HEALTH ASPECTS OF VARIOUS DIGESTIBLE CARBOHYDRATES

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ABSTRACT

The present review addresses the question whether simple and complex carbohydrates may result in different physiological responses with emphasis on glucose tolerance, human energy metabolism, and blood lipid spectrum. Furthermore, the implications of possible different physiological responses are discussed in relation to diabetes mellitus, obesity, and cardiovascular disease.

Previously, it was believed that all starches were digested more slowly than simple carbohydrates, resulting in a slower release of glucose into the bloodstream. The presumed higher insulinemic response of simple carbohydrates would eventually give rise to hyperinsulinemia and diabetes mellitus. At present, thinking in this area has changed and from many acute experimental studies it has become clear that there is a wide range of glycemic responses to both simple and complex carbohydrate foods, so that some complex carbohydrates give comparable glycemic and insulinemic responses to some simple carbohydrates. These responses to both forms of carbohydrates are appreciably influenced by certain other food components such as dietary fibre and antinutrients. Long(er) term studies on the relation between type of ingested carbohydrate and glucose tolerance show inconsistent results with two recent studies indicating a more beneficial effect of simple as compared to complex carbohydrates on glucose tolerance. Further long term well-controlled studies are necessary to elucidate this issue.

Obesity develops under circumstances of a positive energy balance. Recent evidence indicates that energy balance can only be achieved in the case of macronutrient balance and that fat, protein and carbohydrate balances are regulated separately. Current literature indicates a closer regulation of carbohydrate than fat balance, and carbohydrates have been reported to have powerful effects on thermogenesis and energy intake. Differences in thermogenesis among simple carbohydrates have been reported with sucrose and fructose being more thermogenic than glucose. Also, a higher carbohydrate oxidation and more pronounced suppression of lipid oxidation have been reported with fructose ingestion as compared to glucose. Furthermore, it has been reported that there is no difference in the thermogenic efficiency with which the body handles simple and complex glucose saccharides. The implications of these results of acute studies remain uncertain since there is no evidence indicating differences in the effects of various carbohydrates on long(er) term energy and substrate balance.

A change from a Western type of diet to a very high carbohydrate diet causes a reduction in HDL and LDL cholesterol but a possibly transient increase in plasma
triglycerides. In early studies it was claimed that simple carbohydrates, especially sucrose or fructose, would have more adverse effects on blood lipid spectrum than complex carbohydrates. There is, however, no consistent evidence available to support such a presumption. In fact, the majority of studies indicate no difference in the effects of various types of carbohydrates on blood lipid spectrum when ingested in amounts comparable to habitual Western consumption patterns. Hyperlipidemias, obesity, hyperinsulinemia, insulin resistance, diabetes, and hypertension have all been implicated as risk factors for cardiovascular disease. There is no evidence to support an independent relationship between any of these factors and the consumption of simple carbohydrates. Taking the above considerations into account, it can be concluded that there is no evidence to implicate an independent role for simple carbohydrates compared to complex carbohydrates in the etiology of cardiovascular disease.

The available literature indicates that there is no consistent evidence indicating differences in the effect of simple and complex carbohydrates on glucose tolerance, human energy metabolism and blood lipid spectrum. Furthermore, there is no evidence to implicate differences in the effects of simple and complex dietary carbohydrates in the etiology of obesity Diabetes Mellitus or cardiovascular disease.

**KEYWORDS:** Carbohydrate type, Glucose tolerance, Energy metabolism, Lipid spectrum.

**INTRODUCTION**

During the last decades, evidence has accumulated for a possible role of dietary fat in the etiology of cardiovascular disease (1,2), and obesity (3,4,5). As a consequence the nutritional advisory committees in several Western countries strongly recommend a decrease in the consumption of fat, especially saturated fatty acids. This should possibly be achieved by replacement of fat by 'complex' carbohydrates, whereas a restricted use of mono- and disaccharides has been advised (6,7,8). In The Netherlands, it has been recommended that the consumption of mono- and disaccharides should be at a level between 15-25 % of total energy intake (6). Although the average consumption of the Dutch population is generally within these limits, it has often been advised to restrict the use of products which contain added amounts of mono- and disaccharides (6).

The background for a limitation in the use of mono- and disaccharides lies in the facts that their consumption is strongly related to dental caries (8) and that (in the pure form) they are a source of carbohydrates which provide no micronutrients. In addition, claims have previously been made that 'simple' sugars may have adverse effects on several metabolic conditions involved in the etiology of obesity, cardiovascular disease and non-insulin dependent diabetes mellitus (9-14).

The present review addresses the question whether the so called 'simple' and 'complex' carbohydrates may result in different physiological responses, with emphasis on glucose tolerance, human energy metabolism and blood lipid spectrum. If so, this should have the implication for nutritional recommendations to discriminate between simple and complex carbohydrate. Subsequently, the implications of the possible different physiological responses are discussed in relation to human disease.

**TYPES OF CARBOHYDRATES**

Carbohydrates are the most important source of calories for the world's population and comprise on average 40-45% of the energy supply in the Western world. Carbohydrates are a class of
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Chemical compounds composed of carbon, hydrogen and oxygen and contain two atoms of hydrogen for each atom of oxygen, the same as in water. Carbohydrates in food are divided into two categories. The first comprises the digestible carbohydrates, which can be digested in the upper gastrointestinal tract in man, absorbed and utilized. The available carbohydrates can in turn be divided in ‘simple’ and ‘complex’ carbohydrates.

The second category or indigestible carbohydrates consists of indigestible oligosaccharides (raffinose, stachyose) and dietary fibre like cellulose that do not provide significant nourishment to man. They are broken down by bacteria in varying degrees in man, distal to the absorptive sites in the colon (15,16).

Simple carbohydrates represent 40% of the carbohydrates in most Western diets and include monosaccharides, which consist of one saccharide unit per molecule, and disaccharides, which contain two saccharide units per molecule. In The Netherlands the simple sugar intake is estimated to account for 21% of total calories (21 en%), whereby mono- and disaccharides account for 7 and 14 en%, respectively (17). The disaccharides maltose, lactose and sucrose, account for 0.3, 2.7 and 11 en%, respectively. Sucrose (table sugar) is made up of 1 unit each of glucose and fructose per molecule, whereas lactose (milk sugar) consists of one glucose and one galactose unit per molecule. Maltose consists of two glucose units per molecule. Half of the ingested calories of mono- and disaccharides comes from sugars naturally present in certain foods and drinks. The hexose monosaccharides glucose and fructose, and the disaccharides sucrose, maltose and lactose occur naturally in milk, dairy products, fruits and vegetables. The other half of the calories delivered by simple sugars is added during industrial processing and household use. Sugars added during food processing include sucrose, lactose, fructose and syrups that contain glucose and/or fructose.

Complex carbohydrates are large molecules consisting of many glucose units. Starch (polymers of glucose) comprises the majority (50-60%) of carbohydrates in the Western diet and are found in many foods including cereal grains, legumes and potatoes. Starch is composed of the straight chain glucose polymer amylose and the branched chain polymer amyllopectin. The amylose chain of starch contains straight chain $\alpha_1,\alpha_4$ linked glucose residues, whereas the amyllopectin chain also consists of $\alpha_1,\alpha_6$ branching links occurring approximately every 25 glucose residues along the chain. The ratio of amylose to amyllopectin in starch varies widely but is usually about 1:4. Maltodextrins are made by hydrolyzing corn starch and contain glucose, maltose and higher polymers of glucose and are predominantly added to food as main carbohydrate source (15,16).

Certain related compounds and close derivatives are conveniently considered with the carbohydrates although they are not carbohydrates in strict chemical terms. One of these are the sugar alcohols, like sorbitol, mannitol and xylitol, which differ from carbohydrates only in having an alcohol group in place of a keto or aldehyde group on one of the carbons atoms. These compounds are added to food as alternative sweeteners but may also be added to other products for various reasons (i.e. to toothpaste or detergents, 8,15,16). Table 1 summarizes the different types of carbohydrates in common foods.

