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Sugar issues

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Since the first doctor noticed, hundreds of years ago, that the urine of a diabetic patient tasted sweet, it has been common to call the condition the sugar disease, or sugar diabetes, and since nothing was known about physiological chemistry, it was commonly believed that eating too much sugar had to be the cause, since the ability of the body to convert the protein in tissues into sugar wasn't discovered until 1848, by Claude Bernard (who realized that diabetics lost more sugar than they took in). Even though patients continued to pass sugar in their urine until they died, despite the elimination of sugar from their diet, medical policy required that they be restrained to keep them from eating sugar. That prescientific medical belief, that eating sugar causes diabetes, is still held by a very large number, probably the majority, of physicians.

Originally, diabetes was understood to be a wasting disease, but as it became common for doctors to measure glucose, obese people were often found to have hyperglycemia, so the name diabetes has been extended to them, as type 2 diabetes. High blood sugar is often seen along with high blood pressure and obesity in Cushing's syndrome, with excess cortisol, and these features are also used to define the newer metabolic syndrome.

Following the old reasoning about the sugar disease, the newer kind of obese diabetes is commonly blamed on eating too much sugar. Obesity, especially a fat waist, and all its associated health problems, are said by some doctors to be the result of eating too much sugar, especially fructose. (Starch is the only common carbohydrate that contains no fructose.) Obesity is associated not only with diabetes or insulin resistance, but also with atheroslcerosis and heart disease, high blood pressure, generalized inflammation, arthritis, depression, risk of dementia, and cancer.

There is general agreement about the problems commonly associated with obesity, but not about the causes or the way to prevent or cure obesity and the associated conditions.

In an earlier newsletter, I wrote about P. A. Piorry in Paris, in 1864, and Dr. William Budd in England, in 1867, who treated diabetes by adding a large amount of ordinary sugar, sucrose, to the patient's diet. Glucose was known to be the sugar appearing in the diabetics' urine, but sucrose consists of half glucose, and half fructose. In 1874, E. Kulz in Germany reported that diabetics could assimilate fructose better than glucose. In the next decades there were several more reports on the benefits of feeding fructose, including the reduction of glucose in the urine. With the discovery of insulin in 1922, fructose therapy was practically forgotten, until the 1950s when new manufacturing techniques began to make it economical to use.

Its use in diabetic diets became so popular that it became available in health food stores, and was also used in hospitals for intravenous feeding.

However, while fructose was becoming popular, the cholesterol theory of heart disease was being promoted. This was the theory that eating foods containing saturated fat and cholesterol caused heart disease. (My newsletter, Cholesterol, longevity, intelligence, and health, discussed the

development of that theory.)

A Swedish physician and researcher, Uffe Ravnskov, has reviewed the medical arguments for the theory that lipids in the blood are the cause of atherosclerosis and heart disease, and shows that there has never been evidence of causality, something which some people, such as Broda Barnes, understood from the beginning. In the 1950s, an English professor, John Yudkin, didn't accept the idea that eating saturated fat was the cause of high blood levels of triglycerides and cholesterol, but he didn’t question the theory that lipids in the blood caused the circulatory disease. He argued that it was sugar, especially the fructose component of sucrose, rather than dietary fat, that caused the high blood lipids seen in the affluent countries, and consequently the diseases. He was sure it was a specific chemical effect of the fructose, because he argued that the nutrients that were removed in refining white flour and white sugar were insignificant, in the whole diet.

Following the publication of Yudkin's books, and coinciding with increasing promotion of the health benefits of unsaturated vegetable oils, many people were converted to Yudkin's version of the lipid theory of heart disease, i.e., that the "bad lipids" in the blood are the result of eating sugar. This has grown into essentially a cult, in which sugar is believed to act like an intoxicant, forcing people to eat until they become obese, and develop the "metabolic syndrome," and "diabetes," and the many problems that derive from that.

The publicity campaign against "saturated fat" as an ally of cholesterol derived its support from the commercial promotion of the polyunsaturated seed oils as food for humans. Although the early investigators of vitamin E knew that the polyunsaturated oils could cause sterility, and others later found that their use in commercial animal foods could cause brain degeneration, there were a few biologists (mostly associated with George Burr) who believed that this type of fatty acid is an essential nutrient.

George and Mildred Burr had created what they claimed to be a disease in rats caused by the absence of linoleic or linolenic acid in their food. Although well known researchers had previously published evidence that animals on a fat free diet were healthy--even healthier than on a normal diet--Burr and his wife published their contradictory claim without bothering to discuss the conflicting evidence. I haven't seen any instance in which Burr or his followers ever mentioned the conflicting evidence. Although other biologists didn't accept Burr's claims, and several researchers subsequently published contrary results, he later became famous when the seed oil industry wanted scientific-seeming reasons for selling their product as an "essential" food. The fact that eating the polyunsaturated fats could cause the blood cholesterol level to decrease slightly was advertised as a health benefit. Later, when human trials showed that more people on the "heart healthy" diet died of heart disease and cancer, more conventional means of advertising were used instead of human tests.

