*Proceedings of the Nutrition Society* (2006), **65**, 125–134 DOI:10.1079/PNS2005485


# Glycaemic index and metabolic disease risk

Louise M. Aston
*MRC Collaborative Centre for Human Nutrition Research, Elsie Widdowson Laboratory, 120 Fulbourn Road, Cambridge CB1 9NL, UK*

There is growing evidence that the type of carbohydrate consumed is important in relation to metabolic disease risk, and there is currently particular interest in the role of low-glycaemic-index (GI) foods. Observational studies have associated low-GI diets with decreased risk of type 2 diabetes and CHD, and improvements in various metabolic risk factors have been seen in some intervention studies. However, findings have been mixed and inconsistent. There are a number of plausible mechanisms for the effects of these foods on disease risk, which arise from the differing metabolic responses to low- and high-GI foods, with low-GI foods resulting in reductions in hyperglycaemia, hyperinsulinaemia and late postprandial circulating NEFA levels. Low-GI foods may also increase satiety and delay the return of hunger compared with high-GI foods, which could translate into reduced energy intake at later time points. However, the impact of a low-GI diet on body weight is controversial, with many studies confounded by dietary manipulations that differ in aspects other than GI. There is currently much interest in GI from scientists, health professionals and the public, but more research is needed before clear conclusions can be drawn about relationships with metabolic disease risk.

**Glycaemic index: Metabolic disease: Carbohydrate**

Obesity and obesity-related metabolic diseases are major public health concerns. More than one billion adults worldwide are overweight, with ≥300 million clinically obese (World Health Organization, 2002). Obesity is an important predisposing factor for chronic non-communicable diseases, including type 2 diabetes and CVD. Non-communicable diseases account for approximately 75% of deaths worldwide, and this percentage is predicted to increase as rates rise in developing countries (World Health Organization, 2003). These diseases are also related to diet and lifestyle independently of body weight. It is therefore vital to develop strategies to prevent and treat obesity that target these diet and lifestyle factors.

Evidence for adverse effects of high-fat diets on metabolic disease risk has led to recommendations in the UK that total dietary fat should contribute ≤33% energy intake, with <10% energy intake from saturated fats (Department of Health, 1994). Reductions in fat usually lead to reciprocal increases in carbohydrate intake. However, less-detailed recommendations have been issued in relation to the quality of dietary carbohydrate. Different types of carbohydrate have differing metabolic effects, especially in the extent to which they raise blood glucose and insulin levels. It is therefore hypothesised that they will affect metabolic risk profiles in different ways. Carbohydrates are commonly classified according to their chemical and physical properties, e.g. 'simple' (mono- and disaccharides) *v.* 'complex' (polysaccharides), based on the belief that the digestion rate of a carbohydrate is determined by its saccharide chain length. This assumption is now known to be inaccurate, and a more physiologically-relevant classification system has been sought (Food and Agriculture Organization/World Health Organization, 1998).

## The glycaemic index

The glycaemic index (GI) is a system for the classification of carbohydrate-containing foods that is based on their blood-glucose-raising potential. It is defined as 'the incremental area under the glucose response curve to a test food providing a fixed amount of carbohydrate, relative to the response to a standard control food (glucose or white bread) providing the same amount of carbohydrate' (Jenkins *et al.* 1981; Food and Agriculture Organization/World Health Organization, 1998). Foods with a high GI produce

**Abbreviations:** GI, glycaemic index; GL, glycaemic load.

**Corresponding author:** Louise Aston, fax +44 1223 437515, email Louise.Aston@mrc-hnr.cam.ac.uk

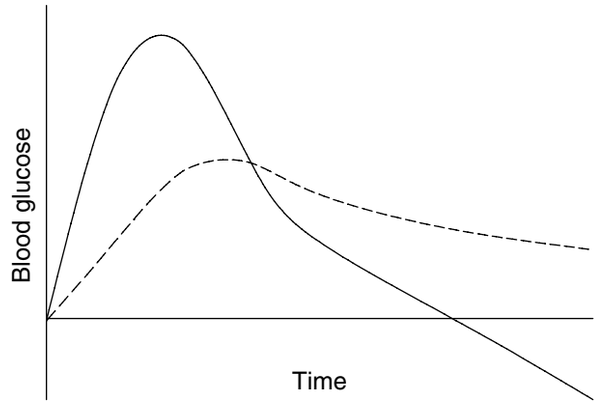


**Fig. 1.** Glycaemic responses to high (——)-glycaemic-index and low (- - -)-glycaemic-index foods.

a higher peak and greater overall blood glucose response than those with a low GI, which release glucose into the blood at a slower rate (Fig. 1). A low-GI food is defined as having a GI of $\leqslant 55$, and a high-GI food has a GI of $\geqslant 70$.

The blood-glucose response to a food, and thus the GI, is determined by the rate of digestion and absorption of the carbohydrate, which is affected by a number of factors. These factors include chemical properties: the type of monosaccharide (fructose and galactose give a lower GI than glucose; Englyst *et al*. 2003); amylose : amylopectin in starch (the branched amylopectin is more rapidly digested than the straight-chain amylose, and so gives a higher GI; Granfeldt *et al*. 1995); the presence of viscous soluble fibres such as guar and β-glucan, which can lower GI because of their gel-forming properties (Björck *et al*. 2000). Physical properties of foods also influence the GI: foods with an intact botanical structure tend to have lower GI values, as the starch is protected from enzymic degradation by the outer layer of the grain kernel (Juntunen *et al*. 2002); GI tends to increase with the extent of ripeness (Hermansen *et al*. 1992), cooking, processing and refining (Jenkins *et al*. 1988; Holt & Miller, 1994), which render the carbohydrate more digestible, although some methods of processing, such as parboiling, can lower GI (Larsen *et al*. 2000). The presence of other food components also influences the GI: fat and protein in foods lower GI by slowing gastric emptying; α-amylase inhibitors lower GI by slowing starch digestion (Augustin *et al*. 2002).

### *The glycaemic load*

It is not only the GI of the carbohydrate in the diet that affects glucose and insulin responses, but also the quantity of carbohydrate consumed. Both these variables are represented by the glycaemic load (GL). A low-GL diet can be achieved either by reducing carbohydrate intake or by reducing the GI of the carbohydrates consumed. The GL is calculated as the amount of carbohydrate in a food, multiplied by its GI and the quantity eaten, summed for all foods ($GL = \Sigma$ (amount of food consumed $\times$ carbohydrate content of food $\times$ GI); Willett *et al*. 2002).

### *Measurement of the glycaemic index of various foods*

The GI of a food cannot easily be predicted from the basic food components, and must be measured as an *in vivo* response relative to a standard. Lists of the GI values of many foods have been published (Foster-Powell *et al*. 2002). However, these lists are by no means complete, especially since GI can vary with only subtle differences in processing. Thus, it may not always be appropriate to apply published GI values to similar products that differ in brand or country of origin from those that have been measured. Inappropriate application of data is a potential problem in studies of GI and health in which published values are frequently used to calculate dietary GI or to determine intervention diets.