METABOLISM

Digestion

Intraluminal digestion of starch

Digestible carbohydrates are progressively broken down by the action of enzymes within the gut lumen. The $\alpha_1,\alpha_4$ links are cleaved by salivary amylase and pancreatic amylase which are identical in their action. Starch digestion is initiated in the mouth by the action of salivary alpha-amylase, but this action is limited (due to pH-changes). Starch remains only a short period in the mouth prior to amylase
inactivation by the low pH in the stomach. For this reason, most starch is digested in the small intestine where pancreatic alpha-amylase acts on starch in the lumen (fig 1). The final products of amylase hydrolysis are maltose, maltotriose (containing 2 or 3 α1, 4-linked glucose residues, respectively) and α-limit dextrins (α1,6- and α1,4-linked glucose residues). The latter are not digested by amylase since that enzyme has very little activity against α1,4 bonds near α1,6 bonds. These products of intraluminal starch hydrolysis are further digested by the action of brush border enzymes (15,16).

**TABLE 1.**
Major Dietary Carbohydrates (based on ref 15,16)

<table>
<thead>
<tr>
<th>Carbohydrate</th>
<th>Food source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Digestible</strong></td>
<td></td>
</tr>
<tr>
<td>Monosaccharides</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>Milk, sugar cane, starches</td>
</tr>
<tr>
<td>Galactose</td>
<td>Milk products</td>
</tr>
<tr>
<td>Fructose</td>
<td>Vegetables, fruit, honey, soft drinks</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>Alternative sweetener, diet gums</td>
</tr>
<tr>
<td>Oligosaccharides</td>
<td></td>
</tr>
<tr>
<td>Lactose</td>
<td>Milk products</td>
</tr>
<tr>
<td>Maltose</td>
<td>Corn syrups</td>
</tr>
<tr>
<td>Sucrose</td>
<td>Sugar cane, sugar beet</td>
</tr>
<tr>
<td>Corn syrups</td>
<td>Corn, rice, potatoes</td>
</tr>
<tr>
<td>Polysaccharides</td>
<td></td>
</tr>
<tr>
<td>Starches</td>
<td>Plants</td>
</tr>
<tr>
<td>Maltodextrins</td>
<td></td>
</tr>
<tr>
<td><strong>Indigestible</strong></td>
<td></td>
</tr>
<tr>
<td>Oligosaccharides</td>
<td></td>
</tr>
<tr>
<td>Raffinose, stachyose</td>
<td>Legumes</td>
</tr>
<tr>
<td>Polysaccharides</td>
<td></td>
</tr>
<tr>
<td>Cellulose, hemicellulose, gums</td>
<td>Vegetables, fruits</td>
</tr>
</tbody>
</table>

The rate of starch hydrolysis can be influenced by many factors like the nature of the starch, the rate of gastric emptying, the composition of the ingested food, and the presence of intraluminal substances that may alter amylase hydrolysis (16,18). These factors will be considered in more detail in the section on glucose tolerance. Overall, the rate of intraluminal starch hydrolysis is an efficient process and it has been reported that the available luminal hydrolytic capacity is greatly in excess of that needed to account for the observed rates of starch hydrolysis in man (19).

**Brush border digestion and absorption**
Brush border digestion of carbohydrate involves two major substrates: ingested disaccharides
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(sucrose and lactose) and the oligosaccharide products of starch digestion. Most enzymes are active against a specific glycosidic bond. The short oligosaccharide products of starch are cleaved by glucoamylase, isomaltase (both for cleaving α1,4-bonds) and α-limit dextrinase (α1,6- and α1,4-bonds). Other brush border enzymes include lactase responsible for lactose digestion and sucrase which can hydrolyze both maltose and sucrose. The realized monosaccharides glucose, fructose, and galactose are available for subsequent absorption in the small intestine (15,16).

![Image](image_url)

**FIG 1.**

Cleavage of the straight chain starch amylose and the branched chain starch amylpectine by pancreatic alpha-amylase to final products in the intestinal lumen. Each circle represents a glucose unit, (circle with line is reducing glucose unit), attached to its neighbour by either α1,4 (horizontal) or α1,6 (vertical) linkages (based on ref 15,16).

Glucose and galactose are probably predominantly absorbed by active Na⁺coupled-dependent transport (15,16), whereas fructose absorption is still poorly understood (20,21). Fructose is absorbed at a slower rate than the actively transported galactose and glucose, but more efficiently than passively transported sugars (i.e sugar alcohols: sorbitol, xylitol). From several studies it has appeared that malabsorption of pure fructose may be considered a normal phenomenon in the healthy state and that glucose may facilitate fructose absorption (15,16,20,21). Two separate mechanisms for the absorption of fructose have been suggested. One mechanism could involve glucose independent facilitated transport and another glucose dependent fructose cotransport (20), which would be additive to the transport of a saturating level of free fructose. It can be speculated that the lower glycemic effect of fructose as compared with glucose may be partly due to an incomplete absorption of fructose (see section glucose tolerance).

Brush border digestion of oligosaccharides has been reported to be a relatively efficient process. Several investigators have studied the relation between the hydrolysis of disaccharides and the absorption of the resulting monosaccharides. The glucose absorption from sucrose has been reported to be the same as from an isotonic equimolar glucose-fructose mixture (15,22), indicating that the hydrolysis of sucrose provides more than enough monosaccharide for final transport. It has previously been reported that there may be differences in the rate of glucose absorption from maltose and lactose as compared to free glucose. Jones and coworkers (23) reported that maltotriose and glucose polymers with degrees of polymerization <6 were more rapidly absorbed than was free glucose. These results could, however, not be confirmed in several other in vivo studies in man.
(24,25,26,27), where the absorption rates of maltose and glucose have been reported to be similar.

Even in normal individuals who have optimal levels of lactase activity, hydrolysis of lactose was found to be a relatively slow process which does not provide enough glucose and galactose to saturate the final transport system (15,16,22). It has been shown that the absorption of glucose from lactose is slower than from an equimolar glucose-galactose mixture (15,16,22), indicating that the lactose hydrolysis is rate limiting for absorption. Taken together, the available literature indicates that the hydrolytic step may be rate-limiting in the overall process of lactose hydrolysis-monosaccharide absorption, whereas hydrolysis is apparently not the rate limiting step for sucrose or maltose absorption.

**Colonic absorption**

The colon plays an important role in salvaging calories from malabsorbed sugars and dietary fiber. The colon cannot absorb monosaccharides but does passively absorb the short chain fatty acids resulting from metabolism of carbohydrates by colonic flora (15,16,18, see also section 'different glyemic responses to carbohydrate foods').

**Post-ingestive metabolism**

After absorption from the small intestine glucose has been reported to be taken up and metabolized by extraspinalchic and splanchnic tissues (28-31). Excess glucose may be stored as the glucose polymer glycogen in both liver and skeletal muscle, providing a readily mobilizable energy source when energy needs increase. Glycogen stores in man has been reported to be on average 15 g/kg body weight (32,33). Acheson and coworkers showed that glycogen stores in normal young men can increase by 350-400 g after one large carbohydrate meal (33). In addition, they showed that glycogen storage capacity can accommodate a gain of about 500 g during carbohydrate overfeeding before net lipid synthesis from carbohydrate occurs (32). These data indicate that man has a higher storage capacity for carbohydrate than generally believed and suggest that net synthesis of lipid from carbohydrates does not occur to a large extent under normal dietary conditions in the Western world.

