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Glycemic Index

From Research to Nutrition Recommendations?

TemaNord 2005:589

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ISBN 92-893-1256-4

Print: Ekspressen Tryk & Kopicenter
Copies: 250

Printed on environmentally friendly paper

This publication can be ordered on www.norden.org/order. Other Nordic publications are available at www.norden.org/publications

Printed in Denmark

Nordic Council of Ministers
Store Strandstræde 18
DK-1255 Copenhagen K
Phone (+45) 3396 0200
Fax (+45) 3396 0202

Nordic Council
Store Strandstræde 18
DK-1255 Copenhagen K
Phone (+45) 3396 0400
Fax (+45) 3311 1870

www.norden.org

The Nordic Food Policy Co-operation

The Nordic Committee of Senior Officials for Food Issues is concerned with basic Food Policy issues relating to food and nutrition, food toxicology and food microbiology, risk evaluation, food control and food legislation. The co-operation aims at protection of the health of the consumer, common utilisation of professional and administrative resources and at Nordic and international developments in this field.

Nordic co-operation

Nordic co-operation, one of the oldest and most wide-ranging regional partnerships in the world, involves Denmark, Finland, Iceland, Norway, Sweden, the Faroe Islands, Greenland and Åland. Co-operation reinforces the sense of Nordic community while respecting national differences and similarities, makes it possible to uphold Nordic interests in the world at large and promotes positive relations between neighbouring peoples.

Co-operation was formalised in 1952 when *the Nordic Council* was set up as a forum for parliamentarians and governments. The Helsinki Treaty of 1962 has formed the framework for Nordic partnership ever since. The *Nordic Council of Ministers* was set up in 1971 as the formal forum for co-operation between the governments of the Nordic countries and the political leadership of the autonomous areas, i.e. the Faroe Islands, Greenland and Åland.

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1 Preface

The concept of glycemic index (GI) has been widely studied and debated in the scientific literature since its appearance in 1981 (Jenkins et al., 1981). Epidemiological and intervention studies have increased both public and expert awareness of the possible importance of blood sugar regulation and the varying glycemic effect of foods in the etiology and treatment of chronic diseases and obesity. However, the practical implications of these studies on nutrition recommendations for the prevention or treatment of diseases still have to be clarified. Great public attention has been given to these studies, and popular weight reduction schemes have been tailored accordingly using the GI concept.

In 2003 the "Nordiska Komiteen for Ernæringsmedel (NKE)" on behalf of The Nordic Council of Ministers asked professor Inga Thorsdóttir, at the Unit for Nutrition Research at Landspitali-University Hospital and University of Iceland, to apply for a project in the field of the glycemic index. The objective was to get experts together in order to clarify the importance of glycemic index of foods in nutrition of Nordic populations. The report has been approved by NKE. However, the interpretations of the scientific litterature and the conclusions presented are those of the authors.

The Nordic countries publish common nutrition recommendations (Nordic Nutrition Recommendations, 2004), and harmonization of these is one of the main elements of nutrition cooperation in the Nordic countries. It is therefore important to evaluate the evidence for and against using the GI concept in prevention or treatment of diseases in a Nordic food reality today.

A Seminar: "Glycemic Index: From Research to Nutrition Recommendations" was held on June 20th 2004 as a satellite meeting to the 8th Nordic Nutrition Congress, June 20th-23rd 2004 in Tönsberg, Norway (see Appendix 1). Preparations were made, by collaborating with experts in all the Nordic countries. The organizers, chairs and speakers were from Iceland, Sweden, Finland, Norway and Denmark as well as speakers providing information about the extensive studies on the subject performed in Toronto, Canada and at Harvard University, USA. The lectures were on different aspects of the glycemic index and time was allocated for questions and panel discussions. This gave basis for analysis of the evidence for using the glycemic effect of foods in prevention and treatment of overweight and diseases in the Nordic populations. The results from the seminar have been presented as a poster at the 22nd International Symposium on Diabetes and Nutrition, held by the Diabetes and Nutri-

tion Study Group (DNSG) of the European Association for the Study of Diabetes (EASD), in Sweden 2004.

Following the seminar a comprehensive evaluation of the literature was mainly done in Iceland, based on the lectures and discussions from the seminar as well as by contacting the experts through the Internet.

Authors responsible for the contents of the report:
Prof. Inga Thorsdóttir, project-coordinator Unit for Nutrition Research, Landspitali-University Hospital and University of Iceland.
Dr. Bryndís Eva Birgisdóttir, Unit for Nutrition Research, Landspitali-University Hospital and University of Iceland.

Working group of the project - report and/or seminar:
Dr. Laufey Steingrimsdóttir, The Public Health Institute of Iceland, former chairman of the Working Group on Diet and Nutrition (NKE) a sub-group of the Nordic Committee of Senior Officials on Food (AK-livs) and the Nordic Council of Ministers.
Dr. Brita Karlström, Unit for Clinical Nutrition Research, Institute for public Health and Caring Sciences, Uppsala University.
Prof. Inger Björck, Applied Nutrition and Food Chemistry, Department of Food Technology, Engineering and Nutrition, Lund University, Sweden
Associate professor Anne Flint, Institute of Human Nutrition, Royal Veterinary and Agricultural University, Centre of Food Studies, Denmark
Prof. Svein Olav Kolset, Department of Nutrition, University of Oslo, Norway
Prof. Matti Uusitupa, Rector of the University of Kuopio, former Head of the Department of Clinical Nutrition, University of Kuopio, Finland
Dr. Matthias B. Schulze, Department of Epidemiology, German Institute of Human Nutrition, Germany, former research fellow at the Department of Nutrition, Harvard School of Public Health, Harvard University, Massachusetts, USA
Prof. David J.A. Jenkins, Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Canada

Other Nordic experts in the field of glycemic index participated as well and are greatly acknowledged for their valuable input, especially Professor Nils-Georg Asp at Lund University, for his review and comments. These experts were found through national channels, through both government officials and scientific study groups on diabetes and glycemic index.

We thank the organizers of the 8th Nordic Nutrition Conference for their co-operation as well as Elva Gísladóttir at the Unit for Nutrition Research in Iceland for her part in organizing the Seminar.

2 Summary

2.1 Summary in English

Epidemiological and intervention studies have increased both public and expert awareness of the possible importance of blood sugar regulation and the varying glycemic index (GI) of foods in the etiology and treatment of chronic diseases. The practical implications of these studies on nutrition recommendations for the prevention or treatment of diseases have to be clarified.

Generally low GI food is considered beneficial due to less incremental increase in blood levels of glucose than after consumption of food with a high GI. Examples of food with low GI are whole cereal grains and whole kernel bread (pumpernickel), beans, and many fruits while examples of high GI food are common bread, highly processed cereal grains and potatoes. The concept of glycemic load (GL) is the arithmetic product of GI and total available carbohydrates in a portion, or the overall diet.

For evaluation of the GI of different food items, it is important to have an internationally standardized GI methodology to be able to compare GI data from different research groups. Furthermore, studies have found that present international table values are often not good predictors of measured GI for various reasons, such as differences between countries in methodology and cooking methods; this indicates a need for local information. When measuring the GI of different food items, information on the insulin index might give important additional information.

It has been suggested that GI and GL values should only be applied for food items that have at least 15-20 grams of available carbohydrates per normal portion. Furthermore, comparison of GI values should only be made between foods in the same food group such as different types of bread, morning cereals, etc. If these principles are followed, GI and GL could be used to stimulate an alternative choice without disturbing the nutritional value of the diet and prevent the misuse and misunderstanding that has occurred.

Epidemiological studies indicate that a low GI diet decreases the risk of chronic diseases, such as type 2 diabetes and coronary heart disease and of developing risk factors for these diseases as well as decreasing the risk for cancer, especially among those who are overweight or obese. The association between high GL and type 2 diabetes is stronger when the diet is also low in cereal fiber. According to the Finnish diabetes prevention study, there is evidence that low GI, dietary fiber, whole grain products and healthy modification of dietary fatty acids all play a role in preventing type 2 diabetes, but the evidence is strongest for ideal body

weight and physical activity. The interaction between all these factors needs further investigation. Other intervention studies have shown that a low GI diet may improve impaired glucose tolerance and even dyslipidemia. For example, the mere exchange of common high GI bread for low GI bread products with low GI and rich in dietary fiber in a mixed diet for three weeks improved insulin economy in young women at high risk of type 2 diabetes. When giving dietary advice to people with diabetes, products with low GI are often recommended. The importance of GI in weight maintenance or weight loss has to be further studied.

For individuals with diabetes or impaired glucose tolerance, a low GI diet might be of importance; this holds as well for those prone to diabetes due to overweight, which is a large and expanding group of people. More evidence is needed to draw more secure conclusions on the importance of low GI food for healthy individuals. As a low GI diet often goes hand in hand with a healthy diet rich in fiber and nutrients, it is often hard to evaluate the real reason for a positive association seen between a low GI diet and decreased risk of chronic diseases or beneficial effect on health by diminishing risk factors. This must be resolved in future studies, and there is an urgent need for well-controlled, long-term, randomized clinical intervention trials as well as well-designed prospective epidemiological cohort studies to establish clearly the role of low GI foods and diets in maintenance of health and prevention of chronic disease or overweight.

In order to perform such studies in a realistic way, a variety of low GI foods is needed. Many of the habitual food items consumed in the Nordic countries are likely to have a high GI, such as common breads and cereals, and might thus be suboptimal for a large group of people. Compiling a Nordic GI database for carbohydrate rich food items would therefore enhance evaluation of the importance of GI in the Nordic diets. Today the applicability of the GI concept is partly limited by the shortage of low GI foods on the market, but a number of food factors have been identified that can be exploited for this purpose.

It should always be kept in mind that the glycemic index is only one measure of many which together indicate a healthy diet.

2.2 Summary in Swedish

Epidemiologiska studier och interventioner har ökat både experters och allmänhetens medvetenhet om att blodsockerreglering och kostens varierande glykemiska index (GI) kan vara viktig både i etiologi och vid behandlingen av kroniska sjukdomar. Betydelsen av dessa studier för näringsrekommendationer behöver utvärderas.

Allmänt har mat med lågt GI ansetts vara bra eftersom blodsockerstegringen är mindre än efter intag av livsmedel med högt GI. Hela spannmålskärnor, fullkornsbröd typ pumpernickel, bönor och många frukter är exempel på livsmedel med lågt GI medan exempel på mat med högt GI är vanliga bröd, mycket processerade ceralier och potatis. Ett annat koncept, "Glycemic Load" (GL), används också och är ett livsmedels GI multiplicerad med andelen kolhydrater i portionen.

Vid bestämning av GI för olika livsmedel är det viktigt att det finns en internationellt standardiserad GI-metod för att kunna jämföra data från olika forskningsgrupper. Studier har visat att internationella tabellvärden inte alltid förutsäger GI för livsmedel som har analyserats i samband med studier i andra länder. Orsaken är till exempel olikheter i mätmetoder och matlagning vilket indikerar att lokala tabellvärden behövs. Parallell analys av insulinstegring i blodet i samband med GI-analyser skulle kunna addera viktig information till GI-forskningen.

GI- och GL-värden borde endast användas för livsmedel som har minst 15-20g kolhydrater per normal portion. Man borde också endast jämföra livsmedel inom samma grupp, dvs. olika typer av bröd, frukostflingor osv. Om man följer dessa principer skulle GI- och GL-värden kunna användas för att stimulera ett alternativt val utan att störa kostens näringsvärde. Detta förhindrar dessutom felaktigt användande och missförstånd av GI- och GL-värden.

Epidemiologiska studier indikerar att en kost med lågt GI minskar risken för kroniska sjukdomar som typ 2-diabetes och hjärtkärlsjukdomar och även risken för vissa cancertyper, särskilt hos de som är överviktiga. Kopplingen mellan kost med högt GL och typ 2-diabetes är starkare när kosten samtidigt innehåller en liten mängd fiber. Den finska diabetespreventionsstudien visade att lågt GI, kostfiber, helkornsprodukter och hälsosam modifikation av fettsyror alla spelade roll i att förhindra typ 2-diabetes, men bevisen var starkast för normalvikt och fysisk aktivitet. Interaktionen mellan alla dessa faktorer behöver studeras ytterligare. Andra interventionsstudier har indikerat att kost med lågt GI skulle kunna förbättra glukostoleransen och i somliga fall även blodfettrubbningar. Det har till exempel visat sig att utbyte av vanligt bröd mot bröd med lågt GI och rikt av fibrer i en blandad kost i tre veckor förbättrade insulinekonomin hos unga kvinnor som hade hög risk att utveckla

typ 2-diabetes. När kostinformation ges till de som har diabetes, rekommenderas ofta produkter med lågt GI. Hur viktig kost med lågt GI är för att bibehålla normalvikt eller för viktminskning måste studeras ytterligare.

En kost med lågt GI kan vara av värde för individer med diabetes eller glukosintolerans eller för de som har risk för diabetes för att de är överviktiga (en stor andel av befolkningen). Ytterligare studier behövs dock innan man kan dra säkra slutsatser angående hur viktig en kost med lågt GI är för friska. Eftersom en kost med lågt GI ofta går hand i hand med en hälsosam kost som är rik på fiber och näringsämnen är det ofta svårt att utvärdera vad som är orsaken till den positiva relation som många studier visat mellan en kost med lågt GI och minskad risk för kroniska sjukdomar eller förbättrad effekt på hälsan genom att förhindra uppkomsten av eller förbättra riskfaktorer för dessa sjukdomar. Detta måste framtida studier lösa och det är viktigt att utföra välkontrollerade, randomiserade långtidsinterventioner samt välkonstruerade prospektiva epidemiologiska studier för att etablera om kost med lågt GI är viktig för att bibehålla god hälsa och förhindra uppkomsten av kroniska sjukdomar och övervikt.

För att kunna göra sådana studier på ett realistiskt sätt, behövs ett stort urval av matvaror som har lågt GI. Mycket av den kolhydratrika mat som konsumeras idag i de nordiska länderna har troligtvis ett högt GI, såsom vanligt bröd och processerade cerealier. Det skulle underlätta utvärderingen av låg GI-kosts betydelse för befolkningen i de nordiska länderna och deras hälsa, om det fanns en nordisk GI-databas för kolhydratrik mat. I dag begränsar det relativt låga utbud av mat med lågt GI i de nordiska länderna delvis användningen av GI-konceptet, men en rad faktorer och egenskaper i maten har pekats ut som är användbara för att sänka GI-värden hos vanliga livsmedel.

Det är viktigt att komma ihåg att glykemiskt index enbart är en faktor av många som tillsammans indikerar en hälsosam kost.

2.3 Summary in Icelandic

Faraldsfræðilegar og íhlutandi rannsóknir hafa aukið þekkingu bæði fræðimanna og almennings á blóðsykurstjórnun og breytilegum glýkemíustuðli matvæla og á hugsanlegu mikilvægi þessa fyrir þróun og meðhöndlun sjúkdóma. Varpa verður ljósi á þýðingu þessara rannsókna fyrir næringarfræðilegar ráðleggingar sem miða að því að koma í veg fyrir eða meðhöndla sjúkdóma.

Fæðutegund með lágan glýkemíustuðul er almennt talin æskileg vegna þess að hún veldur minni aukningu á styrk glúkósa í blóði en fæðutegund með háan glýkemíustuðul. Dæmi um mat með lágan glýkemíustuðul eru lítið unnar heilkornavörur, baunir og margir ávextir. Dæmi um matvæli með háan glýkemíustuðul eru algengar brauðtegundir, mikið unnið korn og kartöflur. Glýkemíuhleðsla er margfeldi blóðsykurstuðuls fæðutegundar og kolvetna í einum skammti.

Til að meta glýkemíustuðul mismunandi matvæla er mikilvægt að til sé alþjóðleg stöðluð aðferð til þess að upplýsingar frá mismunandi rannsóknarhópum séu sambærilegar. Rannsóknir hafa sýnt að núverandi alþjóðleg töflugildi gefa oft ekki réttar upplýsingar um glýkemíustuðul matvæla, þetta stafar af breytileika í aðferðafræði við að mæla glýkemíustuðul og mismunandi matreiðslu á einstökum fæðutegundum milli landa. Þetta sýnir mikilvægi staðbundinna mælinga á glýkemíustuðli algengra matvæla. Upplýsingar um aukningu insúlínstyrks í blóði um leið og glýkemíustuðull matvæla er mældur geta í sumum tilfellum verið mikilvægar.

