHO exchange system. Furthermore, the rates of excessive hyperglycemia were significantly lower while using the low GI diet. Both the parents and the children preferred the low GI diet to using the exchange system and stated it was easier to learn and follow. Other aspects of quality of life were also reported as improved by the low GI diet.

Some clinicians note that there are no known adverse effects of recommending a low GI/GL dietary approach, and that there may be a number of positive results. Therefore, diabetes associations and health care professionals in many countries advocate low GI foods and low GL diets as tools for the treatment of diabetes and related conditions. A recent ILSI review suggested that low GI/GL diets might be useful for diabetics.<sup>139</sup>

A recent cross-over study with 901 diabetics corroborated this. It showed that regular selection of low-glycemic index foods was valuable in improving HbA1 and post meal glucose levels in the everyday life of type 2 diabetic patients.<sup>147</sup>

## Glycemic Index, Glycemic Load and Gestational Diabetes

Dietary GL was related to the risk for gestational diabetes mellitus (GDM) according to analysis resulting from a prospective cohort study among 13,110 eligible women in the Nurses' Health Study II.<sup>141</sup> As had been observed for other endpoints, there is an interaction between dietary GL and dietary fiber. While total fiber in the diet reduced the OR to 0.74, GL was positively associated with the risk of gestational diabetes with an OR of 1.61. When the diet was both low in fiber and had a high GL, the OR was 2.15. While these data would indicate that GL of the diet might be important, a Cochrane Review of studies concluded that "while a low glycemic index diet was seen to be beneficial for some outcomes for both mother and child, results from the review were inconclusive."<sup>142</sup> More studies need to be done.

## Pre-Diabetes and the Insulin Resistance Syndrome and GI/GL

The insulin resistance syndrome, or metabolic syndrome (MetS) is a cluster of metabolic abnormalities characterized by high levels of circulating insulin, high blood glucose, high blood pressure, central (visceral) obesity, low HDL cholesterol, high triglycerides (TG), small, dense LDL particles, elevated markers of inflammation and abnormal fibrinolysis. It is thought to be due to a defect in insulin action and abnormalities in adipose tissue metabolism, but the actual cause remains under investigation. The cluster of metabolic abnormalities increases risk of diabetes, coronary disease and all cause mortality.

All agree that a sedentary lifestyle, obesity, and genetics are factors involved in the development of insulin resistance and the MetS. As with other clinical endpoints the role of CHO and GI and GL in the development and treatment of MetS is unclear.<sup>143,144,145</sup> Diets low in saturated and trans fat and balanced in CHO intake, rich in dietary fiber, as well as high fruit and vegetable intake and including low-fat dairy foods such as the DASH or the Mediterranean diet were related to MetS prevention. These diets were not necessarily low in total fat or total CHO. However, one review concluded that the data at this time cannot show that any individual dietary component could be considered wholly responsible for the association of diet with MetS. Rather, it is the overall quality of the diet and lifestyle.<sup>146</sup>

Some studies point to CHO in the diet but fail to look at the GI or GL of the diet. For example, in the Third Korea National

Health and Nutrition examination survey, CHO intake was related to incidence of MetS.<sup>147</sup> While it might be assumed that the Korean diet based on white short-grain rice would have a high GL, only total CHO was assessed, not the GI and GL of the diet.

The role of GI or GL in the diets for treating MetS and its many abnormalities is also controversial.<sup>139</sup> Some, but not all, data indicate that a diet characterized by low GI foods not only improves some metabolic effects of insulin resistance, but also reduces insulin resistance *per se*. However, this was not the case in 29 MetS subjects on a calorie-restricted diet. Insulin sensitivity improved to the same degree regardless of the GI or GL of the diet.<sup>78</sup>

Some studies show that low GI and GL diets are associated with reducing markers related to MetS including obesity, abnormal lipid profiles and elevated markers of inflammation in both the elderly and children. However, as with other endpoints, there is much variation. In the Health, Aging and Body Composition Study, a prospective cohort study of adults aged 70-80 y (n = 2,248), GL (not GI) was inversely associated with one marker of MetS – visceral obesity – in men only.<sup>148</sup> Inclusion of low GI foods along with other dietary recommendations, including the increased frequency of meals, had no effect on BMI of 3-6-year-old children,<sup>149</sup> but did in 7-15-year-olds.<sup>150</sup> Markers of inflammation were improved in 14 of 16 subjects on a low GI diet in a small crossover design study. On the high GI diet only 7 of 16 improved.<sup>79</sup>

Lowering the GI and GL by changing the foods improved markers of inflammation in some studies. In a Finnish study the substitution of wheat and potato or wheat and oat diets (high GI diets) with rye or rye and pasta diets improved some markers of MetS such as insulin secretion.<sup>151, 152</sup> Similarly, a diet that is low GI and high in dairy and fruit, rather than one with cereals and potatoes, reduced markers of inflammation and other aspects associated with metabolic syndrome.<sup>73</sup> However, dietary changes that not only lower the GI or GL of the diet, but also change micro-constituents fail to answer the question of the effect of GI/GL because of potential confounding. Thus, the relationship between pre-diabetes and MetS and GI or GL is difficult to clearly characterize for several reasons. First, there are contradictory results in epidemiological studies. Second, many intervention studies have small numbers of subjects. Third, in many cases diets differ not only in GI and GL, but also differ in fiber, micro-nutrients, protein and/or fat content.



## Glycemic Index, Glycemic Load and Markers of Coronary Risk and Cardiovascular Disease

### GI/GL, Blood Lipids and Markers of Coronary Risk

The relationship between GI/GL, blood lipid profiles and coronary disease has been studied ever since the concepts' inception.<sup>153, 154</sup> Many newer epidemiological studies corroborate results of early studies,<sup>155, 156</sup> which show that increases in dietary GI and GL are associated with increased blood lipids and lowered HDL-cholesterol concentrations. The following recent studies showed low GI or GL resulted in improved blood lipids: (1) in the UK Whitehall II study with 7321 subjects (~70% men),<sup>112</sup> (2) wealthy adults in Central Massachusetts (n=574),<sup>157</sup> (3) Asian Indians (n=2043),<sup>158</sup> and (4) in the Insulin Resistance Atherosclerosis Study (IRAS), a cohort of middle aged men and women (n= 1026).<sup>159</sup> However, in the latter study the relationship held only for men. Dietary GI (not GL) was inversely associated with HDL in nearly 1000 men (mean age 57).<sup>73</sup> In Asian Indians dietary GL and total carbohydrate were both inversely related to HDL concentrations.<sup>157</sup> Dietary GL was associated positively with total and LDL cholesterol in the IRAS study in both genders<sup>158</sup> and in a study of Massachusetts adults.<sup>160</sup> GI, but not GL, was related to cholesterol in US women over 45.<sup>161</sup>

