The Glycemic Index: Looking Back 25 Years

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It is now more than 25 years since David Jenkins first proposed the glycemic index (GI) as a physiological basis for carbohydrate exchange (23). At that time, just before I joined the research group, he investigated the effects of fiber and was the first to demonstrate that addition of viscous soluble fiber to food reduces postprandial glucose levels (21). Intrigued by this phenomenon, we went on to test foods with different fiber contents, assuming that only foods with a high fiber content would show lower glucose responses. However, we found that this was not always the case. At that point, it became clear that, irrespective of the fiber content, and for reasons we could not at the time understand, different carbohydrate foods with the same amount of available carbohydrate produced different glycemic responses. As a result, we realized that we would have to systematically test foods one at a time to compare their glycemic response in a standardized fashion, and the most logical way to do this was to index the foods to a common standard. Thus the first GI table was created.

The GI had obvious relevance to diabetes, and we therefore repeated the GI testing in subjects with diabetes (20) and showed that the GI values were the same as in the healthy subjects. This is not really surprising, as the indexing of the response makes the GI value to a large extent independent of the individual response. Hence, GI values apply to everyone, irrespective of their glucose tolerance status (20).

Many research studies exploring the relevance of the GI in health and disease have been undertaken over the last 25 years. The research has been extensive, exploring methodology, mechanism of action, factors influencing the GI, potential health benefits, etc. Only select highlights are covered here.

Methodology

The method for determining the GI is well established; nevertheless, some of the differences seen between laboratories may be due to the use of different methodologies. It is therefore timely that the GI methodology is now being considered by the International Standards Organization. Since establishing the GI of a food in vivo can be costly, it has been argued that a less-expensive in vitro method should be used in its place.

In vitro vs. In vivo. In vitro methods have been used to predict the GI of a food, and good correlations can be obtained, especially with starchy carbohydrate foods. This is not surprising, as the rate of digestion is a major determinant of the glycemic response (16). However, a range of intrinsic and extrinsic factors that alter the rate of gastrointestinal motility, digestion, and absorption also influence the GI, and these cannot always be predicted using an in vitro model. At present, therefore, the GI can be established only using the standard in vivo method.

Variability and Factors Influencing the GI

The GI is a biological measurement and therefore has inherent variability; however, many of these sources of variability can be minimized using the correct methodology (36). It is often argued that the glycemic response varies widely between different subjects or varies from day-to-day for the same subject. It is true that the absolute response to a standard test meal varies within a subject and between subjects. However as already mentioned, expressing the results against a standard measured in the same individual reduces the between-subject variability to such an extent that the GI can be tested in individuals with very different glucose tolerance status (e.g., healthy people vs. those with diabetes). To reduce within-subject variability, the reference food is repeated two to three times, and the mean of these is used to calculate the GI of a food. For the same reason, it is recommended that a minimum of 10 subjects be used. Use of venous vs. capillary blood can also increase variability, with capillary having the lower variability. Several interlaboratory studies have now been undertaken that confirm that, once the methodology is standardized, the agreement between laboratories is good (38).

In addition to methodological differences, variance can also reflect true GI differences. It was noticed early on that the GI values for rice differed significantly between different laboratories; subsequently, it was found that these differences were true physiological differences and dependent on the type of rice or the processing the rice had undergone. Since then, many factors that influence the GI value of a food have been uncovered. Some of the most common ones are listed in Table I.
Mixed Meals
Another criticism of the GI that has been raised is that it cannot predict the GI of a mixed meal. However most (7,35,39) but not all (10) have shown good predictability. More recently, in a very comprehensive study, this issue was revisited. Fourteen different, typical Canadian and Australian meals were consumed, varying in energy (220–450 kcal), protein (0–18 g), fat (0–18 g), available carbohydrate (16–79 g), and GI (35–100). More than 90% of the variation in observed mean glycemic response was explained by the GI and the carbohydrate content in the meals (39).