Burr's experimental diet consisted of purified casein (milk protein) and purified sucrose, supplemented with a vitamin concentrate and some minerals. Several of the B vitamins weren't known at the time, and the mineral mixture lacked zinc, copper, manganese, molybdenum, and selenium. More of the essential nutrients were unknown in his time than in Yudkin's, so his failure to consider the possibility of other nutritional deficiencies affecting health is more understandable.

In 1933, Burr observed that his fat-deficient rats consumed oxygen at an extremely high rate, and even then, the thought didn't occur to him that other nutritional deficiencies might have been involved in the condition he described. Ordinarily, the need for vitamins and minerals corresponds to the rate at which calories are being burned, the metabolic rate. Burr

recalled that the rats on the fat free diet drank more water, and he reasoned that the absence of linoleic or linolenic acid in their skin was allowing water vapor to escape at a high rate. He didn't explain why the saturated fats the rats were synthesizing from sugar didn't serve at least as well as a "vapor barrier"; they are more effective at water-proofing than unsaturated fats, because of their greater hydrophobicity. The condensed and cross-linked keratin protein in skin cells is the main reason for the skin's relatively low permeability. When an animal is burning calories at a higher rate, its sweat glands are more actively maintaining a normal body temperature, cooling by evaporation; the amount of water evaporated is an approximate measure of metabolic rate, and of thyroid function.

In 1936, a man in Burr's lab, William Brown, agreed to eat a similar diet for six months, to see whether the "essential fatty acid deficiency" affected humans as it did rats.

The diet was very similar to the rats', with a large part of the daily 2500 calories being provided at hourly intervals during the day by sugar syrup (flavored with citric acid and anise oil), protein from 4 quarts of special fat-free skimmed milk, a quart of which was made into cottage cheese, the juice of half an orange, and a "biscuit" made with potato starch, baking powder, mineral oil, and salt, with iron, viosterol (vitamin D), and carotene supplemented.

Brown had suffered from weekly migraine headaches since childhood, and his blood pressure was a little high when he began the diet. After six weeks on the diet, his migraines stopped, and never returned. His plasma inorganic phosphorus declined slightly during the experiment (3.43 mg./100 cc. of plasma and 2.64 on the diet, and after six months on a normal diet 4.2 mg.%), and his total serum proteins increased from 6.98 gm.% to 8.06 gm.% on the experimental diet. His leucocyte count was lower on the high sugar diet, but he didn't experience colds or other sickness. On a normal diet, his systolic blood pressure varied from 140 to 150 mm. of mercury, the diastolic, 95 to 100. After a few months on the sugar and milk diet, his blood pressure had lowered to about 130 over 85 to 88. Several months after he returned to a normal diet, his blood pressure rose to the previous level.

On a normal diet, his weight was 152 pounds, and his metabolic rate was from 9% to 12% below normal, but after six months on the diet it had increased to 2% below normal. After three months on the sugar and milk diet, his weight leveled off at 138 pounds. After being on the diet, when he ate 2000 calories of sugar and milk within two hours, his respiratory quotient would exceed 1.0, but on his normal diet his maximum respiratory quotient following those foods was less than 1.0.

The effect of diabetes is to keep the respiratory quotient low, since a respiratory quotient of one corresponds to the oxidation of pure carbohydrate, and extreme diabetics oxidize fat in preference to carbohydrate, and may have a quotient just a little above 0.7. The results of Brown's and Burr's experiments could be interpreted to mean that the polyunsaturated fats not only lower the metabolic rate, but especially interfere with the metabolism of sugars. In other words, they suggest that the normal diet is diabetogenic.

During the six months of the experiment, the unsaturation of Brown's serum lipids decreased. The authors reported that "There was no essential change in the serum cholesterol as a result of the change in diet." However, in November and December, two months before the experiment began, it had been 252 mg.% in two measurements. At the beginning of the test, it was 298, two weeks later, 228, and four months later, 206 mg%. The total quantity of lipids in his blood didn't seem to change much, since the triglycerides increased as the cholesterol decreased.

By the time of Brown's experiment, other researchers had demonstrated that the cholesterol level was increased in hypothyroidism, and decreased as thyroid function, and oxygen consumption, increased. If Burr's team had been reading the medical literature, they would have understood the relation between Brown's increased metabolic rate and decreased cholesterol level. But they did record the facts, which is valuable.

The authors wrote that "The most interesting subjective effect of the 'fat-free' regimen was the definite disappearance of a feeling of fatigue at the end of the day's work."