After absorption from the small intestine fructose is primarily taken up by the liver (34,35,36). Although fructose is absorbed more slowly than glucose, it is more readily metabolized because cellular uptake and the early steps of fructose metabolism differ markedly from those of glucose. Unlike glucose, fructose has only a modest effect on insulin secretion and does not require the presence of insulin to gain access to the intracellular compartment. Once inside the cell, fructose is very rapidly converted to fructose-1-phosphate. This phosphorylation bypasses the early rate-limiting steps of insulin-stimulated transport, which glucose must undergo. Within the liver, fructose (and other monosaccharides i.e. sugar alcohols) are predominantly converted to glucose, which may be stored as glycogen or released to the blood. The rest of the metabolized fructose is released from the liver as lactate. Under normal circumstances, small amounts of fructose are oxidized to carbon dioxide or converted to lipid (34,35,36).

Galactose is most likely predominantly taken up by the liver, where it is only utilized after conversion to glucose-1-phosphate. After mixed meal ingestion the uptake of galactose (and fructose) by forearm muscle has been shown to be negligible (28). Oral galactose ingestion has been reported to have no effect on insulin secretion (37), which suggests that as for fructose the early steps in galactose metabolism do not require insulin.

**GLUCOSE TOLERANCE**

Glucose tolerance tests measure the time course of blood glucose levels after an oral (or intravenous) glucose load. They are often performed with additional measurement of insulin levels,
since glucose tolerance reflects a biofeedback process involving this hormone (and other glucoregulatory hormones like glucagon) and the effect on circulating glucose levels. Plasma glucose values may vary widely after a standardized oral glucose challenge which has been reported to be related to both insulin action and insulin secretion (38). The ability to metabolize a glucose load is influenced by many factors including age, diet, activity, drugs and diseases.

A glucose tolerance test can indicate abnormalities where glucose utilization is impaired and high levels of blood glucose may occur (hyperglycemia, diabetes). At present, it is recognized that different forms of carbohydrates provide varying rates of release of glucose into blood, with a different rate of stimulation of insulin secretion (18). Furthermore, it has previously been suggested that the consumption of simple carbohydrates may result in an increased insulin secretion, hyperinsulinemia and a decreased glucose tolerance (13). A permanent deterioration in glucose tolerance induced as result of carbohydrate consumption would be of great concern because, if found, this may suggest a role for dietary carbohydrates in the etiology of diabetes.

Different glycemic responses to carbohydrate foods

Previously, emphasis has been placed on the difference between complex (starch) and simple sugars. It was believed that all starches were digested similarly and more slowly than simple carbohydrates. As result of the slower digestion or decreased stimulation of intestinal hormone release, glucose from complex carbohydrates was thought to reach the blood stream more slowly, resulting in smaller changes in blood glucose (18). However, current knowledge in this area has changed and it has been convincingly shown that there is a wide range of glycemic responses to both simple and complex carbohydrate foods.

Some starchy foods (e.g. baked potatoes) have been reported to give identical glycemic responses as compared to glucose (18, 40,41). Also, the glycemic responses to sucrose has been reported to be lower than for a wide range of starchy foods (i.e. potatoes, bread, cornflakes, 18, 40,41). In a study of Bantle and coworkers (39) where glucose, sucrose or starch from potatoes or wheat incorporated in a breakfast meal resulted in comparable glucose and insulin responses.

Furthermore, a wide range of glycemic responses has been reported among simple carbohydrates. The glycemic and insulinemic response to fructose has in several studies been reported to be lower than that of glucose and sucrose (18,41,42,44). Also, fructose incorporated as a sweetener in complex foods has been reported to be associated with significantly lower serum glucose and insulin responses as compared to sucrose sweetened foods (41). In addition, it has been shown that glucose and sucrose drinks at doses containing 50 g glucose equivalents resulted in similar plasma glucose curves, but that the insulin response to sucrose was somewhat higher (±20%) than the insulin response to glucose (40). However, another study showed that administration of a similar amount of carbohydrate in the form of a glucose or sucrose load resulted in a twofold higher insulin response after glucose as compared to sucrose ingestion (45). From the above data it can be concluded that the difference between simple and complex carbohydrates seems no longer clearcut in terms of glycemic responses. This is emphasized in several studies where it has been shown that plasma insulin and free fatty acid responses to glucose saccharides were not influenced by chain length (46) and postprandial glucose and insulin curves were independent of the type of carbohydrate consumed in the meals (47). Nevertheless several useful generalisations can be made about the effects of different types of carbohydrates (a) and food-related factors (b) on the postprandial glucose and insulin responses. The factors affecting the postprandial glucose (and insulin) responses are summarized in table 2.

a. Different types of carbohydrate

Crapo et al showed a larger glycemic response to common starchy foods such as baked potatoes and white bread than to white rice and corn starch (40), which may partly be ascribed to the nature of the starch. This is illustrated by studies of starches with a different amylose-amylopectin ratio. Behall
et al reported lower glucose and insulin responses after consuming high amylose crackers than after consuming low amylose crackers, both in volunteers on a normal diet (48) and after several weeks on a controlled experimental diet with different amounts of amylose (49). Also, in a study of Weststrate et al (50) it was found that the amylose content of meals may significantly affect postprandial responses, but the effects reported in this study were small and depended on meal size and composition.

Another factor which may affect the glycemic response to starches is the cooking time and procedure (18). Although amylases can attack raw starch, the gelatinization of starch during cooking does make the starch more accessible to the enzymes and the action more rapid.

In addition, the physical form of the starch may affect the glycemic response. Grinding brown rice before cooking has been shown to greatly enhance the postprandial glucose and insulin profile to comparable responses as found after an oral glucose load, whereas unpolished brown rice resulted in a significantly lower glycemic and insulinemic response (43).

Furthermore, rices with similar amylose content and cooked under the same conditions may differ in glycemic responses due to differences in gelatinization time and required minimum cooking time (51).

Finally, contrast in particle size of starches may result in differences in the postprandial responses due to differences in gastric emptying, since digestible solids empty from the stomach only when they have changed to particles smaller than 2 mm (52).

### TABLE 2.
Factors Affecting the Glycemic Response after Carbohydrate Ingestion

<table>
<thead>
<tr>
<th>Type of carbohydrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylose-amylopectine ratio</td>
</tr>
<tr>
<td>Cooking time and procedure</td>
</tr>
<tr>
<td>Physical form of the starch</td>
</tr>
<tr>
<td>Differences in gelatinization time</td>
</tr>
<tr>
<td>Particle size</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Food-related factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat and protein</td>
</tr>
<tr>
<td>Dietary fibre</td>
</tr>
<tr>
<td>Antinutrients</td>
</tr>
</tbody>
</table>

**b. food-related factors**

Beside the type of carbohydrate the composition of the meal in which the carbohydrate is eaten is of great importance in determining the glycemic response. Fat and protein influence glycemic response by delaying upper gastrointestinal transit and enhancing insulin secretion, respectively (53,54).

In addition, the presence of dietary fibres in a meal has been shown to reduce gastric emptying rate (18,55). Legumes are among the richest sources of dietary fibre, and legume fibre flattens the postprandial glucose response when added to carbohydrate foods.

Furthermore, some foods like legumes are rich in antinutrients (amylase protein inhibitors) which may delay starch hydrolysis and the postprandial glycemia (15,18).

Thus, it has been convincingly shown that the subdivision in simple and complex carbohydrates in terms of glycemic response is an oversimplification of the real situation and that many interrelated
factors may be involved in determining the glycemic and insulinemic response after carbohydrate ingestion. Factors such as the nature of the carbohydrate, its method of preparation, the composition of the meal, i.e. fibre content and the content of antinutrients, may interfere with the postprandial glycemic response. In general, it can be said that slowly digested carbohydrates ('lente carbohydrate foods') produce flatter glycemic and insulinogenic responses than quickly digested carbohydrates. It has been shown that the rate of gastric emptying may account for 34% of the variance in peak plasma glucose levels after a 75 gram glucose load (56) and may account for 36% of the variance in glucose response after four different starchy foods (57). Furthermore, it has been shown in several studies that the rates of digestion of carbohydrates in vitro are related to the glycemic and insulinogenic responses (58,59), also when the carbohydrate food were fed to normal subjects as part of a mixed meal (59).