In terms of triglycerides (TG), the relationship of GI and GL is unclear. Both high GI and GL were associated with higher serum TG levels in 574 Massachusetts adults<sup>150</sup> and in 18,137 healthy women 45 yrs of age and older.<sup>161</sup> For the women the difference in triglyceride between the top and bottom quintile of GI and GL were 12 and 13 mg/dl, respectively. The authors suggested that while this was not a large difference, it might be important when looking at cardiovascular risk of large populations. High GI (not GL) was associated directly with TG levels in several other cohorts: (1) in the Whitehall study, over 70% men,<sup>112</sup> (2) in 1349 Japanese women farmers,<sup>162</sup> (3) in the IRAS study, but only in women,<sup>159</sup> and (4) in older Dutch men.<sup>73</sup> GL was associated with TGs in the study of 2043 Asian Indians.<sup>158</sup>

Some, but not all, intervention studies show that low GI

foods can lower serum TGs and improve blood lipids. In a randomized trial of obese young adults, the low GL diet, compared to a low-fat diet, improved blood lipids, e.g. it raised HDL cholesterol and lowered TGs.<sup>163</sup> In the Ontario Cardiac Rehabilitation Pilot Project, the 120 subjects on the low GL diet showed greater improvement in HDL and drop in TGs than the 1434 'controls' eating according to the Canadian Food Guide.<sup>164</sup> In 32 Japanese postmenopausal women placed on a diet, those eating in the highest tertile of GI had lower HDL-cholesterol concentrations and higher TG concentrations.<sup>165</sup> However, in a randomized, controlled trial with 40 poorly controlled, overweight diabetics, a low GI diet gave the same blood lipid profile as the American Diabetes Association diet.<sup>157</sup>

Dickinson and Brand-Miller<sup>166</sup> posit that the average dietary GI and GL predict cardiovascular disease risk factors, including HDL cholesterol, TGs and markers of inflammation, and, therefore are related to coronary heart disease. Several mechanisms have been suggested as ways that low GI diets can decrease coronary risk factors. First, they can decrease numbers of atherogenic small, dense LDL particles and help maintain high levels of HDL, primarily by mechanisms that involve decreasing plasma TG concentrations.<sup>167</sup> Second, they also decrease chylomicron production.<sup>168</sup> Third, markers of inflammation such as C-reactive protein have been associated with dietary GI or GL. In one study the data showed a stronger association amongst those with BMIs above normal.<sup>169</sup> In the Canadian Trial of Carbohydrates in Diabetes, a low GI diet did not improve blood glucose, but it did lower the level of C-reactive protein (CRP).<sup>126</sup> Low GI was associated with low CRP in another large cohort, however, the effect was small.<sup>161</sup> The authors of the latter study argued that since markers of inflammation are strongly correlated with coronary disease, then dietary patterns that reduce CRP and other pro-inflammatory substances may be an important aspect of prevention.

### GI/GL, Stroke and Cardiovascular Disease

Most studies fail to show an association between dietary GI/GL and cardiovascular disease and stroke, but a few

do. The benefit may be related to gender and BMI of the subjects. For example in Dutch women (n=15,714), there was positive association between high dietary GL and increased risk of coronary heart disease and stroke. The hazard ratios (HR) for the highest quartile of dietary and GI or GL and versus the lowest quartile were 1.47 and 1.33, respectively.<sup>170</sup> If the women had BMIs above normal (>25 kg/m<sup>2</sup>), the HR was even higher. In contrast, no association was found between either GI or GL a large cohort of Dutch older men<sup>73</sup> or in 36,246 Swedish men (aged 45-79 years) for either ischemic cardiovascular disease or mortality. However, in the Swedish study, dietary GL was associated with a greater risk of hemorrhagic stroke.<sup>171</sup> In 4,000 Swedish men with prior cardiovascular disease, neither dietary GI nor GL was associated with cardiovascular or all-cause mortality.<sup>172</sup>

Thus, individual studies fail to give a clear picture. However, when 37 prospective cohort studies were analyzed together, the relative risk (RR) for the highest versus the lowest quintile of dietary GI was 1.25.<sup>66</sup> Promoters of the low GI concept show that diets moderate in fat and low in saturated fat and CHOs with low GI are important for controlling complications of cardiovascular disease, but proof of its clinical value awaits clinical trials with subjects segmented by gender, age, lipid profile, BMI and other factors.

In summary, studies report conflicting evidence on the role of low-GI diets in CHD and risk factors for CHD. Randomized clinical trials report a small reduction in total cholesterol (-6.6 mg/dL) from low-GI diets compared with high-GI diets. There also may be a small effect on markers of inflammation. More research is needed on the role of GI and GL with respect to all cardiovascular diseases. Low GI and GL diets that are high in whole grain fiber, fruits and vegetables and other factors that lower disease risk may be the reason for the impacts seen.

### **Glycemic Index, Glycemic Load and Cancer**

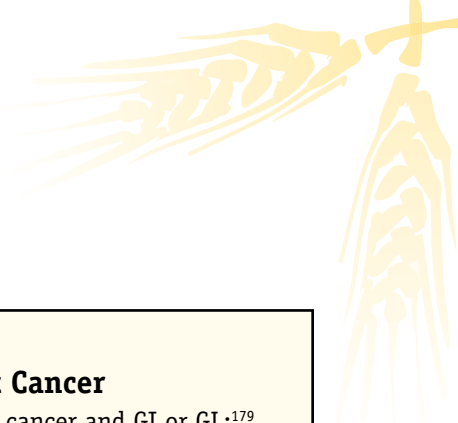
Since 2000, there have been a number of studies looking at the relationship between CHO intake, GI, and GL and cancer risk. It has been postulated that because insulin affects levels of insulin-like growth factor (IGF),<sup>173</sup> and IGF promotes growth in normal and malignant tissues, that GI

or GL might be associated with cancers. This review will look at the relationship between various forms of cancer and GI/GL.

### **Breast Cancer**

Breast cancer risk in many large epidemiological studies is unrelated to dietary GI or GL (Text Box 3). The authors of a review of prospective epidemiologic study concluded that, "There is no association that is consistent, strong, and statistically significant for any dietary variables and breast cancer, including GI or GL."<sup>174</sup> The review noted that the lack of relationship held even when populations were stratified according to body mass index, physical activity, or hormone use.