Glýkemíustuðul og glýkemíuhleðslu ætti einungis að nota fyrir matvæli sem innihalda að minnsta kosti 15-20 grömm af meltanlegum kolvetnum í einum skammti. Ennfremur ætti samanburður á glýkemíustuðulsgildum einungis að eiga sér stað milli matvara í sama matvælahópi svo sem mismunandi brauðgerða, tegunda morgunkorns o.s.frv. Sé þessum grundvallarreglum fylgt, væri hægt að nota glýkemíustuðul og glýkemíuhleðslu til að þróa matvæli og bjóða valmöguleika án þess að breyta næringargildi fæðunnar, og koma auk þess í veg fyrir misnotkun og misskilning á hugtökunum glýkemíustuðull og glýkemíuhleðsla.

Faraldfræðilegar rannsóknir benda til að mataræði með lágum glýkemíustuðli dragi úr líkum á langvinnum sjúkdómum, svo sem sykursýki af tegund 2 og hjartasjúkdómum, og því að áhættuþættir þessara sjúkdóma komi fram, auk þess að draga úr hættu á krabbameini, sérstaklega meðal þeirra sem eru of þungir eða feitir. Tengslin milli glýkemíuhleðslu og sykursýki af tegund 2 eru sterkari þegar mataræðið er einnig snautt af trefjum. Niðurstöður finnskrar rannsóknar á forvörnum gegn sykursýki sýndu að lágur glýkemíustuðull, fæðutrefjar, heilkornaa-

furðir og heilsusamleg samsetning fitusýra hefur allt þýðingu við að koma í veg fyrir sykursýki af tegund 2, en tengsl minni sjúkdómstíðni eru þó sterkust við kjörþyngd og líkamlega hreyfingu. Rannsaka þarf samverkan milli allra þessara þátta. Aðrar íhlutandi rannsóknir hafa bent til þess að mataræði með lágan glýkemíustuðul gæti bætt blóðsykurþol og jafnvel lækkað blóðfitur. Sem dæmi má nefna að með því eingöngu að skipta algengri tegund af brauði með háan glýkemíustuðul út fyrir brauð með lægri stuðul í þrjár vikur varð insúlínnæmi ungra kvenna sem voru í hættu á að fá sykursýki af tegund 2 mun betra. Þegar fólki með sykursýki eru gefnar ráðleggingar um mataræði er oft mælt með afurðum með lágan glýkemíustuðul. Mikilvægi glýkemíustuðuls í að viðhalda kjörþyngd eða til að léttast krefst frekari rannsókna.

Fyrir einstaklinga með sykursýki eða skert sykurþol getur mataræði með lágum glýkemíustuðli verið mikilvægt og eins fyrir þá sem eru í hættu á að fá sykursýki vegna ofþyngdar, sem er stór og stækkandi hópur. Frekari rannsókna er þörf til að gefa öruggari niðurstöður varðandi mikilvægi lágs glýkemíustuðuls matvæla fyrir heilbrigt fólk. Þar sem mataræði sem gefur lágan glýkemíustuðul er oft samstíga mataræði sem er heilsusamlegt að öðru leyti, og ríkt af trefjum og næringarefnum, er oft erfitt að meta raunverulega ástæðu þess að jákvæð tengsl sjást milli mataræðis með lágan glýkemíustuðul og minni hættu á langvinnum sjúkdómum, eða jákvæðum áhrifum á heilsu og minnkun áhættuþátta þessara sjúkdóma. Þetta verður að leysa í rannsóknum framtíðarinnar. Það er því mikil þörf á vel stýrðum klínískum íhlutandi rannsóknum þar sem þátttakendur eru valdir af handahófi, og á vel hönnuðum framsýnum faraldsfræðilegum rannsóknum, til að prófa hlutverk matar og mataræðis með lágum glýkemíustuðli fyrir heilsuna og til að koma í veg fyrir sjúkdóma og ofþyngd.

Til þess að hægt sé að framkvæma rannsóknir á mikilvægi blóðsykurstuðulsins á raunsæjan hátt er þörf á matvælum sem hafa lágan glýkemíustuðul. Mikið af hefðbundnum matvælum á Norðurlöndum hafa að öllum líkindum háan glýkemíustuðul, svo sem algengar brauðtegundir og kornvörur, sem gætu þannig verið lítt ákjósanlegar vörur fyrir stóran hóp fólks. Það myndi þess vegna efla verulega rannsóknir á mikilvægi matvæla með lágan glýkemíustuðul fyrir heilsu Norðurlandabúa ef hægt væri að búa til Norrænan gagnabanka um glýkemíustuðul kolvetnaríkra matvæla. Í dag takmarkast rannsóknir á glýkemíustuðli að hluta til af skorti á matvælum sem hafa lágan glýkemíustuðul, en bent hefur verið á fjölda atriða sem varða innihald og vinnslueiginleika matvæla sem nýta má til að lækka glýkemíustuðul venjulegra matvæla.

Það er mikilvægt að hafa í huga að glýkemískur stuðull er einungis einn mælikvarði af mörgum sem saman geta leitt til heilsusamlegs mataræðis.

3 Introduction

The concept of glycemic index lists food items by virtue of their influence on postprandial blood glucose and was introduced to facilitate blood glucose control in people with diabetes and prevent long term complications (Jenkins et al., 1981).

Earlier it had been assumed, based on chemical properties, that polysaccharides or "complex carbohydrates" i.e. starch, were "slow carbohydrates" whereas sugars (mono- and disaccharides) were considered "rapid". However, many food factors other than the molecular size of the carbohydrate component are important determinants of the glycemic response to composite foods (Bjorck et al., 2000). Many foods containing simple sugar do not raise blood sugar levels to a higher degree than many common starchy foods and here are differences in glycemic responses within food groups containing one and the same carbohydrate source. The results of the study by Jenkins and coworkers and other similar studies (Jenkins et al., 1981; Schauberger et al., 1977) thus demonstrated large differences in the extent to which different carbohydrate foods raise the blood glucose, even in healthy individuals (Jenkins et al., 1981) permitting new insight into the relation between the physiologic effects of carbohydrate rich foods and health (Foster-Powell et al., 2002). Methodologically the concept has developed over the last thirty years and factors affecting the GI of foods have been identified. Furthermore, the concept of Glycemic Load has been identified as the GI of food multiplied by the amount of carbohydrates per portion.

An increasing body of evidence from intervention studies and observational studies have increased expert awareness of the possible importance of blood sugar regulation and consequently the GI of foods in the etiology and treatment of chronic diseases such as type 2 diabetes and coronary heart disease as well as obesity. Thus, the GI of foods has possible practical ramifications for nutrition recommendations both in health and disease.

The importance of low GI diet in the prevention of diseases or obesity and in treatment has been discussed widely in the scientific literature and some concerns over the clinical relevance and use of GI have been raised over the years as different health organizations or official recommendations are not in conformity in if and how to use the concept of GI in prevention and treatment of diseases (Nordic Nutrition Recommendations, 2004; American Diabetes Association, 2000; FAO/WHO, 1998; Mann et al., 2002; FAO/WHO, 2003; Sheard et al., 2004; Wolever et al., 2003a). Furthermore, many popular books on the subject have been written for the public both by experts and laymen as well as numerous magazine

articles resulting in great public attention and weight reduction schemes have been tailored accordingly.

Nordic experts have to date not used the GI concept as such in prevention or to a large extent in treatment of disease, except adjusted in treatment of diabetes (Arvidsson-Lenner et al., 2004; Bjorck et al., 2000; Kolset, 2003). Evaluation of the evidence is important, not least as the Nordic dietary habits include a large number of carbohydrate rich food items, many of which are likely to fall into the category of high GI. There is no logic in being "for" or "against" the concept of glycemic index. It can give very important information regarding glucose and insulin metabolism although it will never give the whole picture of the metabolism of food in the body. This report will try to shed a light to the strengths and weaknesses of the glycemic index.

4 Methodology

4.1 Glucose and insulin – a feedback system

Following a meal, blood glucose concentration rises, stimulating insulin secretion. The insulin induces rapid entry of glucose into cells and cessation of glucose output by the liver, resulting in reduced concentration of glucose in the blood. This removes the stimulus for insulin secretion that then returns to its previous level, i.e., acting as a negative feedback control.

There are many other substances that can cause the release of insulin (coming from the Beta cells of the islets of Langerhans in the pancreas) other than plasma glucose concentration, such as increased plasma concentration of free fatty acids as well as of certain amino acids. Hormones secreted by the gastrointestinal tract in response to eating also stimulate the release of insulin. This means that insulin secretion will rise earlier (an anticipatory component) and to a greater extent than if plasma glucose was the only controller during ingestion of a meal. Another type of anticipatory regulation is how the parasympathetic neurons to the islets of Langerhans increase insulin secretion during ingestion of a meal. Exercise and stress, on the other hand, activate the sympathetic neurons and increase plasma epinephrine concentration, both of which inhibit insulin secretion.

Insulin unquestionably plays the primary role in controlling the metabolic adjustments required for feasting or fasting. Other hormonal and neural factors, glucose counter-regulatory controls, oppose the action of insulin in one way or another. The most important factor is glucagon, a peptide hormone produced by the Alpha cells of the pancreatic islets. The stimulus for glucagon secretion is a decreased plasma glucose concentration, and, conversely, an increase in plasma glucose concentration inhibits the secretion of glucagons, thereby helping to return plasma glucose level to normal (Murrey et al., 1993).

4.2 Glycemic Index definition

The concept of glycemic index (GI) lists food by its effect on postprandial blood sugar. Generally, the carbohydrate component in low GI food is, for many possible reasons, slowly absorbed from the gastrointestinal tract and therefore blood levels of glucose and, subsequently, insulin is lower postprandially than with a high-GI diet.

The GI of a food is defined as the incremental blood glucose area (0-2 h) following ingestion of 50g of available carbohydrates (no fibers or resistant starch included), expressed as a percentage of the corresponding area following an equivalent amount of carbohydrate from a standard reference product (FAO/WHO, 1998; Wolever et al., 2003b). GI values for different food products range from less than 20% to approximately 120% when using glucose as a reference (Bjorck et al., 2000).

4.2.1 What affects the GI of food?

The glycemic response to food, which in turn affects the insulin response, depends on the rate of gastric emptying, as well as on the rate of digestion and absorption of carbohydrates from the small intestine (Jenkins et al.,1987a) and in addition on the effects of other food factors to potentate non-glucose mediated insulin secretion (Ostman et al., 2001). A range of food factors have been identified as important determinants of the glycemic response to carbohydrate foods (Bjorck & Elmstahl, 2003; Bjorck et al., 2000; Jenkins & Jenkins, 1985; Jenkins et al., 1987a; Jenkins et al., 1981; Thorsdottir et al., 1998; Wolever et al., 1991a). Therefore, different food products or composition of meals with the same amount and even type of carbohydrates show differences in glycemic and insulinemic responses. A number of food factors have been identified which affect the GI of foods (Table 1). Studies in this field combine expertise in both nutrition and food science.

	Proposed mechanism	**Effect on GI**
Nutrients		
Dietary fiber (gel-forming type, viscous)	Slower gastric emptying	Lowers
Dietary fiber (naturally occurring levels in whole grain cereals)	Slower digestion	Very small lowering effect
Starch: Granular structure (intact or gelatinized)	Slower digestion	Increased when gelatinized compared to intact
Starch: Amylose (unbranched)	Slower breakdown in intestine if retrograded	Lowers GI compared to amylopectin
Starch: Amylopectin (branched)	Faster breakdown in intestine	Increases GI compared to amylose
Added sucrose (fructose-glucose)	Metabolic transformation of fructose to glucose in liver takes time	Marginal influence if used in small amount as taste or baking enhancer
Fructose or galactose	Metabolic transformation to glucose in liver takes time	Very small effect
Fat	Delays gastric emptying	Lowers
Protein	Some proteins increase insulin secretion	Lowers
Water and carbohydrate in liquid form	More rapid gastric emptying	Increases
Structure-related factors		
Maintenance of and/or inducing high starch crystallinity		Lower
Gross structure		Higher GI when homogenized
Cellular structure (Cell wall integrity)		Higher GI with increased ripe-

		ness
Formation of macromolecular interactions		Promotes lower GI
Larger particle size distribution		Promotes lower GI
Method of food preparation		Low degree of gelatinization gives lower GI
Extended chewing		Increases
Organic acids	Slower gastric emptying or slower digestion	Lowers
Amylase inhibitor	Delays function of amylase in the intestine	Lowers

Table 1. What affects the GI of carbohydrate rich food

4.2.1.1 Nutrients

Dietary fiber

In the original GI paper by Jenkins and co-workers, no correlation was seen between GI and dietary fiber. However, many of the high-fiber foods investigated were wheat products (Jenkins et al., 1981), and highly processed wheat fiber has little effect on blood glucose. Indeed, there was little difference between high-fiber whole meal bread, spaghetti and brown rice and their low-fiber white counterparts. An earlier study also investigating the effect of different foods on blood sugar level gave similar results (Schauberger G, 1977). However, Wolever and coworkers found an inverse relation between total dietary fiber and GI when including a wide range of carbohydrate rich food items (Wolever, 1990).

High dietary fiber content is thus not a prerequisite for low-GI properties, and the naturally occurring levels of viscous fiber in common cereals ofte have only a small impact on glycemia (Bjorck et al., 2000). Whole meal cereal products can thus produce GIs as high as those of white bread, while dietary fiber as part of an intact botanical structure, as in barley kernels and pumpernickel bread, may be effective in reducing glycemia (Liljeberg & Bjorck, 1994).

Legumes (compared to cereals) raise the blood sugar level slowly (Jenkins et al., 1981; Karlstrom et al., 1988; Torsdottir et al., 1989a). The effect is not through gastric emptying rate but is likely to be slow digestion of bean starch in the small intestine (Torsdottir et al., 1989a). Legumes are rich sources of viscous dietary fiber which may in addition have a small lowering effect on GI (Bjorck & Elmstahl, 2003).

It has been known for a very long time that different kinds of dietary fiber tend to have different metabolic effects (Karlstrom et al., 1988). Purified guar and pectin (viscous fibers) added to carbohydrate meals seem effective in lowering postprandial glucose and insulin levels up to a certain level (Jenkins & Jenkins, 1985; Torsdottir et al., 1989b), due to a slower gastric emptying rate and slower movement towards the site of absorption. Furthermore, high levels of beta-glucan fiber has been found to lower GI of food (Jenkins et al., 2002).

Starch

Granular structure is important as higher GI is seen when starch is gelatinized. Amylose (unbranched) gives a lower GI compared to amylopectin, while amylopectin (branched) (Bjorck et al., 2000). When studying the GI of bread from barley flours varying in amylose content, researchers found the GI became lower as the percentage of amylose in the bread increased, particularly when using specific conditions for heat-treatment (pumpernickel baking) which promoted amylose retrogradation (Akerberg et al., 1998).

Resistant starch

Resistant starch (RS) is malabsorbed starch or starch dextrins that for various reasons escapes digestion and is delivered to the colon. The origin of RS may be due to presence of native starch granules, botanical encapsulation or retrogradation, in particular of amylose, and can for some food items reach substantial levels. Examples of foods rich in RS are pumpernickel-type bread and leguminous products (Akerberg et al., 1998).

RS is an accompanying feature of low-GI foods. When plotting the RS of 10 food items and their GI, a very high correlation is seen (Bjorck et al., 2000). For most starch food products, a reduction in GI appears to be accompanied by a higher content of RS (Akerberg et al., 1998). RS can thus be expected to contribute to the colonic generation of short chain fatty acids, particularly butyric acid, with potential beneficial effects on glucose and lipid metabolism (Scheppach et al., 1988; Thorburn et al., 1993; Wolever, 1991), which may suggest a specific role of RS in the maintenance of a healthy colonic epithelium (Bjorck et al., 2000).

