The Science of Sugars, Part 3

Sugars and Chronic Disease Risks

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The prevalence of diabetes, obesity, and hypertension in the United States is concerning. The etiologies of these chronic diseases are multifactorial in nature, involving varying genetic, social, and environmental factors. The relationship between food and food ingredients and risk for chronic disease has been particularly questioned. Specifically, scientific investigators have extensively examined the relationship between sugars and health. Consensus to date includes the following: total sugar intake does not cause type 2 diabetes; evidence linking sugar consumption to obesity is inconsistent; and intake of carbohydrates, including sugars, is not considered an independent risk factor for cardiovascular disease. Although more research is needed in some areas, in general, the available data show no direct link between moderate consumption of sugars and serious diseases or obesity. Nutr Today. 2012;00(0):00–00

Almost everyone enjoys sugars and sweets, but many consumers wonder whether consumption of sugars affects health. Part 3 of the series The Science of Sugars explores associations between intake of sugars and obesity and chronic diseases such as diabetes mellitus and cardiovascular disease (CVD). The first article in the series explored the nomenclature of various sugars and the function of sugars in foods. Part 2 examined the association between sugars and indices of dietary quality as well as dietary recommendations for sugar. Recommendations for changing dietary intake of sugars are often based on suggestive but inconclusive data relating sugar consumption and the incidence of chronic disease or obesity. Part 4 will focus on the relationship between sugar intake and dental health as well as the effect of sugar intake on mental performance and behavior.

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DIABETES

The prevalence of diabetes in the United States has been increasing over time, according to an analysis of data from the 2005–2006 National Health and Nutrition Examination Survey (NHANES).[1] Cowie et al[1] report that 13% of adults 20 years or older have diabetes; however, 40% of them have not been diagnosed. Figures from the Centers for Disease Control are similar, stating that 11.3% of adults have diabetes, 27% of whom are undiagnosed.[2] The prevalence of diabetes has risen steeply since 1980, when 3.7% of the population was diagnosed with the disease[3] (Figure). The National Institute of Diabetes and Digestive and Kidney Diseases notes that the risk factors for diabetes include overweight or obesity, genetics, ethnicity (high incidence among Asians, Native Americans, and non-Hispanic blacks), inactivity, family history, and prior gestational diabetes. Research has identified many lifestyle and dietary risk factors that contribute to the development of type 2 diabetes mellitus (T2DM). Obesity has long been recognized as one of the most significant risk factors for this disease. A sedentary lifestyle is also considered a risk factor, with increased physical activity providing a measure of protection.[4] There is general agreement among the scientific community that total sugar intake does not cause T2DM.[5,6] This has been confirmed by several prospective studies,[7–9] including one that shows a negative association between sucrose intake and diabetes risk.[10]

A number of researchers now believe, and some studies indicate, that people who consume diets with a high glycemic index (GI)[11] or glycemic load (GL), which is GI related to the amount of carbohydrate consumed, may be more likely to develop T2DM.[12–14] However, 2 recent large prospective studies found no relationship between dietary GI or GL and risk of developing diabetes.[9,15]

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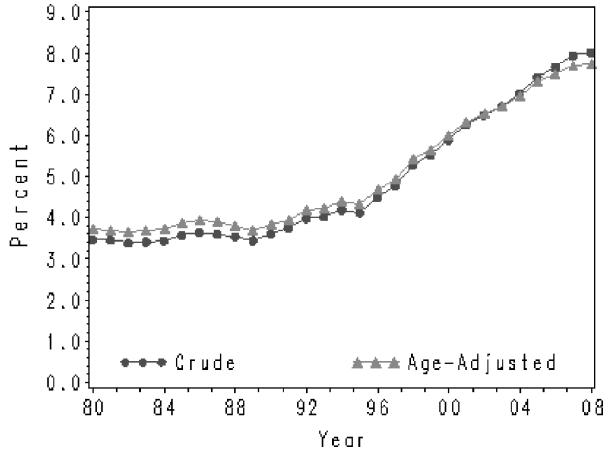

FIGURE. Crude and age-adjusted percentage of civilian, noninstitutionalized adults with diagnosed diabetes in the United States, 1980–2008. Source: Centers for Disease Control and Prevention (http://www.cdc.gov/diabetes/statistics/prev/national/figageadult.htm. Accessed April 16, 2011).