However, some epidemiological and case-control studies show a positive relationship between GI, GL or both and the risk of breast cancer for either a cohort or a subset of it. In a case-control study of 475 Mexican women with histologically-confirmed breast cancer (compared 1,391 controls), those in the quartile with the highest dietary GL, compared with those in the lowest quartile, had a RR of breast cancer of 1.62. When data for the postmenopausal women were analyzed separately, the OR rose to 2.18.<sup>175</sup> In over 5,000 Italian women in a case-control study,<sup>176</sup> there was a slight, but significant, increase in risk for the quintiles ingesting the highest GI and GL. The ORs were 1.4 and 1.3, respectively. High GI foods, such as white bread, were associated with a slight increased risk (OR = 1.3), but medium GI foods such as pasta were not. In a retrospective study, participants in the Nurses Health Study II (n = 47,355) were asked to complete a food frequency that reflected their diet during high school. Those whose recall suggested that they were eating foods with the highest GI, versus the lowest, had a RR of breast cancer of 1.47.<sup>177</sup> In a prospective epidemiological study of 8,926 Northern Italian women, there was a positive association of both GI and GL and increased breast cancer risk. The relative risk (RR) of breast cancer for the highest (versus lowest) quintiles of GI intake was 1.57; for GL, the RR was 2.53. Parsing the data according to menopausal status and body mass index markedly increased the association. For premenopausal women, those in the highest quintile of dietary GL had a RR = 3.89, but if the women were both premenopausal and had normal BMIs (under 25), the RR rose to 5.79.<sup>178</sup>



### Text Box 3:

#### Prospective Studies Which Show No Association of GI and GL with Breast Cancer

- In Australian women (n = 12,273), there were no significant associations between breast cancer and GI or GL;<sup>179</sup>
- In US women in the Nurses' Health Study (n= 88,678), there was no association of GI or GL on either pre- or post-menopausal breast cancer;<sup>180</sup>
- In US women in the Women's Health Study (n= 39,876), they found no relationship between GI and GL and post-menopausal breast cancer;<sup>181</sup>
- In US postmenopausal women (n = 63,307, age 40-87 years) in the Cancer Prevention Study II Nutrition Cohort, there was no association of GI or GL on breast cancer; and<sup>182</sup>
- In US postmenopausal women (n=34,703) in the Iowa Women's Health Study, there was no association of GI or GL on breast cancer.<sup>183</sup>

In some studies there was no relationship between breast cancer risk and dietary GI or GL for the cohort considered in totality, but there was a significant relationship when the cohort was partitioned according to menopausal status and BMI. This was the case in the Western New York Exposure and Breast Cancer Study (1,166 cases, 2,105 controls).<sup>184</sup> For premenopausal women with BMIs > 25, dietary GL was associated with increased risk (OR = 2.21). For postmenopausal women, there is an inverse association with a high GL diet (OR = 0.68), and this was more pronounced in women with BMIs > 25.

Partitioning the cohort in the US Nurses' Health Study II (n= 90,655 premenopausal women aged 26-46 years) also showed some significant associations. However, they were not the same as in the New York study. For premenopausal women with normal BMIs (< 25) in the Nurses' Study, the relative risk of breast cancer decreased with increasing CHO or GL, so that those in the quintile eating the most CHO or highest GL had a 38% lower risk of breast cancer than those eating the least CHO intake or the lowest GL. The opposite was true among premenopausal women with BMIs > 25; that is the relative risk of breast cancer increased with increasing CHO or GL. Those in the quintile with the highest dietary CHO or GL (not GI) had a 47% higher risk of breast cancer than those with the lowest dietary intakes.<sup>185</sup> These latter studies indicate that premenopausal women with BMI above normal have increased risk with high GI diets. On the other hand, premenopausal women with BMIs less than 25 may have lower risk breast cancer risk when dietary GI or GL is high. Postmenopausal women in the New York study showed decreased breast cancer risk with

high GL diets. The precise relationships and the potential mechanisms need to be characterized more fully with more research.

*Summary* – These data suggest that there is no clear relationship of GI or GL with risk of breast cancer. Factors such as menopausal status, body weight, tumor type (estrogen-receptor positive and negative tumors), the effects of body weight, hormones and genetic differences may need to be teased out in future large population studies.

#### Glycemic Index, Glycemic Load and Colon Cancer Risk

Early studies suggested that foods with a high GI or GL could possibly increase the risk of colorectal cancer.<sup>186</sup> Hyperinsulinemia resulting from elevated glucose has been suggested as having an impact. Yet, many epidemiological studies and the existing animal study do not support this thesis. Rats fed a chemical carcinogen showed no difference in the formation of abnormal colonic cells (aberrant crypts), a precursor to colon cancer when the diet varied in GI or GL.<sup>187</sup> Some epidemiological studies even showed that high dietary GI or GL reduced risk. In the Netherlands Cohort Study (n=120,852 men and women),<sup>188</sup> men eating in the highest quintile of GI or GL **reduced** their RR for colorectal cancer by nearly 20% compared with those eating in the lowest quintile of GI and GL. Men and women in the Prostate, Lung, Colorectal, and Ovarian screening trial (n = 34,817) were screened for the development of an adenoma using flexible sigmoidoscopy.<sup>189</sup> Men with high intakes of CHO or high GL (not high GI) decreased their odds ratio (OR) for adenomas to 0.71.

For the women in Breast Cancer Detection Demonstration Project follow-up cohort (n=45,561), the risk of colon cancer was significantly reduced with diets high in CHO intake and GI.<sup>190</sup>

However, dietary GI or GL was not associated with a decrease in risk for the following studies:

1. Women in the Netherlands Cohort Study,<sup>188</sup>
2. Women in a Swedish study (n=61,433),<sup>191</sup>
3. Women in previously cited Prostate, Lung, Colorectal, and Ovarian screening trial.<sup>189</sup>
4. Women and men either in the US Nurses' Health Study and the Health Professionals Follow-up Study. In this cohort neither intakes of dietary CHO, GL, overall GI, sucrose, or fructose were associated with colorectal cancer risk.<sup>192</sup> However dietary GL slightly increased risk in men (RR = 1.32). The association was stronger among men with BMI > 25.

As in the latter study, BMI was shown to affect the association. In the Iowa Women's Health Study (n = 35,197 postmenopausal women),<sup>193</sup> CHO intake, GI, and GL were not associated with risk of colorectal cancer, colon cancer or rectal cancer. However, when segmented by BMI, those women with BMIs > 30, both GI and GL were positively associated with colorectal cancer incidence. The RR for the highest versus lowest quintiles of GI the RR = 1.66 and for GL the RR = 1.79. However, in the cohort of Swedish women, segmentation by BMI failed to change the results.<sup>191</sup> Differences in the data between the US and the European cohorts may be due to a greater percentage of obese and extremely obese women in US cohorts.