When measuring the GI of foods, 50g of "available carbohydrates" are to be used and therefore should not include RS. In practice this can be difficult to ensure as RS is difficult to measure (Foster-Powell et al., 2002). However, different methods for RS determination have been developed and evaluated (Champ, 2004; Englyst et al., 2003). An in vitro method to predict RS content (all major forms) in foods has been developed by Nordic researchers (Akerberg et al., 1998). The method also allows parallel determination of the available starch fraction and of dietary fiber (Akerberg et al., 1998).

In future GI measurements and studies on GI, the amount of RS should preferably be analysed. This is particularly important in the case of tailored low GI products which frequently may contain substantial amounts.

Sugars

Sugar content was not related to blood glucose response even though absorption may have been more rapid (Jenkins et al., 1981). This has

been confirmed in later studies and is presumably due to the very small rise produced by fructose (Brand Miller et al., 1997). Fructose and galactose require metabolic transformation in the liver, a slow process conferring relatively low-GI on these sugars (Wolever & Jenkins, 1986).

Fat and protein

Fat and protein showed negative association with GI (Jenkins et al., 1981). Fat and protein may delay gastric emptying and affect insulin secretion, but their effect on GI is generally not seen unless relatively large amounts (about 30g of protein and 50g of fat per 50g carbohydrates) are added to a meal (Wolever & Bolognesi, 1996; Wolever et al., 1994). It is important to note that although the addition of fat and protein to a meal containing carbohydrates may result in a lower glucose response, the relative difference between starch-rich foods with different GI values remains (Bornet et al., 1987). However, recent studies indicate that certain milk proteins have insulinotropic properties and may substantially increase post prandial levels of insulin (Nilsson et al., 2004; Ostman et al., 2001).

Water

Water (300g added to a meal) has been found to increase GI, most likely due to an increased rate of gastric emptying of carbohydrates (Torsdottir & Andersson, 1989). The difference observed in healthy subjects can be reflected as the difference between fiber-depleted and fiber-containing meals.

4.2.1.2 Structure-related factors

Processing of foods can optimize nutritional properties or diminish them severely, and it can either decrease or increase the GI of different foods. The maintenance of high-starch crystallinity is an important factor in low-GI food.

GI is higher in preheated and flaked cereals, compared with less processed cereals. The GI increases as the degree of gelatinization increases in a product. Cellular structure or cell wall integrity is important as GI increases with increased ripeness, and the same is true for gross structure as higher GI is seen with homogenization. Formation of macromolecular interactions, and larger particle size distribution promotes lower GI (Bjorck et al., 2000).

Pasta is an example of a product that has a low GI because of the physical entrapment of ungelatinized starch granules in a sponge-like network of protein (glutein) molecules in the pasta dough. Pasta is unique in this regard. As a result, pastas of any shape and size have a fairly low GI (30-60). For further explanation: If we put pasta (low GI) or bread (high GI) in a glass of water, the bread dissolves much faster with easier access for enzymes and thus faster breakdown of the starch. This was elegantly

showed in a study on ten type 2 diabetic patients receiving pasta or bread baked from the same durum wheat, where lower postprandial glucose and insulin levels were found after a pasta meal than after a comparable bread meal (Jarvi et al., 1995).

In the same study there was a significantly lower area under the curve for blood glucose and plasma insulin after parboiled rice, red kidney beans and bread made from whole wheat grains, compared with a meal of sticky rice, ground red kidney beans and bread made from ground wheat. The results clearly showed the importance of preserved structure in common foods (Jarvi et al., 1995).

Method of food preparation

The type and extent of cooking may also influence the GI. When using particular heating cycles the retrogradation of starch may be promoted, e.g., pumpernickelbaking at extended time periods (20h, 120°) (Akerberg et al., 1998). Pasta cooked al dente showed lower GI than following prolonged cooking; possibly due to incomplete gelatinization and/or maintained physical structure (Ludwig, 2003a) and simple preparation, such as mashing of potato increase the GI by 25% (Pi-Sunyer, 2002).

4.2.1.3 Organic acids

The addition of organic acids (formed during fermentation or present in pickled products) has a blunting effect on postprandial glycemia and insulinemia to cereal-based meals. Studies have been done on the metabolic impact of lactic acid, acetic acid or the sodium salt of propionic acid when added to bread meals. Inclusion of the respective acids/salts gives a significantly lower area under the glucose curve (AUC) as well as a lower insulin area in healthy subjects (Ostman et al., 2005; Ostman et al., 2002a; Ostman et al., 2002b; Liljeberg & Bjorck, 1998). The mechanism for the propionic and acetic acids is a slower gastric emptying rate (Darwiche et al., 2001) and the lactic acid creates some sort of barrier for the starch degrading enzymes (Ostman et al., 2002b).

4.2.1.4 Enzyme inhibitors

Enzyme inhibitors (found for example in wheat kernels and some herbs) such as amylase inhibitor, lowers postprandial glycemia as it affects the breakdown of starch by amylase in the intestine (Heacock et al., 2005).

4.2.1.5 Other

The glycemic response to the same food or meal may be influenced by the time consumed and GI of a previous meal (second-meal effect, see 4.6).

As seen above, several food factors, processing and cooking conditions affect GI. Differences in GI due to the above-mentioned factors are some-

times perceived as a particular shortcoming when using GI data of foods from international tables, which should preferably include more detailed information regarding raw material and processing conditions used. However, the knowledge regarding operative food factors also composes tools for optimization of the GI of food (see chapter 9.1).

4.2.2 A standardized method for measurements of GI

To be able to evaluate the GI of a food or meal correctly there are some important methodological considerations (Table 2).

Tested in the morning
Standardization of physical activity and previous meal
At least 10 fasting test subjects (healthy)
50g of available carbohydrates
Reference product: glucose (or white bread)
Capillary blood
Two-hour incremental area

Table 2. Examples of methodological considerations in measurements of the GI

Over the years, different research groups have used somewhat different blood sampling techniques (venous or capillary), different subjects (healthy or subjects with diabetes) and reference product (glucose vs. white bread). The use of bread as a reference product, for example, has been criticized due to differences in type of wheat, products and baking procedures between countries. Research groups have also used different time frame for calculating the glucose response area (1.5-3 hours) (Foster-Powell et al., 2002; Arvidsson-Lenner et al., 2004; Colombani, 2004).

Furthermore, determining the available carbohydrates in food has differed between laboratories. Convenient and standardized methods are now available for RS analysis making it possible to attain an available starch content, analytical problems still remain for "partially available" carbohydrates such as e.g. certain sugar alcohols which are incompletely absorbed, at least at high doses (Foster-Powell et al., 2002). This does probably not cause problems in the case of most common foods but need to be considered in the case of foods to which e.g. sugar alcohols have been added.

Methodological differences have thus impaired the comparison of GI data from different groups (Chlup et al., 2004) in the past. However, a recent inter-laboratory study, using a method in line with the procedures recommended by FAO/WHO (FAO/WHO 1998), measured the GI of five identically, centrally distributed foods, in 7 experienced GI laboratories around the world, using a local white bread as a standard. The mean GI values for the different foods did not differ considerably between laboratories, although individual determinations for the same food varied by 17-34 GI units (Wolever et al., 2003b). A random within-subject variation seemed to be the major reason for variation in the GI determination,

but using local white bread as a standard can be criticized. This paper was an important step in the evaluation of GI measurements of different laboratories.

Furthermore, an ILSI Europe invited working group has recently published recommendations for a standardized method for GI measurements (Brouns et al., 2005). The accuracy and reproducibility of the proposed methodology will be verified in inter-laboratory tests to become an internationally standardized GI methodology.

4.2.3 Predicted GI of foods

The GI of food can be predicted from in vitro assays (pGI) (Granfeldt et al., 1992; Sayago-Ayerdi et al., 2005), for example, by using a chewing/dialysis digestion protocol, which is cheaper and less time consuming than using subjects in the determination of GI of food (Foster-Powell et al., 2002). In vitro assays have been used to identify the GI of different starchy foods in various studies (Jarvi et al., 1999). For example, the GI of lactic acid containing sourdough bread can be predicted from the rate of in vitro starch hydrolysis (Bjorck & Elmstahl, 2003). However, only a limited number of food items have been subjected to both in vitro and in vivo testing. It is not recommended that current in vitro techniques be used in clinical research applications or for food labeling purposes (Foster-Powell et al., 2002), and they remain mainly a tool for optimization and quality assurance purposes.

4.3 GI tables

In 1981 the GI concept was introduced by Jenkins with a list of GI values of 62 food items (Jenkins et al., 1981). In 1995 the first International GI review of available GI values was published with 565 entries, and in 2002 an update with the latest International GI values was published, now with 1300 entries from both published and unpublished, verified sources (Foster-Powell et al., 2002). This table also lists the GL, as portion sizes are evaluated for each food item (see 4.4).

Low or medium GI food is thus for example whole kernel bread and cereal, pasta, legumes, and most fruit and sometimes cakes while **high GI food is** for example common types of bread and crackers, common ready-to-eat cereals and processed white rice, potatoes and candy.

The GI data in the international table has been compiled over time from different laboratories, (although GI value of some items such as jasmine rice is based on one study only). They are derived from products of different origins and brands, different types of test subjects (healthy or diabetic), and somewhat different procedures for measuring and calcula-

ting GI have been used with different reference foods, local bread or glucose (Arvidsson-Lenner et al., 2004; Foster-Powell et al., 2002).

For many food items, however, the GI database confirms the reproducibility of GI results around the world, and retests only give ±5% variation. However, for some food items there is a considerable variation of reported GI values (Foster-Powell et al., 2002). Two examples are long grain/parboiled rice (GI=38-72) and boiled potatoes (GI=24-101). One explanation is less accuracy or experience of some GI testing groups, not using or only partially adhering to a WHO protocol for GI measurement. Another explanation is large difference in the GI of similar products. The variability of potatoes, rice and oats can be real as different types of these contain, for example, different types of starch, which affects the degree of starch gelatinization. Methods of cooking are also different around the world, a factor affecting the GI of food. In future GI tables the processing conditions should preferably accompany the GI values.

A GI value obtained from an international GI table should not be seen as an exact value but may be useful as an indication of the expected glycemic response (Arvidsson-Lenner et al., 2004). However, the tables clearly show the variation in GI and are instrumental for improving the quality of research examining the relation between GI and health.

Ideally the GI values of international food tables should be determined using an internationally standardized GI methodology (Brouns et al., 2005). For the Nordic countries it is important to evaluate the GI of local foods as most of the food items in the international tables represent foods from Australia, Canada and UK (Foster-Powell et al., 2002). Furthermore, only using the concept for foods with a certain minimum of available carbohydrates per portion and only compare similar food groups might be necessary to prevent misuse and misunderstanding.

Box 1

Glycemic index range (glucose as reference food)
Low GI = 55 or less
Medium GI = 56-69
High GI = 70 or more

4.3.1 The GI concept is only valid for food with substantial amounts of carbohydrates

Misuse of the GI tables frequently occurs in communication to the public, which may have undesirable consequences. For example, carrots are sometimes blacklisted due to their high GI value, whereas salted peanuts are found to be excellent food – according to GI. A carrot has a GI value of 101. However, to get 50g of carbohydrates from a carrot one needs to eat 575g, i.e., 9 normal-sized carrots. Peanuts have a GI of 21, which is low. To get 50 carbohydrates from a peanut you need to eat 500g (i.e., 8

dl of salted peanuts). This amount gives 2925 kcal, of which 245g are fat. This is more than the daily energy intake of most people (Jarvi et al., 1998). These examples describe how unrealistic it can be to evaluate food as healthy or not only by its GI value.

Given the definition of GI, the concept is only useful for foods providing substantial amounts of available carbohydrates in a normal to large portion. GI values for low carbohydrate foods, such as vegetables or foods mainly containing fat and protein, are difficult to determine and may be misleading when used in practice, as suggested above.

It has therefore been suggested that the GI concept should be applied only to foods providing at least 15g, and preferably 20 g, of glycemic carbohydrates per portion, i.e., products, such as bread, cereal, pasta, rice and potatoes (Arvidsson-Lenner et al., 2004). Furthermore, comparison of GI values should generally be done within the same food groups. This prevents misunderstanding such as blacklisting carrots for example. In the literature this has also been tackled by using the concept of GL.

4.4 What is Glycemic Load?

The dose response curves for glucose, bread and lentils, in the early paper by Jenkins and coworkers, demonstrated that when more than 50g of carbohydrate from any source was eaten, the increase in GI was smaller than expected. However, the relative differences between the three carbohydrate sources was, if anything, accentuated, indicating that simple increases in meal size would not invalidate tables based on 50g carbohydrate portions (Jenkins et al., 1981).

However, in practice the actual carbohydrate load from a normal portion varies considerably between food products, and actual blood glucose levels, are determined by the GI of the carbohydrate (quality) and quantity of the carbohydrate. Therefore, the concept of glycemic load (GL) was introduced (Salmeron et al., 1997a; Salmeron et al., 1997b), aiming at giving a comparable basis of comparison that include both the quality and quantity of the carbohydrates in a food or meal.

GL is the arithmetic product of GI and the total available carbohydrates (g) (Box 2) and has been physiologically validated for glucose response as well as insulin response in lean adults and overweight subjects. However, more studies with differing subject populations are now needed to establish the general validation of the concept (Atkinson et al., 2004). Further investigation of the biological validity of the GL concept is needed.

GL allows comparisons of the likely glycemic effect of realistic portions of different foods, calculated as the amount of carbohydrate in one serving times the GI of the food. For example, spaghetti has a lower GI than boiled potatoes, but the normal portion of spaghetti is commonly

larger than normal portions of potatoes. (Arvidsson-Lenner et al., 2004). Therefore, GL may or may not differ between these two carbohydrate sources, depending on the applicable GI values and portion sizes.

The carrots mentioned above illustrate rather well the leveling effect of GL. A carrot has a high GI, but because it contains relatively little carbohydrate, it ends up with a modest GL (Salmeron et al., 1997a). It should therefore be emphasized that the GI concept is applicable for high carbohydrate foods only.

Box 2

GL of a food item=(GI*carbohydrates (g) in one serving)/100

Box 3

The GL of all food consumed in a meal or in one day can be summed up. GL of a diet=(average GI*carbohydrates consumed during the day)/100 Average GI is calculated as shown in Box 4.

4.4.1 Difference between GI and GL

GL might overestimate the glycemic impact of certain low-GI foods, which are slowly absorbed, when eaten in large portions (Bjorck presentation 2004). The use of GL has also raised concerns that this would lead to decreased consumption of carbohydrates, as that would be a way to decrease the overall GL of the diet. A small amount of rapidly digested carbohydrates (high GI food) does not produce similar metabolic effects as a large carbohydrate amount from slowly absorbed food (low GI food), even though the GL would be the same. Substantial documentation is present from interventions and observational studies regarding the beneficial effect of a low GI diet with respect to reduced risk factors and reduced risk of disorders related to insulin resistance, the documentation concerning benefits of a low carbohydrate diet is scarce.

4.5 Mixed meals

One concern over the years regarding the clinical relevance and use of GI has been its applicability to mixed meals, based on the weighted GI of the individual ingredients (Coulston et al., 1984). It has even been concluded that differences in GI between foods are diminished when incorporated in composite meals (Coulston et al., 1984; Hollenbeck & Coulston, 1991) and even simple water ingested by healthy subjects and type 2 diabetic patients with a meal increases the glycemic effect (Torsdottir & Andersson, 1989). Although the addition of fat and protein to a meal containing

carbohydrates may result in a lower glucose response, the relative difference between starch-rich foods with different GI values remains if fat and protein content is kept steady (Bornet et al., 1987). In 1998 a FAO/WHO report included an equation for calculating GI of mixed meals, see Box 4 (FAO/WHO, 1998).

The applicability of the GI in the context of mixed meals and diets was debated in a recent Danish study on 28 healthy young men investigating the predictability of measured GI in 13 composite breakfast meals, calculated from table values, and all of them differed considerably in energy and macronutrient composition. No relationship between the GI of a mixed meal and the GI calculated by international table values (Foster-Powell et al., 2002) and the WHO equation was found (Flint et al., 2004). Furthermore, the prediction models used in the study showed that the GI of mixed meals was more strongly correlated either with fat and protein content or energy content than with carbohydrate content alone (Flint et al., 2004).