Researchers continue to explore the idea that GI and GL may be useful tools for measuring diabetes risk. Results from 2 large prospective studies, the Nurses' Health Study[14,16] and the Health Professionals' Follow-up Study,[13] showed a positive association between dietary GI and diabetes risk. However, results from the Iowa Women's Health Study[10] did not show a consistent association between the GI and diabetes risk. The American Diabetes Association notes that current information is neither sufficient nor consistent to conclude that low-GI diets reduce risk for diabetes.[17] More recently, the 2010 Dietary Guidelines Advisory Committee (DGAC) report addressed the relationship between GL and T2DM, with the report explicitly concluding, "Strong, convincing evidence shows little association between glycemic load and type 2 diabetes."[18]

Further analysis of the Nurses' Health Study data found that women who increased their consumption of sugar-sweetened beverages (SSBs) from fewer than 1 per week to more than 1 a day over time (1991–1995, 1995–1999) gained more weight and had a higher risk of developing T2DM than did women who maintained a consistent SSB intake.[19] The authors suggest that dramatically increasing the intake of SSBs over time may contribute to obesity and thus indirectly increase diabetes risk. On the other hand, 1.95% of the cohort (1007 nurses) in the Nurses' Health Study II, who changed their SSB consumption from low to high, had more weight gain than did the other groups mentioned above (about 1.5 kg more than the constant-consuming group during the first 4 years and 2 kg more during the second 4 years). The other 1.98% of the cohort (1020 nurses), who changed their SSB consumption from high to low, had less weight gain (about 2 kg less than the constant-consuming groups in each 4-year period). Based on these outcomes from less than 4% of the total study cohort, the authors concluded, "Higher consumption of sugar-sweetened beverages is associated with a greater magnitude of weight gain." However, this conclusion was not reconciled with the data from the 96% of nurses who did not change their dietary beverage pattern.

Van Horn et al[20] cite the same analysis but assert that about half the increase in incidence of T2DM is attributable to consumption of SSBs and above that due to obesity. Body mass index and calorie intake attenuated the positive relationship between SSBs and diabetes[19]; however, the authors cautioned that increasing the intake of sugar-containing beverages could increase the GI of the diet, which may also increase diabetes risk. Because the preponderance of evidence shows that total sugar intake is not related to diabetes risk, it is clear that more research is needed to put these findings into perspective. In addition, women in this study who consumed the highest levels of SSBs tended to be physically less active, smoked more, had higher daily caloric intake, and had lower intake of protein, alcohol, and cereal fiber compared with women in the study who drank sugared soft drinks at a low level (<1 per week).

Laville and Nazare reviewed a variety of studies (intervention, prospective, cross-sectional) on the relationship between sugars, insulin resistance, and diabetes.[21] The studies failed to demonstrate an obvious relationship between sucrose intake and glycemic control or diabetes risk. With regard to fructose, the authors noted discrepancies among studies' conclusions about its long-term effect on diabetes development.

Management of Diabetes

Although sugar is not directly implicated in causing T2DM, investigators have examined the role of dietary sugars in disease management. The challenge is that some studies examine total sugar, whereas others investigate the type or source of sugar or the GI of the diet.

Manders et al[10] compared the effects of consumption of sucrose-containing beverages on lean and obese diabetic and nondiabetic men. They found that moderate consumption (approximately 2 cans per day) did not further increase the prevalence of hyperglycemia in subjects with type 2 diabetes or in normoglycemic lean or obese men. The introduction[11] of the GI in 1981 stimulated a number of studies examining the body's blood glucose response to different carbohydrates and the implications for meal planning for people with diabetes. Research on GI established that sugars do not increase plasma glucose concentrations to a greater extent than do isocaloric amounts of dietary starch. This finding led to the relaxation of previous restrictions and to the current recommendation that moderate amounts of sugars can be safely incorporated in diets for people with diabetes.