Case-control studies were more likely than prospective cohort studies to show a slight increase in risk of colon cancer related to dietary GI. Colorectal cancer risk of 1,125 Italian men and 828 women with histologically-confirmed incident cancer of the colon or rectum was higher for those in the quintile eating diets with the highest GI or GL compared to those eating in lowest quintile.<sup>194</sup> The ORs were 1.7 and 1.8, respectively. One study suggested that subjects with a high GL diet (relative to lowest intake) were more likely to have mutations of p53<sup>iii</sup> that could lead to increased cancer risk.<sup>195</sup>

In summary, many of the studies show that dietary GI or GL is not associated with increased risk of colorectal

cancer, and a few studies suggest the dietary GI or GL is associated with reduced risk. A few studies suggest that dietary GI or GL might not affect colorectal cancer risk in the population overall, but that it might be affected by gender or BMI. The puzzling thing about these attributes is that there is not consistency among studies. Perhaps the variation is due to differences in diet quality (dietary fiber and its co-travelers) in diets that are low or high GI. Low GI or GL diets may contribute resistant starch, which can have positive impacts on colonic health.

### Glycemic Index, Glycemic Load and Pancreatic Cancer

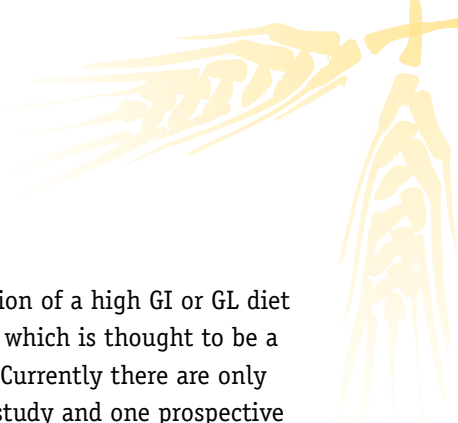
Epidemiological evidence strongly suggests that glucose intolerance and T2DM are risk factors for pancreatic cancer, thus some predicted that GI or GL would be a risk factor for pancreatic cancer. However, this was not shown to be the case. GL/GI was not related to pancreatic cancer risk in various prospective studies:

1. 124,907 men and women in the American Cancer Society Cancer Prevention Study II (CPS-II) followed for 9 years,<sup>191</sup>
2. 49,613 Canadian women enrolled in the National Breast Screening Study followed for 16.5 years,<sup>197</sup>
3. 88,802 women participating in the Nurses' Health Study for 18 years,<sup>198</sup> and
4. 162,150 participants in the Hawaii-Los Angeles Multiethnic Cohort.<sup>199</sup>

In the latter two studies, BMI and other dietary constituents might impact the risk. For the women in the Nurses' Health study, there was a statistically, non-significant increase in risk of pancreatic cancer for women with a high GL, which became stronger among sedentary women with BMIs > 25. In the Hawaii-Los Angeles Multiethnic Cohort, pancreatic cancer risk did not seem to be related to dietary GI or GL but was increased for those who had both high BMIs and high sucrose intakes.

In summary, the data to date indicate that an association between GI or GL pancreatic cancer is not likely. If such an association does exist in the overweight, the elevation of risk appears to be small. Further research is needed to

<sup>iii</sup> *Inactivation of the p53 tumor suppressor gene is a common event in the development of colon cancer.*



see how BMI, other aspects of the diet such as total CHOs or sugars impact the relationship of GI/GL and pancreatic cancer.

### Glycemic Index, Glycemic Load and Other Cancers

Cancers of the **thyroid**, stomach and upper gastrointestinal tract have been related to intake of refined grain intake.<sup>200</sup> Some hypothesize that the relationship could also be related to dietary GI and GL. This was observed in the only study on the thyroid cancer and GI and GL referenced in MedLine, which was a case-control study conducted in Italy with 399 patients with thyroid cancer and 616 controls.<sup>201</sup> Those in the highest tertile versus the lowest tertile of GI or GL intake had an increase RR of 1.73 and 2.17, respectively.

In terms of **stomach** cancer, a case-control study conducted in Italy with nearly 800 cases looked at the relationship, those in the quintile eating a diet with a high GL, compared to those eating a low GL diet, had a RR of stomach cancer of 1.94. The RR increased in a dose related manner as GL increased. The authors suggested that the increase in risk could be linked to excess circulating insulin and related IGFs. No association was seen between dietary GI and stomach cancer risk.<sup>202</sup>

Three case-control studies in Italy assessed the association of GI or GL with upper **digestive tract cancers** (oral and pharyngeal cancer, squamous cell esophageal cancer and laryngeal cancer). The odds ratios (OR) for the highest versus the lowest quintile of dietary GI and GL were 1.5 and 1.8, respectively.<sup>203</sup> Similar ORs were observed for various cancer sites. The association was stronger in women and in those with high BMIs.

In terms of risk for **prostate** cancer, there was a dose-related association between GI and GL and risk in an Italian case-control study with 1,204 cases and matched controls. The OR for the highest versus the lowest quintile of intake of GI was 1.57 and GL was 1.41.<sup>204</sup> A 6-week intervention study with prostate cancer patients suggested a possible mechanism. A low-fat/low-GL diet was associated with significant gene expression changes in human prostate epithelium. The authors suggested that diet can modify the effects on the prostate.<sup>205</sup>

**Ovarian** – Long-term consumption of a high GI or GL diet may elevate circulating insulin, which is thought to be a potential risk factor for cancer. Currently there are only two studies – one case-control study and one prospective study – assessing the association between GI, GL and ovarian cancer. In the case-control study of women from four Italian regions with over 1,000 cases and twice as many controls, high GI or GL increased ovarian cancer risk by 70%. The associations were observed in pre- and postmenopausal women, and they remained consistent across strata of major covariates identified. A more recent prospective study on 49,613 women enrolled in the Canadian National Breast Screening Study (NBSS), GI and total carbohydrate and sugar intakes were not associated with ovarian cancer risk in the total cohort. GL was positively associated with a 72% increase in risk of ovarian cancer for the entire population. The risk was even slightly greater for post-menopausal women.