A relatively small part of the starch in many foods is not absorbed in the small intestine and enters the colon. It has been reported that freshly cooked potatoes are well digested with 3% of the potatoes escaping small intestinal digestion, but this percentage may vary with the manner of food processing (60). Breath hydrogen and ileostomy studies indicate that 7-20% of the starch in bread enters the colon (16,18). With legumes and other foods the percentage entering the colon may be higher. The colon plays an important role in salvaging calories from malabsorbed sugars and dietary fibre. The colon does not absorb monosaccharides, but does passively absorb the short chain fatty acids resulting from the metabolism of carbohydrates by colonic flora. Although these small intestinal losses may relate to the in vivo rate of digestion, the differences in the percentage malabsorbed carbohydrates between foods is much smaller than the percentage difference between the glycemic responses. Therefore, the flatter glycemic response of 'lente carbohydrate foods' cannot be accounted for by increased losses from the small intestine (15,16,18).

**Long term effects on glucose tolerance**

Most of the above indicated studies are acute experimental studies, which may not provide direct answers to the question of the physiological effects of long term carbohydrate consumption. In a study of Wolever et al (61) foods with a low glycemic response eaten at dinner reduced the glycemic response to the subsequent breakfast. This overnight second meal effect supported the hypothesis that slowly absorbed carbohydrates have a longer term metabolic effect (table 3).

Several studies have reported that simple carbohydrates, in particular sucrose, may adversely affect glucose tolerance and insulin sensitivity. Reiser and coworkers (62) performed studies looking at the effect of diet on glucose tolerance in subjects preselected on an exaggerated insulin response after oral sucrose loading. These 'carbohydrate sensitive' subjects are also hypertriglyceridemic (Type IV hyperlipoproteinemia). During a 6 week period a diet containing sucrose as 5, 18 or 33% of calories, (fed in a gorging pattern: food is consumed in a sort period of time daily) increased fasting serum insulin concentrations in a dose dependent fashion. However, the pretest fasting insulin levels in this study were lower than those determined during the experiment in the group consuming 5% of calories as sucrose, which indicates that there is no simple dose-response relationship. In addition, a major confounding variable in this study was the introduction of the gorging pattern (25% of calories at breakfast, 75% at dinner) which may in itself affect glucose tolerance (63). Furthermore, the same group studied 19 healthy men and women to determine whether replacement of utilizable complex carbohydrate by sugars (mono- and disaccharides) in a high fibre-low fat diet would affect indices of glucose tolerance (12). Diets differed in that the 50% of calories from carbohydrate was administered as 35% complex and 15% simple sugars or vice versa. It was concluded that the high simple sugar diet may adversely affect insulin binding and may adversely affect indices of glucose tolerance. Although these data suggest an adverse effect of sucrose ingestion on glycemic control, most of the added simple sugars in the high sugar diet were administered as lemon-lime drinks. This makes it uncertain whether these results can be extrapolated to a situation where the mono and disaccharides
are incorporated into the food.

Beck-Nielsen et al (9) reported that supplemental feeding with 250 g/day of sucrose in addition to the normal diet of 23 to 33 year old male and female volunteers decreased insulin sensitivity and insulin-binding capacity to monocytic leukocytes. To determine whether the glucose or fructose moiety of the sucrose molecule was responsible for these effects, in a subsequent study (64) 250 g/day of glucose or fructose was added to the diet of 21-35 y old males and females. The fructose supplemented group showed a decrease in insulin binding to leukocyte, whereas glucose caused no changes. These data suggest that extremely high sucrose and fructose supplements may adversely affect insulin sensitivity.

Besides the above studies reporting an adverse effect of simple carbohydrates on glucose tolerance there are as many studies indicating a positive effect of simple sugars on glucose tolerance.

Thompson and coworkers (65) evaluated changes in glucose tolerance as result of a 10 day diet period with 45 or 65% of the calories as carbohydrate in the form of either sucrose or corn syrup. Glucose tolerance was improved in both the 65 and 45% carbohydrate group. Furthermore, sucrose diets resulted in a more pronounced increase in insulin sensitivity than the corn syrup diets as indicated by less postprandial glycemic excursions and a lower 24h plasma insulin curve. The above findings are consistent with a study of Anderson et al (66) who observed an improvement in glucose tolerance in 18-22 year old males after 2 weeks of high liquid carbohydrate consumption (either sucrose or glucose up to 80% calories) as compared to a control diet (40% of calories as carbohydrate). However, the diet in these studies was provided in a liquid form, which makes extrapolation to the solid food situation difficult.

One prospective feeding study (67) is of special interest since few data on long term interventions are available. Subjects were maintained on a diet containing sucrose, xylitol or fructose as sole sweetening agent. A versatile assortment of food stuffs containing sucrose, xylitol and fructose was given to the subjects. They were instructed to avoid ingestion of sweet fruit and other sucrose-containing food stuffs. In all other respect the diet was similar to that in the pre-trial period. Two-year dietary change of sucrose to fructose or xylitol did not affect fasting serum triglycerides, fasting blood glucose and insulin levels. Glucose tolerance was not affected by the kind of sugar (or sugar alcohol) consumed.

In a recent study of Piatti et al (68) the effect of a hypocaloric solid food diet with a high complex carbohydrate content (60% high complex, high starch and fibre, 20% fat) or with a high simple carbohydrate (60% simple/high natural fibre and 20% fat) were compared with respect to several parameters including insulin resistance in obese subjects. Peripheral insulin resistance increased on the high complex carbohydrate diet whereas a a tendency towards the opposite effects was observed as result of the simple carbohydrate diet, suggesting a beneficial effect of simple carbohydrates on glycemic control. These data are consistent with the results of a study on the relationship between dietary intake and glucose tolerance using data of the Zutphen study (69). In this study an oral glucose tolerance test was performed in a sample of the original study population and the relationship between specific dietary factors and aspects of glucose tolerance was analyzed. It was shown that the intake of mono- and disaccharides and pectin were independently negatively associated with the area under the curve after oral glucose ingestion, suggesting a beneficial effect of simple carbohydrates on glucose tolerance. Table 3 represents a summary of the studies dealt with in this paragraph.

Taken together, data on the relationship between type of carbohydrate and glucose tolerance are contradictory. In several studies it was suggested that simple carbohydrates may result in an increased insulin secretion, which would eventually give rise to hyperinsulinemia and diabetes mellitus. However, in several acute and long(er) term studies this hypothesis could not be confirmed. Moreover, several recent studies suggest a beneficial effect of simple carbohydrates on glucose tolerance. These findings must however be treated with caution and further long term well controlled studies are necessary to elucidate this issue.
### TABLE 3.
Overview of Major Studies investigating the 'Long term' Effects of Different Carbohydrates on Glucose Tolerance