With respect to the role of sugars in the nutritional management of diabetes, consensus recommendations do not

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support the widespread use of the GI.[22] The 2010 DGAC stated, "A moderate body of inconsistent evidence supports a relationship between high glycemic index and type 2 diabetes."[18] According to the 2010 European Food Safety Authority Panel on Dietetic Products, Nutrition, and Allergies, the evidence is inconclusive for a relationship of GI and GL with diet-related disease.[23] The American Diabetes Association recommends a balanced diet that includes carbohydrate from fruits, vegetables, whole grains, legumes, and low-fat milk. Monitoring carbohydrate is a key element of glycemic control, and sucrose-containing foods can be substituted for other carbohydrates in the meal plan. Excess energy intake should be avoided.[17]

Although fructose produces a lower postprandial glucose response than sucrose does, the American Diabetes Association does not recommend the use of added fructose as a sweetening agent in the diabetic diet owing to evidence that fructose may adversely affect plasma lipids.[17] Bantle[24] noted that fructose ingestion results in lower circulating insulin and leptin, which might inhibit appetite less than other carbohydrates. However, he added that, as yet, there is no convincing experimental evidence that dietary fructose actually stimulates excess energy intake.

Experimental evidence indicates that fructose reacts with protein molecules to form advanced glycation end-products, which may accelerate the aging process and contribute to complications of diabetes.[25] Schalkwijk et al[26] postulates that although direct evidence is not available, it is likely that fructose, as a highly reactive sugar in the Maillard reaction, promotes the formation of advanced glycation end-products to a greater extent than other reducing sugars do (eg, glucose and lactose). However, a review of fructose and metabolic syndrome and diabetes by Bantle[27] found no evidence that fructose accelerates protein glycation.

Within the context of a dietary pattern that meets caloric and nutrient requirements, moderate intake of sugars may benefit individuals, such as those with diabetes, by increasing satisfaction and improving adherence to prescribed diets.[28–31]

The chemistry of sugar alcohols (polyols) was addressed in part 1 of this series. Sugar alcohols may be beneficial in managing diabetes because no insulin is required for absorption and the slow metabolism of the compounds does not produce spikes in blood sugar. In addition, they have fewer calories (gram for gram) than other carbohydrates. However, sugar alcohols and other products that may be labeled as "sugar-free" do contain carbohydrates and calories and must be accounted for in meal planning for people with diabetes.[32]

OBESITY

It is well accepted that increases in body weight and body fat content occur only when energy intake exceeds energy expenditure. Behind this simple statement is the inescapable fact that obesity is a complex condition with multiple causes, with research providing only partial answers to the obesity puzzle. Increasing prevalence in the United States and other developed countries has led to examination and reexamination of possible dietary habits that may contribute to obesity.

Because sugars are ingredients in many popular foods, it may be logical to suspect that they have a role in contributing to overconsumption and increased body weight. However, some epidemiologic studies find a surprising but clear inverse relationship between sucrose intake and body weight or body mass index (BMI), as well as sucrose intake and total fat intake.[33–35] These studies found that body weight and BMI decrease as the percentage of sugar in the diet increases. Other investigators show a positive relationship between added sugars, particularly SSBs, and BMI.[36,37] The American Heart Association (AHA) noted that the relationship between SSBs and obesity is inconsistent.[38] Similarly, the Institute of Medicine (IOM) found "no clear and consistent association between increased intake of added sugars and BMI." In fact, it was noted that higher intakes of total or added sugars are associated with a lower incidence of obesity.[5] The report states that "a negative correlation between total sugar intake and BMI has been consistently reported for children and adults" and "a negative correlation between added sugar intake and BMI has been observed."

Furthermore, high-sucrose diets are not incompatible with weight loss. In one study, 42 women consumed identical low-fat, low-calorie diets except that one diet was high in sugar (43% of total daily energy intake) and one was high in complex carbohydrates. The 2 groups showed no difference in weight loss, mood, concentration levels, or hunger. Both groups exhibited an equal decrease in blood pressure, percentage of body fat, resting energy expenditure, stress hormone levels, thyroid hormones, and plasma lipids.[39]

The causal relationship between calorically sweetened beverages and obesity is still controversial.

Benton[40] examined the hypothesis that an addiction to sucrose could play a role in obesity and eating disorders. Epidemiologic data show that "although high intake of dietary fat is positively associated with indexes of obesity, high intake of sugar is negatively associated with indexes of obesity." After examining and comparing data from animal and human studies, he concluded: "There is no support from the human literature for the hypothesis that sucrose may be physically addictive or that addiction to sugar plays a role in eating disorders."[40]

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Scientists have also studied the effect of sugars on total food intake, finding that under laboratory conditions, sucrose contributes to satiety and reduces subsequent food intake.[41,42] Anderson and Woodend[41] reported that food intake is reduced when 50 g of sucrose is ingested in drinks 20 to 60 minutes before a meal. Larger amounts prolong satiety as expected.[41] The literature does not address the effects of corn syrups or of high-fructose corn syrup (HFCS) on satiety, but because HFCS is similar in composition to sucrose, Anderson and Woodend noted: "It seems unlikely that there would be a difference in satiety between a beverage containing sucrose and one containing high-fructose corn syrup."