**Endometrial Cancer** – Studies assessing the association between dietary GI or GL and endometrial cancer risk also yielded contradictory findings, which possibly suggest the need for subject segmentation by hormone use, body weight or other measures. For example, there was no significant association between dietary GL and GI, and endometrial cancer risk in the 288,428 women in the European Prospective Investigation into Cancer and Nutrition cohort (1992-2004).<sup>206</sup> However, further segmentation of the data beyond quartiles indicates that there could be a modest positive association of total CHOs, total sugars, and total dietary GL, especially among those who have never used hormones. In the Swedish Mammography Cohort (n=61,226),<sup>207</sup> there was no overall association between CHO intake, GI or GL and the incidence of endometrial cancer. However for overweight women (BMI > 25) who also reported low physical activity, both CHO intake and GL were positively related to endometrial cancer risk. Both GI and GL were associated with increased risk in a prospective study of 49,613 Canadian women aged between 40 and 59 at baseline.<sup>208</sup> The HRs for the highest versus the lowest quartile level of overall GI and GL were 1.47 and 1.36, respectively. For women with BMIs greater than 30, the HR increased to 1.88. Risks also went up for premenopausal women and postmenopausal women who use hormone replacement therapy. Case-control studies from Italy and Switzerland (410 cases) show that those

with diets in the highest quintile versus the lowest quintile of GI and GL are associated with HRs of 2.1 for and 2.7, respectively.<sup>209</sup> The associations were stronger in older women, in those with higher body mass index and in hormone replacement therapy users.

### Summary for Glycemic Index and Glycemic Load for all Cancers

Most case-control studies showed positive associations between GI and GL intake and these cancers. However, pooled cohort study results showed no associations between colorectal cancer risk and either dietary GI (5 studies) or GL (8 studies). Furthermore, no significant associations were observed in meta-analyses of cohort study results of colorectal cancer subsites and GI and GL intake. Similarly, no significant associations emerged between pancreatic

cancer risk and dietary GI (5 studies) or GL intake (6 studies) in combined cohort studies. The findings from the meta-analyses indicate that GI and GL intakes are not associated with risk of colorectal or pancreatic cancers. There were insufficient data available regarding other digestive tract cancers to make any conclusions about GI or GL intake and risk.<sup>210</sup> The association between GL and breast cancer disappeared when publication bias was taken into account. No association was found for pancreatic cancer. A recent comprehensive meta-analysis of GI and GL and cancer risk suggested an overall direct association with colorectal and endometrial cancer. Associations between GL and breast cancer disappeared when publication bias was considered. There was significant between-study heterogeneity for colorectal cancer.<sup>211</sup>

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## Glycemic Index for Athletics

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A continuous and adequate fuel supply is crucial to athletic performance especially in endurance events such as marathons. For optimal competition an athlete's daily diet needs to fuel the exercising muscle and replenish muscle glycogen between events. General dietary recommendations include CHO-rich foods with a moderate GI to provide a readily available source of CHO for muscle glycogen synthesis and a regimen of CHO loading prior to endurance events. Glycogen recovery after an exercise bout may also require readily available CHO. New findings on GI and GL with respect to athletics will be discussed.

CHO loading prior to such an endurance event to increase muscle glycogen has been the practice for over 25 years. Despite long years of use, there is controversy about whether the CHO's GI or GL for the loading regimen mattered. Early studies with both diabetics and trained athletes<sup>212</sup> failed to show any change in perceived exertion, endurance or other measures of performance when high and low GI foods were compared. More recent studies show that while the GI and GL are important, the quantity of carbohydrate is the most important factor.

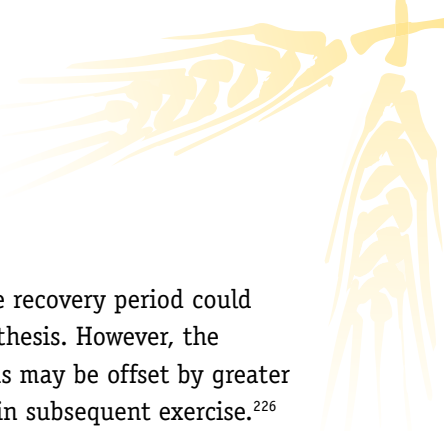
Nonetheless, the glycemic response of the pre-event meal also has been debated and researched. Pre-match meals composed of low GI CHO foods, rather than high GI foods, were shown to be more satiating and to produce more stable

blood glucose concentrations during the event, according to a review from the Loughborough University School of Exercise and Sports Science.<sup>213</sup> This conclusion was based on reports of improved endurance capacity and better times after low-GI CHO pre-exercise meals for trained, and recreational runners.<sup>214,215</sup> While low GI meal contributed less CHO to muscle glycogen synthesis in the 3-h postprandial period compared with the high GI meal, the reduced synthesis of muscle glycogen was compensated for by reduced muscle glycogen utilization during exercise.<sup>216</sup>

The GI or GL of the diet may have little impact for certain types of exercise or for those with different levels of training. For example, the GI of a breakfast eaten by women prior to brisk walking had no measurable impact,<sup>217</sup> and the GI/GL of the diet of seven male semi-pro soccer players made no difference with respect to fatigue during an event or a shuttle run looking at sprint and distance performance during the 22 hour recovery.<sup>218</sup>

The timing of the food prior to the event appears to matter. While the GI of a pre-event meal (~3 hours prior) did affect performance, the GI of the evening meal did not.<sup>219</sup>

A possible way that the GI/GL of the diet can impact exercise performance is by changing fuel use patterns and fat oxidation rates. Low GI meals caused higher



fat oxidation rates for both recreational cyclists and in exercising women.<sup>220</sup> Increasing fat oxidation spares CHO thus making the fuel supply last longer. In addition, ingestion of low to moderate GI foods increased the availability of nonessential fatty acids during exercise and decreased the reliance on intramuscular lipid during moderate intensity exercise.<sup>221</sup> Another reason that CHO type may be important is that it appears to affect oxidative stress. High GI foods appeared to aggravate inflammatory processes after exercise in lean, young adults.<sup>222,223,224</sup>

Post-exercise CHO replenishment helps restore muscle glycogen, but again the GI or GL of foods used for glycogen recovery is also a subject of debate. Some argue that since plasma glucose and serum insulin concentrations following high GI meals are higher, then high GI meals would be advantageous for muscle glycogen recovery. This was shown in a study with eight trained males.<sup>225</sup> Serum insulin concentrations following lunch were higher in the high GI trial compared to the low GI trial. The increased

insulin concentrations during the recovery period could facilitate muscle glycogen re-synthesis. However, the advantages of greater re-synthesis may be offset by greater subsequent glycogen utilization in subsequent exercise.<sup>226</sup> Thus, low GI CHO may offer greater overall benefit during the postprandial periods by maintaining plasma glucose concentrations better during subsequent exercise.

Carbohydrate foods are important for providing the steady fuel supply needed for exercise. For CHO-loading regimens prior to endurance exercise, total carbohydrate is a much more important consideration than the GI or GL of the foods/diets chosen. For the meal prior to endurance exercise, there appears to be competitive advantage to selecting low-to-moderate GI/GL foods, however the GI/GL of the meal prior to activities such as brisk walking was not important. There was also a slight, but limited, advantage of a higher GI/GL diet or food for replenishing glucose after exercise.