These studies clearly demonstrate the difficulties of applying international table values to predict the GI of a specific mixed meal in daily life, and the tables need to be extended with GI values of local foods. However, the same is true for the validity of e.g. nutrient content of a mixed meal based on figures from food composition tables. In addition to the considerable range of values for the same food, which makes it difficult to choose the relevant value from international tables, different countries might have different names for the same foods or the same name for foods with different compositions.

In contrast, studies using measured GI values of the key foods responsible for differences in GI have shown that the GI of a composite meal can be predicted from the GI values of the different carbohydrate-rich foods included (Collier et al., 1986; Jarvi et al., 1999; Jarvi et al., 1995; Wolever et al., 1986). Thus, properly determined GI values for individual foods have been used successfully to predict the glycemic response of a meal, while table values have not.

Box 4

GI of a mixed meal
Average GI= $\sum$ (glycemic index*carbohydrate content*servings per day)/ total carbohydrates

An example of GI calculations for a mixed meal (Jarvi et al., 1998).

	Portion	Carbohydrates in the portion	Proportion of carbohydrates in the meal (a)	GI [1](b)	GI of the meal (a*b)
Yoghurt	250g	11.8g	0.23	51	11.7
Cornflakes	25g	19.7g	0.39	119	46.4
White bread	40g	19.4g	0.38	100	38.0
Total		51	1		96

[1]bread as reference food

The consumption of a mixed meal containing protein and fat combined with carbohydrate may lower the total glycemic and insulinemic response of the carbohydrate food alone (Wolever & Jenkins, 1986). Repeated consumption of high-glycemic-index mixed meals has been found to result in higher mean 24-hour blood glucose and insulin concentrations, compared with low-glycemic-index mixed meals of identical caloric content in both healthy as well as people with diabetes (Jenkins et al., 1987b; Miller, 1994).

As research evolves, different aspects of what affects the glycemic response come to light. Recent studies have for example suggested that caffeine consumption is associated with a substantial reduction in insulin-mediated glucose uptake, indicating that any study of the GI of foods needs to carefully control for caffeine ingestion and/or withdrawal (Lee et al., 2005).

4.6 Second-meal effect

Many studies have shown that if subjects (healthy or diabetic) are given test meals at breakfasts with either a high or low GI, the acute effects on glucose in blood seems to "carry over" to the subsequent standardized meal four hours later. The subjects consuming the low-GI breakfast thus frequently display an improved glucose tolerance at the subsequent lunch (Bjorck et al., 2000; Jenkins et al., 1982; Liljeberg et al., 1999; Wolever et al., 1988) (Figure 1). Some low-GI foods give a prolonged insulinemic response, providing sustained, slightly elevated insulin levels at the time of the next meal (lunch). This may improve peripheral glucose uptake, i.e., glucose tolerance, as well as the removal of circulating lipoproteins. The cause of the second-meal effect is probably that a prolonged absorption phase following breakfast will favor more efficient suppression of free fatty acids, thus improving insulin sensitivity at the time of the next meal (Wolever & Miller, 1995).

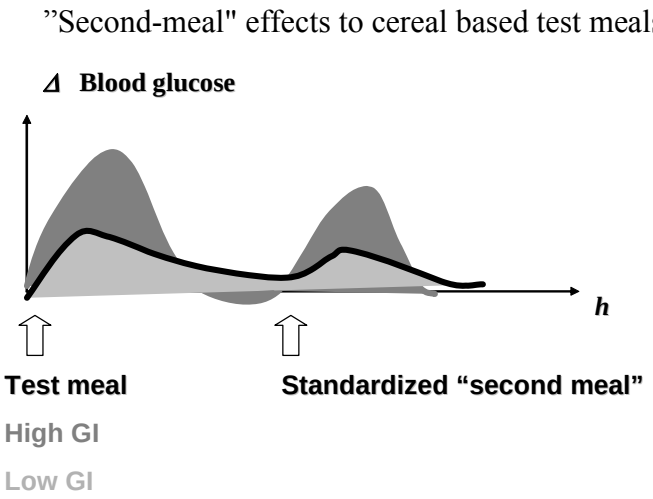

Figure 1. Higher glucose response after the same lunch meal (standardized second meal) among healthy subjects consuming a high-GI breakfast (test meal) compared to those consuming a low-GI breakfast (test meal). Similar effects are seen overnight.

When this experiment is performed overnight, starting with a high- or low-GI evening meal and the same breakfast, the same effect is seen (Axelsen et al., 1999; Axelsen et al., 1997; Nilsson et al., 2004; Wolever et al., 1988). However, there seems to be a larger discrepancy between low-GI cereal foods with respect to their capacity to improve glucose tolerance from an evening meal to breakfast. In the overnight perspective the variation is probably mediated through differences in type and/or content of indigestible carbohydrates reaching the colon for fermentation (Liljeberg et al., 1999). Colonic fermentation of dietary fiber, resulting in elevated serum levels of short-chain fatty acids may reduce serum-free fatty acids and hepatic glucose output.

Thus, low-GI cereal foods appear to vary in their potential in improving glucose tolerance at subsequent meals in healthy subjects. In addition to the slow release properties of such foods, the content of dietary fiber appears to play a role. A reduction in dietary GI improved glucose and lipid metabolism and normalized fibrinolytic activity in type 2 diabetics, while maintaining a similar amount and composition of dietary fiber. However, the higher dietary fiber content frequently associated with low-GI foods may add to the metabolic merits of a low-GI diet. Consequently a low-GI barley meal rich in dietary fiber (GI=53) improved glucose tolerance from an evening meal to breakfast, whereas an evening meal with pasta had no effect (GI=54) (Bjorck & Elmstahl, 2003).

The second-meal effect should be given serious consideration when discussing the GI concept as it may reveal mechanisms for long-term metabolic benefits of low-GI foods. However, the implications for health and clinical applications remain to be demonstrated (Arvidsson-Lenner et al., 2004).

4.7 Other measurements

It has been discussed whether the glycemic response is always the most correct measurement in studies investigating effects of carbohydrate rich food and health. The GI was put forward in a study designed to help diabetic people to control their blood sugar, which is of high importance for this group (Jenkins et al., 1981). It has however been pointed out that if the concept is to be used for others, measuring the insulin response (insulin index) might be of equal importance (Flint et al., 2004, Schenk et al., 2003).

Certainly, there is a linear correlation between postprandial blood glucose and insulin response where high GI products also have high II, at least in the case of starchy food (Bjorck et al., 2000; Ciok et al., 2004). Thus, GI and GL represent indirect measures of dietary insulin demand. Until recently this consistency was believed to be a general characteristic of carbohydrate foods.

However, some types of food are insulintropic i.e., insulin is not secreted solely as a response to a rise in blood glucose. Milk, for example, produces much higher insulin response than expected from a comparatively low-GI meal (Ostman et al., 2001). Increased insulin response has also been seen for other food items, for instance the exotic fruit papaya (Fatema et al., 2003a).

In a recent study by Ostman et al. the GI and II for milk products were measured in healthy subjects (Ostman et al., 2001). The test products were regular milk, two types of fermented milk or a carbohydrate equivalent of pure lactose. With white bread as a reference, the GIs were very low for the milk products, ranging from 12-30. This low range in GI is in accordance with data in the literature. However, the IIs of the milk products were high and similar to that of white bread. The fact that lactose induced a substantially lower II than the milk products indicates that some other milk component adds to the insulin response (Bjorck et al., 2000). These data imply that in the case of certain products and meals, GI may be different in subjects that are capable of responding with insulin, i.e. with normal glucose tolerance, compared with those who do not (type 1 diabetics) (Karlstrom et al., 1988). It should be noted that certain individuals may produce deviating glycemic responses to milk for other reasons, for example lactose intolerant subjects.

Further studies by the same study group showed that the milk proteins have the insulinotropic properties, and that the whey fraction contains the predominating insulin secretagogue. The effect might be either through bioactive peptides either present in the milk or formed during digestion or through the amino acid concentration in the blood (Nilsson et al., 2004).

A Danish study recently found increased serum-insulin and insulin resistance in eight-year-old boys after consumption of a large amount of milk (>1.5L/day) for 7 days, while this effect was not seen with an increased intake of low fat meat (Hoppe et al., 2005), indicating differences between food proteins.

This feature of dairy proteins is likely to increase insulinemia from mixed meals containing milk. Moreover, even a realistic amount of milk (200ml) added to a low GI meal (pasta) significantly increased the postprandial insulin response to the same level seen with white bread (Liljeberg et al., 2001). The potential metabolic consequences of this insulinotrophic capacity of milk need to be elucidated and the effect of protein from different sources on the glucose-insulin metabolism needs further study (Hoppe et al., 2005).

This is of importance not least because it has been pointed out that the link between a high-GI diet and diabetes may relate to elevated postprandial blood glucose peaks but also to increased insulin demand (Augustin et al., 2004a). Insulin resistance and hyperinsulinemia are often observed concomitantly, and elevated insulin concentrations can cause insulin resistance even in healthy subjects (Del Prato et al., 1994).

Furthermore, a recent study showed that GI is not necessarily correlated with II in the context of meals of varying composition, not even when removing meals including milk (Flint et al., 2004). This result indicates that on a study basis one should measure both glucose and insulin response to food as GI may not always be a good marker to predict insulin response (Wylie-Rosett et al., 2004). Due to the metabolic relevance of insulin response, testing in healthy subjects appears preferable.

Furthermore, a recent study found that in healthy subjects, the cause of lower GI of bran cereal compared with cornflakes has been found to be not due to lower rate of appearance of glucose into blood but instead to an earlier postprandial hyperinsulinemia and an earlier increase in the rate of disappearance of glucose, which attenuated the increase in the plasma glucose concentration (Schenk et al., 2003). Some researchers find peak glucose level and related rebound effects (valley glucose) gives additional information (Fatema et al., 2003b).

5 Studies on GI and Health

Over the last decades studies investigating the relationship between low-GI and health have accumulated resulting generally in either a positive or no relationship. It is hard to find studies where high-GI food or diet is beneficial to health.

5.1 Epidemiological studies

Hypotheses regarding the protective effects of low-GI and GL diets against chronic disease, such as coronary heart disease, diabetes and cancer have been tested in a number of epidemiological studies. The mechanisms behind a possible protective effect of a low-GI diet against diabetes and coronary heart disease probably include effects on risk factors, such as triglycerides (TG), total HDL and LDL cholesterol, insulin levels and insulin sensitivity, coagulation factors and protein glycation, and these are therefore also end points in epidemiological studies. Few epidemiological studies on GI and body weight are found.

5.1.1 Body weight

A recent prospective observational study suggested an association between GI and body weight. The subjects were 572 healthy adults (mean BMI 27.4 kg/m^2) whose diets were evaluated by seven-day dietary recalls, collected quarterly over one year. Body mass index was found to be positively associated with the GI of the diet, but not with daily carbohydrate intake, E% carbohydrates or GL (Ma et al., 2005). As those consuming low GI food are often consuming food rich in fiber, which is related to satiety, it is hard to relate the relationship seen entirely on the GI of the food. Further research is needed to deepen the understanding on the relation between body-weight, the quality of dietary carbohydrates and dietary fiber.

5.1.2 Type 2 diabetes

The first epidemiological study using GL as a variable was the Nurse's Health Study published in 1997 by Salmeron and coworkers. It involved 65173 women. After six-years of follow-up using quintile analysis (lowest vs. highest) RR for type 2 diabetes was higher among those consuming high GI and GL diets, after adjustment for cereal fiber and energy

intake as well as other non-dietary factors (Table 3). The RR of type 2 diabetes was lowest among the highest consumers of cereal fiber compared to those consuming the least (Salmeron et al., 1997b), all showing a clear trend over the quintiles ($p<0.05$). Furthermore, the combination of a low intake of cereal dietary fiber and high GL gave the highest relative risk of developing type 2 diabetes. A 15 unit increase in GI gave a 37% increased risk of diabetes type 2. In a recently published follow-up (16 years) of the same study, the relation between high GL and higher risk of diabetes was confirmed (Hu et al., 2001).

	RR (95%GI)			
Study population	**GI**	**GL**	**Cereal fibre**	**Publication**
65.173 women after 6-years of follow up (*Nurse's Health Study*)	1.37 (1.09-1.71)	1.47 (1.16-1.86) and high GI and low cereal fibre 2.50 (1.14-5.51)	0.72 (0.58-0.90)	Salmeron et al 1997, association confirmed in a 16-year follow up by Hu et al 2001
91.249 women (*Nurse´s Health Study II*)	1.59 (1.21-2.10)	NS	0.64 (0.42-0.86)	Schulze et al 2004
42.759 men after 6-years of follow up (*Health Professionals Follow up Study*)	1.37 (1.02-1.83)	NS but high GL and low cereal fibre 2.17 (1.04-4.54)	0.70 (0.51-0.96)	Salmeron et al 1997, b
12.251 middle aged men and women after 9-years of follow-up (*The ARIC Study*)	NS	NS	0.75 (0.6-0.92) *(HZ ratio)*	Stevens et al 2002
35.988 older women (*Iowa Women's Health Study)*	NS	NS	0.64 (0.53-0.79)	Meyer et al 2000
31.641 men and women 40-69 years *(Melbourne Collaborative Cohort Study)*	1.32 (1.05-1.66) *(OR per 10 units)*	NS	NS	Hodge et al 2004
2.834 men and women* (*Framingham Offspring Study)*	1.41 (1.04-1.91) OR	NS	0.62 (0.45-0.86) *OR*	McKeown et al 2004

* end point: metabolic syndrome

Table 3. Overview of studies investigating the association between GI or GL of the diet and cereal fibre and the relative risk of type 2 diabetes

The Health Professionals Follow-up study on 42759 men gave similar results with highest risk among those consuming the diet with the highest GI compared to those with the lowest GI, after adjustment for cereal fiber and energy intake as well as other non-dietary factors. GL was not significant but men in the lowest tertile of cereal fiber as well as highest GL had a twofold risk of diabetes type 2 compared to those consuming a diet with the lowest GL and highest in cereal fiber (Salmeron et al., 1997a). Men with the highest intake of cereal fiber were also of lower risk of type 2 diabetes compared to those in the lowest range (Table 3).

Stevens and coworkers found the hazard ratio for cereal fiber regarding risk of type 2 diabetes to be 0.75 in the ARIC Study on 12251 middle-aged men and women. In this study the association with GI or GL was

not significant after 9 years of follow-up (Stevens et al., 2002), although modeling GI and GL as continuous variables in this study may have led to an underestimation of the effect, relative to a quintile based analysis (Table 3). The Iowa Womens Health Study (n=35988) found similar results for total dietary fiber and cereal fiber (Table 3) as well as whole grain (0.78; 0.65-0.96), but no relation to GI or GL (Meyer et al., 2000; Montonen et al., 2003).

In a recent study (Schulze et al., 2004a) on 91.249 women of the Nurses' Health Study II, the RR of type 2 diabetes was highest in the highest quintile of GI compared to the lowest, non-significant for GL, but a negative association was found for cereal fiber, after adjustments for age, BMI, and other potential confounders such as diet. A recent Australian study showed similar results, although they did not find dietary fiber to be related to type 2 diabetes. They however found a positive relationship with increased intake of starch and white bread, while inverse relationship was found with total carbohydrate, sugars and magnesium. The authors concluded that reducing dietary GI while maintaining a high carbohydrate intake may reduce the risk of type 2 diabetes (Hodge et al., 2004).

In another study (n=2834) McKeown and coworkers found low GI food to be related to insulin resistance (HOMA-IR) as well as lower prevalence of the metabolic syndrome. Intake of cereal fiber and whole grain food was also related to insulin resistance and lower prevalence of the metabolic syndrome (McKeown et al., 2004) (Table 3).

Some studies have not evaluated the GI or GL but have found lower risk of diabetes among men and women consuming higher amount of whole grain (Fung et al., 2002; Liu, Manson et al., 2000; Montonen et al., 2003) and higher risk for those consuming refined grains (Liu et al., 2000a).

Based on the available epidemiological evidence, a diet with a low-GI may play a role in the prevention of type 2 diabetes, and the same is true with a diet rich in dietary fiber and whole grain foods. However, on the basis of these studies one cannot rule out that other factors in whole grains, or factors associated with whole grain consumption, may contribute to the preventive effect rather than the direct effect of GI or GL on glucose and insulin response (Arvidsson-Lenner et al., 2004).