The evidence available to date continues to show no direct connection between total sugar intake and obesity.[43] Nevertheless, nutrition researchers have continued investigating whether sugars might have a role in obesity apart from the caloric contribution. Various possibilities for a connection between sugar intake and obesity have been proposed. Moran[44] reviewed research on the impact of fructose-containing sweeteners on feelings of satiety. Results depended on a variety of factors ranging from how the sweeteners were administered to the timing of hunger measurements. "On balance, the case for fructose being less satiating than glucose or HFCS being less satiating than sucrose is not compelling," he concluded. Melanson et al[45] state that HFCS and sucrose are similar but consider that excessive consumption of pure fructose may be problematic to energy intake regulation. Therefore, short-term studies show no significant differences in satiation and energy intake when HFCS is compared with sucrose.

A review by Dolan[46] found no convincing evidence that ingestion of up to approximately 100 g/d of fructose (the highest level of intake used in studies designed to assess the effect of fructose on blood lipids) instead of glucose or sucrose is associated with an increase in food intake or body weight. Bachman and colleagues[36] reviewed several mechanisms that could explain a possible association between SSBs and obesity, including satiety issues. "Assessing the contributions of one food group (e.g., sweetened beverages) to obesity is a difficult task, because energy balance is likely a function of total caloric intake and total caloric expenditure," they wrote. A number of areas for further research were suggested. Pereira[37] dubbed the evidence to date "equivocal" and called for more high-quality randomized trials on this topic.

Other theories relating SSBs to obesity have to do with the composition of HFCS, the most prevalent sweetener found in soft drinks and other beverage products in the United States. Noting that the rise in obesity has paralleled the increased use of HFCS in beverages and other processed foods, some studies hypothesize that it is the increasing consumption of fructose that is at least partly responsible for the current obesity epidemic.[47] These studies posit that fructose is a less satiating sweetener than sucrose.[47,48]

To study this question, Akhavan and Anderson[49] compared the effects of a variety of sugar solutions on appetite and satiety in 31 subjects. They found no significant differences among 3 test solutions (sucrose, HFCS, and 50% glucose/50% fructose) in effects on satiety. Similarly, Monsivais and colleagues[50] compared the effects of various beverages on appetite suppression and found no difference between sugar-sweetened cola, HFCS-sweetened cola, and 1% milk.

Soenen and Westerterp-Plantenga[51] compared the satiating effects of HFCS and sucrose with that of milk. They found that the energy balance consequences of HFCS-sweetened soft drinks are not different from those of other isoenergetic drinks.

Bantle[27] noted that "although increasing fructose consumption is temporally associated with the increasing worldwide prevalence of obesity, there is little or no evidence proving cause and effect." Use of HFCS is almost entirely limited to the United States, although the epidemic of obesity is a global phenomenon. As several experts have pointed out, it is important to consider that fructose and HFCS are different sweeteners and despite its name, HFCS is not high in fructose. Akhavan and Anderson[49] note that "HFCS is a nutritive sweetener containing an unbound form of the same monosaccharides as sucrose (sugar)." In another study comparing the metabolic effects of sucrose and HFCS, Melanson et al[52] found that "when fructose is consumed in the form of HFCS, the measured metabolic responses do not differ from sucrose in lean women."

Forshee et al[53] also point out that HFCS and sucrose have similar monosaccharide compositions and sweetness values. In an extensive literature review plus original analysis, the researchers found that the ratio of fructose to glucose in the US food supply has not changed appreciably. "It is unclear why HFCS would affect satiety or absorption and metabolism of fructose any differently than would sucrose." They concluded that HFCS does not contribute to overweight and obesity any differently than do other energy sources. However, the group noted the absence of studies on whether HFCS is metabolized differently than sucrose, and they recommended future research in this and several other areas.