Intervention studies that use prescribed foods should first establish the GI of the foods by means of standardised methodology (Food and Agriculture Organization/World Health Organization, 1998). In studies at MRC Human Nutrition Research, Cambridge, UK, foods were tested in ten subjects who each performed three tests with a 50 g glucose standard. Glucose was measured in capillary blood obtained by finger-prick in the fasted state and at six further time points over the 2 h following commencement of consumption of the test food. The portions of food tested contained 50 g glycaemic carbohydrate, defined as total carbohydrate minus dietary fibre. As values for fibre (the manufacturers' values) are determined according to the AOAC International (1995) procedure, some, but not all, resistant starch is included. Foods were tested as they might typically be consumed: breakfast cereals with semi-skimmed milk, which provided 15% of the available carbohydrate in the test portion; other foods (breads, potatoes, pasta and rice) with 10 g margarine per test portion. Although this procedure would have affected the absolute GI of the foods, adding the same quantity to each food should not have affected their hierarchical relationship (Collier *et al*. 1986). As the intention was to identify high- and low-GI versions of foods that could be substituted for each other, it was this relative difference in GI that was of primary importance.

In general, results were found to be close to published values for similar foods; e.g., low GI values (43–54) for pastas and relatively high ratings (69–102) for all potatoes. The differences between GI values for various cereals were found to be smaller than expected, with many clustering at approximately 60–65. Cereals were tested with milk, which has a disproportionately large insulinaemic effect for the glucose response it produces (Östman *et al*. 2001), and the resulting high insulin : glucose may have attenuated glucose responses. The magnitude of the inter-individual variability across foods was found to be large, with the 95% CI for a number of foods spanning low, medium and high GI ranges. This variability raises concerns where foods with only small GI differences are used in interventions.

The findings illustrate some of the factors affecting GI. Porridge made from larger more-intact oats was found to have a lower GI (40) than that made from more-finely-ground oats (61; $P = 0{\cdot}019$). Differing effects of different types of fibre were also observed; while wheat fibre was

https://doi.org/10.1079/PNS2005485 Published online by Cambridge University Press

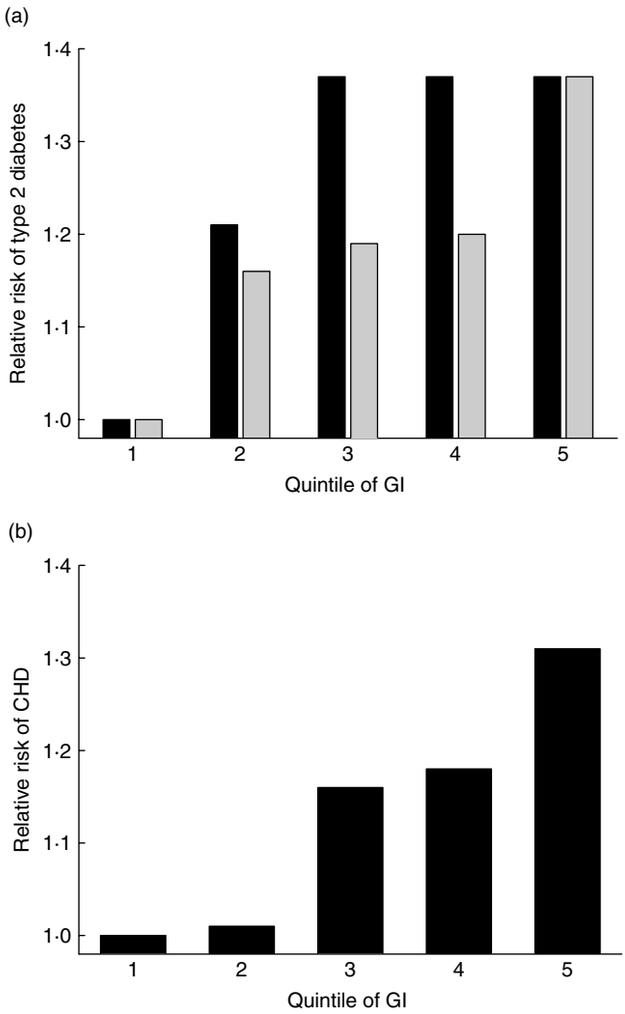


**Fig. 2.** (a) Glycaemic index (GI) and risk of type 2 diabetes. (■), US women (*n* 65 173) aged 40–65 years from the Nurses' Health Study, followed up for 6 years. Median energy-adjusted GI for the lowest and highest quintiles were 64 and 77 respectively. $P=0{\cdot}005$ for trend across quintiles; (□), US men (*n* 42 759) aged 40–75 years from the Health Professionals' Study, followed up for 6 years. Median energy-adjusted GI for the lowest and highest quintiles were 65 and 79 respectively. $P=0{\cdot}03$ for trend across quintiles. (Data from Salmerón *et al.* 1997*a*,*b*.) (b) GI and risk of CHD. (■), US women (*n* 75 521) aged 38–63 years from the Nurses' Health Study, followed up for 10 years. $P=0{\cdot}008$ for trend across quintiles of energy-adjusted GI. (Data from Liu *et al.* 2000.)

found to have no effect on GI, with similar values for white (70) and wholemeal (71) breads, GI was shown to be significantly lowered when a jacket potato was eaten with the skin (69) rather than without the skin (98; $P=0{\cdot}007$). Increasing maturity or ripeness of a food also tends to increase GI, and waxy small new potatoes were found to have lower GI values (79 and 80) than floury large old white potatoes (96; not significantly different). As potatoes mature, the extent of amylopectin branching in the starch increases, rendering it more digestible, and thus increasing the GI (Soh & Brand-Miller, 1999).

## Metabolic effects of low- and high-glycaemic-index diets

### *Evidence from observational studies*

Observational studies indicate that the GI of the diet may be an important determinant of metabolic risk. The major sources of carbohydrate in the Western diet (highly-refined cereal and potato products) tend to have high GI values, which has been linked to the widespread occurrence of type 2 diabetes and CVD.

Lower dietary GI has been associated with reduced risk of developing type 2 diabetes in large cohorts of both men (Salmerón *et al.* 1997*a*) and women (Salmerón *et al.* 1997*b*), with risk increased by 37% in the highest quintiles of energy-adjusted GI compared with the lowest quintiles, after adjustment for potential confounders including cereal fibre intake (Fig. 2(a)). However, this difference in risk is not a totally consistent finding, as no relationship was found between GI and diabetes risk in a 6-year follow-up of 35 988 post-menopausal women from the Iowa Women's Health Study (median GI for lowest and highest quintiles: 53 and 89; Meyer *et al.* 2000). These disparities may relate to imprecision in the assessment of GI, especially since many studies have used food-frequency questionnaires that were not designed to measure GI.