Further evidence for a role of GI/GL in diabetes comes from a recent prospective cohort analyses conducted from 1991 to 1999 among women in the Nurses' Health Study II (n= 51.603 women) where women consuming one or more sugar-sweetened soft drinks per day (high GI) had a relative risk [RR] of type 2 diabetes of 1.83 (95% confidence interval [CI], 1.42-2.36; P<.001 for trend), compared with those consuming less than one of these beverages per month after adjustment for potential confounders. Similarly, consumption of fruit punch was associated with increased diabetes risk (RR for $\geq$ 1 drink per day, compared with <1 drink

per month, 2.00; 95% CI, 1.33-3.03; P =.001). Higher consumption of sugar-sweetened beverages was also associated with greater weight gain and thus soft drinks may increase risk for the development of type 2 diabetes in women, possibly by providing excessive calories but also large amounts of rapidly absorbable sugars (Schulze et al., 2004b).

5.1.3 Cardiovascular dieseases and related metabolic factors

The Zutphen Study investigating elderly men (n=646) over a period of ten years, found no association between GI and CHD (van Dam et al., 2000) and no significant relations were found between GI and blood lipid values (total cholesterol, HDL and triglycerides). In this study GL was not calculated.

However, in a 10-yr follow-up of the Nurses Health Study (n=75.521), where diet was evaluated through a food frequency questionnaire, a high dietary GL (highest quintile) from rapidly digested and absorbed carbohydrates was related to an increased risk of coronary heart disease, most evident in overweight women (BMI$\geq$23kg/m^2) (RR=1.98 (95%CI=1.41-2.77:p for trend<0.001) (Liu et al., 2000b) after adjustment for age, smoking and total energy intake. In this study an increased risk of developing CHD due to a high-GL diet was supported by the observation of a negative influence on the lipid risk profile.

A study of 1.077 patients with existing CVD showed, by calculating from FFQ, that dietary GI (p<0.001) and GL (p<0.001) were significantly inversely related to plasma HDL cholesterol concentrations. This is supported by other large observational studies showing an inverse correlation between GI or GL and HDL cholesterol, i.e., that low GL diet is associated with increased HDL (Ford & Liu, 2001: Frost et al., 1999). Low GL has even been found to be a stronger predictor of serum HDL cholesterol than dietary fat intake (Frost et al., 1999). Similar relation between GI and GL with HDL and also with lower fasting triglycerides was found in a study by Liu and coworkers (Liu et al., 2001).

In a recent study on 32 healthy males and females, aged 11-25y, the subjects registered their consumption for 3 days. Negative correlations between HDL cholesterol and GL were seen as well as with GI. GL accounted for 21% of the variation in HDL cholesterol in this group (Slyper et al., 2005). Furthermore, a strong positive association was found between dietary GL and plasma C-reactive protein (CRP), which is a moderate predictor of CHD (Danesh et al., 2004), in 244 apparently healthy women, independent of conventional risk factors for the disease. The association was significantly modified by BMI as the difference was larger in the group of women with BMI $\geq$ 25 (Liu et al., 2002).

In addition, a 18-year follow up on the Nurses Health Study (n=78.779) dietary GL was positively associated with risk of total stroke when extreme quintiles were compared (RR=1.61, 95%CI:1.15, 2.27;

p_{trend} =0.01) in women with BMI $\geq$ 25 kg/m^2 when adjusting for non-dietary risk factors, energy and dietary fiber. This was not found in normal weight women and GI was not related to risk of stroke. Furthermore, the findings suggested that high intake of refined carbohydrates is associated with hemorrhagic stroke risk among overweight and obese women and high consumption of cereal fiber was associated with a lower risk of total and hemorrhagic stroke (Oh et al., 2005).

5.1.4 Cancer

Several epidemiological studies have found a relationship between GI and GL or both and different types of cancer, while others do not support such an association. Augustin and co-workers analyzed data, including 769 cases of *gastric cancer* and 2081 controls, which all had answered a reproducible food frequency questionnaire. The odds ratio for subsequent quartiles of dietary GL were, 1.44 (1.11-1.87), 1.62 (1.24-2.12) and 1.94 (1.47-2.55). The association was consistent in different strata of age and education but was stronger in women than in men. In addition the associations appeared to be particularly relevant among subjects with underlying insulin resistance, e.g., the association was stronger in individuals with BMI>25 kg/m^2 (Augustin et al., 2004b).

In two prospective cohort studies the Nurses Health Study and the Health Professionals Follow-up study, which contributed 1809 *colorectal cancer* cases during up to 20 years of follow-up. Intakes of dietary carbohydrate, GL, overall GI, sucrose and fructose were not associated with colorectal cancer risk in women. However, a small increase in risk was observed in men with high GL, sucrose or fructose. Associations were slightly stronger among men with elevated BMI >=25 (Michaud et al., 2002).

A case (n=1204) control (n=1352) study on *prostate cancer* risk found direct relations with both dietary GI and GL. Correcting for potential confounding factors, among them energy, fiber and lycopenes, did not substantially modify these associations (Augustin et al., 2004a).

In a systematic analysis of data from a series of case-control studies (a total of 12000 cases in Italy), intake of whole grain foods was related to reduced risk for several types of cancer, particularly in the *upper digestive tract,* while refined grain and consequently GL and GI were associated with increased risk of different types of cancer, including *colorectal cancer and breast cancer* (La Vecchia, 2004).

Earlier, Augustine and co-workers observed a direct association between *breast cancer* and both GI and GL in a case control study evaluating 2569 cases against 2588 controls using a FFQ to evaluate the diet (Augustin et al., 2001).

In a cohort study on 90655 women, aged 26-46 years after 8-years of follow-up, the relative risk of *breast cancer* increased with carbohydrate

consumption and GL among women with BMI $\geq$ 25, while this relationship was not found in the whole cohort. The authors suggest that this might be linked to the substantially greater insulin response to dietary carbohydrate among overweight women, than women who are not overweight (Cho et al., 2003).

A prospective cohort of 49613 Canadian women, who completed a self-administered FFQ between 1980-1985, found after a 17-year follow-up that GI, GL, total carbohydrate and total sugar intake were not associated with *breast cancer* risk in the total cohort. However, the data suggested that a high-GI diet may be associated with increased risk of breast cancer among postmenopausal women, possibly more so among subgroups defined by participation in vigorous physical activity, ever use of HRT and those who are not overweight (Silvera et al., 2005).

A cohort study of 23870 Danish postmenopausal women (aged 50-65), where tumor estrogen receptor status was taken into consideration, did not find an association between GI or GL nor different carbohydrates and *breast cancer* after adjusting for confounding factors. However, a borderline significant positive association was found between GI of the diet and estrogen receptor negative breast cancer (Nielsen et al., 2005).

In a cohort study of 88802 US women, 180 cases of *pancreatic cancer* were diagnosed during 18 years of follow-up and the study findings suggested that a diet high in GL may increase the risk of pancreatic cancer in women already with some degree of insulin resistance (Michaud et al., 2002).

In epidemiological studies on cancer, it is clear that confounding factors can affect the results between GI and GL and cancer as low-GI food is often also food that is considered “anticancer food”. For example fruits and fiber-rich or kernel cereals and legumes are not only low in GI/GL but are rich in nutrients, fibers and other constituents that may be important for health. Although some studies correct for these factors, it is hard to identify them all (Augustin et al., 2004b), and other types of studies are needed to confirm whether the mechanism is through the low GI of the diet per se or other factors reflecting low GI such as resistant starch for colon cancer as it is found to be important in the maintenance of a healthy colonic epithelium (Bjorck et al., 2000; Scheppach et al., 1988; Thorburn et al., 1993; Wolever et al., 1991). More research is needed in this field.

5.1.5 Evaluation of epidemiological studies

The epidemiological studies on the GI concept and health have been criticized. A shortcoming of some of the epidemiological studies is the use of data produced by dietary assessment methods not geared to the study of GI and GL. Another shortcoming shared with epidemiological studies in general is the lack of relevant analytical data for foods, in this case the shortage of standardized GI values relevant to the foods consumed by the

population under investigation (Arvidsson-Lenner et al., 2004). However, the methology of the studies have the advantage of real life circumstances and it can be argued that an experimental situation does not describe the true effects of life. Additionally some relationship between food and health or disease, such as cancer, is hard to study without long term epidemiological studies.

It is hard to distinguish between low-GI food and healthy food, such as fruits, legumes and high fiber whole kernel cereals. Therefore epidemiological studies do not give as clear evidence of the importance of the GI concept as controlled intervention studies (Arvidsson-Lenner et al., 2004), although some epidemiological studies find GL to be an independent risk factor after adjusting for fiber content, energy and macronutrient content (Liu et al., 2000b; Salmeron et al., 1997a; Salmeron et al., 1997b).

The most positive studies originate from one research group only (Hu et al., 2001; Liu et al., 2000b; Salmeron et al., 1997a; Salmeron et al., 1997b), using a certain type of food frequency questionnaires for GI and GL calculations. To provide convincing evidence, similar results should be published from other research groups using adequate dietary assessment methods.

5.2 Intervention studies

Due to the character of intervention studies they more often focus on the relationship of GI and the risk factors for diseases for example diabetes and coronary heart disease such as TG, total HDL and LDL cholesterol, insulin levels and insulin sensitivity and even coagulation factors. For body weight and obesity the link might be through insulin levels, regulation of food intake (hunger and satiation) and basic metabolic processes (Ma et al., 2005).

5.2.1 Body weight and regulation of food intake

The possible role of the GI of foods in appetite and body weight regulation is supported by the fact that low-GI foods reduce postprandial glucose and often insulin responses. As obesity has been associated with increased insulin levels, foods that have a lower glycemic response would be encouraged (Wylie-Rosett et al., 2004). The slower glucose and insulin response after low-GI foods is also believed to result in decrease hunger or promote satiety and give decreased ad libitum energy intake, i.e., prevent overeating (Ludwig, 2002, Ludwig 2003b). This would also be due to the absence of reactive hypoglycemia and alter the expression of rate limiting enzymes (Brand-Miller et al., 2002; Pawlak et al., 2002). The lower responses have also been found to reduce carbohydrate oxida-

tion and fat storage and to increase fat oxidation, relative to high-GI foods although this is not supported in a very recent study on sedentary, obese women (Diaz et al., 2005).

Whether GI is a useful concept in the treatment of obesity has been debated in recent years (Pawlak et al., 2002; Raben, 2002).

5.2.1.1 Short term – regulation of food intake and appetite

A crossover study on 12 obese teenage boys that consumed high- or medium-GI, identical test meals at breakfast and lunch was designed to have similar macronutrient composition, fiber content and palatability, with equal energy content for each subject. Ad libitum food intake was determined in the five-hour period after lunch. After the high-GI meal voluntary energy intake was 53% greater than after the medium-GI meal (and 81% greater than after a low-GI meal, which, however, had a different macronutrient composition). The study concluded that the rapid absorption of glucose after consumption of high-GI meals induces food intake in obese subjects (Ludwig et al., 1999).

This study was included in a Danish review of 31 short-term studies (<1d) on appetite sensations; 15 studies concluded that a low-GI diet resulted in less hunger and more satiety. In two studies a high-GI diet resulted in less hunger and more satiety, while 14 studies showed no difference. In 15 studies with ad libitum intake, 7 studies found less energy intake on a low-GI diet, while 8 studies found no difference (Raben, 2002).

Later studies have both shown a positive relation or none. A randomized crossover study of 16 overweight adolescents found an increase in satiety with a low-GI, whole-food meal and low-GI meal replacement (shake and nutrition bar), compared with a moderately high-GI meal replacement (Ball et al., 2003) as well as differences in insulin response. The authors suggest that the prolonged satiety associated with low-GI foods may prove effective for reducing caloric intake and achieving long-term weight control.

Furthermore, a 3-way crossover study on 37 children, both normal and overweight, comparing a breakfast with low GI, low GI with 10% added sucrose and a high-GI breakfast showed that the low-GI foods had a significant impact on food intake at lunch. However, this might at least in part be attributable to differences in macronutrient content ((E% carbohydrates 60, 77 and 75 respectively) (E% protein 15, 15, 9, respectively) and (dietary fiber 6, 6 and 1g, respectively)) (Warren et al., 2003).

However, a Danish four-hour study with a single-meal test gave 45 overweight subjects a low-GI or a high-GI breakfast corresponding to the diet they had received during a previous 10-week intervention. Rye bread was served with cheese, jam, butter and yogurt, which gave 20% of estimated daily energy requirements (57E% carbohydrate, 29E% fat and 14E% protein). While resting for the next four hours, appetite sensations

and energy metabolism were measured and in the end, an ad libitum lunch was served. No differences in postprandial appetite, energy expenditure, substrate oxidation or energy intake, were found. The study gave no clear picture of the role of GI on energy balance and body weight (Sloth et al., 2004).

The results are therefore not uniform in this regard. It is likely that both high and low glycemic carbohydrates could influence satiety, but that their effects have different time courses (Anderson & Woodend, 2003). High-GI carbohydrates would be associated with a reduction in appetite and food intake in the short term (e.g., one hour), whereas the satiating effects of lower GI carbohydrates appear to be delayed (e.g., by 2-3 hours). The type of low- and high-GI food given might also be of importance.

The Danish review also looked at studies on total energy expenditure in response to changes in GI, with the majority of studies looking at single sugars. In 15 acute studies (3-6 h after meal intake), 11 compared fructose (or sucrose) with glucose. Nine out of 15 found increased total energy expenditure with low-GI (i.e., fructose). However, this only shows that fructose metabolism is energetically more costly (Raben, 2002). Evidence is therefore still lacking for increased energy expenditure after low-GI diets.

The Danish review concluded that the data do not support the contention that a low-GI diet is more beneficial than a high-GI diet in decreasing postprandial sensations of hunger, increasing satiety and/or lowering subsequent ad libitum energy intake, in inducing a higher energy expenditure or altering substrate oxidation (Raben, 2002).

The review by Raben has been discussed by Pawlak and coworkers (Pawlak et al., 2003) on several points, such as the choice of underpowered studies, as pointed out by the author as well, studies where important confounding factors were not controlled for, or the actual differences in glycemic responses among test foods or meals were not demonstrated. They state that it is misleading to weigh all studies equally, and to consider only whether differences in each end point reached statistical significance in the hypothesized direction. They find the conclusion too decisive and not in accordance with the review as there is a clear trend towards beneficial effects of low GI, and finally suggest that a formal meta-analysis be done.

5.2.1.2 Long-term - body weight and energy expenditure

The previously mentioned critical review by Raben (Raben, 2002) also included 20 long-term human intervention studies (defined as long-term if lasting longer than 6 days) on GI in relation to body weight, later adding four more studies to the calculation (Brynes et al., 2003; Heilbronn et al., 2002; Sloth et al., 2004; Wolever & Mehling, 2003). When summarizing the data from these 24 studies, a larger weight loss was seen on a

low-GI diet in four studies, on a high-GI in 3 studies, but no differences were observed in 17 studies.

However, of the 24 studies, only 11 used test and control diets with comparable macronutrient compositions, which is the appropriate design for specifically studying the effect of dietary GI on body weight. In 10 of these studies, there were no significant differences in body weight changes, but in one study greater loss was seen on a low-GI versus a high-GI diet. The mean weight change in these 11 studies was a reduction of 3.4 kg on the low-GI diet and 2.8 kg on the high-GI diet, a non-significant difference. Only four studies allowed ad libitum intake (2-10 weeks duration), and in these the average weight change was a reduction of 0.55 kg on the low-GI diet and 0.50 kg on the high-GI diet.

The Danish review therefore concluded that the data do not support the contention that a low-GI diet is more beneficial than a high-GI diet in the regulation of body weight or body composition (Raben, 2002). Pawlak and coworkers have pointed out that most of the studies in the paper were statistically underpowered to pick up clinically relevant differences in weight loss between the two types of diet, as pointed out by the author as well (Raben, 2002) and that many of the studies were very short or included normal-weight subjects (Pawlak et al., 2003).