After studying current research, the American Medical Association issued a policy statement concluding that "high fructose corn syrup does not appear to contribute more to obesity than other caloric sweeteners."[54] The American Medical Association called for further independent research on the health effects of HFCS and other sweeteners. This reinforces a conclusion highlighted in part 1 of this series that "…high fructose corn syrup and sucrose are similar and one is not 'better or worse' than the other."[55] Citing recent studies, Anderson[56] made the case for putting the HFCS-obesity theory to rest. He noted the

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"multidimensional determinants of obesity" and the generally accepted fact that neither sugar nor carbohydrate consumption has been clearly delineated as a direct cause of obesity. Anderson acknowledges the challenges to address lifestyle factors that create energy imbalance and obesity, but holds that "a reductionist approach that focuses on one food…is unlikely to succeed."

OBESITY AND INSULIN RESISTANCE

McMillan-Price and Brand-Miller[57] propose that insulin resistance is more prevalent now than in the past and that reducing the GI of the carbohydrate portion of the diet would aid fat loss by promoting higher satiety, higher metabolic rate, and increased fat oxidation. Sloth and Astrup[58] respond that the evidence is insufficient to establish that a low-GI diet is more effective than traditional weight loss plans. Because it is difficult to distinguish the effects of GI from other factors that influence satiety, they suggest that future studies focus on individual food factors, such as the effects of whole grains, fiber, energy density, and preparation methods.

Coulston and Johnson[59] note that insulin resistance is a genetic trait characterized by an impaired biological response to insulin. Although many older children and adults who are overweight or obese have insulin resistance, the notion that insulin resistance leads to obesity is unfounded, they state. People with insulin resistance "live a perfectly healthy life unless they overeat and markedly decrease their physical activity."

SUGAR-SWEETENED BEVERAGES

In a secondary analysis of a prospective study of 548 schoolchildren, Ludwig et al[60] examined the association between baseline and the change in consumption of sugar-sweetened drinks, finding that for each additional serving of sugar-sweetened drink consumed, both BMI and frequency of obesity increased. Bray and colleagues[47] proposed that the increased intake of soft drinks and other beverages sweetened with HFCS was at least partially responsible for the current epidemic of obesity. Researchers at the Harvard School of Public Health reviewed more than 30 studies conducted between 1966 and 2005 and found a positive association between greater intakes of SSBs and weight gain and obesity in both children and adults.[61] The authors of these studies acknowledged the multifactorial nature of obesity and that their study results do not establish causality.

Several other studies have produced different results. Forshee and colleagues[62,63] used data from the third NHANES to examine the relative importance of demographics, beverage consumption, physical activity, and sedentary behavior for maintaining a healthy body weight. No statistically significant association between consumption of SSBs and fruit drinks and BMI was found. Television viewing was positively associated with BMI, whereas participation in sports demonstrated a negative association.

In addition, in the largest cross-sectional study to date, Janssen et al[64] looked at intakes of more than 120,000 children and adolescents in 34 countries and found no association between SSB consumption and obesity levels. A further quantitative meta-analysis and qualitative review of longitudinal and randomized controlled trials (RCTs) found the association between sweetened beverage consumption and BMI to be near zero.[65] Research by Sun and Empie[66] also found that frequent versus infrequent consumers of sweetened soft drinks had similar percentage obesity. The cross-sectional study found that higher obesity rates were related to other factors, such as television and computer screen time and high-fat diets. A review by Van Baak and Astrup[67] concludes that although observational studies suggest a possible relationship between consumption of sweetened beverages and body weight, there is currently insufficient supporting evidence from RCTs.

Using dietary recall data from the 2003–2004 NHANES, Wang and colleagues[68] examined the impact of sweetened beverage consumption on calorie intake by estimating the amount of kilocalories that could be replaced by drinking water. They predicted that a significant reduction in total energy intake would occur that would not be offset by a compensatory increase in food or beverage consumption and found that, "Overall, because SSBs represent 35% of all beverage weight consumed, replacing all SSBs among NHANES respondents with water would translate to a net reduction of 235 kcal/d (95% CI, 215 to 255 kcal/d) in total energy intake, on average."

Bleich and colleagues[69] examined trends in SSB consumption by age, race/ethnicity, and weight loss intention and found higher SSB consumption among populations at greater risk for obesity and T2DM.

According to Bremer et al,[70] high levels of SSB consumption and low levels of physical activity are 2 lifestyle behaviors associated with obesity, insulin resistance, and metabolic syndrome. Analyzing NHANES data for a nationally representative sample of US adolescents, the researchers found that low SSB intake and high physical activity levels had the effect of decreasing insulin resistance and triglyceride concentrations and increasing high-density lipoprotein (HDL) cholesterol concentrations. They called for prospective studies of how dietary modifications and exercise patterns may affect the health of pediatric populations.