Associations have also been observed between both GI and GL of diets and CHD risk in the Nurses' Health Study (Liu *et al.* 2000). After adjustments for potential confounders, including dietary fibre intake, risk of CHD was shown to be increased by 98% in the highest quintile of energy-adjusted GL *v.* the lowest quintile, and by 31% in the highest quintile of energy-adjusted GI *v.* lowest quintile (Fig. 2(b)). No association with total carbohydrate intake was found, indicating that the majority of the effect of GL is related to GI. Again, this association is not a consistent observation, as no relationship was found between GI and CHD risk in 646 men aged 64–85 years from the Zutphen Elderly Study (van Dam *et al.* 2000), although this study was much smaller and may not have had sufficient power to detect a relationship.

GI has also been shown to be positively associated with the prevalence of the metabolic syndrome and insulin resistance in a cross-sectional study of 2834 subjects from the Framingham Offspring cohort (McKeown *et al.* 2004). Odds of having metabolic syndrome were reported to be 41% higher in the highest quintile of dietary GI compared with the lowest quintile (median GI values 84 and 72 respectively), and insulin resistance was found to be increased across quintiles ($P<0{\cdot}001$ for trend). Other dietary carbohydrate factors that were shown to be related to lower insulin resistance include higher intakes of total fibre, cereal fibre and whole grain. In contrast, no association between GI and insulin resistance was found in a cohort of 5675 subjects aged 30–60 years from the Danish Inter99 study, after adjustment for potential confounders including dietary fibre (Lau *et al.* 2005).

Associations have also been reported between GI and both unfavourable lipid profiles and raised inflammatory status. In 280 women aged 45–70 years from the Nurses' Health Study fasting triacylglycerol levels were shown to be positively related to GI (Liu *et al.* 2001). Serum HDL levels have been found to be negatively related to GI in

https://doi.org/10.1079/PNS2005485 Published online by Cambridge University Press

1420 subjects aged 18–64 years from the 1986–7 Survey of British Adults 18–64 years (Frost *et al*. 1999), in which GI was the only dietary factor found to be significantly associated with HDL levels in multiple linear-regression analysis. Plasma levels of high-sensitivity C-reactive protein, a sensitive marker of systemic inflammation, were found to be positively associated with both GI and GL in 244 women from the Nurses' Health Study, aged 45–82 years, with a stronger relationship in overweight women than in normal-weight women (Liu *et al*. 2002).

### *Evidence from intervention studies*

The effect of GI on health outcomes in intervention studies has been mixed. Studies have varied widely in duration, sample size, subject type and intervention diet, and many have used diets not matched for energy, macronutrient or fibre content. There have, however, been some reports of improvements in insulin sensitivity, β-cell function, dyslipidaemia and thrombolytic function.

Several studies have investigated the effects of a low-GI diet on insulin sensitivity. In thirty patients with advanced CHD insulin sensitivity was found to be improved in 4 weeks in the low-GI group, with the dietary GI reduced by 10 (from 86 to 76), compared with the high-GI group (Frost *et al*. 1996). In sixteen women at increased risk of CHD as a result of parental history of the disease, those randomised to a low-GI diet for 3 weeks, with the dietary GI reduced by 24 (from 91 to 67), were found to have improved insulin sensitivity compared with the high-GI group (Frost *et al*. 1998). No effects of lowering GI were seen in control subjects with no parental history of CHD, suggesting that benefits may only be achievable in those subjects either predisposed to, or already having some extent of, insulin resistance. In support of this explanation no effects of a low-GI diet on insulin sensitivity were seen in seven lean insulin-sensitive men, following nutrient-matched high- and low-GI diets (mean GI difference 24) for 30 d (Kiens & Richter, 1996). Furthermore, no effect on insulin sensitivity or β-cell function was found in a 10-week parallel study of forty-five overweight women when low- or high-GI foods were incorporated into *ad libitum* habitual diets (Sloth *et al*. 2004).

There is some evidence to suggest that low-GI diets may improve insulin secretion. First, the glucose disposition index (the ability of β-cells to compensate for changes in insulin sensitivity by increasing insulin secretion) was found to be improved in subjects with impaired glucose tolerance after 4 months on a low (mean GI 54·4, *n* 13)-GI diet compared with high (mean GI 59·3, *n* 11)-GI diet (Wolever & Mehling, 2002). While a trend towards improvements in insulin sensitivity was reported with the low-GI diet, it did not reach significance. However, the fibre intake in the low-GI group was shown to be higher, so the effects cannot confidently be attributed to GI. Second, an 8-week cross-over study in twenty post-menopausal women has compared the effects of high-fibre rye bread and white wheat bread (Juntunen *et al*. 2003). The rye bread was found to enhance insulin secretion without any effect on insulin sensitivity, suggesting an improvement in β-cell function. While the rye bread had a lower GI than the wheat bread, it was also higher in soluble fibre, phytates and tannins, which could act by reducing GI, or via other independent effects.

Some studies in subjects with type 2 diabetes and impaired glucose tolerance, in whom dyslipidaemia is common, have demonstrated improvements in lipid profiles with lowered GI. These improvements include decreases in total cholesterol, LDL-cholesterol and triacylglycerol, and increases in HDL-cholesterol with differences in dietary GI of 20–28 over 4–6-week periods (Fontvieille *et al*. 1992; Wolever *et al*. 1992; Järvi *et al*. 1999; Luscombe *et al*. 1999; Wolever & Mehling, 2002). However, a 6-month study in subjects with type 2 diabetes with a GI difference of 10 has reported no effects on blood lipids (Tsihlias *et al*. 2000). Evidence suggests any beneficial effects of low-GI diets are most marked in those subjects with the worst dyslipidaemia (Brand-Miller, 1994). In forty-five overweight women LDL was found to be different between groups after 10 weeks on low- or high-GI diets, with a reduction of 10% in the low-GI group, and a slight increase (2%) in the high-GI group (Sloth *et al*. 2004). A tendency towards a greater decrease in total cholesterol in the low-GI group was observed, but it was not significant. These findings are not conclusive, however, and a Cochrane meta-analysis investigating the role of low-GI diets in CHD risk (Kelly *et al*. 2004) that has reviewed fifteen randomised controlled trials in subjects with pre-existing CHD risk factors has concluded that whilst there is some limited evidence for slight reductions in total cholesterol with low-GI diets, there is no evidence for effects on other lipids.

A low-GI diet may have beneficial effects on thrombolytic function. The activity of plasminogen activator inhibitor-1, a thrombolytic factor that increases clot and plaque formation, has been found to be 53% lower after 24 d on a low (56·8)-GI diet compared with a high (82·7)-GI diet in twenty subjects with type 2 diabetes (Järvi *et al*. 1999). Plasminogen activator inhibitor-1 has also been shown to be decreased in the low-GL group of a weight-loss intervention compared with a low-fat-diet group, despite no differences in weight loss (Ebbeling *et al*. 2005); however, the low-GL diet was also lower in carbohydrate.

## Potential mechanisms for effects of low-glycaemic-index diets

The mechanisms by which low-GI diets may reduce metabolic disease risk are still unclear. They may include direct metabolic effects, and also reductions in body weight with concomitant improvements in health. A number of plausible biological mechanisms arise from the differing metabolic responses to low- and high-GI foods, which may underpin differential effects on metabolic disease risk.