They state that as GI can be related to obesity through plausible physiological mechanisms a low GI diet might have important effects on obesity. They conclude in a recent review that obese patients should be counseled to follow a low-GI diet as part of a weight control program (Pawlak et al., 2003, Pawlak et al., 2002).

More recent studies still find low GI food to either increase weight loss compared to a high GI diet or to make no difference at all. A recent randomized control trial on 14 obese adolescents, consisting of a six-month intervention and a six-month follow-up, showed that those following an ad libitum, reduced-GL diet lost more weight and fat mass, compared with those following an energy-restricted, reduced-fat diet (Ebbeling et al., 2003). The macronutrient composition was around 45-50E% carbohydrates and 30-35 E% fat in the low-GL diet, while the other diet had 55-60 E% carbohydrates and 25-30 E% fat. The selection of carbohydrate-rich food was low- to moderate-GI in the low GL group.

A randomized parallel design study on 39 overweight or obese young adults, aged 18-40, who received an energy-restricted diet for five months, of either low-GL (43E% carbohydrates, 27E% protein, 30E% fat, GI 50, 1500kcal) or low fat (65 E% carbohydrates, 17E% protein, 18E% fat, GI 82, 1500 kcal), found less decrease in resting energy expenditure by 80 kcal per day on the low-GL diet than on the low-fat diet. Participants receiving the low-GL diet reported less hunger than those receiving the low-fat diet. Insulin resistance, serum triglycerides, C-reactive protein and both systolic and diastolic blood pressure improved more on the low-

GI diet. Changes in body weight and composition in both groups were very similar (Pereira et al., 2004).

In a one-year behavioral weight loss program, education on the GI of foods failed to improve treatment outcomes (Carels et al., 2005). Two groups were formed, with each being put on a behavioral weight loss program (emphasizing a low-calorie, low-fat diet and increased physical activity), but one got additional education on GI and was found to use the information in their daily habits. The average weight loss was 7.6 kg over one year, but one year later the participants had regained 59% of their treatment weight loss, with no difference between groups (Carels et al., 2005).

Animal studies are also not in consistence regarding GI and obesity (Pawlak et al., 2001; Raben, 2002).

Despite the disagreement mentioned above over the strength of the evidence, both debating parties as well as other research groups totally agree that well-designed, longer-term studies (> 6 months) are needed on the role of GI in body weight regulation (Ebbeling et al., 2003; Pawlak et al., 2003; Raben, 2002; Warren et al., 2003). As many carbohydrate-rich foods with a low GI also have high fiber content (e.g., beans) and thereby a more pronounced satiating effect, and due to substantial crossover between slowly absorbed low-GI foods and low energy dense food, the studies should be conducted with an ad libitum design, and only the GI should be manipulated (not protein, fat, carbohydrate, dietary fiber or energy density) (Carels et al., 2005). Further research into the rate of absorption of food as well as a consistently reproducible way to measure that effect is needed, as is further research into satiety and appetite control. As these factors become better understood, the development of clearer guidelines become possible (Wylie-Rosett et al., 2004).

It has been pointed out regarding the strength of the evidence (with regard to advising the public to revise their current view of a healthy diet and replace high-GI food with low-GI food) that it might prove damaging to public credibility and the perceived reliability of the scientific community if future well-powered, randomized, long-term trials later show no difference in weight loss between high- vs. low-GI diets. Or if the classification of foods into high and low GI is later found to be too simplistic with respect to appetite and energy balance control, and some low-GI foods are discovered to be less satiating than high-GI foods (Astrup, 2002). On the other hand it is important to be alert, evaluate the evidence at any point in time and enlighten the public about the current strength of the evidence, such as for body weight control.

In this regard it is worth mentioning that a weakness of GI in relation to the obesity epidemic is that GI does not address other metabolic issues related to food consumption and satiety, such as effect of food on leptin or ghrelin. Opposite to glucose ingestion, fructose, which has a low GI,

does not suppress ghrelin but reduces leptin resulting in less satiety (Wylie-Rosett et al., 2004).

Furthermore, it is possible that some people are more genetically susceptible to a high-GI diet (i.e., to increases in glucose and insulin concentrations) as has been indicated for dietary fat (Heitman et al., 1995).

5.2.2 Diabetes

5.2.2.1 Prevention of type 2 diabetes

Exchanging common bread for tailored low-GI/high dietary fiber bread in a mixed diet improved insulin economy in women at risk of type 2 diabetes (Östman et al., 2005; Bjorck & Elmstahl, 2003) and other studies have shown similar results between high- and low-GI diets when investigating subjects with impaired glucose tolerance or hyperinsulinemia or otherwise at risk of type 2 diabetes (Ebbeling et al., 2003; Slabber et al., 1994; Wolever & Mehling, 2002). Thus, macronutrient quality may be important (as well as macronutrient quantity) in prevention of type 2 diabetes (Ludwig, 2003a).

A recent Cochrane Database Systematic Reviews investigating the current evidence from randomized controlled trials found limited and weak evidence of a small reduction in HbA1c after 12 weeks on a low-GI diet. Participants included were adults with at least one major risk factor for coronary heart disease (Kelly et al., 2004).

Overall, the findings suggest that conventional high-carbohydrate diets, with their high GI, may be suboptimal, particularly in insulin-resistant individuals. Because around one in four adults has impairments in postprandial glucose regulation (Dickinson & Brand-Miller, 2005; Jenkins & Jenkins, 1985; Jenkins et al., 1987a) and with increasing obesity a low GI diet might be beneficial to a large group of people.

Furthermore, beneficial effects of a low GI diet, has also been found in healthy subjects. A redution in fasting glucose and mean glucose was found when changing to a low GI diet for 1 week, with energy and macronutrient composition unchanged (Brynes et al., 2005). An earlier study found reductions in serum fructoseamine and urinary C-peptide levels in healthy subjects after a low GI diet compared to a high GI diet (Jenkins et al., 1987b). The prevention of hyperglycemic situations might therefore also be targeted in healthy people (Colombani, 2004). However, overall large-scale, randomized, controlled trials are needed to further evaluate the effectiveness of reduced GL and GI diets in the prevention of type 2 diabetes (Ebbeling et al., 2003).

5.2.2.2 The Finnish Diabetes Prevention study

The Finnish Diabetes Prevention Study is an individually randomized, controlled, clinical trial to test the feasibility and efficacy of lifestyle modification in high-risk subjects. 522 overweight men and women with

impaired glucose tolerance were randomly assigned (mean age 55) to either the lifestyle intervention or control group. Each subject in the intervention group received individualized counseling aimed at reducing weight and intake of total and saturated fat and increasing intake of fiber and physical activity. An oral glucose test was performed annually to detect incident cases of diabetes and to measure changes in metabolic parameters (Lindstrom et al., 2003; Tuomilehto et al., 2001).

The risk of type 2 diabetes was reduced by 58% after six years in the intervention group, compared with the control group. The reduction in the incidence of diabetes was directly associated with the number and magnitude of lifestyle changes made. Risk reduction was found for weight loss >5% (strong), total fat < 30%, saturated fat < 10%, fiber > 15g/1000kcal (relationship found with both dietary fiber and whole grain food products) and exercise > 4 hours a week (strong). Furthermore, a small association was found for GI.

The Finnish Diabetes Prevention Study found that that type 2 diabetes can be prevented by changes in lifestyle in high-risk subjects (Laaksonen et al., 2005; Lindstrom et al., 2003a; Lindstrom et al., 2003b; Tuomilehto et al., 2001). However the scientists found it difficult to classify the diet according to GI due to many methodological issues, not least due to the lack of good data on GI of Finnish food items.

5.2.2.3 Treatment of type 1 and type 2 diabetes

The overall main goal in the treatment of diabetes is to achieve as normal glycemia as possible. Type 2 diabetes is characterized by a delayed insulin response to a meal and enhanced postprandial blood glucose concentrations. Against this background the use of a diet with a low GI seems rational to reduce the mismatch between insulin secretion and the absorption rate of food in type 2 diabetic patient. Finding the correct match between food intake and insulin dosage is the primary focus for the person with type 1 diabetes and care providers. (Colombani, 2004). The benefit of a low-GI diet is perhaps most obvious in the treatment of type 1 and 2 diabetes with a large majority of studies positive.

In treatment of type 2 diabetes, the potential of a diet with a low GI has been documented by improved blood glucose control, lowered HbA1c and improved glucose tolerance, insulin sensitivity and fibrinolytic capacity (Jarvi et al., 1999; Brand et al., 1991; Miller, 1994). A study on type 2 diabetes patients showed that a moderate amount of leguminous seeds in a mixed diet resulted in lower mean postprandial glucose concentration compared with controls. The diets contained the same energy, protein, fat and amount of available carbohydrates (Karlstrom et al., 1987).

A recent meta-analysis supported the use of the GI as a scientifically based tool to enable selection of carbohydrate-containing foods to improve the overall metabolic control of diabetes as the low-GI diets signifi-

cantly improved blood glucose control in type 2 diabetes subjects. These findings are in accordance with other meta-analyses conducted on markers of carbohydrate metabolism (Opperman et al., 2004).

An observational study on type 1 diabetes (the EURODIAB study), involving more than 3000 subjects with type 1 diabetes in 31 clinics throughout Europe, showed that the GI rating of self-selected diets was independently related to blood concentrations of glycated hemoglobin in men and women (Buyken et al., 2001) and to waist circumference in men (Toeller et al., 2001). Another study found that by simply exchanging conventional high-GI breakfast for a low-GI meal, metabolic control was improved for type 1 diabetic patients (Golay et al., 1992).

Furthermore, a recent meta-analysis of randomized controlled trials on both type 1 and type 2 diabetes patients identified 14 studies compromising 356 subjects treated for 12 days to 12 months duration. The low-GI diets reduced HbA1c significantly over that produced by high GI diets. Although most of the studies were on small numbers of people it found a small but clinically useful effect on medium term glycemic control in patients with diabetes (Brand-Miller et al., 2003a).

5.2.2.4 Glycation end products

A high GI diet might also increase the risk of complications in diabetes such as nephropathy, i.e., a disease of the kidneys. Advanced glycation end products (AGE) are formed by initial non-enzymatic reactions between glucose and lysine residues in patients with hyperglycemia. AGE increase with consistent high blood glucose in glucose-intolerant persons and may be a specific risk factor for disease (Bangstad et al., 1999).

5.2.3 Cardiovascular diseases and related metabolic factors

5.2.3.1 Treatment of dyslipidemia

No direct intervention studies support that a low GI diet lower the risk for CHD. On the other hand a low-GI diet has been found to be useful in the management of dyslipidemia in a number of studies (Jarvi et al., 1999; Jenkins et al., 1987c; Sloth et al., 2004; Wolever et al., 1992). In studies where energy intake has been thightly controlled, low-GI diets have not had a large effect on dyslipidemia although there are exceptions such as a well-controlled Swedish study on type 2 diabetes subjects (Jarvi et al., 1999). It showed a significant reduction of LDL cholesterol and a reduction of PAI-1 on the low-GI diet, suggesting an improvement of the lipid profile and the fibrinolytic capacity.

When investigating the current evidence from randomized controlled trials, a recent Cochrane Database Systematic Reviews found no evidence that low-GI diets affect LDL cholesterol, HDL cholesterol or triglycerides. However, limited and weak evidence of a relationship between low GI diets and slightly lower total cholesterol, compared with higher GI

diets was found. Participants included were adults with at least one major risk factor for coronary heart disease. The review concluded that evidence from randomized, controlled trials showing that low-GI index diets is beneficial to risk factors for CHD is weak. Many of the trials identified were short-term, of poor quality and conducted on small sample sizes (Kelly et al., 2004).

However, another recent meta-analysis found a low-GI diet useful in lowering total cholesterol, and it tended to reduce LDL cholesterol in type 2 diabetic subjects, compared with high-GI diets. No changes were observed in HDL cholesterol and triglyceride concentrations (Opperman et al., 2004).

In this regard it is interesting to note that when carbohydrates are used to replace saturated fats in a low-fat diet, LDL and HDL decrease similarly, and the LDL/HDL ratio is not improved. Triglycerides increase as well when carbohydrate increases, except when low-GI foods are used (Sacks & Katan, 2002).

There still is a need for well-designed, adequately powered, randomized, controlled studies of more than 12 weeks duration to assess the effects of low GI diets on CHD risk factors (Kelly et al., 2004).

5.2.4 Evaluation of intervention studies

Regarding intervention studies, most protocols used for collecting dietary data are poorly designed to identify the GI of the diet, and most long-term intervention studies with free-living persons comparing diets with different GI values lack a careful description of the details of the diet. The volunteers in the studies may only have been encouraged to change their major source of carbohydrates to either low- or high-GI food without any further guidance (Frost et al., 1996). If so, this approach might result in only small differences between high-GI and low-GI diets, and it is almost certain that other macronutrients, e.g., dietary fiber (many low-GI foods are also high in fiber) and fat will be changed if no specific dietary advice or menus are given to the volunteers (Frost et al., 1996; Frost et al, 1998). This might influence the results, and it becomes hard to differentiate whether a positive effect is seen, for example, because of fiber content, macronutrient composition (even micronutrient composition) or the low GI of the diet (Kolset, 2003).

A well-controlled Nordic study found a difference between low and high GI even when macronutrient and fiber composition was controlled for (Jarvi et al., 1999). However, long-term intervention studies where GI differs but not micronutrients or fiber or even energy are very hard to perform in practice. Thus it can be hard to obtain maximum differences in GI and control for confounding variables in practical circumstances over a long period. However, to be able to come to terms with the GI concept this is necessary.

5.3 To summarize the evidence

Many studies have investigated the role of GI in the treatment of diabetes and impaired glucose tolerance, and to date an increasing body of evidence supports a therapeutic potential of low-GI diet. Indications of a beneficial effect in subjects with dyslipidemia are not as consistent.

Many observational studies have shown preventive potential of low GI diets against type 2 diabetes, cardiovascular disease and even certain types of cancer, such as breast cancer and colon cancer. The benefit of low GI food is less when the diet is also high in fiber. Some studies attribute the relationship to the fiber content alone, while in other studies the relationship remained after adjustment for fiber content. Although not consistent, the relationship is often stronger in those overweight or obese.

Regarding body weight control, the evidence clearly demonstrates the need for longer-term, better controlled studies to provide conclusive evidence for the benefits of low-GI foods in this regard although some US obesity centers have included a low GI diet as part of their treatment of overweight and obesity.

5.3.1 Is the GI concept important for healthy, non-overweight people?

There is still an ongoing discussion about the benefits of low GI in the prevention of lifestyle disease (Nantel, 2003). “Slow carbohydrates” have often been considered advantageous for healthy people to avoid an excessive insulin response and hypoglycemia between meals (Arvidsson-Lenner et al., 2004), and the published tables of GI values are a testimony to the effect of low-GI foods in reducing blood glucose in normal individuals (Leeds, 2002). Whatever strategy is employed to avoid recurrent hyperglycemic situations, there is evidence that controlling postprandial glycemia is an important target in maintaining health and preventing disease (Colombani, 2004). However, overall large-scale, randomized, controlled trials are needed to further evaluate the importance of reduced GL and GI diets for maintainence of health in non overweight, healthy individuals (Arvidsson-Lenner et al., 2004). Overall it must be clarified that the health effect of a low-GI diet is not solely attributed to fibre or other nutrients, which act as a proxy for low GI, but that the beneficial effect seen is really due to differences in glucose and insulin response to different diets.

How important low GI food is for healthy people when evaluated against the benefits of other dietary recommendations, such as high fiber and low saturated fat diet and adequate amounts of micronutrients remains to be seen.

In summary the low-GI diet has emerged as an interesting tool in combating diseases and conditions linked to the metabolic syndrome, but more information is needed before adding information regarding low GI

food to public recommendations on an evidence based level. As put forward at the Seminar, the concept of GI is only part of the picture; there are more factors that must be considered – the metabolic picture of body is complex.

5.3.2 Cognitive performance and athletes

Short term aspects of low GI food are also interesting. In healthy subjects, a low-GI breakfast, for example, allowed better *cognitive performance* later in the morning (2.5-3.5 hours later) than a high-GI breakfast (Benton et al., 2003) although glucose levels were similar in both groups.