Science establishing a causal association between SSB consumption and obesity is imperfect. A 2010 systematic review and meta-analysis of 12 RCTs found that "the current evidence does not demonstrate conclusively that nutritively sweetened beverage (NSB) consumption has uniquely contributed to obesity or that reducing NSB consumption will reduce BMI levels in general."[71]

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A longitudinal cohort study of roughly 260 children followed for 18 months to assess the impact of physical activity, screen time, and dietary habits on body weight found no correlation between SSB intake and BMI.[72] Similarly, a randomized trial of 1140 students aged 9 to 12 years focused on determining whether an educational program aimed at discouraging students from drinking SSBs could prevent excess weight gain found, as a general matter, that "[a] statistically significant decrease in the daily consumption of carbonated drinks in the intervention compared to control…was followed by a nonsignificant overall reduction in BMI."[73] These studies suggest that SSBs do not play a unique role in adiposity in children and adolescents. The AHA Nutrition Committee also noted that evidence regarding an association between SSBs and obesity is inconsistent. The committee recommended in 2011 that women limit SSB intake to 450 or less kcal/wk for CVD prevention,[74] although it acknowledged in 2009 that "because overweight and obesity are complex metabolic conditions, it is unlikely that a single food or food group is causal."[38]

The 2010 DGAC report noted mixed results on the topic. Although it concluded that "A moderate body of epidemiologic evidence suggests that greater consumption of sugar-sweetened beverages is associated with increased body weight in adults," it also states that "A moderate body of evidence suggests that under isocaloric controlled conditions, added sugars, including sugar-sweetened beverages, are no more likely to cause weight gain than any other source of energy."[18] In examining existing research on the subject, the DGAC concluded that "RCTs [randomized controlled trials] report that added sugars are not different from other calories in increasing energy intake or body weight. Prospective studies report relationships between SSB and weight gain, but it is not possible to determine if these relationships arise from additional calories, as opposed to added sugars per se. The systematic reviews in this area are also inconsistent, and may be relying on different measures used to determine added sugars intake or intake of SSB."[18]

SATIETY: LIQUIDS VERSUS SOLIDS

Researchers have investigated whether sugar is less satiating in liquid (as a beverage) than in solid form.[41,75] Some investigators hypothesize that liquids may not trigger physiological satiety mechanisms, so the body does not compensate completely for liquid calorie intake. A basic question is whether there is a plausible physiological mechanism to explain the suggested hypothetical difference between calories from liquid sources and calories from solid foods. Almiron-Roig and colleagues[76] noted that some studies found liquids to be less satiating than solids, whereas other studies found the converse. Drewnowski and Bellisle[77] reviewed a variety of studies and concluded that "the notion that liquid calories are not perceived by the body rests on inconclusive evidence." In particular, they cited a number of studies showing that SSBs used as meal replacements in calorie-controlled diets are effective weight loss tools, and, therefore, the claims that liquids have particular obesity-inducing properties are unfounded. Anderson[78] agreed, noting that "the associations between sugars-sweetened beverages and obesity must be viewed as circumstantial because biological plausibility, based on known physiologic mechanisms regulating food intake and energy balance, and short-term experimental studies, does not support cause and effect conclusions."

The hypothesis that solids are more satiating than liquids remains unproven.

The 2010 DGAC concluded that "A limited body of evidence shows conflicting results about whether liquid and solid foods differ in their effects on energy intake and body weight except that liquids in the form of soup may lead to decreased energy intake and body weight." They further note that "Americans are advised to pay attention to the calorie content of the food or beverage consumed, regardless of whether it is a liquid or solid. Calories are the issue in either case."[18]

CARDIOVASCULAR HEALTH

Intake of carbohydrates, including sugars, is not considered an independent risk factor in the etiology of CVD.[5] Dietary advice to help reduce heart disease risk urges intake of fruits and vegetables, whole-grain high-fiber foods, fish, foods prepared with little or no salt, and minimized intake of added sugar.[79] In addition, the AHA focuses on controlling the amount and types of fats in the diet because certain fats increase low-density lipoprotein (LDL) cholesterol in the blood. However, replacing dietary fat with carbohydrates may result in increased blood triglyceride levels, a phenomenon known as carbohydrate-induced hypertriglyceridemia.[80] Short-term studies indicate that diets high in carbohydrates (60% of energy), particularly sugars (>20% of energy), increase serum triglyceride levels and decrease serum HDL cholesterol levels.[81] Longer term studies show that the hypertriglyceridemic effects of high-sugar, high-carbohydrate diets may dissipate with time.[82,83] Moreover, diets that meet recommendations for fiber, saturated fat, and unsaturated fat lessen the effect of sugars on triglycerides.[84]