Glycemic Index vs. Glycemic Load
Within the ranks of those who don’t dismiss the GI in its entirety but feel that the GI may have some value, there has arisen conflict with the introduction of the glycemic load (GL) concept. The GI gives a ranking of foods based on their acute blood glucose response, while the GL takes into account also the amount of available carbohydrate being consumed in the portion (GL = [GI × amount of available carbohydrate]/100). Thus the GL may be a truer reflection of the exposure of the subject to glycemic foods. However, because the GL is dependent on two factors (the GI of the food and the serving size), increases and decreases in GL can be achieved by varying either term or both. Therefore, a low-GL diet can be achieved either by decreasing the GI of the food consumed or by eliminating most of the carbohydrate from the diet. This may be the reason that, in epidemiological studies, the GI seems to correlate more consistently with risk of diabetes, heart disease, and cancer than the GL does (9). Acutely, the GL and GI may also produce significantly different effects. One of the advantages of ingesting a low-GI (i.e., low-GL and low-GI) meal is that the postprandial response to the subsequent meal will be attenuated. If a meal containing a small amount of high-GI carbohydrate is consumed (i.e., high GI, low GL), the subsequent postprandial glucose response may be worsened rather than improved (Fig. 1).

Possible Mechanisms of Action
The hypothesis for the underlying mechanism of action that leads to low-GI foods is that the carbohydrate in those foods is absorbed slowly. Studies were undertaken by our lab to explore this concept (22). Subjects were given a glucose drink, which they either drank within 5 min or sipped at an even rate over 3 hr. Four hours after the start of the first meal, subjects were also given a standard IV glucose bolus. When subjects sipped their glucose rather than drinking it in 5 min, much lower postprandial glucose levels were observed. Furthermore, the fall in blood glucose levels during the IV glucose tolerance test was significantly more rapid following the sipping paradigm, which suggested reduced insulin resistance. Insulin levels were reduced even more dramatically than glucose levels, which may account for the increases in insulin sensitivity seen in people following a low-GI diet. A commercial product, the α-glucosidase inhibitor Acarbose, inhibits the digestion and therefore simulates the reduced rate of carbohydrate absorption seen with low-GI foods. In the STOP-NIDDM trial (5,6), Acarbose was shown to significantly delay the progression of impaired glucose tolerance to diabetes and also significantly reduced the development of cardiovascular disease. Many of the features that are associated with low-GI foods, such as viscous fiber, a high amylose-to-amylopectin ratio of the starch, or traditional food processing such as parboiling all influence the rate of carbohydrate absorption (Table I). The mechanism of action through which these factors reduce the rate of absorption may range from decreasing the rate of gastric emptying, as seen with foods such as sourdough bread, to reducing accessibility of enzymes to the carbohydrate, as is seen with viscous fiber (21,33). It is interesting to note that many of the traditionally eaten starchy staples, such as bulgur, couscous, pasta, and parboiled rice, are low-GI foods.

Glycemic Index and Health
Epidemiological studies using the NHANES II database and the 1986–87 British Adults Survey data have shown a negative relationship between glycemic index and high-density lipoprotein cholesterol (11,13). This supports the data from both the Nurses Study and the Health Professionals Study, which have shown correlations between low-GI diets and decreased incidence of diabetes (28, 29) and risk of cardiovascular disease (26). No association

Table I. Aspects of foods that influence their glycemic index (GI)