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Diet conditions</th>
<th>Results</th>
<th>ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, female</td>
<td>Low or high GI dinner, breakfast of cornflakes</td>
<td>Breakfast glucose tolerance is improved after low GI dinner previous evening</td>
<td>61</td>
</tr>
<tr>
<td>'Carbohydrate sensitive'</td>
<td>Diet containing sucrose as 5,18 or 33% of calories (gorging pattern)</td>
<td>Diet increased serum insulin in dose dependent manner, fasting serum insulin is lower than fasting insulin at 5 en% sucrose</td>
<td>62</td>
</tr>
<tr>
<td>Male, female</td>
<td>Diet: 35 en% as complex and 15 en% as simple carbohydrate or vice versa</td>
<td>High simple sugar diet (added mainly in form of lemon lime drinks) adversely affected insulin binding and indices of glucose tolerance</td>
<td>63</td>
</tr>
<tr>
<td>Male, female</td>
<td>250 g sucrose per day added to normal diet for 2 weeks</td>
<td>Decreased insulin sensitivity and insulin binding capacity to monocyte leukocytes</td>
<td>9</td>
</tr>
<tr>
<td>Male, female</td>
<td>250 g glucose or fructose added to normal daily diet for 7 days</td>
<td>Fructose supplemented group showed a decrease in insulin binding to the leukocytes</td>
<td>64</td>
</tr>
<tr>
<td>Male volunteers young</td>
<td>10 day diet period with 45 or 65 en% in form of sucrose or corn syrup</td>
<td>Glucose tolerance improved in both diet groups; sucrose diet resulted in more pronounced increase in insulin sensitivity</td>
<td>65</td>
</tr>
<tr>
<td>Males</td>
<td>Liquid 80 en% CHO diet (sucrose or glucose) vs 40 en% CHO solid diet</td>
<td>Improvement in glucose tolerance after high carbohydrate liquid diet</td>
<td>66</td>
</tr>
<tr>
<td>Volunteers</td>
<td>Replacement of sucrose by fructose or xylitol in regular diet for two years</td>
<td>No change in fasting serum glucose, insulin or glucose tolerance</td>
<td>67</td>
</tr>
<tr>
<td>Obese, 2 male, 23 female,</td>
<td>3 hypocaloric diets 60% high complex/20% fat, 60% high simple/20% fat, 20% simple, complex/60% fat</td>
<td>Insulin resistance increased on high complex CHO diet, tendency towards decrease on high simple CHO diet</td>
<td>68</td>
</tr>
<tr>
<td>394 men</td>
<td>Relationship between glucose tolerance and diet was determined</td>
<td>Intake mono-, disaccharides negatively associated with AUC after oral glucose</td>
<td>69</td>
</tr>
</tbody>
</table>
ENERGY BALANCE AND MACRONUTRIENT BALANCE

Energy balance is determined by the rate of energy intake and expenditure. There has been a general consensus that a stable body weight is maintained by a tight control of energy balance and that the body is 'energy blind'. When energy balance is positive, the excess energy will be stored and when this continues over longer periods of time obesity will develop. When energy balance is negative the rate of expended energy exceeds the energy intake which will result in a loss of body weight. This concept implies that each calorie has the same value in the balance, independent of whether the energy is derived from fat, protein or carbohydrate. However, evidence is accumulating that energy balance can only be achieved in the case of macronutrient balance and that protein, fat and carbohydrate balances are regulated separately (3,70). Achievement of macronutrient balance requires that the net oxidation of each nutrient equals the average amounts of the same macronutrients in the diet. In addition, most recent literature suggests that protein and carbohydrate balance are regulated more closely than fat balance (3,5,70,71,72). Regulation of carbohydrate balance has the highest priority in the hierarchy, since carbohydrate stores are only capable of covering carbohydrate balance for a few days. Less attention has been paid to possible differences of various types of carbohydrates in the regulation of energy and macronutrient balance.

Carbohydrate induced thermogenesis and substrate utilization

After the ingestion of glucose or other nutrients there is an increase in resting energy expenditure that has been referred to as diet induced thermogenesis (±10% of daily energy expenditure). The increment in energy expenditure can partly be accounted for by the conversion of the ingested nutrients into their major storage forms, i.e., the conversion of glucose to glycogen requires 2 ATP. The energy required for storage of nutrients into the body has been traditionally called the obligatory component of the diet induced thermogenesis. However, it has been long recognized that the energy expended after meal ingestion exceeds the theoretical costs for the storage of nutrients. This difference has been called the regulatory component of the diet induced thermogenesis and it has been attributed to several factors i.e. an increased activity of the sympathetic nervous system, an increased recycling of substrates and other (34,36,73,74,75).

It has been shown that ingestion of carbohydrates elicits a higher thermogenic response than ingestion of fat (76,77). Excess carbohydrate promotes its own oxidation by stimulating the cellular uptake and oxidation of glucose (see section on metabolism). It has been demonstrated that over a 9 hour period the same amounts of carbohydrates, fat and protein are oxidized whether or not the test meal is supplemented with extra fat, indicating that fat intake does not promote its own oxidation (71). Thus, there are indications that carbohydrate and protein stores are regulated with the excess being metabolized, whereas excess fat intake is channelled directly into the fat stores (3,5,70,71).

As indicated above, the ingestion of different types of carbohydrates may lead to varying metabolic postprandial responses, which implies the possibility that different types of carbohydrates have varying effects on thermogenesis and substrate utilization. Indeed, differences in postprandial thermogenesis among various types of carbohydrates have been reported with sucrose or fructose being more thermogenic than glucose in both lean and obese volunteers (34,36,78,79, see table 4). These differences have been attributed to differences in postingestive metabolism between glucose and fructose (see also section on metabolism). Because fructose avoids the first rate limiting enzymes of glycolysis it is metabolized more rapidly than glucose resulting in the accumulation of three-carbon components which are available for gluconeogenesis and glycogen formation. Carbohydrate oxidation, glycogen formation and the decrement in lipid oxidation have been reported to be higher after fructose than glucose ingestion. It has been found that the β-adrenergic nervous system contributes (34,36), at least in part, to fructose-induced thermogenesis, but these findings are not consistent (75).

In previous studies it has been documented that the increase in energy expenditure and
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carbohydrate oxidation that normally accompanies glucose ingestion or glucose/insulin infusion is impaired in several insulin resistant states, like type II diabetes and obesity (73). On the basis of these studies insulin has been considered to be an important determinant of the carbohydrate induced thermogenesis. Other experiments indicated that insulin per se did not stimulate thermogenesis to any great extent but that via sympathetic nervous system stimulation it could explain the facultative thermogenesis observed in glucose clamp experiments (74). The finding that fructose ingestion results in a higher thermogenic response than glucose ingestion despite the fact that fructose ingestion has only a very slight effect on insulin secretion, indicates that the thermogenesis after carbohydrate ingestion is related to an augmentation of cellular metabolism and is not dependent on an increase in the plasma insulin concentration per se.

In a study of Ritz et al (80, table 4) substrate oxidation and energy expenditure was followed in 6 healthy volunteers for 6 hours after ingesting glucose or cooked manioc starch (contains 16% amylose). Although there were no differences in the total thermogenic response and glucose storage, and total fat oxidation, total carbohydrate oxidation was lower from 200 to 360 min after the glucose load. Since glucose storage was similar in both experiments, the higher glucose oxidation 3-6 h after the manioc starch load may indicate an increased use of endogenous glycogen stores. It was speculated by the authors that this increased use of endogenous glycogen stores could result in a better glucose tolerance by controlling the entry of glucose into the cell. However, as indicated in the section on glucose tolerance no consistent evidence from long term studies is available to substantiate such a conclusion. The thermogenic response to glucose and manioc starch was similar over the 6h period after ingestion, which indicates that there are no differences in the thermogenic efficiency with which the body handles glucose saccharides with varying chain lengths.

It is difficult to extrapolate the above findings on acute carbohydrate ingestion to a situation of long(er) term energy or substrate balance. It can be speculated that the higher postprandial thermogenic responses after fructose or sucrose as compared to glucose ingestion may result in a higher 24h energy expenditure when part of the carbohydrates consumed in the form of glucose or glucose polymers are replaced by sucrose or fructose containing products. In addition, the higher increase in carbohydrate oxidation and more pronounced suppression of lipid oxidation with ingestion of fructose as compared to glucose may result in a lesser effect on daily fat oxidation when fructose is (partly) substituted for glucose (polymers). However, evidence for differences in the effects of various carbohydrates on long term energy or substrate balance is lacking, as discussed in the next section.

Dietary carbohydrate and energy and substrate balance

As mentioned above, most recent literature suggests that carbohydrate balance is under strict metabolic control, whereas fat intake and fat oxidation are not under any metabolic control (3,5,70,71,72).