### *Metabolic responses to high- and low-glycaemic-index foods*

The rapid large rise in blood glucose following consumption of high-GI foods triggers a large insulin response and

https://doi.org/10.1079/PNS2005485 Published online by Cambridge University Press

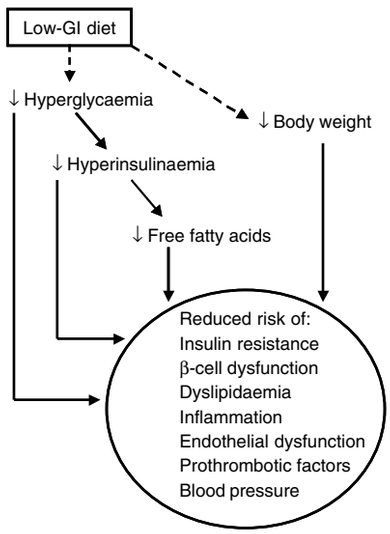


**Fig. 3.** Summary of potential effects of low-glycaemic-index (GI) meals on metabolic risk factors. ↓, Reduced; →, established link; - -→, possible link.

strongly inhibits glucagon release. For most foods a good correlation exists between glycaemic and insulinaemic responses, with high-GI foods eliciting large insulin responses (Björck *et al*. 2000), which trigger rapid uptake of nutrients by insulin-responsive tissues and suppress nutrient mobilisation. Glucose uptake and glycogen synthesis in skeletal muscle and liver, and lipogenesis in adipose tissue, are increased. Simultaneously, gluconeogenesis and glucose output by liver and lipolysis and NEFA release by adipose tissue are suppressed. Low-GI foods produce an attenuated glucose response, and so the resulting hormone responses and effects are less dramatic.

As a result of the rapid absorption of nutrients from a high-GI meal the rate of entry of exogenous glucose into the circulation decreases sooner than it would following a low-GI meal. However, the effects of the high insulin : glucagon persist, so that nutrient storage continues and mobilisation from tissues remains suppressed. Blood glucose falls rapidly, often dropping below fasting levels. This hypoglycaemic undershoot triggers release of counter-regulatory hormones, including glucagon, adrenaline and growth hormone. These hormones act to restore circulating fuel levels by increasing hepatic glucose output and decreasing glucose uptake by skeletal muscle. However, they also trigger lipolysis and NEFA release by adipose tissue, causing a rebound in circulating NEFA levels (Wolever *et al*. 1995). In contrast, as a result of the prolonged and continued absorption of nutrients from the gastrointestinal tract following a low-GI meal, the hypoglycaemic undershoot does not occur, and the fasted state is not reached until much later. This slower release of nutrients and gradual drop in blood glucose levels allows adjustment of hepatic glucose output to maintain circulating glucose levels without dramatic rises and falls, or a large rebound in NEFA levels.

Low-GI diets therefore give a more stable diurnal profile, reducing postprandial hyperglycaemia and hyperinsulinaemia, and attenuating late postprandial rebounds in circulating NEFA, all factors that exacerbate various components of the metabolic syndrome (Fig. 3).

### *Insulin resistance*

High circulating NEFA levels result in lipid accumulation in skeletal muscle and liver, causing insulin resistance in these normally insulin-responsive tissues (Frayn, 2001; Petersen & Shulman, 2002), which reduces insulin-stimulated glycogen synthesis in skeletal muscle (the primary pathway for non-oxidative glucose disposal in normal subjects; Kelley *et al*. 2002) and decreases the ability of insulin to suppress hepatic glucose production and output. High circulating NEFA levels also inhibit insulin-stimulated suppression of NEFA release from adipose tissue, so further increasing circulating levels, and triggering a vicious cycle of insulin resistance and increased fatty acid levels (Frape *et al*. 2000).

Attenuation of the NEFA rebound may be a mechanism by which low-GI diets could improve insulin sensitivity. This mechanism is supported by findings from 'second meal' studies showing that low-GI-preload meals compared with high-GI-preload meals may improve (attenuate and prolong) glycaemic responses to standard subsequent meals (Jenkins *et al*. 1982; Liljeberg & Björck, 2000). The glucose response curve to a standard lunch has been shown to be related to plasma NEFA concentration immediately before the lunch (Wolever *et al*. 1995), and preload meals that improve glucose and insulin responses to a standard lunch are those that prevent a hypoglycaemic undershoot until the second meal (Liljeberg *et al*. 1999).

### *Insulin secretion*

There are several plausible explanations for a beneficial effect of low-GI diets on β-cell function. The large insulin demand created by high-GI meals leads to overstimulation of β-cells, which may cause β-cell 'exhaustion' (Ludwig, 2002). High glucose levels have a glucotoxic effect on β-cells, probably as a result of free radical oxidative damage (Augustin *et al*. 2002). Hyperinsulinaemia may reduce β-cell function by causing excess amyloid deposition (Wolever, 2000). High NEFA levels lead to triacylglycerol accumulation in β-cells, which reduces insulin secretion (Goldstein, 2002). Accordingly, by reducing hyperglycaemia, hyperinsulinaemia and NEFA levels low-GI foods may decrease the factors contributing to β-cell failure.

### *Dyslipidaemia*

Low-GI diets may reduce insulin-stimulated activity of 5-hydroxy-3-methylglutaryl-CoA reductase, the rate-limiting enzyme involved in cholesterol synthesis, by reducing insulin levels. The benefits of low-GI diets may also be associated with attenuation of NEFA rebounds, since raised circulating NEFA increase triacylglycerol-rich lipoproteins. Other benefits may arise as a result of a typically high fibre content of low-GI foods. Dietary fibre tends to reduce bile acid and cholesterol re-absorption from the ileum, and also increases colonic fermentation

https://doi.org/10.1079/PNS2005485 Published online by Cambridge University Press

and production of the SCFA propionate, which may inhibit hepatic cholesterol synthesis (Augustin *et al*. 2002).

### *Other cardiovascular risk factors*

Hyperglycaemia is a continuous risk factor for CVD morbidity and mortality (Coutinho *et al*. 1999), and reductions in chronic hyperglycaemia associated with low-GI diets may impact on a number of cardiovascular risk factors. Hyperglycaemia exacerbates oxidative stress, which is associated with inflammation, increased blood pressure, accelerated clot formation and decreased endothelium-dependent blood flow (Augustin *et al*. 2002; Ludwig, 2002), and which may also worsen insulin resistance (Ceriello, 2000). Reduced hyperinsulinaemia associated with a low-GI diet may reduce CVD risk through effects on oxidative stress, blood pressure, serum lipids, coagulation factors, inflammatory mediators, endothelial function and thrombolytic function (Ceriello, 2000; Augustin *et al*. 2002; Goldstein, 2002; Ludwig, 2002; Davy & Melby, 2003).