## Conclusions

Since the development of GI and GL in the 1980s by Jenkins and co-workers, volumes of research have been conducted on its relationship to human health. A number of health promotion organizations around the world have recommended their use as one dietary component to prevent and treat diabetes, gestational diabetes, metabolic syndrome, obesity, cardiovascular disease and certain cancers. Others advocate its use for modulation of blood glucose and fuel supplies as way to improve athletic performance and overall health. Yet, there is far from unanimous support for its use to inform dietary recommendations or health guidelines<sup>227</sup> for a number of reasons including inconsistent results for nearly all health and disease end points and methodological issues. There is the most support for its use in treating and preventing diabetes. Thus, the American Diabetes Association, in its evidence-based recommendations, rates the evidence supporting its use with a “B” in terms of both preventing and treating diabetes. Translated this means that there is fair scientific evidence for the benefit and that using it as clinical advice outweighs the potential risks.

Data associating dietary GI or GL with respect to blood triglyceride levels and markers of inflammation are fairly

consistent, findings regarding the association between cardiovascular disease risk and GI/GL do not show the same consistency. Furthermore, associations between low GI/GL and the reduction of obesity, metabolic syndrome and many cancers are not consistent among the studies. Some studies show no association. Others show that high GI/GL foods and diets increase risk, especially if the cohort is segmented by gender, BMI or other lifestyle factors. Perhaps more studies, which segment the cohorts, will give a clearer picture of the effects of GI/GL. However, existing studies, even with carefully segmented populations, often fail to bring clarity.

The lack of clarity may be related to potentially large errors associated with using GI tables to assign foods a specific GI/GL. The tables often fail to give values for different varieties and cooking methods and fail to account for effects when foods are eaten in combination with other foods. Further, the large standard deviation of the index for many foods limits both its accuracy and precision. The use of existing GI tables to determine the GI or GL of the diet raises concerns. First, there is concern about foods that were once high GI foods but are modified to attain a low GI label value through the addition of fat or replacement of

sucrose and high fructose corn syrup (moderate glycemic sweeteners) with low GI sweeteners such as fructose or agave syrup, up to 95% fructose. Second, there is concern about the avoidance of foods labeled as high GI such as carrots or watermelon because consumers fail to understand that the high GI value results because of inordinately large volume of the food required to get 50 grams of available CHO. Third, there is concern about labeling of foods with GI values. Many fruits and vegetables are high in water and provide little CHO per serving, so it makes little sense to use the GI for these foods. In like manner, putting a GI label on foods, which inherently have little or no CHO, fails to promote consumer clarity or improve consumer choice. In fact, the presence of a GI label may lead to consumers to make poor nutritional choices. For example, a consumer using GI as a guide for food selection might choose deep-fried pork rinds or fat-laden summer sausage as a snack and instead of a whole grain bagel. Fourth, food preparation and storage can markedly change GI from the value in the table or on a food label (for instance the same cake baked conventionally and in the microwave have different GIs and as a cake is stored there is still a lower GI).<sup>228</sup> Fifth, lack of accuracy and precision associated with the measure itself creates difficulty placing foods into arbitrary high, medium and low GI categories. The high standard deviation associated with the measure, even when the analysis is done by experienced laboratories, documents this problem.

Confounding may also occur because low GI/GL diets can be achieved in dramatically different ways. Diets high in fruits, vegetables, nuts and whole grains are naturally low in GI or GL and tend to be higher in fiber and nutrients. These may not only improve the diet, but also may, in their own right, reduce the risk of a variety of chronic diseases. So the measurement of dietary GI or GL is merely a surrogate measure for a good diet. However, low GI/GL diets can be constructed with moderate GI sugars (e.g. sucrose, table sugar or high fructose corn syrup) and low GI sugars (e.g. fructose), with added fat and the elimination of many or nearly all CHO foods. Such a low GI/GL diet could be very high in meat, fat and saturated fat, and other items that could potentially increase disease risk. Thus a low GI/GL diet can vary markedly in types of food, dietary fiber and nutrients delivered. Each of these could have as much impact on disease as the GI/GL either alone or in combination.

Another cause of inconsistency among studies is differences among countries in terms of GI/GL values from the food frequency questionnaires and differences among raters. Some authors have pled for more consistent methodology to attribute GI values to foods and validated dietary questionnaires in order to derive meaningful GI/GL estimates for nutritional epidemiology.<sup>66</sup>

Despite these numerous drawbacks, many feel that dietary advice not only to consider quality of fat and protein, but also to consider quality of CHO. The US Dietary Guidelines and Canada's Food Guide to Healthy Eating, both recommend that consumers choose a diet with 45-65% of the calories or approximately 50% of each day's calories coming from CHOs. The Canadian guide and many diabetes organizations caution that not all CHOs are the same. These guides recommend that selecting fruits, nuts, vegetables and whole grains – foods providing fiber, nutrients and phytonutrients – is one potential way to select CHO foods. Using the GI to rank ONLY CHO-rich foods, and not other food categories, according to their glycemic response may be used as an additional consideration when selecting foods and planning diets. It may be useful to some diabetics and to those with elevated TGs.

More research is needed on the use of the GI/GL concept to show that it is a desired system for food selection and meal planning. Recommendations must be evidence-based and must show that such a plan creates diets and health outcomes equal to or better than those plans, which have been shown to be beneficial in preventing a number of chronic diseases. These include plant-rich diets such as the DASH<sup>229</sup> or Mediterranean diet plans.<sup>230,231,232</sup> Use of the GI or GL to further refine food choices as a way to modify existing recommendations from the government and health-related organizations such as the American Health Association or the ADA may offer benefits especially to those with diabetes and other conditions. However, exclusion of nutritious foods because they or their GI or GL may fail to improve the diet, might eliminate some important aspect of the diet. Data continue to show that diets high in fiber and rich in fruits, vegetables, nuts, legumes and whole grains help maintain health and reduce the risk of chronic disease and such diets tend to be low in both GI and GL.



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## List of Acronyms

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ADA	American Diabetes Association	HR	hazard ratio
AUC	area-under-the-curve	IGF	insulin growth factor
BMI	body mass index	IRAS	Insulin Resistance Atherosclerosis Study
CHO	carbohydrate	IRR	incident relative risk
CRP	C-reactive protein	MetS	metabolic syndrome
EPIC	European Prospective Investigation into Cancer and Nutrition	OR	odds ratio
GGE	glycemic glucose equivalent	RR	relative risk
GI	glycemic index	SAG	slowly available glucose
GL	glycemic load	T2DM	type 2 diabetes mellitus
HbA(1c)	hemoglobin A 1c	USDA	United States Department of Agriculture
		SCFA	short chain fatty acid

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## Glossary

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**Adenoma** – Benign tumor that can occur in many organs. In the colon, it is referred to as a polyp.