In several studies it is proposed that carbohydrate and fats may have different effects on appetite regulation. The satiation power of protein exceeds that of carbohydrate which in turn exceeds that of fat when given in a mixed diet (3,72). Consumption of a minimal amount of carbohydrates is necessary to maintain carbohydrate stores and satiety coincides with a carbohydrate intake corresponding to the daily carbohydrate oxidation (5). Thus, diet composition may have in itself effects on energy intake and energy balance. This is illustrated by several studies where it was shown that over 2 weeks compensation was less accurate with diets that had been diluted by removal of fat than by removal of carbohydrates (81). The underlying mechanisms for these differences between macronutrients are not entirely clear but may be related to the fact that fat is not metabolized as readily as protein or carbohydrate. Carbohydrates are rapidly absorbed thereby contributing to thermogenesis, cellular glucose uptake and oxidation (see above), which may be factors involved in appetite control. In addition, the body has a limited glycogen storage capacity. Fat digestion is relatively slow and fat does not augment its own oxidation (71,72). When fat is incorporated into
TABLE 4.
Overview of Studies dealing with the Relationship between Type of infused or Ingested Carbohydrate and Energy expenditure and Substrate utilization

<table>
<thead>
<tr>
<th>Studied</th>
<th>Results</th>
<th>ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Greater thermic effect of intravenous fructose than glucose is probably due to continued gluconeogenesis and energy cost fructose metabolism to glucose in liver</td>
<td>34</td>
</tr>
<tr>
<td>Male, Female</td>
<td>Increment in energy expenditure greater after oral fructose than glucose. With fructose greater increment in carbohydrate oxidation and greater decrement in lipid oxidation</td>
<td>36</td>
</tr>
<tr>
<td>Male, Female</td>
<td>Increase in metabolic rate (3-h period) greater after oral sucrose or glucose + fructose mixture than after glucose or galactose; RQ higher after sucrose or fructose + glucose than after glucose; RQ after galactose higher than after glucose but not as high as after sucrose</td>
<td>79</td>
</tr>
<tr>
<td>Male</td>
<td>Ingestion of glucose or manioc starch did not result in differences in postprandial thermogenesis, but total glucose oxidation was higher with starch</td>
<td>80</td>
</tr>
<tr>
<td>Rats</td>
<td>No differences in energy balance between rats fed a high starch vs a high simple carbohydrate diet</td>
<td>91</td>
</tr>
<tr>
<td>Rats</td>
<td>Isocaloric feeding of different types of simple carbohydrates and starch did not result in different effects on energy expenditure, energetic efficiency and energy repartitioning during refeeding after low food intake</td>
<td>92</td>
</tr>
<tr>
<td>Obese, 2 male, 23 female</td>
<td>With 3 hypocaloric diets (high complex CHO/low fat, high simple CHO/low fat and low CHO/high fat) the decreases in body weight, fat mass and fat free mass were comparable</td>
<td>68</td>
</tr>
<tr>
<td>Overweight male, female</td>
<td>The addition of 0.48 MJ as sucrose to a 4.2 MJ diet did not affect the rate of weight loss</td>
<td>93</td>
</tr>
</tbody>
</table>

Adipose tissue, it essentially has almost no satiety value since it represents a negligible fraction of total adipose tissue fat stores (3).

Thus, carbohydrates appear to have a potent effect on appetite regulation. In current literature, there are no indications that various types of carbohydrates may differ in their effects on appetite regulation or energy intake. However, it is a popular belief that the simple and complex carbohydrates may have varying effects on energy intake and that the attractiveness of sugar-rich foods may promote overeating and may thereby contribute to the development of obesity (13). In man, taste preferences for both fat and sugar have been investigated. Studies examining sweetness have not revealed any differences in sensory functioning between normal weight and obese individuals (82,83,84). In addition, several studies indicated a negative relationship between preference for sweet taste and degree of body fatness and a strong positive relationship between body fatness and preferences for...
fatty foods (85,86). This seems consistent with reports on the relationship between diet and the prevalence of obesity, showing that a higher fat intake is associated with a lower carbohydrate and sugar intake, which is in turn associated with a higher body mass index (87-90). Taken together, there is no reason to assume that the powerful effect of carbohydrates on appetite regulation and energy intake varies with the type of carbohydrate.

Several studies have compared the effects of different types of carbohydrates on energy balance and rates of weight loss. In a study of Dulloo et al (91), it was shown that there were no differences in energy balance between rats fed a high starch vs a high simple carbohydrate diet. The same group showed more recently that isocaloric feeding of different types of simple carbohydrates and starch did not result in different effects on energy expenditure, energetic efficiency and energy partitioning during refeeding after low food intake in rats (92). These data, indicating no effect of the type of carbohydrate on energy balance, are consistent with studies in man. In a recent study in man (68) the effects of three hypocaloric diets (3 weeks, 800 kcal) with a high content of complex carbohydrates (45 en%), simple carbohydrates (45 en%) or fat (60 en%), respectively, were compared. With all hypocaloric diets the decrease in body weight, fat mass and fat free mass was comparable. Also, in a study of Mc Creery et al (93), the addition of 0.48 MJ as sucrose to a 4.2 MJ diet in overweight volunteers did not affect the rate of weight loss. Table 4 summarizes the acute and long(er) term studies dealing with the relationship between type of carbohydrate and energy expenditure and substrate utilization.

In summary, it can be said that the available literature indicates a closer regulation of carbohydrate as compared to fat balance and that there is no evidence indicating differences between simple and complex carbohydrates on energy and substrate balance.

**BLOOD LIPIDS**

Hyperlipidemia, the elevation in the concentration of blood lipids such as cholesterol or triglycerides, is believed to be an important risk factor for atherosclerotic disease (1,2). In the 1960s, Keys et al (94) and Hegstedt et al (95) carried out investigations on how the major nutrients affect levels of serum cholesterol in normal humans. The two groups developed similar equations to quantify changes in total cholesterol as they occur in response to alterations in diet composition. It was found that saturated fatty acids raised serum cholesterol levels as compared to carbohydrates, whereas polyunsaturated fatty acids lowered serum cholesterol levels. Carbohydrates and monounsaturated fatty acids were regarded neutral in their action on serum cholesterol levels. From these equations many nutritionists concluded that the polyunsaturated to saturated (P/S) ratio is the key determinant of serum cholesterol levels. More recently, several investigators have begun to reexamine the influence of various nutrients on lipid metabolism with emphasis on serum lipoproteins and apolipoproteins. Blood lipids are carried by lipoproteins, of which four major classes are characterized: the chylomicrons, very low density lipoproteins (VLDL), low density lipoproteins (LDL), and high density lipoproteins (HDL). The lipoprotein fractions are considered to represent different risk factors, in general terms it can be said that VLDL is essentially neutral, high LDL is a positive risk factor and high HDL is a negative risk factor ('protective' against atherogenesis).

Diets high in carbohydrates and low in fat have been reported to cause a reduction of HDL and LDL cholesterol and to raise serum triglyceride levels (96,97,98), which has been suggested by some investigators to be transitory (99). Several early studies suggested that serum lipid concentrations are affected differently depending on the type of dietary carbohydrate. It has been shown that plasma triglycerides rose when starch was replaced by sucrose in a diet in which 50 (100) or 70% (10,11) of the energy came from carbohydrate. Since then many studies have been performed comparing the effect of different types of carbohydrates on blood lipids, which has yielded inconsistent results. This section provides a global overview of studies reporting on the relationship between type of
carbohydrate and the changes in plasma triglycerides, cholesterol and lipoprotein levels.

**Plasma triglycerides**

A change from a Western type of diet to a very high carbohydrate, low fat diet (more than 60% of calories from carbohydrate) has been reported to increase fasting triglyceride concentrations (96-98), which decline again after several weeks to months on the high carbohydrate diet (99). These increased triglyceride levels may result from an enhanced hepatic synthesis of VLDL triglycerides, but other mechanisms may also be involved in this effect (101). It has previously been hypothesized that the selection of foods that minimize the glucose and insulin responses may reduce the stimulus for hepatic triglyceride synthesis, i.e., hyperinsulinemia can promote hypertriglyceridemia. Indeed, it was shown in a study of Jenkins et al (102) that a reduction in the mean glycemic index of the diet in 12 hyperlipidemic patients for a 1 month period led to a reduction in serum triglycerides and total serum and LDL cholesterol. In this context it was suggested that simple sugars would be more hypertriglyceridemic than complex sugars (103). As must be evident from the above section on glucose tolerance, consistent evidence to support such a hypothesis is lacking since the glycemic and insulineic response to diet depend on many interrelated factors and it is by no means proven that long(er) term ingestion of simple carbohydrates would result in a more pronounced hyperinsulinemia.