## Effects on body weight

Modest weight loss, or reduction of weight gain, is an additional potential mechanism by which low-GI diets may contribute to reduced risk of metabolic disease. The most likely mechanism for this effect is via reductions in energy intake. Low-GI foods may increase satiety and delay the return of hunger in comparison with high-GI foods, which may be translated into reduced energy intake at later meals. The hormonal environment following a high-GI meal reduces the availability of the two major metabolic fuels (glucose and fatty acids), signalling a fasted state. Hypoglycaemia is a signal for hunger, and the rate of change of blood glucose may also be important, with more rapid falls triggering more rapid return of hunger (Pawlak *et al*. 2002). The hypoglycaemic undershoot frequently seen following high-GI meals would therefore be predicted to trigger hunger. In one study (Ludwig *et al*. 1999) in which subjects ate more following a high-GI breakfast than following a low-GI breakfast the *ad libitum* energy consumption at lunch has been shown to be strongly predicted by the blood glucose nadir. Initial low levels of NEFA as a result of the high insulin response to high-GI foods may also trigger hunger. Low circulating NEFA levels caused by the consumption of high-GI foods predict intra-subject variability in energy intake following meals of differing GI (Ludwig *et al*. 1999). Together the NEFA levels and area under the glucose response curve following the preload meal predict 85% of the intra-subject variability in energy intake. Satiety is also inversely related to the area under the insulin response curve for various meals, with increased processing of grains increasing glucose and insulin responses and decreasing satiety ratings (Holt & Miller, 1994).

Low-GI foods may also delay the return of hunger by slowing gastric emptying. Many low-GI foods are high in fibre, which prolongs distension of the gastrointestinal tract, causing increased and prolonged secretion of the gut peptides cholecystokinin, ghrelin, glucagon, glucagon-like-peptide-1 and glucose-dependent insulinotropic polypeptide, all of which have been suggested as potential satiety factors (Burton-Freeman *et al*. 2002; Pawlak *et al*. 2002).

A number of short-term feeding studies have investigated the effects of low-GI meals on subsequent satiety, hunger and energy intake. However, many of these studies are confounded by the use of meals that differ in aspects other than GI, and findings have not been wholly consistent. One meta-analysis of cross-over studies investigating the effects of low- and high-GI preloads matched for energy and macronutrient content (Roberts, 2000) has found that subsequent energy intake averages 29% more after high-GI meals *v*. low-GI meals ($P=0{\cdot}005$). Another review of studies using low-GI preloads *v*. high-GI preloads with similar energy, macronutrient and fibre contents (Raben, 2002) has found that in twelve of twenty-four studies low-GI meals decrease hunger or increase satiety, and in six of twelve studies energy intake is lower at a later meal following a low-GI meal compared with a high-GI meal.

If low-GI foods do increase satiety, they may aid compliance to hypoenergetic diets. However, longer-term effects on body weight are unclear. In a study in which a low-GI diet was compared with a standard hypoenergetic reduced-fat diet for 4 months in 107 obese, but otherwise healthy, children (Spieth *et al*. 2000), with the low-GI diet not being energy-restricted and subjects instructed to eat to satiety, reductions in weight and BMI were achieved with the low-GI diet, but not with the standard treatment. However, subjects were not randomised, so selection bias cannot be discounted.

Comparing diets with differing nutrient contents is a problem in many interventions, such that effects cannot confidently be attributed to GI. A review of studies using diets with similar energy, macronutrient and fibre contents (Raben, 2002) has identified six studies with isoenergetic weight-maintaining diets, but none observed any difference in weight between diets. Of three studies using energy-restricted diets only one study reported weight loss in the low-GI group. However, prescribing energy intake reduces the possibility of effects via satiety mechanisms, and few studies have investigated effects of *ad libitum* low-GI diets on weight. In a recent 10-week parallel trial in forty-five overweight women (Sloth *et al*. 2004) subjects were instructed to incorporate certain minimal quantities of low- or high-GI versions of key carbohydrate-rich foods into their diets, to replace 75% of the carbohydrate intake. Subjects consumed the rest of their habitual diets *ad libitum*. Low- and high-GI intervention foods were matched for energy, macronutrient and fibre content, and differed in GI by 24. It was reported that weight decreased for both groups, but no significant differences were found between the groups. Furthermore, no differences in energy intake or fat mass were found. In a randomised cross-over study of eleven overweight men consuming low- or high-GI diets for 5 weeks each (Bouché *et al*. 2002) a trend towards greater decreases in body weight and energy intake on the low-GI diet compared with the high-GI diet was found, but the differences were not significant. However, a significant decrease ($P<0{\cdot}05$) in fat mass and a

https://doi.org/10.1079/PNS2005485 Published online by Cambridge University Press

**Table 1.** Glycaemic index (GI) values of intervention foods

| Low-GI foods | | High-GI foods | |
|---|---|---|---|
| Breakfast cereals | 40–60 | Breakfast cereals | 74–80 |
| Bread | 55 | Bread | 70 |
| Basmati rice | 43 | Easy-cook basmati rice | 68 |
| Penne pasta | 43 | White potatoes | 69–98 |

tendency to increase lean mass more ($P=0{\cdot}07$) on the low-GI diet were reported. Subjects in this study were provided with substitution lists allowing exchanges of low-GI or high-GI foods within food groups. GI was found to be different between diet periods (41 *v*. 71), but fibre content was also found to be higher for the low-GI diet. The potential importance of fibre above GI is also highlighted in a cross-over study of twenty normal-weight women in which *ad libitum* high-starch and high-sucrose diets (with the high-sucrose diet having a lower GI than the high-starch diet; Raben *et al*. 2001) were compared for a period of 14 d (Raben *et al*. 1997). A decrease in weight was found with the high-starch (higher-GI) diet, but no change was found with the high-sucrose (lower-GI) diet. However, the high-starch diet was also higher in fibre content and had a lower energy density than the high-sucrose diet.

From animal studies there is evidence for an effect on nutrient partitioning. Rats fed high-GI diets develop larger epididymal fat pads and adipocyte volumes than those fed low-GI diets (Brand-Miller *et al*. 2002; Pawlak *et al*. 2002). This outcome could plausibly be explained by the differing metabolic responses to high-GI and low-GI foods. The hormonal environment following high-GI foods may favour fat deposition, with nutrients directed towards storage rather than oxidation. Physiological changes observed in the rats fed high-GI diets *v*. low-GI diets would also tend to favour adipogenesis. These changes include increased expression and activity of fatty acid synthase complex in adipose tissue, increased glucose uptake into adipocytes, increased GLUT4 expression in adipose tissue and increased hepatic lipogenesis (Brand-Miller *et al*. 2002). However, the effects on nutrient partitioning during weight loss in human subjects are not clear. In one study, despite no differences in weight loss between low- and high-GI diets, selective loss of fat mass with an increase in lean mass has been reported (Bouché *et al*. 2002). However, a study investigating the acute effects of low- and high-GI meals on fuel partitioning has found that, despite higher insulin levels following the high-GI meal, there are no differences in substrate oxidation (Díaz *et al*. 2005).