**Abdominal obesity** – See visceral obesity.

**Adiponectin** – A hormone secreted by fat cells to regulate the metabolism of lipids and glucose. Adiponectin is also anti-inflammatory. Low levels are associated with obesity and increase risk of disease.

**Atherogenic** – Describing a substance that will raise blood lipids and encourage their deposition on the artery wall, thus promoting the risk of coronary disease.

**Available Carbohydrate** – Available carbohydrate is carbohydrate that is released from a food in digestion and which is absorbed as monosaccharides and metabolized by the body.

**Body mass index BMI** – A measure of the relationship between weight and height that is associated with body fat and health risk. It is expressed as weight in kg<sup>2</sup> over the height in m<sup>2</sup>. Persons with BMIs > 25 are considered overweight and BMIs > 30 are considered obese.

**C-Reactive Peptide** – C-reactive protein is one of the markers of inflammation. It is produced by the immune system in response to an immune challenge. It attaches to the membrane of a microorganism and activates the complement cascade, initiating the destruction

of cells or viruses. Higher levels of C-reactive protein in the blood indicate low-grade inflammation and are associated with higher risk of obesity and other chronic disease.

**Carbohydrate Loading** – This refers to the practice of eating large amounts of carbohydrate foods prior to an endurance event such as a marathon with the objective of increasing the amount of glucose available to the muscle while exercising.

**Chylomicron** – Relatively large lipoprotein particles that transport absorbed dietary lipids throughout the body.

**Cochrane Reviews** – Comprehensive, highly-credible, independent reviews of effects or intervention and observational studies about medical topics and risks. The results of these systematic reviews are published as “Cochrane Reviews.”

**Cross-over design** – Studies designed in subjects who act as their own controls because the subject completes all the interventions including the control treatment.

**Diabetes** – The term diabetes mellitus describes a metabolic disorder characterized by chronic hyperglycemia (elevated blood glucose) with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.

**Type I Diabetes Mellitus (T1DM)** – This refers to diabetes where the pancreas produces insufficient insulin. Exogenous insulin is required for the treatment of this disorder. (This was formerly referred to as juvenile-onset diabetes.)

**Type II Diabetes Mellitus (T2DM)** – This refers to diabetes where the pancreas produces insulin, but where the insulin is ineffective in transporting glucose from the bloodstream into the cells, so called insulin resistance. In this case, subjects usually have high levels of circulating blood glucose and insulin. This is the most common type of diabetes in the North America and was formerly referred to a maturity-onset diabetes. It can be treated with weight-loss, diets, oral glucose agents, and in some cases, exogenous insulin.

**Down-regulation** – This is the decrease in the quantity of a cellular component, such as RNA, a hormone or an enzyme, in response to a dietary component or other factor.

**Fructosamine** – This is one of three measures of elevated blood glucose. (See HbA1c.)

**Fermentable Carbohydrate** – Dietary fibers including resistant starch and oligosaccharides such as inulin, which are not metabolized in the small intestine and are metabolized by the bacteria in the large intestine to produce short-chain fatty acids and other compounds.

**Fibrinogen** – Is a fibrous protein involved in the clotting of blood. Elevated levels are one marker of disease risk and can mean that the blood is more likely to clot.

**Gestational Diabetes** – Diabetes that is found for the first time when a woman is pregnant.

**Glycemic Index (GI)** – This term refers to the relative degree to which the concentration of glucose in the blood rises after consumption of a food, i.e., the so-called “glycemic response.” Testing of the GI requires ingestion of 50g of available carbohydrate from a variety of foods, and measuring the blood glucose response over 2 h. After the blood glucose concentration over the two hours is graphically represented (with glucose concentration on the vertical axis and time on the

horizontal axis) the area under the blood glucose curve is measured for each food and compared to that observed after the consumption of 50g of glucose as the reference. The glycemic index is given as a percentage, i.e., the percentage of the area under the blood glucose curve for the test food compared to that for glucose. Accordingly, a GI of 70 indicates that consuming 50g of the food in question yields an increase of blood glucose 70% as great as that for ingesting 50g of pure glucose.

**Glycemic Load (GL)** – This is the glycemic index multiplied by the amount of carbohydrate in the food.

**Glycated or glycosylated** – This means that glucose is attached to another type of molecule.

**Hazard Ratio** – Relative risk of any measured outcome at any given time.

**HbA(1c) or hemoglobin A(1c)** – This is a measure of the reaction between glucose and hemoglobin. When glucose is not cleared from the blood stream and is left circulating, as occurs in diabetes and prediabetes, it can interact with proteins of various tissues. Once glycated, the protein may be unable to carry out its specific role in the cell. Since access to blood is relatively easy, glycosylation of hemoglobin is measured as HbA1c. This measure is a marker of potential glycosylation of proteins through out the body.

**IGF-1 - Insulin-like Growth Factor-1** – This protein hormone promotes growth of tissues.

**Inclusion criteria** – A list of criteria that must be met by all subjects (or studies in a meta-analysis) in order to be included in a study.

**Insulinemic Index** – This term refers to the relative degree to which the concentration of insulin in the blood rises after consumption of a food, i.e., the so-called “insulinemic response.” Testing of the insulinemic index requires the same protocols as described for measuring the glycemic index except that blood concentrations of insulin are measured and used to calculate the index.

**Insulin Resistance Syndrome**, also called **Metabolic Syndrome** (formerly referred to as Syndrome X) – The Insulin Resistance Syndrome or Syndrome X is

characterized by high blood pressure, increased triglyceride levels and decreased HDL (or “good” cholesterol), obesity and high levels of circulating glucose and insulin. The insulin is ineffectual or hence insulin resistant. Insulin resistance, which is indicated by consistently high levels of glucose in the body, is the key marker for this syndrome. High levels of glucose in conjunction with high levels of insulin, put stress on the arteries, affecting the blood flow in the system and increasing chances of coronary heart disease, hypertension and diabetes. Thus development of these symptoms is a warning sign for more serious diseases.

**Insulin Sensitivity** – This refers to the ability of insulin to help move glucose from the bloodstream in to the cell.

**Markers of Inflammation** – Components that are elevated in the bloodstream to fight infection or stress. They can predict risk of coronary artery disease, diabetes and obesity. Fibrinogen and high-sensitivity C-reactive protein (CRP) are examples of such markers.

**Meta Analysis** – A meta-analysis is a statistical technique that combines data from several studies that address a related topic. The result can yield a more powerful estimate of the true effect size than any single study alone.

**Odds ratio (OR)** – This ratio compares whether the probability of a disease or other outcome is the same for two groups. An OR = 1 means that the outcome is equally likely in both groups. An OR > 1 implies that the outcome is more likely in the first group; whereas an OR < 1 implies that the outcome is less than in the first group.