Nordmann et al[85] pointed out that choosing between a low-fat diet and a low-carbohydrate diet involves weighing potential favorable changes in triglyceride and HDL

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cholesterol against potential unfavorable changes in LDL cholesterol. Parks[80] notes that it is difficult to predict whether carbohydrate-induced hypertriglyceridemia will have negative health consequences because of the concurrent reduction in LDL cholesterol concentration.

Researchers have identified factors, such as abdominal obesity and insulin resistance, that exacerbate the effects of sugars on triglycerides. Increased physical activity and weight reduction can improve insulin resistance and minimize the tendency of high-carbohydrate diets to boost triglyceride levels.[82,86–88]

McCarty[87] suggests that the increased coronary risk associated with elevated triglycerides in Western epidemiology reflects the fact that high triglycerides serve as a marker for insulin resistance syndrome, rather than pointing to an inherent pathogenic role of triglycerides per se. Thus, attention has been focused on metabolic syndrome as a risk factor for cardiovascular and other diseases. Triglyceride levels are more likely to increase in obese individuals with metabolic syndrome who consume a high-sugar diet (29%–34% of energy).[82] However, studies indicate that modest weight loss coupled with a shift to a diet rich in fruits, vegetables, and whole grains prevents a rise in triglyceride levels even when diets are high in sugars.[82,84]

Several investigators have examined the relationship of sugar to blood pressure. Brown et al[89] did a cross-sectional association between blood pressure and SSBs for US and UK adult participants of the Intermap Study. They noted a 1.6–mm Hg rise in systolic pressure and 1.1–mm Hg rise in diastolic pressure among those consuming more than 1 serving per day. Elevated fructose intake has been associated with increases in blood pressure in rodents and dogs; however, extrapolations to usual human intakes of HFCS have not been published.[90]

The AHA statement on added sugars and cardiovascular health states that cross-sectional studies suggest an association between excessive fructose consumption and hypertension.[38] Many questions remain about whether there is a direct relationship between sugar intake and high blood pressure and, if so, whether the relationship exists at usual intakes.

Gao et al[91] analyzed data from the 2001–2002 NHANES on the relationship between the intakes of added sugars and SSBs and serum uric acid concentrations. They found that higher intakes of added sugars or sugar-sweetened drinks were associated with higher serum uric acid concentrations in men but not in women. They noted that hyperuricemia might play a causal role in metabolic syndrome, hypertension, and other chronic diseases and suggested further research to clarify these associations and the observed gender differences.

To date, only 1 study has evaluated the potential relationship between SSBs and CVD risk. Fung et al[92] analyzed data from the Nurses' Health Study to prospectively examine consumption of SSBs and the risk of coronary heart disease (CHD). They found an association between regular consumption of SSBs and a small increased risk of CHD in women. This risk was significantly attenuated after adjustment for other known risk factors.

Short-term studies suggest a link between high consumption of calories from sugars (eg, >20%) and increased triglyceride levels, but hypertriglyceridemic effects of sugars are diminished by diets that meet recommendations for fiber and fats.

The 2010 European Food Safety Authority Panel on Dietetic Products, Nutrition, and Allergies concluded that "Although there is some evidence that high intakes (>20% energy) of sugars may increase serum triglyceride (TG) and cholesterol concentrations, and that >20 to 25% of energy might adversely affect glucose and insulin response, the available data are not sufficient to set an upper limit for (added) sugar intake."[23] Similarly, the IOM concluded that there are insufficient data for setting an upper level for sugars based on increased risk for CHD.[5]

The AHA Nutrition Committee scientific statement on sugars and health reviewed selected studies on sugars and blood pressure. They concluded that increased intake of added sugars might raise blood pressure, but results are inconsistent and chronic effects of a high intake of simple sugars remain uncertain.[38]

It is generally agreed that long-term clinical studies are needed to clarify the relationships among carbohydrates and sugar intake and triglycerides. Uncertainty about the role of type of carbohydrate, type of sugar, or just a specific sugar moiety on cardiovascular health continues to prevail. Some research shows that Americans are consuming more fructose, primarily from sucrose and HFCS, and that fructose per se might adversely affect the heart health of Americans. The increasing consumption of fructose may be related to the obesity problem in the United States and may also be a potential risk factor for CVD.[93,94]

Fructose is metabolized in the liver, in a metabolic pathway that can lead to an increase in serum triglycerides.