Finally, there is limited evidence to suggest that the magnitude of the decreases in resting energy expenditure associated with hypoenergetic diets is smaller on low-GI diets *v*. high-GI diets, thus contributing to a greater energy deficit. A randomised cross-over study of high- and low-GI diets for 9 d each in ten overweight men (Agus *et al*. 2000) has found that resting energy expenditure decreases by 10·5 % on the high-GI diet compared with 4·6 % on the low-GI diet ($P=0{\cdot}04$). Another study comparing a low-GL diet with a conventional low-fat hypoenergetic diet (Pereira *et al*. 2004) has found that, with a 10 % body-weight loss on each diet, resting energy expenditure decreases more on the low-fat diet compared with the low-GL diet (10·6 % *v*. 5·9 %, equivalent to 334 kJ (80 kcal)/d, $P=0{\cdot}05$;). However, these diets were not matched for macronutrient content.

## Ongoing research

To address some of the limitations of previous trials a dietary intervention study has been designed to assess how carbohydrates of varying GI affect metabolic disease risk and to explore some potential mechanisms for any effects. It is a randomised cross-over study of low-GI and high-GI diets in forty-four women aged 18–65 years with a BMI of $\geq 25\,kg/m^2$ and fasting insulin level of $\geq 40$ pmol/l (sample size calculated to be sufficient to detect a 10 % difference in insulin sensitivity). The study consists of two consecutive 12-week periods of low-GI and high-GI diets, with measurements of a number of markers of metabolic disease risk at baseline and at the end of each diet period.

Subjects are provided with low-GI and high-GI versions of breakfast cereals, breads and rices, plus pasta during the low-GI period and potatoes on the high-GI period (intervention foods being selected by measurement of the GI of a number of carbohydrate-rich UK 'staple' foods; Table 1). Subjects maintain their normal habitual diets, substituting the intervention foods where they would normally eat them, in the quantity they would normally consume. They are asked to eat the foods approximately three times daily, but quantity is not specified, and subjects are instructed to eat *ad libitum*. They are given guidance for foods to choose and avoid when eating away from home, but are not told of the GI concept. This dietary intervention is designed to avoid broader dietary changes that frequently occur when individuals are advised to follow a low-GI diet, such as increases in pulse, fruit, vegetable and whole-grain consumption. By concentrating on 'staple' foods it is intended to be easily achievable, and so maximise applicability to public health.

Measurable changes have been seen in other studies in which GI has been reduced by ≥11 by exchanging approximately half the dietary carbohydrate from high-GI to low-GI foods (Brand-Miller, 1994). Data from the National Diet and Nutrition Surveys reveal that the types of foods provided in the intervention supply 60–70 % of the total dietary carbohydrate (assuming a diet with 45–55 % energy from carbohydrate; Office of National Statistics, 2002). An estimated achievable difference of approximately 15 in dietary GI has been calculated from the GI values of the intervention foods (Table 1), and assuming a total daily carbohydrate intake of 250 g (calculated as: dietary GI = (carbohydrate provided by food (g)/total dietary carbohydrate (250 g)) × GI).

The study will investigate a range of outcomes, covering many potential effects of low-GI foods. These outcomes include: insulin sensitivity measured by the fasting indices of fasting glucose, insulin and homeostasis model assessment index of insulin resistance, and in the dynamic state by the area under the insulin response curve for a 75 g oral glucose load and also by a novel orally-stimulated

https://doi.org/10.1079/PNS2005485 Published online by Cambridge University Press

intravenous glucose tolerance test, using isotopically-labelled glucose; glucose tolerance, assessed by fasting and postprandial glucose levels after a glucose load and after a mixed meal; body weight, waist circumference and body fat (determined by dual-energy X-ray absorptiometry); blood pressure; fasting lipid profile; various markers of inflammatory status and thrombolytic function.

The study is not powered to look at weight change, but does have sufficient power to investigate a 10% difference in subjective ratings of appetite (Flint *et al*. 2000). An appetite investigation day is incorporated during each diet period. Subjects are given a fixed low-GI or high-GI breakfast and then they complete subjective ratings of hunger and fullness over the following 4 h. They are given an *ad libitum* snack 2 h after breakfast and an *ad libitum* lunch after a further 2 h. The intention is to investigate the short-term impact of low GI on between-meal snacking and on energy intake at the subsequent meal to determine whether any differences in intake of the snack are compensated for at lunch. Intake at main meals may be more strongly habituated than between-meal snacks, and so may be less affected by perceived hunger.

Compliance is being monitored by completion of food-frequency questionnaires, 4 d food diaries and day-to-day recording of intervention foods consumed. Subjects are also fitted with continuous glucose monitors for 24 h during each diet period to determine whether the intervention foods consumed *ad libitum* as part of a mixed diet have differing effects on day-long glucose levels.

This work and other ongoing work into the effect of low-GI diets on health, including large studies funded by the Food Standards Agency (RISCK, 2005) and EU (The Diogenes Project, 2005) will, over the next few years, provide clearer answers to some of the many questions that the present review has raised. Until then, the specific effects of GI on metabolic health and body weight remain uncertain.

## Acknowledgements

The author would like to thank S.A. Jebb for her supervision, many other colleagues at MRC HNR for their expertise and involvement in the studies described here, and all the volunteers for their time and commitment. L.M.A. is supported by a Medical Research Council Studentship.

## References

Agus MS, Swain JF, Larson CL, Eckert EA & Ludwig DS (2000) Dietary composition and physiologic adaptations to energy restriction. *American Journal of Clinical Nutrition* **71**, 901–907.

AOAC International (1995) Total, soluble and insoluble dietary fiber in foods. AOAC official method 991.43. *Official Methods of Analysis*, 16th edition. Gathersburg, MD: AOAC International.

Augustin LS, Franceschi S, Jenkins DJ, Kendall CW & La Vecchia C (2002) Glycemic index in chronic disease: a review. *European Journal of Clinical Nutrition* **56**, 1049–1071.

Björck I, Liljeberg H & Östman E (2000) Low glycaemic-index foods. *British Journal of Nutrition* **83**, Suppl. 1, S149–S155.

Bouché C, Rizkalla SW, Luo J, Vidal H, Veronese A, Pacher N, Fouquet C, Lang V & Slama G (2002) Five-week, low-glycemic index diet decreases total fat mass and improves plasma lipid profile in moderately overweight nondiabetic men. *Diabetes Care* **25**, 822–828.

Brand-Miller JC (1994) Importance of glycemic index in diabetes. *American Journal of Clinical Nutrition* **59**, 747S–752S.

Brand-Miller JC, Holt SH, Pawlak DB & McMillan J (2002) Glycemic index and obesity. *American Journal of Clinical Nutrition* **76**, 281S–285S.

Burton-Freeman B, Davis PA & Schneeman BO (2002) Plasma cholecystokinin is associated with subjective measures of satiety in women. *American Journal of Clinical Nutrition* **76**, 659–667.

Ceriello A (2000) Oxidative stress and glycemic regulation. *Metabolism* **49**, 27–29.

Collier GR, Wolever TM, Wong GS & Josse RG (1986) Prediction of glycemic response to mixed meals in noninsulin-dependent diabetic subjects. *American Journal of Clinical Nutrition* **44**, 349–352.

Coutinho M, Gerstein HC, Wang Y & Yusuf S (1999) The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care* **22**, 233–240.