Furthermore, information on low- and high-GI values of food might be important for *athletes*. Carbohydrate ingestion before, during and in recovery following exercise makes a very positive contribution to substrate availability and, in most cases, leads to enhanced exercise and work performance and promotes recovery from strenuous exercise (Burke & Hawley, 1999; Kirwan et al., 1988). The GI of the carbohydrates consumed has been found to be of importance in this regard in some instances.

Food with high GI as a post-exercise meal results in higher muscle glycogen levels within 24 hours *after exercise* when compared to the same amount of carbohydrates from a low-GI meal (Burke et al., 1993). *During exercise,* combinations of multiple transportable carbohydrates may increase the total carbohydrate absorption and total exogenous carbohydrate oxidation (Jeukendrup & Jentjens, 2000). A low-GI meal *pre-exercise* leads to enhanced performance when compared with high-GI meals (DeMarco et al., 1999; Kirwan et al., 2001; Thomas et al., 1991). The usefulness and application of a high-GI food after exercise must be considered in conjunction with the athlete's overall diet and should be reserved for occasions when maximizing post-exercise glycogen synthesis is critical.

6 Current official recommendations

Current international dietary guidelines agree on stressing the importance of a diet rich in fruits and vegetables, pulses and whole grain cereals (less processed food), but vary regarding the importance of the GI concept.

As early as 1998 the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) stated in a report on "Carbohydrates in Human Nutrition" (FAO/WHO, 1998) that people in industrialized countries base their diets on low-GI foods in order to prevent the most common diseases of affluence, such as coronary heart disease, diabetes and obesity. They stated that the bulk of carbohydrate containing foods consumed [$\geq$ 55 E%] should be rich in non-starch polysaccharides and with a low GI finding appropriately processed cereals, vegetables, legumes and fruits particularly good food choices.

The report also had proposals for the role of the GI in food choice:

-That, for healthful food choice, both the chemical composition and physiological effects of food carbohydrates should be considered, because the chemical nature of the carbohydrates in foods does not completely describe their physiological effects.

-That, in making food choices, the GI be used as a useful indicator of the impact of foods on the integrated response of blood glucose. Clinical application includes diabetes and impaired glucose tolerance. It is recommended that the GI be used to compare foods of similar composition within food groups.

-That published glycemic response data be supplemented where possible with tests of local foods as normally prepared, because of the important effects that food variety and cooking can have on glycemic responses" (FAO/WHO, 1998). A later publication from the same organizations stated that for healthy people the effect of low-GI food for prevention of obesity and diabetes was "possible" (FAO/WHO, 2003). Concerning obesity it stated "Low-glycaemic foods have been proposed as a potential protective factor against weight gain and there are some early studies that support this hypothesis. More clinical trials are, however, needed to establish the association with great certainty".

The recent US Food and Nutrition Board macronutrient report concluded: "Due to lack of sufficient evidence on the prevention of chronic diseases in generally healthy individuals, no recommendations based on GI are made" (Food and Nutrition Board 2002). In the Nordic Nutrition Recommendations the GI concept is not used as such in recommendations and more long-term intervention studies are found to be needed to

establish the role of low GI foods and diets for maintenance of health and prevention of chronic disease (Nordic Nutrition Recommendations, 2004).

In their nutrition recommendations for people with diabetes, the Canadian Diabetes Association supports that within the same food category, low GI foods should be consumed in place of high GI foods (Wolever et al., 2003a) and is thus in favor of supplying consumers with information about the GI of foods and beverages. Diabetes Australia has similar recommendations (www.dav.org.au). The European Association for the Study of Diabetes Guidelines also puts the GI concept forward as a part of their guidelines for diabetic patients (Mann et al., 2002).

However, although based on the same available scientific data, other organizations, such as The American Diabetes Association (American Diabetes Association, 2002), come to a different conclusion regarding diet in diabetes and do not favor linking GI to health and disease prevention. However, they give a broader view in a recent publication, deeming that the GI in addition to total carbohydrate may be helpful in controlling postprandial blood glucose levels (Sheard et al., 2004).

The evidence for recommending low-GI diets to the public as well as to diabetic patients and others is under constant reevaluation within official bodies in different countries. It is more frequently used in diabetes patient education and is presented in different ways, either as table values or otherwise integrated into dietary advice. Different scientific opinions and emphasis in different countries can be confusing as well as the varying quality of information to the public regarding the concept.

7 Scientists and laymen write popular books for the public

Information regarding the GI concept has reached the public in the Nordic countries through numerous popular books and articles in both magazines and newspapers, where the benefit of a low-GI diet is put forward. Sometimes well balanced, but often the results of studies are either over- or misinterpreted with lists of GI of foods of very different quality.

Respected scientists from Australia and Canada, actually two of those with the highest number of publications in the field of GI, have also published a very popular book for the public on the GI "*The New Glucose Revolution – The Authoritative Guide to the Glycemic Index, the Dietary Solution for Lifelong Health."* The cover also states:

The Scientifically Proven Plan that Helps You to

- Loose weight
- Control Blood Sugar
- Tackle Syndrome X
- Reduce Your Risk of Heart Disease
- Manage Type 1 and Type 2 diabetes

It is written by Jennie Brand Miller, Thomas MS Wolever, Kaye Foster Powell and Stephen Colagiuri, a New York Times Bestseller, sold in at least 750,000 copies (Brand-Miller et al., 2003).

The third large scientific group, which has been studying the GI of food and relationship to diseases, is at Harvard School of Public Health and is headed by Walter Willet. He wrote a book for the public called: *Eat Drink and Be Happy*. Partly on the basis of studies linking low GL and health, the professor proposed an adapted food pyramid, in which white bread, potatoes and white rice are put at the top, indicating a recommendation to use these foods sparingly (Willett, 2001). The Danish Nutrition Council wrote a report evaluating the new pyramid and did not find the current arguments for using it strong (Richelsen et al., 2005).

The GI concept has become a hot topic in the media. However, often those with little knowledge of nutrition present the diet in magazine articles or through other media and have a hard time distinguishing between low GI food and its potential benefits and low-carbohydrate diets, such as the Atkins diet. This adds to public confusion on nutrition.

In the Nordic countries books have been written on the subject by Nordic individuals working in the health sector (nutritionists and physicians), which have sold very well.

With public interest high, the food industry or companies working with weight loss have shown much interest in the GI concept (Kolset, 2003). To date many people have heard of the concept, and even followed a proposed diet, although the concept and what it stands for is frequently misunderstood.

7.1 GI labeling outside the Nordic countries

Usage and even marketing of the GI concept has come very far in Australia and New Zealand. This is organized under a program called "GI symbol program," which is a non-profit company formed by the University of Sidney, Diabetes Australia and the Juvenile Diabetes Research Foundation. It represents Australia's peak body of GI research and education. Information about the program can easily be found on the website www.glycemicindex.com.

Which foods will have the GI symbol?

According to the website, food companies in Australia and New Zealand can apply to use the GI symbol on their products. This symbol has been specially designed for the purpose. The product must show the GI value and the words high (>70), medium (56-69) or low (<55). According to the program, the product must also fulfill certain nutritional requirements. Provided a food has been properly GI-tested, contains 10 grams of carbohydrate per serving, and meets the set nutritional criteria for its food group (in terms of fat, sodium, fiber, etc.), it will be eligible for the symbol, regardless of its GI. This is to ensure that consumers can mix and match low-, medium- and high-GI foods to meet their various needs. According to the information on the website foods with added sugar will not be excluded, as this is not a guide to the overall nutritional profile of a food. GI gives more useful information about the effect of the carbohydrate on blood glucose levels than the sugar content per se.

There is no prohibition in the program on providing information on the GI of food combinations, such as breakfast cereal and milk. If the GI values of each of the meal components are known, and no further cooking takes place that could affect the GI, the GI of the meal can be calculated using the GI values and the carbohydrate content of each of the components.

The GI rating of individual food items must be tested physiologically, and foods in the program will be required to undergo retesting for their GI if there is any change in product formulation. Glycemic Index Limited is not responsible for the accuracy and legality of labels and marketing

claims of the foods in the program. All product labels and advertising using the symbol or mentioning the program are pre approved by Glycemix Index Limited.

It is very clear that different parts of the world vary in their valuation of the GI concept and how far one should go in directing the public. However, official bodies in most countries regularly evaluate whether GI labeling might be appropriate, and the food industry is often very interested. Many of the large food companies act globally. Thus, presenting information on the glycemic responses of foods and drinks, if relevant, may become a global action of industrial relevance.

8 Why do scientists not concur?

Why are scientists not quite in consensus regarding the usefulness of the GI concept in the prevention or treatment of diseases?

8.1 Methodological considerations

Lack of a standard method to measure GI of foods has delayed research, but using an easily applied, internationally validated method is important, as the one presented recently by Brouns and coworkers (ILSI document) (Brouns et al., 2005). The insulin index should be measured along with the GI as foods giving a high glucose and high insulin response have different metabolic consequences than foods, such as milk, giving a low incremental glucose response but a high insulin response. Studies sometimes lack or have questionable definitions of high- versus low-GI foods or diet (Arvidsson-Lenner et al., 2004), and international table values have limitations, calling for the construction of local GI tables as references in different countries or areas. Only a few research groups have been working with the concept in the Nordic countries. Studies on GI are expensive, and when the applicability or importance of the results is not clear, analysis is not prioritized. However, the GI concept is clearly important for people with diabetes, and the information would always be useful even though the importance of the GI concept for healthy people might later prove slight.

8.1.1 GI is not a nutrient

If the GI was a nutrient and not the more diffuse "effect on blood sugar" that it is, the scientific discussion would be much easier. However, and this is a very important point, the GI is not a nutrient although sometimes discussed as if it were in the literature. Unlike a nutrient, it cannot be isolated (or held in your hand) and, therefore, cannot be measured as such (even if it may be affected by processing and/or storage, as nutrients often are). But bowing to tradition and thinking of GI as a nutrient might produce irritation in the long run as the concept does not conform to the rules of regular nutrient analysis. It takes a lot of effort to measure the GI of a single food item or meal, and the result is very easily affected by other factors.

8.1.1.1 A new generation of guidelines?

On the other hand the GI concept gives an opportunity to look at nutrition from a different angle, i.e., as the physiological effect of food rather than as an effect of certain nutrients and might be part of a new generation of dynamic dietary guidelines focusing on the postprandial response (Colombani, 2004), the direct metabolic effect of food in the body.

8.2 Not enough evidence?

Two recent Nordic papers concluded that the implications of the GI concept have yet to be demonstrated for healthy people (Arvidsson-Lenner et al., 2004: Kolset, 2003). More evidence is needed before using and incorporating the GI concept into recommendations, and the recent version of the Nordic Nutrition Recommendations 2004 did not find the evidence strong enough to include the concept in the recommendations for healthy people (Nordic Nutrition Recommendations, 2004).

8.2.1 Current nutrition recommendations enough?

It is regularly asked whether the current nutrition recommendations i.e., increased consumption of fruits (and vegetables), legumes and whole grains and food rich in fibre and lower in sugar, are not enough, i.e., if it is not too complicated to add the GI concept to these recommendations, especially for healthy people (Colombani, 2004; Kolset, 2003). The current recommendations automatically lead to lower GI for most individuals and adding GI to the recommendations would not change them (Kolset, 2003).

Although high-fibre and low GI are not equivalent, they tend to be related because certain dietary fibres and foods in which the natural cell wall architecture remains intact (e.g., legumes and whole grains) generally have lower GI. However, many products high in fibre can also be found at the highest end of the GI scale. These are products like high-fibre breakfast cereals, which are often highly processed, and even high-fibre bread (generally not considered processed by the public). On the other hand low-fiber processed food such as pasta can be found at the lower end of the GI scale and other factors than fiber and intact structure affect the GI of food (see 4.2.1.). Therefore, recommending only a diet high in fiber, preferably from wholegrain cereals fruits and vegetables and less processed food (Nordic Nutrition Recommendations, 2003; FAO/WHO 2003) does not give the same scope as including information on GI in dietary advice, although the current recommendations reach a very long way towards a low GI diet.

8.2.2 GI cannot stand alone

However, the GI concept was never meant to be used in isolation and must always be presented in a balanced way, like other nutritional advice. It should always be clearly stated that exchanging foods based on the GI should generally be done within the same food groups, and the concept should only be used for high-carbohydrate foods, looking especially at the breakfast and the second-meal effect and regular meals. The focus should always be on the diet as a whole, including the portion size and composition of nutrients and fibre.

When discussing the GI concept, it is the "quality" of carbohydrates in the food that is under discussion (within the same daily energy need), and the concept can easily be used within the current macronutrient recommendation for E% of carbohydrates. This should be clear to everyone working with the concept and explaining it.

8.2.3 A heterogeneous group

For example, fructose has been considered a low-GI food as it does not cause a rapid rise in blood glucose or trigger an insulin response. However, high intake of refined sugars (>20E% sucrose or 5E% fructose) has resulted in elevated triglyceride levels (Nordic Nutrition Recommendations, 2004; Bantle et al., 2000; Swanson et al., 1992). It may also contribute to insulin resistance through its unique ability among all sugars to cause a shift in balance from oxidation to esterification of serum-nonesterified free fatty acids (Cordain et al., 2005). Recently fructose was found to be associated with increased adiposity, which may result from its effect on hormones, such as leptin and ghrelin, associated with satiety (Elliott et al., 2002; Wylie-Rosett et al., 2004).

The above is a reminder that low-GI food is a heterogeneous group, which although giving a low glycemic response, can have many other effects in the body. A food item found to be beneficial due to its low-GI might turn out to be less beneficial in other ways such as due to its effect on other hormones (even despite good macro- and micronutrient composition).

8.2.4 Looking at the whole picture

The GI concept is part of a larger picture of the metabolic effect of different food on postprandial response and metabolic effects in the body. Only looking at the glucose and insulin response is an oversimplification as other hormones are also important, for example, in appetite response as well and affect the body in different ways. The measurements used commonly today, i.e., LDL and HDL cholesterol, glucose and insulin, are those we know well, but as science progresses, other factors become

standard measurements, such as C-reactive protein (CRP), leptin, even ghrelin, adding to our knowledge.

Today we lack an overview of all the processes and interactions that different foods stimulate in the human body, which makes all changes in ingredients or changes in the processing of common food items a potential source of serious health consequences. The glycemic index concept brings us one step closer to the answer. However, until we have the whole picture of the effect of different foods on the body in sickness and in health, it is almost impossible to answer the question of how important low-GI food is for health.

8.2.5 The cautious mind of a scientist

Finally, it must be stated that it is the nature of science to be cautious when new ideas come to light. The great public attention and output of popular writing from some very respectable scientists working in the field of GI might have made others more sceptical towards the concept as they found the evidence as well as the international GI tables weak at the time.

Chocolate cake can be a low-GI alternative. The amount of fatty and sometimes unhealthy diet found at the lower end of the GI scale in the international tables, such as cakes and chocolate, annoys many experts as this might mislead the public to eat unhealthy food in pursuit of health. Some of the books and articles written for the public have done exactly that.

However, when looking at the GI concept from a public health perspective, it is very important not to be prejudiced and close one's eyes to the important possibility that low GI might promote public health and the development of quality foods that not only lower the GI but are also rich in fibre and dense in micronutrients. The concept might be a tool for diet education, and the public health focus should be on both fibre and carbohydrate quality and quantity.

Furthermore, it is good to remember that when the GI concept has been criticized, the focus is usually on either methodology or low-GI or GL diets' classification as not being superior to other diets (Raben, 2004), but not on potentially negative health outcomes (Colombani, 2004).

Is it possible to identify the research needed and the emerging issues requiring clarification in order to gain a consensus regarding the value of GI to the public as a whole?

8.3 What studies are needed?

First, it is important to evaluate the GI (and II) of Nordic food. Furthermore, the food or diets used in the studies must be clearly described, for example, whether it is industrially made low-GI bars and shakes or con-

ventional food. Macronutrient content must be known as well as processing and cooking methods, and the difference in GI between the food or diets must be clear. This requires adequate dietary assessment methods as it must be clarified that the health effect of a low-GI diet is not solely attributed to fibre or other nutrients, which act as a proxy for low GI, but that the beneficial effect seen is really due to differences in glucose and insulin response between the two diets or food items. This also requires more conventional and palatable low-GI food on the market, which is a limiting factor in studies today.