Lê and Tappy[95] compared animal and human studies with respect to the metabolic aspects of fructose. In rodents, consuming large amounts of fructose can lead to metabolic syndrome. The researchers found that in humans, fructose consumption increases blood triglycerides in the short-term but does not cause muscle insulin resistance. Further human studies were recommended to delineate the effects of fructose in humans.

Stanhope and Havel[96] conducted a human study in which feeding very high levels of fructose caused an increase in blood triglycerides compared with glucose. Results from

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this and another study by Stanhope et al[97] also indicated that a high-fructose diet decreased insulin sensitivity. Jones[98] commented that such studies "are important to understand the effects of extremes in dietary consumption, but studies that reflect what is commonly consumed are needed to understand the impact of its use."

Teff and colleagues[99] compared the effects of glucose and fructose-sweetened beverages on 17 obese men and women, finding that triglyceride levels increased in all subjects. However, consumption of the fructose-sweetened beverages resulted in a total amount of triglycerides almost 200% higher over a 24-hour period than consumption of the glucose-sweetened beverages. The study used pure fructose, which is not typically used alone as a sweetener. The researchers conclude: "Additional short-term and long-term dose-response studies in both metabolically normal and 'at risk' subjects will be required to determine the amounts of dietary fructose that have adverse effects on lipid metabolism in different populations."

In a comprehensive review, Schaefer et al[100] found that many studies showed no difference in lipid metabolism in either diabetic or normal subjects when comparing glucose or sucrose to fructose. However, in studies in which subjects consumed the highest levels of fructose, triglycerides were elevated, highlighting the need for further studies of dietary fructose at customary intake levels.

Reviewing studies on the dose effects of fructose, Livesey[101] found that the balance of beneficial and adverse metabolic effects of fructose is "difficult to assess." The effects of consuming very high levels of fructose (>100 g/d) can be very different and may be diametrically opposite to effects produced by low (<50 g/d) or moderate (50–100 g/d) consumption.

According to Dolan,[46] a possible reason for inconsistent study results on the effects of fructose on triglycerides is that they are dependent on study population, study design, and/or the amount of fructose administered. The results of their critical evaluation of existing evidence indicate that "fructose does not cause biologically relevant changes in TG or body weight when consumed at levels approaching 95th percentile estimates of intake."[46]

SUMMARY

Sugar consumption has generated significant scientific investigation in the face of rising rates of diabetes, obesity, and hypertension. Investigators have examined the questions of whether sugar causes type 2 diabetes and the effects on glycemic control and insulin resistance for those with the illness. There is no evidence for sugar causing diabetes; diets to control the disease must account for total carbohydrate, not merely the sugar component. No differences have been found between the effects of sucrose or HFCS on diabetes, but pure fructose differs from these sugars and from glucose. More research is needed to better understand the effects of fructose.

Sugar is not an independent risk factor for CVD. Nonetheless, sugar raises blood triglyceride, but not LDL cholesterol, levels. High intakes of fructose may adversely affect lipid profiles, but whether intake at typical levels are of any concern remains to be determined. Dietary advice to limit sugar will depend upon the lipid profile, BMI, and risk of CVD. Consuming added sugars may increase blood pressure, but the results are inconsistent and no conclusions may be drawn.

The etiology of obesity is multifactorial, involving genetic, social, and environmental factors. No single food or ingredient has been shown to cause obesity or excess calorie consumption. In fact, evidence that sugar consumption leads to obesity is inconsistent and parallels diverse studies showing both reduced and enhanced satiating effects. Although there is evidence that SSBs may be less satiating than solid forms of carbohydrate and increasing consumption of such beverages has generated scientific concern, most of the evidence is observational and well-designed intervention trials are lacking.

Thus, the evidence for an effect of sugars on chronic diseases is generally not conclusive and sugars can be a component of a diet that is designed to achieve and maintain normal body weight.

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