Davy BM & Melby CL (2003) The effect of fiber-rich carbohydrates on features of Syndrome X. *Journal of the American Dietetic Association* **103**, 86–96.

Díaz EO, Galgani JE, Aguirre CA, Atwater IJ & Burrows R (2005) Effect of glycemic index on whole-body substrate oxidation in obese women. *International Journal of Obesity* **29**, 108–114.

Department of Health (1994) *Nutritional Aspects of Cardiovascular Disease*. *Report on Health and Social Subjects* no. 46. London: H. M. Stationery Office.

Ebbeling CB, Leidig MM, Sinclair KB, Seger-Shippee LG, Feldman HA & Ludwig DS (2005) Effects of an ad libitum low-glycemic load diet on cardiovascular disease risk factors in obese young adults. *American Journal of Clinical Nutrition* **81**, 976–982.

Englyst KN, Vinoy S, Englyst HN & Lang V (2003) Glycaemic index of cereal products explained by their content of rapidly and slowly available glucose. *British Journal of Nutrition* **89**, 329–340.

Flint A, Raben A, Blundell JE & Astrup A (2000) Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. *International Journal of Obesity and Related Metabolic Disorders* **24**, 38–48.

Fontvieille AM, Rizkalla SW, Penfornis A, Acosta M, Bornet FR & Slama G (1992) The use of low glycaemic index foods improves metabolic control of diabetic patients over five weeks. *Diabetic Medicine* **9**, 444–450.

Food and Agriculture Organization/World Health Organization (1998) *Carbohydrates in Human Nutrition*. *Report of a Joint FAO/WHO Expert Consultation. FAO Food and Nutrition Paper* no. 66. Rome: FAO.

Foster-Powell K, Holt SH & Brand-Miller JC (2002) International table of glycemic index and glycemic load values: 2002. *American Journal of Clinical Nutrition* **76**, 5–56.

Frape DL, Williams NR, Carpenter KL, Freeman MA, Palmer CR & Fletcher RJ (2000) Insulin response and changes in composition of non-esterified fatty acids in blood plasma of middle-aged men following isoenergetic fatty and carbohydrate breakfasts. *British Journal of Nutrition* **84**, 737–745.

Frayn KN (2001) Adipose tissue and the insulin resistance syndrome. *Proceedings of the Nutrition Society* **60**, 375–380.

Frost G, Keogh B, Smith D, Akinsanya K & Leeds A (1996) The effect of low-glycemic carbohydrate on insulin and glucose response in vivo and in vitro in patients with coronary heart disease. *Metabolism* **45**, 669–672.

Frost G, Leeds A, Trew G, Margara R & Dornhorst A (1998) Insulin sensitivity in women at risk of coronary heart disease and the effect of a low glycemic diet. *Metabolism* **47**, 1245–1251.

Frost G, Leeds AA, Dore CJ, Madeiros S, Brading S & Dornhorst A (1999) Glycaemic index as a determinant of serum HDL-cholesterol concentration. *Lancet* **353**, 1045–1048.

Goldstein BJ (2002) Insulin resistance as the core defect in type 2 diabetes mellitus. *American Journal of Cardiology* **90**, 3G–10G.

Granfeldt Y, Drews A & Bjorck I (1995) Arepas made from high amylose corn flour produce favorably low glucose and insulin responses in healthy humans. *Journal of Nutrition* **125**, 459–465.

Hermansen K, Rasmussen O, Gregersen S & Larsen S (1992) Influence of ripeness of banana on the blood glucose and insulin response in type 2 diabetic subjects. *Diabetic Medicine* **9**, 739–743.

Holt SH & Miller JB (1994) Particle size, satiety and the glycaemic response. *European Journal of Clinical Nutrition* **48**, 496–502.

Järvi AE, Karlstrom BE, Granfeldt YE, Bjorck IE, Asp NG & Vessby BO (1999) Improved glycemic control and lipid profile and normalized fibrinolytic activity on a low-glycemic index diet in type 2 diabetic patients. *Diabetes Care* **22**, 10–18.

Jenkins DJ, Wesson V, Wolever TM, Jenkins AL, Kalmusky J, Guidici S, Csima A, Josse RG & Wong GS (1988) Wholemeal versus wholegrain breads: proportion of whole or cracked grain and the glycaemic response. *British Medical Journal* **297**, 958–960.

Jenkins DJ, Wolever TM, Taylor RH, Barker H, Fielden H, Baldwin JM, Bowling AC, Newman HC, Jenkins AL & Goff DV (1981) Glycemic index of foods: a physiological basis for carbohydrate exchange. *American Journal of Clinical Nutrition* **34**, 362–366.

Jenkins DJ, Wolever TM, Taylor RH, Griffiths C, Krzeminska K, Lawrie JA, Bennett CM, Goff DV, Sarson DL & Bloom SR (1982) Slow release dietary carbohydrate improves second meal tolerance. *American Journal of Clinical Nutrition* **35**, 1339–1346.

Juntunen KS, Laaksonen DE, Poutanen KS, Niskanen LK & Mykkanen HM (2003) High-fiber rye bread and insulin secretion and sensitivity in healthy postmenopausal women. *American Journal of Clinical Nutrition* **77**, 385–391.

Juntunen KS, Niskanen LK, Liukkonen KH, Poutanen KS, Holst JJ & Mykkanen HM (2002) Postprandial glucose, insulin, and incretin responses to grain products in healthy subjects. *American Journal of Clinical Nutrition* **75**, 254–262.

Kelley DE, Goodpaster BH & Storlien L (2002) Muscle triglyceride and insulin resistance. *Annual Review of Nutrition* **22**, 325–346.

Kelly S, Frost G, Whittaker V & Summerbell C (2004) *Low Glycaemic Index Diets for Coronary Heart Disease*. *The Cochrane Database of Systematic Reviews* 2004, Issue 4. Chichester, West Sussex: John Wiley & Sons Ltd.

Kiens B & Richter EA (1996) Types of carbohydrate in an ordinary diet affect insulin action and muscle substrates in humans. *American Journal of Clinical Nutrition* **63**, 47–53.

Larsen HN, Rasmussen OW, Rasmussen PH, Alstrup KK, Biswas SK, Tetens I, Thilsted SH & Hermansen K (2000) Glycaemic index of parboiled rice depends on the severity of processing: study in type 2 diabetic subjects. *European Journal of Clinical Nutrition* **54**, 380–385.

Lau C, Faerch K, Glumer C, Tetens I, Pedersen O, Carstensen B, Jorgensen T & Borch-Johnsen K (2005) Dietary glycemic index, glycemic load, fiber, simple sugars, and insulin resistance: the Inter99 study. *Diabetes Care* **28**, 1397–1403.

Liljeberg H & Björck I (2000) Effects of a low-glycaemic index spaghetti meal on glucose tolerance and lipaemia at a subsequent meal in healthy subjects. *European Journal of Clinical Nutrition* **54**, 24–28.

Liljeberg HG, Akerberg AK & Björck IM (1999) Effect of the glycemic index and content of indigestible carbohydrates of cereal-based breakfast meals on glucose tolerance at lunch in healthy subjects. *American Journal of Clinical Nutrition* **69**, 647–655.