Future studies should continue to explore the difference between different low-GI foods, such as the difference in second-meal effects. For those with an operating pancreas, foods giving a high glucose response and high insulin response have different metabolic consequences than food giving low glucose response but a high insulin response due to proteins like milk proteins. Thus the effect of protein from different sources on glucose-insulin metabolism needs further study (Hoppe et al., 2005). Furthermore, certain low-GI foods may be more efficient in modulating metabolism in the long term (Bjorck et al., 2000), which has to be investigated further.

Generally, the participants at the seminar all agreed that there is an urgent need for well-designed, long-term (preferably longer than 6 months), adequately powered, randomized clinical intervention trials to establish the role of low-GI foods and diets clearly in the maintenance of health and prevention of different chronic disease, such as cardiovascular disease and type 2 diabetes. These and epidemiological studies should look at the relation of GI of food to different diseases dividing the subjects into groups according to BMI. It is also important to study possible gender differences. It would also be interesting to divide a group of overweight or obese individuals into insulin-resistant and non-insulin-resistant groups and see whether low GI is beneficial in both groups. This might also partly answer the question of whether some individuals are more sensitive to high-GI food than others.

Interventions for the prevention and treatment of overweight and obesity should be performed, preferably with an ad libitum design and, as in the previously mentioned studies, only the GI should be manipulated (not protein, fat, carbohydrate, dietary fibre or energy density) (Carels et al., 2005). In the field of satiety, it would be interesting, for example, to see a well-designed study on high-fibre, low-GI food and low-fibre, low-GI food, keeping macronutrient and energy intake similar. To date most intervention studies have focused mainly on people with glucose or lipid disturbances, but these studies should be performed on apparently healthy people as well.

Low-GI diets are probably less important to health than following other dietary advice, such as eating less candy, sodas, cakes, ice cream and snacks and eating more fibre as well as fruits and vegetables and

maintaining normal weight. Nevertheless, to evaluate this it is important to compare the effects of conventional recommendations regarding healthy food and additional information on moderate- and low-GI food.

Furthermore, studies looking at the whole picture of the metabolic effects of food in the body should be promoted as GI does not address other metabolic issues related to food consumption and satiety, such as the effect of food on leptin or ghrelin. Fructose, for example, has a low GI but has been suggested to be associated with increased adiposity, which may result from its effect on the hormones associated with satiety (Wylie-Rosett et al., 2004).

8.3.1 Different stages of life

Furthermore, it is important to look at the GI concept at different stages of the life cycle. Early life nutrition is receiving increased attention as a factor in setting the stage for future health. Well-designed prospective studies looking at GI and glucose and insulin levels in infancy and childhood should be constructed. The GI concept and resulting low glucose and insulin levels might also be especially relevant to years of growth spurt and pregnancy as well as elderly people (particularly those over 60).

Very little is known about the applicability of the GI concept in childhood. However, a recent study found significantly reduced postprandial glucose and C-peptide levels after a spaghetti meal, compared with a reference meal of white bread; this was observed in two-year-old children (unpublished data) (Vidgard, Axelson, & Bjorck).

For infants the weaning food in industrialized countries, for example, flaked gruels, liquids and mashed foods, is often low in fibre, i.e., likely to be high GI. Moreover, the type of processing used for precooking cereal flours renders the starch more or less completely gelatinized (Granfeldt et al., 1995). Consequently, a high GI could be expected in cereal foods intended for young children (Nilsson et al., 2005). However, a recent study on glucose and insulin responses to porridge and gruel meals intended for infants showed unexpectedly low GI. In contrast high insulin increments were noted. The inconsistency between GI and II could probably be explained by the insulinotropic effect of the milk component in the products. The fruit and fruit juice added to some of the products had only a minor effect on postprandial glycemia (Nilsson et al., 2005). To date, this area of research is rarely explored.

8.3.2 Dietetics

The acceptance of low-GI food is an important issue in the study of the GI concept. Older studies found acceptance of low-GI food dependent on health beliefs and ease of preparation (Jenkins et al., 1984). It is however

interesting to investigate how low-GI food is accepted over a longer period of time, how it is adopted in the population. Furthermore, what happens when people change their dietary habits; what other dietary constituents change? For example, the effects arising when sucrose is replaced by saturated fat may be very different from those arising when sucrose is replaced by whole grains and fruit (Daly, 2003). When using the concept, what is the best way of explaining it to the public; how are the explanations understood? Several studies of low-GI diets have involved self-selection of food by patients which found the diets simple and practical (Pawlak et al., 2002). One study gave parents of obese children (aged 5-12) brief instructions and a handout from the paediatrician aimed at lowering the GI of the food consumed by their children. Of the 34 children initially enrolled, 15 completed the study, and of these 14 lowered their GI score. All these parents described the diet as easy to understand, and 12 children decreased in BMI (Young et al., 2004).

Others have found an alternative way to explain the GI concept to patients, i.e., as "slow" and "fast" carbohydrate-rich food, as an integral, balanced part of the whole diet (Jarvi et al., 1998). In treating diabetes, for example, the GI concept might be considered as one more tool for teaching people to eat healthy food.

All these studies would give a much clearer picture of where low-GI food fits into the larger picture of food and health.

9 From a Nordic perspective

In the Nordic countries, health professionals include a modified version of the GI concept when giving dietary advice to diabetic patients for the control of blood sugar. People have thus been advised to use more "slowly absorbed" and less "fast absorbed" carbohydrates, and this is explained without giving GI tables to the patient (Jarvi et al., 1998). Although the GI concept has proved to be a useful educational tool for people with diabetes as a part of nutritional advice, a certain degree of care is required with patients and the public to prevent misinterpretation and misunderstanding (Jarvi et al., 1998), i.e., the concept must be an integral part of whole-diet evaluation.

The Nordic countries are typical industrialized nations, with the same public health diseases as the other European countries and the USA. However, food habits and food choices have their distinctions. Over the last decades most of the Nordic countries have slowly been reaching the preferred Nordic nutritional goal of 50-60E% from carbohydrates (Nordic Nutrition Recommendations, 2004). The food is thus typically rich in carbohydrates. From a Nordic perspective there is a lack of data for a variety of carbohydrate-rich foods, such as typical Scandinavian bread products, breakfast cereals, potato products, gruels, porridges, certain vegetables and legume products, such as pea soup and pickled brown beans (Arvidsson-Lenner et al., 2004), but according to Nordic dietary studies and international GI tables, many of the common starchy staple foods in the Nordic countries most likely have a high GI although there are traditional, indigenous starchy products with a low GI, such as legumes, pasta, some rice and sourdough bread products.

Nevertheless, without knowledge of the GI of common Nordic food items, studies on the GI concept in the Nordic countries will never be of high quality, as clearly shown by Danish researchers (Flint et al., 2004). The lack of data has been known for a very long time as local GI tables were called for over 20 years ago (Thorsdottir, 1989).

Further study is required on whether the health effects of a low-GI diet seen in some studies are due to varying glucose or insulin levels, or whether they are due to other factors accompanying a low-GI diet (such as fibre). However, it is clear from the studies that small changes, like promoting low-GI wholegrain bread and whole kernels, along with seeds and legumes, etc., are likely to result in a more nutritious diet of great benefit to the public. Furthermore, to date virtually no deleterious effects of low-GI diets have been documented, whereas many such effects have been documented for high-GI diet. Therefore, studies on GI should be supported, and regular evaluation of evidence should be continued to

decide whether the GI concept should be integrated into dietary recommendations. Furthermore, with the increasing prevalence of overweight and obesity in the Nordic countries accompanied by increasing incidence of insulin resistance, it is clear that a large portion of the public might benefit as well as from establishing the GI of Nordic food.

9.1 Optimising the GI of food

The shortage of commercial, low-GI products that can be exchanged for the high-GI food already eaten, such as common breads and breakfast cereals, limits the utility and research of the concept (Nordic Nutrition Recommendations, 2004; Bjorck et al., 2000). This is reflected in the results of studies on GI (Brekke et al., 2004). Recent papers have been calling for more GI alternatives on the market (Hodge et al., 2004) to be able to implement low-GI diets in a natural way and without compromising dietary variety and palatability (Brand-Miller et al., 2003a). Low-GI cereal food, when developed, should preferably be rich in dietary fibre (Bjorck & Elmstahl, 2003), partly on the grounds that the second-meal effect is clearly seen overnight with such products, but not in products like pasta although the GI is the same. Furthermore, fibres have other good qualities important for the digestive tract. Certain low-GI foods may be more efficient in modulating metabolism in the long term (Bjorck et al., 2000), an attribute that has to be investigated further.

Today most of the differences in GI between foods can be explained and the food factors identified (see 4.2.1). This provides a tool that can be used to optimize the GI of food products when designing new low-GI food. Sometimes even modest modifications of current food processes may significantly reduce GI. Some are related to the choice of raw material (such as new cereal genotypes rich in amylose or beta-glucans) and others to the choice food process and processing conditions, fermentation, minimal processing and pumpernickel baking (Bjorck et al., 2000). Within a few years it will be possible to design and much more consciously select the nutritional properties of food ingredients. However, this ability to be able to affect the GI of food has also been perceived as a particular shortcoming of the concept per se (Bjorck et al., 2000).

As always when working with food, it should be kept in mind that adding chemicals to the food in larger amounts than can be consumed naturally might not always be beneficial in the long run (e.g., fructose), and the beneficial effect of a chemical or food processing on glycemic response is not proof of its total beneficial effect on health. Caution is therefore in order, as always, when designing new food items, especially food items commonly used.

9.2 GI labelling in the Nordic countries

In Australia the concept of GI is used in health education, and food items on the market can be marked with a GI symbol on the package after applying for and having the GI of the food verified as low, medium or high (Section 7.1).

Within the EU there is a proposed Regulation on Nutrition and Health Claims Made on Foods, which will be referred to in all the Nordic countries. The proposal covers nutrition claims, such as "rich in vitamin C" or "low in fat" and health claims, e.g., of a positive relationship between a specific food and improved health. As it is now the proposal sets rules for making such claims and also allows health claims, including those regarding reduction of disease risk, that were previously prohibited in the EU, provided such claims can be scientifically substantiated and authorized at the EU level. The Concerted Action PASSCLAIM has established principles and criteria for assessing the scientific support of health. Whether claims will be approved in Europe regarding the glycemic effect of food, or even later GI-labelling of food items, remains to be seen.

In Sweden health claims on food are handled within a Code of Practice (Health Claims in the Labelling and Marketing of Food Products. The Food Sector's Code of Practice, (www.hp-info.nu / www.snf.ideon.se), awaiting entry into force of the EU regulation. Within this Code, claims regarding GI are considered as "Product Specific Physiological Claims". Products providing at least 15g and preferably 20g of digestible carbohydrates per normal serving that have two independent determinations showing a GI below 55 (glucose reference) will be listed and may now carry the claim "low GI".

10 Conclusion

For evaluation of GI of different food items, it is important to have an internationally standardized GI methodology to be able to compare GI data from different research groups. Furthermore, studies have found present international table values often are not good predictors of measured GI for various reasons, such as differences between countries in methodology and cooking methods, indicating a need for local information. When measuring the GI of different food items, information on the insulin index might give important additional information.

It has been suggested that GI and GL values should only be applied for food items that have at least 15-20g available carbohydrates per normal portion. Furthermore, comparison of GI values should only be made between foods in the same food group such as different types of bread, morning cereals, etc. If these principles are followed, GI and GL can be used to stimulate an alternative choice without disturbing the nutritional value of the diet and prevent the misuse and misunderstanding that has occurred.

For individuals with diabetes or impaired glucose tolerance a low-GI diet might be of importance; this holds as well for those prone to diabetes due to overweight. More evidence is needed to be able to draw more secure conclusions on the importance of low GI food for healthy individuals. As a low GI diet often goes hand in hand with a healthy diet rich in fibre and nutrients, it is often hard to evaluate the real reason for a positive association seen between a low GI diet and decreased risk of chronic diseases or a beneficial effect on health by diminishing risk factors. This must be solved in future studies, and there is an urgent need for well controlled, long-term, randomized clinical intervention trials as well as well-designed prospective epidemiological cohort studies to establish clearly the role of low GI foods and diets in the maintenance of health and prevention of chronic disease or overweight.

In order to perform such studies realistically, a variety of low-GI foods are needed. Many of the habitual food items consumed in the Nordic countries today are likely to have a high GI, such as common breads and cereals. Compiling a Nordic GI database for carbohydrate-rich food items would enhance evaluation of the importance of GI in the Nordic diets. Today the applicability of the GI concept is partly limited by the shortage of palatable low GI foods on the market, but a number of food factors have been identified that can be exploited for this purpose.

In summary, the low-GI diet has emerged as an interesting tool in combating diseases and conditions linked to the metabolic syndrome, but more information is needed before adding information regarding the GI

concept to public recommendations on an evidence-based level. Furthermore, it should always be kept in mind that the glycemic index is only one measure of many which together indicate a healthy diet.

11 Abbreviations

AGE Advanced Glycation End Products
AUC Area under the curve
BMI Body Mass Index
CHD Coronary Heart Disease
CRP C-reactive protein
CVD Cardiovascular Disease
DNSG Diabetes and Nutrition Study Group
EASD European Association for the Study of Diabetes
EURODIAB Europe and Diabetes Study
FFQ Food Frequency Questionnaire
GI Glycemic index
GL Glycemic load
HDL High density lipoprotein
II Insulin index
ILSI International Life Sciences Institute
LDL Low density lipoprotein
NKE Nordiska Komiteen for Ernæringsmedel
REE Resting Energy Expenditure
TC Total Cholesterol

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13 Appendix

Nordic Seminar on Glycemic Index: From Research to Nutrition Recommendations

June 20th 2004, 14:00 – 17:30

Træleborg Konferansesenter
Træleborgveien 11
Tönsberg, Norway

Satellite Meeting: 8th Nordic Nutrition Congress

Project supported by the Nordic Council of Ministers, Nordic Committee of Senior Officials for Food Issues

Project co-ordinator:
Professor Inga Thorsdottir, Unit for Nutrition Research,
Landspitali-University Hospital & Department of Food Science University of Iceland

Chairs:
Dr. Laufey Steingrimsdottir, Public Health Institute, Reykjavik, Iceland
Dr. Brita Karlström, Clinical Nutrition Research, Public Health and Caring Sciences Institute, Uppsala, Sweden

PROGRAM

14:00 – 14:05 **Welcome**
Professor **Inga Thorsdottir**, Unit for Nutrition Research, Landspitali-University Hospital & Department of Food Science, University of Iceland

14:05 – 14:45 **Overview of the glycemic index and its implications for the prevention of chronic disease**
Professor **David D. J. Jenkins**, Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Canada

14:50 – 15:05 **Glycemic index of mixed meals & glycemic index in relation to appetite and body weight**
Associate professor **Anne Flint**, Institute of Human Nutrition, Royal Veterinary and Agricultural University, Centre of Food Studies, Denmark

15:10 – 15:25 **Epidemiological and trial evidence of glycemic index in prevention of diabetes**
Professor **Matti Uusitupa**, Rector of the University of Kuopio, former Head of the Department of Clinical

Nutrition, University of Kuopio, Finland

15:30 - 16:00 **---------- BREAK with a taste of Norwegian delicatessen ----------**

16:00 – 16:25 **Glycemic load - quality vs. quantity of carbohydrates**
Research fellow **Matthias B. Schulze**, Department of Nutrition, Harvard School of Public Health, Harvard University, Massachusetts, USA

16:30-16:45 **Means and motives to optimize the GI of foods**
Professor **Inger Björck**, Applied Nutrition and Food Chemistry, Centre for Chemistry and Chemical Engineering, Lund University, Sweden

16:50-17:05 **Hyperglycemia - AGE and the kidney filtration network**
Professor **Svein Olav Kolset**, Department of Nutrition, University of Oslo, Norway

17:10 – 17:30 **DISCUSSION and CONCLUSION**

Unit for Nutrition Research
Landspitali University Hospital and
University of Iceland
Hringbraut
101 Reykjavik
http://www.landspitali.is/nutrition
mailto:elvag@landspitali.is