A comparable effect of different carbohydrates on fasting triglyceride concentrations has been emphasized in studies of Thompson and coworkers (65). In these studies it was reported that the complexity of dietary carbohydrate (10 day period, 50% of carbohydrates provided as glucose, maltose, corn syrup or corn starch) did not affect fasting triglyceride levels and the 24-h integrated triglyceride concentration. In addition, it was shown that when 8 healthy volunteers were fed either sucrose or corn syrup at 45 or 65% of calories for ten days fasting triglyceride concentration was significantly affected by the amount of dietary carbohydrate, but was not influenced by the source of carbohydrate. These data are in agreement with the majority of short-term metabolic studies showing that glucose, sucrose, fructose and starch appear to have comparable effects on fasting triglyceride concentrations in normal man (104-110). Beside the above studies reporting a comparable effect of simple carbohydrates on fasting triglycerides levels it was suggested in a recent study that a simple carbohydrate diet may have a more beneficial effect on lipid spectrum than a complex carbohydrate diet (68). In this study obese subjects were allocated to three hypocaloric diets (800 kcal) containing 60 % complex carbohydrate and 20% fat, 60% high simple or 20% carbohydrate and 60% fat (all diets 20% protein). The high simple carbohydrate diet resulted in contrast to the complex carbohydrate diet in a decrease in fasting serum triglyceride concentrations, suggesting that triglyceride VLDL synthesis is more stimulated on the complex carbohydrate diet. Further long term studies are, however, necessary to elucidate this issue.

Although in normal men different types of carbohydrates seem to have comparable effects on fasting triglycerides, several studies suggested that the postprandial triglyceride concentrations are higher when substituting sucrose for starch in the diet. It has been shown that the acute postprandial serum triglycerides were higher when 23% (w/w) starch was replaced by sucrose in a (55 en% carbohydrate) mixed meal (105), but these findings are not consistent (110). Furthermore, in studies of Thompson and coworkers (65) it has been reported that the 24-h triglyceride concentrations were higher during a diet containing sucrose than during a diet containing corn syrup (both 45 or 65% of total calories). However, the amount of sucrose in the diets used by Thompson et al are higher than the levels generally consumed in the Western world, which raises doubt whether sucrose-induced increased postprandial triglyceride levels are of any significance in the normal Western diet.

In several studies the effects of fructose and sucrose ingestion on plasma triglycerides were investigated in subjects exhibiting hyperinsulinemia, hypertriglyceridemia or diabetes. In studies of Reiser et al (111,112) and Gardner and Reiser (113) it was shown that replacing starch by sucrose at 30% of the total calories (6-week period) in 19 subjects, 9 of whom were hypertriglyceridemic, resulted in higher plasma triglycerides, an effect that was more pronounced in males than in females.
As mentioned in other sections there are a number of problems with these studies which makes interpretation of these findings difficult. Firstly, the starch or sucrose was provided in the form of a patty which was presumably consumed at one moment of the day. Secondly, the food was provided in a gorging pattern (food is consumed in a short period of time daily) which may have interfered with the effects of type of carbohydrate on the studied parameters (63). The same group showed in a more recent study that fructose feeding (20 en%, for 5 wk, 3 meals a day) resulted in slightly increased plasma triglycerides in normal subjects and in pronounced increased levels in hypertriglyceridemic subjects as compared to high amylose corn starch (114). However, other studies using comparable subject groups as Reiser and coworkers have failed to detect an increase in plasma triglycerides as result of fructose or sucrose ingestion (115,116). Furthermore, although it has been reported that fructose or sucrose may have adverse effects on lipid spectrum in diabetics (117), the majority of studies report no effect of the ingestion of these carbohydrates on plasma triglycerides when administered in amounts comparable to the habitual consumption (116,118-120).

In summary, in early studies it was claimed that simple sugars caused a greater increase in serum triglycerides than complex digestible carbohydrates. Evidence in support of this claim is, however, relatively weak and it is by no means proven that simple sugars are more hypertriglyceridemic in normal man than starches. Thus, the majority of studies in normal, diabetic, hypertriglyceridemic or hyperinsulinemic subjects indicate no differences in the effects of different types of carbohydrates when consumed in amounts comparable to habitual consumption patterns (for summary see table 5). Nevertheless, on basis of the studies of Reiser and coworkers we cannot exclude that there is a subpopulation which may be particularly sensitive to added fructose or sucrose. Saying this we have to take into account that the prevalence of such a subgroup of 'carbohydrate-sensitive', type IV hyperlipoproteinemic subjects is unknown, that more research is needed to elucidate if the hypertriglyceridemic effect is due to fructose or sucrose ingestion per se and that the treatment of type IV hyperlipoproteinemic subjects is most often a restriction of carbohydrate and alcohol intake.

### Plasma cholesterol levels

Generally, high carbohydrate, low fat diets have been reported to result in, beside the probably transient increase in plasma triglycerides, a decrease in serum LDL and HDL cholesterol (65,96,98,121). Thompson and coworkers (65) showed that the complexity of the dietary glucose in the diet (10 day period, 50% of carbohydrates provided as glucose, maltose, corn syrup or corn starch) did not affect total serum cholesterol and the LDL/HDL cholesterol ratio. In addition, total plasma cholesterol did not significantly vary as result of a sucrose or corn syrup diet (10 day period both diets carbohydrate was 45 or 65% of total calories). A study of Bosetti and coworkers (107) showed that when normal subjects were fed conventional foods in normal eating patterns there was no difference between the effects of adding moderate amounts of sucrose or fructose (50 to 70 g/ day, 1/3 of carbohydrate) on total triglycerides, total cholesterol, and LDL or HDL cholesterol. The above studies are consistent with several other short term studies showing that when different types of carbohydrates are incorporated in normal eating patterns they do no differ in their effects on total cholesterol, LDL and HDL cholesterol levels (105,122).

In a recently performed study in the Netherlands the effects of a diet according to the Nutrition Council guidelines on several health parameters was evaluated. For this, the subjects received three isoenergetic diets (122). One diet represented the average Dutch diet (23 en % mono- and disaccharides) and in the other diets the content of saturated fat was reduced whereas the content of simple vs complex carbohydrates varied (one diet: complex 38 en%, simple 16 en%, the other diet: complex 38 en%, simple; 26 en%). In this study it was found that restricting saturated fat decreased total and HDL cholesterol levels, irrespective of the amount of simple carbohydrates. However, at the relatively lower simple sugar diet (16 en%) lower apolipoprotein AI (major lipoprotein of HDL) and...
apoprotein A1 levels were found than on the diets containing 23 en% or 26 en% simple carbohydrates. This finding is consistent with data of a study of Piatti and coworkers (68) who found that a simple carbohydrate hypocaloric diet in obese volunteers resulted in a significant increase in serum apolipoprotein A1 (and HDL cholesterol), whereas the opposite was seen with a high complex carbohydrate diet. Since apolipoprotein A1 levels have been reported to be decreased in humans with coronary heart disease (123), the increase of this parameter when a higher proportion of the diet is provided as simple carbohydrates may suggest a beneficial effect of these sugars.