A lowered metabolic rate and energy production is a common feature of aging and most degenerative diseases. From the beginning of an animal's life, sugars are the primary source of energy, and with maturation and aging there is a shift toward replacing sugar oxidation with fat oxidation. Old people are able to metabolize fat at the same rate as younger people, but their overall metabolic rate is lower, because they are unable to oxidize sugar at the same high rate as young people. Fat people have a similar selectively reduced ability to oxidize sugar.

Stress and starvation lead to a relative reliance on the fats stored in the tissues, and the mobilization of these as circulating free fatty acids contributes to a slowing of metabolism and a shift away from the use of glucose for energy. This is adaptive in the short term, since relatively little glucose is stored in the tissues (as glycogen), and the proteins making up the body would be rapidly consumed for energy, if it were not for the reduced energy demands resulting from the effects of the free fatty acids.

One of the points at which fatty acids suppress the use of glucose is at the point at which it is converted into fructose, in the process of glycolysis. When fructose is available, it can by-pass this barrier to the use of glucose, and continue to provide pyruvic acid for continuing oxidative metabolism, and if the mitochondria themselves aren't providing sufficient energy, it can leave the cell as lactate, allowing continuing glycolytic energy production. In the brain, this can sustain life in an emergency.

Many people lately have been told, as part of a campaign to explain the high incidence of fatty liver degeneration in the US, supposedly resulting from eating too much sugar, that fructose can be metabolized only by the liver. The liver does have the highest capacity for metabolizing fructose, but the other organs do metabolize it.

If fructose can by-pass the fatty acids' inhibition of glucose metabolism, to be oxidized when glucose can't, and if the metabolism of diabetes involves the oxidation of fatty acids instead of glucose, then we would expect there to be less than the normal amount of fructose in the serum of diabetics, although their defining trait is the presence of an increased amount of glucose. According to Osuagwu and Madumere (2008), that is the case. If a fructose deficiency exists in diabetes, then it is appropriate to supplement it in the diet.

Besides being one of the forms of sugar involved in ordinary energy production, interchangeable with glucose, fructose has some special functions, that aren't as well performed by glucose. It is the main sugar involved in reproduction, in the seminal fluid and intrauterine fluid, and in the developing fetus. After these crucial stages of life are past, glucose becomes the primary molecular source of energy, except when the system is under stress. It has been suggested (Jauniaux, et al., 2005) that the predominance of fructose rather than glucose in the embryo's environment helps to maintain ATP and the oxidative state (cellular redox potential) during development in the low-oxygen environment. The placenta turns glucose from the mother's blood into fructose, and the fructose in the mother's blood can pass through into the fetus, and

although glucose can move back from the fetus into the mother's blood, fructose is unable to move in that direction, so a high concentration is maintained in the fluids around the fetus.

The control of the redox potential is sometimes called the "redox signalling system," since it coherently affects all processes and conditions in the cell, including pH and hydrophobicity. For example, when a cell prepares to divide, the balance shifts strongly away from the oxidative condition, with increases in the ratios of NADH to NAD+, of GSH to GSSG, and of lactate to pyruvate. These same shifts occur during most kinds of stress.

In natural stress, decreased availability of oxygen or nutrients is often the key problem, and many poisons can produce similar interference with energy production, for example cyanide or carbon monoxide, which block the use of oxygen, or ethanol, which inhibits the oxidation of sugars, fats, and amino acids (Shelmet, et al., 1988).

When oxygen isn't constantly removing electrons from cells (being chemically reduced by them) those electrons will react elsewhere, creating free radicals (including activated oxygen) and reduced iron, that will create inappropriate chemical reactions (Niknahad, et al., 1995; MacAllister, et al., 2011).

Stresses and poisons of many different types, interfering with the normal flow of electrons to oxygen, produce large amounts of free radicals, which can spread structural and chemical damage, involving all systems of the cell. Ethyl alcohol is a common potentially toxic substance that can have this effect, causing oxidative damage by allowing an excess of electrons to accumulate in the cell, shifting the cells' balance away from the stable oxidized state.

Fructose has been known for many years to accelerate the oxidation of ethanol (by about 80%). Oxygen consumption in the presence of ethanol is increased by fructose more than by glucose (Thieden and Lundquist, 1967). Besides removing the alcohol from the body more quickly, it prevents the oxidative damage, by maintaining or restoring the cell's redox balance, the relatively oxidized state of the NADH/NAD+, lactate/pyruvate, and GSH/GSSH systems. Although glucose has this stabilizing, pro-oxidative function in many situations, this is a general feature of fructose, sometimes allowing it to have the opposite effect of glucose on the cell's redox state. It seems to be largely this generalized shift of the cell's redox state towards oxidation that is behind the ability of a small amount of fructose to catalyze the more rapid oxidation of a large amount of glucose.