<table>
<thead>
<tr>
<th>Food Factor Affecting GI</th>
<th>Reference</th>
</tr>
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<tbody>
<tr>
<td>Nature of the starch</td>
<td>2</td>
</tr>
<tr>
<td>Ratio of amylose to amylopectin</td>
<td>3</td>
</tr>
<tr>
<td>Degree of retrogradation (e.g., refrigeration)</td>
<td>9, 38</td>
</tr>
<tr>
<td>Degree of hydration, i.e., method of cooking (e.g., parboiling)</td>
<td>19, 20</td>
</tr>
<tr>
<td>Particle size (e.g., pumpernickel bread, tabouli, coarse bread)</td>
<td>3</td>
</tr>
<tr>
<td>Food form (e.g., ground vs. whole, pasta)</td>
<td>18</td>
</tr>
<tr>
<td>Protein-starch interaction in wheat products</td>
<td>22, 35</td>
</tr>
<tr>
<td>Fiber (e.g., β-glucan, glucomannan, guar)</td>
<td>32, 41</td>
</tr>
<tr>
<td>Antinutrients, (e.g., enzyme inhibitors, phytates, lectins, tannins)</td>
<td>26, 31</td>
</tr>
<tr>
<td>Acidity of food (e.g., sourdough bread, addition of vinegar)</td>
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between dietary GI and cardiovascular disease was seen in men with a body weight below 23 kg/m², suggesting that the GI of the diet may be increasingly important in those with a greater degree of insulin resistance. However, the Zutphen study (32) did not show a significant relationship of GI or GL with cardiovascular disease in older men. These results may relate to the relatively small number of subjects (1,500) and their age at the start, since large numbers of the original cohort had already died or were excluded due to diabetes and cardiovascular disease. High insulin levels have been implicated in the incidence of diet-related cancers, and recent studies have explored the possible relationship between the incidence of these cancers and GI. A case control study from Italy reported that high dietary GI was also related to increased breast cancer risk (1), and similar results were seen with the Nurses Cohort Study (14). Two studies also support the relationship with colon cancer (12,15). Epidemiological studies, therefore, seem to support a role of GI in disease.

Many prospective studies have also been conducted in populations with diabetes and hypercholesterolemia. Two meta-analyses of studies with type 2 diabetes demonstrated that the use of a low-GI diet in the treatment of diabetes improved control, as indicated by a significant decrease in A1c (4) and fructosamine (27). Improvements in cardiovascular risk factors also have been demonstrated (27). None of these data in themselves are definitive, but they suggest a potential therapeutic utility of the GI.

Conclusion
The GI allows foods to be ranked on the basis of the postprandial glucose these foods produce. Consumption of low-GI diets has been associated with reduced incidence and prevalence of heart disease, diabetes, and also some forms of cancer. Although not all studies have been able to demonstrate the positive effects of low-GI foods, nevertheless the GI may be an important element in the armamentarium required to preserve good health. Currently, one of the major limitations of following a low-GI diet is a lack of acceptable low-GI foods. Not only do we demand food that can be prepared rapidly, modern food processing seems predisposed to create palatable pleasing, but rapidly absorbed, high-GI foods. We therefore must look to the food industry to use its ingenuity to produce foods that are not only palatable and fast to prepare but also slow to digest. Armed with foods such as these, we will be able to implement the wealth of knowledge we have acquired on the GI over the last 25 years and maybe make a difference.

References
25. Liljeberg, H. G., and Bjorck, I. M. Delayed gastric emptying rate as a potential mechanism for lowered glycemia after eating sourdough bread: Studies in humans and...

Alexandra Jenkins began her research career in 1979, in Oxford, where she was part of the research team that developed the glycemic index concept. Subsequently she obtained her B.Sc. from the University of Toronto and completed a dietetic internship at St Michael’s Hospital. She completed her Ph.D. at the University of Surrey in the United Kingdom. Her major research focus has been the nutritional treatment of diabetes. She has volunteered extensively for the Canadian Diabetes Association (CDA); she chaired the Applied Research Grant Committee from 1996 to 2000, and presently she is an associate editor of the Canadian Journal of Diabetes. In recognition of her contributions, Jenkins received the Eli Lilly Graduate Scholarship Award in 2000 and, in 2001, a Special Dedication Award from the CDA. She is currently the director of research at Glycemic Index Laboratories Inc. and a research associate at the Risk Factor Modification Centre at St Michael’s Hospital in Toronto. She can be reached at alexandrajenkins@gilabs.com.