**p53** – a transcription factor associated with apoptosis (programmed cell death). Cancer inhibitors up-regulate this gene whereas promoters down regulate it.

**Plasminogen activator inhibitor-1** – Plasminogen activator inhibitor-1 is one of the markers of inflammation and a risk marker of atherosclerosis.

**Phytochemical, also phytonutrient** – A component

of plants (phyto) that have positive effects of the body by reducing chronic disease or enhancing function but are not considered absolutely essential as are vitamins and other nutrients.

**Prediabetes** – A term used to describe impaired glucose tolerance or impaired fasting glucose. In this state one has fasting blood sugar levels above normal (blood sugar between 110-125 mg/dl) but the blood sugar levels are not high enough to diagnose diabetes (fasting blood sugar above 126 mg/dl). Prediabetes or diabetes risk increases with overweight or obesity, a family history of diabetes, ethnicity of Hispanic/Latino, Asian American/Pacific Islander, Native American, or African American, high blood pressure, low HDL cholesterol and high triglycerides, having a history of **gestational diabetes** (diabetes during pregnancy) or giving birth to a baby weighing more than 9 lbs. This condition is estimated to affect 16 million people in the USA.

**Prospective study** – A study in which the subjects are identified and then followed forward over time to see if a certain dietary or other variable affects an endpoint such as risk of diabetes.

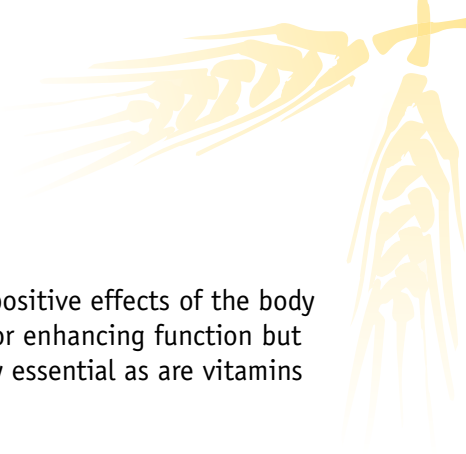
**Postprandial hyperglycemia** – Increase in blood glucose observed in the few hours after eating.

**Relative risk** – The ratio of the risk of disease or death among those exposed to the risk among those exposed to a certain dietary or other element.

**Unavailable Carbohydrate** – Carbohydrate in food that is not absorbed in the small intestine of humans.

**Small, dense low density lipoprotein (LDL)** – Low density lipoprotein, the so-called bad cholesterol, is one of the lipid/protein components of the blood that can increase the risk for coronary heart (ischemic) disease. When the LDL particles are small and dense, they are more atherogenic than when they are larger.

**Visceral obesity** – A form of obesity due to excessive deposition of fat in the abdominal organs rather than under the skin. It is associated with elevated lipids and disease risk.



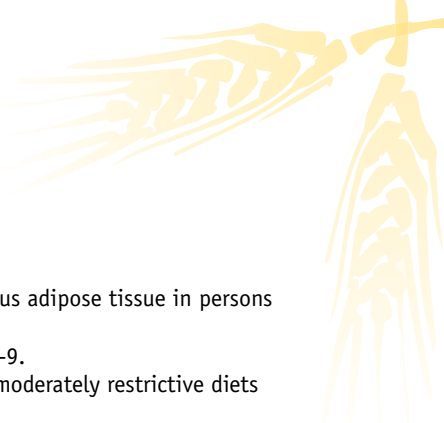
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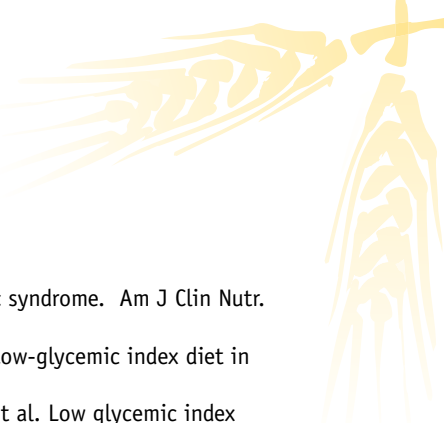
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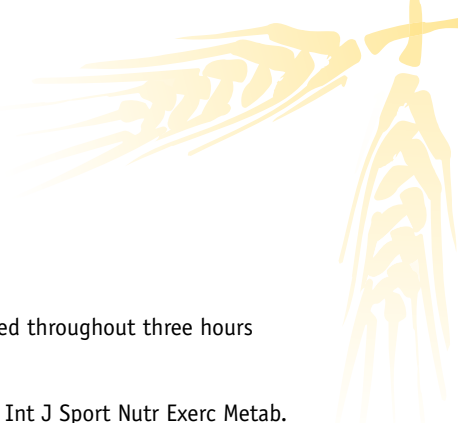
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# The Author

## A Brief Resume of Julie Miller Jones, Ph.D., L.N., C.N.S.

Julie Jones, a Board-Certified Nutrition Specialist and Licensed Nutritionist, received her BS degree from Iowa State University and her Ph.D. in Home Economics and Food Science and Nutrition from the University of Minnesota. Currently she is professor emeritus of nutrition in the Department of Family, Consumer and Nutritional Sciences at St. Catherine University in St. Paul. She has twice been named St. Catherine's outstanding professor. She was awarded The Myser Award by the alumnae as a professor "who made a difference in people's lives." She held the 3M Endowed Chair in Science and was made a Distinguished Scholar.

She authored *Food Safety* (Eagan Press) and edited a book *Dietary Fibre: Food and Feed and Bio-active Ingredients*. She is very interested in all aspects of nutrition science but is especially interested in whole grains and food-based solutions such as the DASH diet. She regularly writes and speaks about whole grains and dietary fiber, carbohydrates, sugars, starch including resistant starch, the glycemic index, fat, vitamins and antioxidants; whey, food safety issues such as microbial safety, irradiation, pesticides; and issues affecting women, such as dieting and body image.

She has been active in many professional organizations. For the national American Association of Cereal Chemists (AACC) International, she is past-President and Chair of the Board of the national organization and has served in many capacities, both nationally and locally. Currently, she heads the Whole Grains Task Force and led the Glycemic Carbohydrate Definition Committee. She has been awarded the highest award of the AACC, the Geddes Award in 2004, and named the Twin Cities Home Economist of the Year in 2006. She is a scientific advisor for the Joint Institute of Food Safety and Nutrition for the University of Maryland and the US Food and Drug Administration, the carbohydrate committee of the International Life Sciences Institute of North America, and the Grains Food Foundation.



**Julie Miller Jones**

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