Liu S, Manson JE, Buring JE, Stampfer MJ, Willett WC & Ridker PM (2002) Relation between a diet with a high glycemic load and plasma concentrations of high-sensitivity C-reactive protein in middle-aged women. *American Journal of Clinical Nutrition* **75**, 492–498.

Liu S, Manson JE, Stampfer MJ, Holmes MD, Hu FB, Hankinson SE & Willett WC (2001) Dietary glycemic load assessed by food-frequency questionnaire in relation to plasma high-density-lipoprotein cholesterol and fasting plasma triacylglycerols in postmenopausal women. *American Journal of Clinical Nutrition* **73**, 560–566.

Liu S, Willett WC, Stampfer MJ, Hu FB, Franz M, Sampson L, Hennekens CH & Manson JE (2000) A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *American Journal of Clinical Nutrition* **71**, 1455–1461.

Ludwig DS (2002) The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *Journal of the American Medical Association* **287**, 2414–2423.

Ludwig DS, Majzoub JA, Al-Zahrani A, Dallal GE, Blanco I & Roberts SB (1999) High glycemic index foods, overeating, and obesity. *Pediatrics* **103**, E26.

Luscombe ND, Noakes M & Clifton PM (1999) Diets high and low in glycemic index versus high monounsaturated fat diets: effects on glucose and lipid metabolism in NIDDM. *European Journal of Clinical Nutrition* **53**, 473–478.

McKeown NM, Meigs JB, Liu S, Saltzman E, Wilson PW & Jacques PF (2004) Carbohydrate nutrition, insulin resistance, and the prevalence of the metabolic syndrome in the Framingham Offspring Cohort. *Diabetes Care* **27**, 538–546.

Meyer KA, Kushi LH, Jacobs DR Jr, Slavin J, Sellers TA & Folsom AR (2000) Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. *American Journal of Clinical Nutrition* **71**, 921–930.

Office of National Statistics (2002) *The National Diet and Nutrition Survey: Adults Aged 16–64 Years. Types and Quantities of Foods Consumed*. Norwich: The Stationery Office.

Östman EM, Liljeberg Elmstahl HG & Bjorck IM (2001) Inconsistency between glycemic and insulinemic responses to regular and fermented milk products. *American Journal of Clinical Nutrition* **74**, 96–100.

Pawlak DB, Ebbeling CB & Ludwig DS (2002) Should obese patients be counselled to follow a low-glycaemic index diet? Yes. *Obesity Reviews* **3**, 235–243.

Pereira MA, Swain J, Goldfine AB, Rifai N & Ludwig DS (2004) Effects of a low-glycemic load diet on resting energy expenditure and heart disease risk factors during weight loss. *Journal of the American Medical Association* **292**, 2482–2490.

Petersen KF & Shulman GI (2002) Pathogenesis of skeletal muscle insulin resistance in type 2 diabetes mellitus. *American Journal of Cardiology* **90**, 11G–18G.

Raben A (2002) Should obese patients be counselled to follow a low-glycaemic index diet? No. *Obesity Reviews* **3**, 245–256.

Raben A, Holst JJ, Madsen J & Astrup A (2001) Diurnal metabolic profiles after 14 d of an ad libitum high-starch, high-sucrose, or high-fat diet in normal-weight never-obese and postobese women. *American Journal of Clinical Nutrition* **73**, 177–189.

Raben A, Macdonald I & Astrup A (1997) Replacement of dietary fat by sucrose or starch: effects on 14 d ad libitum energy intake, energy expenditure and body weight in formerly obese and never-obese subjects. *International Journal of Obesity and Related Metabolic Disorders* **21**, 846–859.

RISCK (2005) The RISCK Study. www.risck.org.uk

Roberts SB (2000) High-glycemic index foods, hunger, and obesity: is there a connection? *Nutrition Reviews* **58**, 163–169.

Salmerón J, Ascherio A, Rimm EB, Colditz GA, Spiegelman D, Jenkins DJ, Stampfer MJ, Wing AL & Willett WC (1997*a*) Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care* **20**, 545–550.

Salmerón J, Manson JE, Stampfer MJ, Colditz GA, Wing AL & Willett WC (1997*b*) Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *Journal of the American Medical Association* **277**, 472–477.

Sloth B, Krog-Mikkelsen I, Flint A, Tetens I, Bjorck I, Vinoy S, Elmstahl H, Astrup A, Lang V & Raben A (2004) No difference in body weight decrease between a low-glycemic-index and a high-glycemic-index diet but reduced LDL cholesterol after 10-wk ad libitum intake of the low-glycemic-index diet. *American Journal of Clinical Nutrition* **80**, 337–347.

Soh NL & Brand-Miller J (1999) The glycaemic index of potatoes: the effect of variety, cooking method and maturity. *European Journal of Clinical Nutrition* **53**, 249–254.

Spieth LE, Harnish JD, Lenders CM, Raezer LB, Pereira MA, Hangen SJ & Ludwig DS (2000) A low-glycemic index diet in the treatment of pediatric obesity. *Archives of Pediatrics and Adolescent Medicine* **154**, 947–951.

The Diogenes Project (2005) The Diogenes Project. Targeting the obesity problem: seeking new insights and routes to prevention. www.diogenes-eu.org

Tsihlias EB, Gibbs AL, McBurney MI & Wolever TM (2000) Comparison of high- and low-glycemic-index breakfast cereals with monounsaturated fat in the long-term dietary management of type 2 diabetes. *American Journal of Clinical Nutrition* **72**, 439–449.

van Dam RM, Visscher AW, Feskens EJ, Verhoef P & Kromhout D (2000) Dietary glycemic index in relation to metabolic risk factors and incidence of coronary heart disease: the Zutphen Elderly Study. *European Journal of Clinical Nutrition* **54**, 726–731.

World Health Organization (2002) *The World Health Report 2002: Reducing Risks, Promoting Healthy Life*. Geneva: WHO.

World Health Organization (2003) *The World Health Report 2003: Shaping the Future*. Geneva: WHO.

Willett W, Manson J & Liu S (2002) Glycemic index, glycemic load, and risk of type 2 diabetes. *American Journal of Clinical Nutrition* **76**, 274S–280S.

Wolever TM (2000) Dietary carbohydrates and insulin action in humans. *British Journal of Nutrition* **83**, Suppl. 1, S97–S102.

Wolever TM, Bentum-Williams A & Jenkins DJ (1995) Physiological modulation of plasma free fatty acid concentrations by diet. Metabolic implications in nondiabetic subjects. *Diabetes Care* **18**, 962–970.

Wolever TM, Jenkins DJ, Vuksan V, Jenkins AL, Wong GS & Josse RG (1992) Beneficial effect of low-glycemic index diet in overweight NIDDM subjects. *Diabetes Care* **15**, 562–564.

Wolever TM & Mehling C (2002) High-carbohydrate-low-glycaemic index dietary advice improves glucose disposition index in subjects with impaired glucose tolerance. *British Journal of Nutrition* **87**, 477–487.