Several studies have been performed investigating the effect of different carbohydrates in hypertriglyceridemic subjects. Reiser and coworkers (124) performed studies in subjects preselected on an exaggerated insulin response to a sucrose load, which have a type IV hyperlipoproteinemia. These studies have shown an adverse effect of sucrose ingestion on total cholesterol, and VLDL, LDL and HDL cholesterol levels. However, as indicated in other sections the fact that in these studies sucrose intake was concentrated in the form of a patty and that diet was provided in the form of a gorging pattern makes interpretation of these findings difficult. Halfrish et al (125) showed that when 12 carbohydrate sensitive men consumed a diet with 60% of calories derived from carbohydrates with graded levels of fructose or wheat starch, plasma cholesterol and LDL cholesterol were observed to be higher after 7.5 and 15% dietary fructose consumption than after a fructose free diet. This effect was also observed in healthy volunteers and suggests that moderate amounts of fructose may have adverse effects on lipid spectrum. However, these data are not consistent with several other studies in hypertriglyceridemic and diabetic subjects (and in normal volunteers, see above, 116,118,119,126).

**TABLE 5.**

Summary of results on the relationship between type of carbohydrate and plasma triglycerides and cholesterol

<table>
<thead>
<tr>
<th>Results</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma triglycerides</strong></td>
<td></td>
</tr>
<tr>
<td>Increase in plasma triglycerides as result of dietary fructose or sucrose in normal, diabetic or hypertriglyceridemic man</td>
<td>10,11,100,111-113,117</td>
</tr>
<tr>
<td>Comparable effects of different types of carbohydrates on plasma triglycerides in normal, hypertriglyceridemic or diabetic man</td>
<td>65, 104-110, 115,116, 118-120</td>
</tr>
<tr>
<td>Decrease in plasma triglycerides with hypocaloric high simple CHO diet and not with high complex CHO diet in obese volunteers</td>
<td>68</td>
</tr>
<tr>
<td><strong>Plasma cholesterol</strong></td>
<td></td>
</tr>
<tr>
<td>Sucrose or fructose ingestion may result in an increase in total cholesterol, and LDL cholesterol and a decrease in HDL cholesterol in normal or hypertriglyceridemic man</td>
<td>124,125</td>
</tr>
<tr>
<td>Different types of carbohydrates do not differ in their effects on total cholesterol, LDL or HDL cholesterol in normal, diabetic or hypertriglyceridemic subjects</td>
<td>65, 105, 107,116,118,119,122</td>
</tr>
<tr>
<td>A high simple CHO, hypocaloric diet results in higher increase in serum apolipoprotein A1 and HDL cholesterol than a high complex CHO diet in obese volunteers</td>
<td>68</td>
</tr>
</tbody>
</table>
In summary, there are no consistent data to indicate that various types of absorbable carbohydrates differ in their effect on serum cholesterol, and LDL and HDL-cholesterol concentrations (for overview see table 5). In several recent studies it has been suggested that the type of the carbohydrate in the diet may be responsible for differences in apo A1 levels with a more beneficial effect of simple carbohydrates. These observations require, however, further research.

CARBOHYDRATES IN THE ETIOLOGY OF HUMAN DISEASE

In this section will be dealt with the effect of the various types of carbohydrates in the etiology of human diseases, in particular diabetes mellitus, obesity and cardiovascular disease. This will be done on basis of the above described chapters on glucose tolerance, energy metabolism and blood lipids in combination with data of several dietary surveys or epidemiological studies.

Diabetes mellitus

Diabetes mellitus frequently occurs in urbanized societies, such as Western countries, and is more rare in developing countries. Non-insulin dependent diabetes mellitus is especially associated with urbanization. Some investigators have suggested that the intake of refined sugars, especially sucrose may be an important etiological factor in the development of diabetes mellitus (13). It has previously been proposed that simple carbohydrates may result in an increased insulin secretion, which would eventually give rise to hyperinsulinemia and diabetes mellitus. As must be clear from the above section on glucose tolerance this hypothesis could not be confirmed in several acute and long term studies. Furthermore, in most epidemiological studies no association could be observed between the intake and sugars or total carbohydrate and increased risk of non-insulin dependent diabetes mellitus, as reviewed elsewhere (8,14). Moreover, in several studies an inverse association between sugar and carbohydrate intake and the prevalence of diabetes mellitus has been observed (8). However, care has to be taken in interpreting this since these associations may be confounded by variables such as obesity and caloric expenditure. In conclusion, there is little evidence to implicate dietary carbohydrates, either simple or complex, in the etiology of diabetes.

Obesity

Obesity, defined as an excessive accumulation of body fat as compared to fat free mass, is one of the major nutritional disorders in the developed world and has been reported to be associated with major health hazards such as coronary heart disease, hypertension, and diabetes mellitus (127). Over a third of the population of many European countries can be considered overweight, also depending on the definition of overweight.

As indicated in the above section on energy metabolism, obesity develops under circumstances of a positive energy balance. In addition, recent evidence indicates that a situation of energy balance within the body can only be achieved in the case of macronutrient balance. Most recent literature indicates a closer regulation of carbohydrate compared to fat balance, and carbohydrates have been reported to have powerful effects on thermogenesis and appetite. Several suggestions on a possible role of simple carbohydrates in the etiology of obesity have been done: they may produce changes in metabolic efficiency, they may stimulate lipogenesis and they may produce changes in appetite and energy intake. As indicated above in the section on energy metabolism, there is no physiological evidence to support a difference in the effects of simple and complex carbohydrates on energy balance and substrate metabolism. These findings are confirmed in several dietary surveys. It has been convincingly shown that an inverse association exists between sugar (and carbohydrate) intake and body mass index and a positive association between fat intake and the degree of body fatness (87-89).
From the above considerations it can be concluded that there is no evidence to support a role for carbohydrates and in particular simple carbohydrates, in the etiology of overweight.

**Cardiovascular disease**

Cardiovascular disease is the leading health problem in most Western countries. It has been shown that food habits and dietary intake are foremost among the factors that influence the risk of coronary heart disease. Variations in the prevalence of coronary heart disease correlated directly with the proportion of calories derived from fat and thus inversely with the proportion of energy derived form carbohydrates. Yudkin (13) compared the per capita sugar consumption in several countries with the mortality from CHD and proposed that sucrose contributes to the occurrence of cardiovascular disease. However, several subsequent studies have failed to substantiate this, as reviewed elsewhere (8).

The pathophysiology of coronary heart disease is complicated and influenced by many interrelated factors. The association between blood lipids and coronary heart disease has been known for some time, so it is possible that diet could influence the disease through its effect on blood lipids (1,2). A change from a Western type of diet to a very high carbohydrate diet (60% of calories from any type of carbohydrate, e.g. simple or complex) has been shown to cause a reduction of HDL, and LDL cholesterol and a possibly transient increase in fasting triglycerides (see section on blood lipids). As indicated in the section on blood lipids there is no consistent evidence for the presumption that different types of carbohydrates consumed in a normal Western diet may differ in their effects on blood lipid spectrum. Furthermore, obesity, hyperinsulinemia, insulin resistance and diabetes have been implicated as risk factors for cardiovascular disease (128) and have all a potential link with eating habits. As described in this review there is no evidence to support an independent relationship between any of these risk factors and the consumption of simple carbohydrates. In addition, as reviewed elsewhere, evidence is lacking for a role of simple carbohydrate consumption in the development of hypertension or atherosclerosis (14).

In summary, it can be concluded that on basis of the above considerations, there is no evidence to implicate an independent role for simple carbohydrates in the etiology of cardiovascular disease. This is consistent with the findings of several prospective epidemiological studies, where men who developed cardiovascular disease had significantly lower carbohydrate intakes (129) or consumed less total carbohydrates, starches and simple carbohydrates than did those without cardiovascular disease (130).

**CONCLUSION**

Previously claims have been made that simple sugars may have adverse effects on several metabolic conditions involved in the etiology of obesity, cardiovascular disease and diabetes mellitus. On basis of the available literature it can be concluded that there is no consistent evidence to implicate differences in simple and complex dietary carbohydrates in the etiology of these human diseases. Moreover, there are indications that simple carbohydrates may have beneficial effects on glucose tolerance and blood lipid spectrum. These findings require, however, further research.

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