Besides protecting against the reductive stresses, fructose can also protect against the oxidative stress of increased hydrogen peroxide (Spasojevic, et al., 2009). Its metabolite, fructose 1,6-bisphosphate, is even more effective as an antioxidant.

Keeping the metabolic rate high has many benefits, including the rapid renewal of cells and their components, such as cholesterol and other lipids, and proteins, which are always susceptible to damage from oxidants, but the high metabolic rate also tends to keep the redox system in the proper balance, reducing the rate of oxidative damage.

Endotoxin absorbed from the intestine is one of the ubiquitous stresses that tends to cause free radical damage. Fructose, probably more than glucose, is protective against damage from endotoxin.

Many stressors cause capillary leakage, allowing albumin and other blood components to enter extracellular spaces or to be lost in the urine, and this is a feature of diabetes, obesity, and a variety of inflammatory and degenerative diseases including Alzheimer's disease (Szekanecz and Koch, 2008; Ujiie, et al., 2003). Although the mechanism isn't understood, fructose supports capillary integrity; fructose feeding for 4 and 8 weeks caused a 56% and 51% reduction in capillary leakage,

respectively (Chakir, et al., 1998; Plante, et al., 2003).

The ability of the mitochondria to oxidize pyruvic acid and glucose is characteristically lost to some degree in cancer. When this oxidation fails, the disturbed redox balance of the cell will usually lead to the cell's death, but if it can survive, this balance favors growth and cell division, rather than differentiated function. This was Otto Warburg's discovery, that was rejected by official medicine for 75 years.

Cancer researchers have become interested in this enzyme system that controls the oxidation of pyruvic acid (and thus sugar) by the mitochondria, since these enzymes are crucially defective in cancer cells (and also in diabetes). The chemical DCA, dichloroacetate, is effective against a variety of cancers, and it acts by reactivating the enzymes that oxidize pyruvic acid. Thyroid hormone, insulin, and fructose also activate these enzymes. These are the enzymes that are inactivated by excessive exposure to fatty acids, and that are involved in the progressive replacement of sugar oxidation by fat oxidation, during stress and aging, and in degenerative diseases; for example, a process that inactivates the energy-producing pyruvate dehydrogenase in Alzheimer's disease has been identified (Ishiguro, 1998). Niacinamide, by lowering free fatty acids and regulating the redox system, supporting sugar oxidation, is useful in the whole spectrum of metabolic degenerative diseases.

A few times in the last 80 years, people (starting with Nasonov) have recognized that the hydrophobicity of a cell changes with its degree of excitation, and with its energy level. Recently, even in non-living physical-chemical systems, hydrophobicity and redox potential have been seen to vary together and to influence each other. Recent work shows how the oxidation of fatty acids contributes to the dissolution of mitochondria (Macchioni, et al., 2010). At first glance it might seem odd that the presence of fatty material could reduce the "fat loving" (lipophilic, equivalent to hydrophobic) property of a cell, but the fat used as fuel is in the form of fatty acids, which are soap-like, and spontaneously introduce "wetness" into the relatively water-resistant cell substance. The presence of fatty acids, impairing the last oxidative stage of respiration, increases the tendency of the mitochondrion to release its cytochrome c into the cell in a reduced form, leading to the apoptotic death of the cell. The oxidized form of the cytochrome is more hydrophobic, and stable.

Burr didn't understand that it was his rats' high sugar diet, freed of the anti-oxidative unsaturated fatty acids, that caused their extremely high metabolic rate, but since that time many experiments have made it clear that it is specifically the fructose component of sucrose that is protective against the antimetabolic fats.

Although Brown, et al., weren't focusing on the biological effects of sugar, their results are important in the history of sugar research because their work was done before the culture had been influenced by the development of the lipid theory of heart disease, and the later idea that fructose is responsible for increasing the blood lipids.

In 1963 and 1964, experiments (Carroll, 1964) showed that the effects of glucose and fructose were radically affected by the type of fat in the diet. Although 0.6% of calories as polyunsaturated fat prevents the appearance of the Mead acid (which is considered to indicate a deficiency of essential fats) the "high fructose" diets consistently add 10% or more corn oil or other highly unsaturated fat to the diet. These large quantities of PUFA aren't necessary to prevent a deficiency, but they are needed to obscure the beneficial effects of fructose.

Many studies have found that sucrose is less fattening than starch or glucose, that is, that more calories can be consumed without gaining weight. During exercise, the addition of fructose to glucose increases the oxidation of carbohydrate by about 50% (Jentjens and Jeukendrup,

2005). In another experiment, rats were fed either sucrose or Coca-Cola and Purina chow, and were allowed to eat as much as they wanted (Bukowiecki, et al, 1983). They consumed 50% more calories without gaining extra weight, relative to the standard diet. Ruzzin, et al. (2005) observed rats given a 10.5% or 35% sucrose solution, or water, and observed that the sucrose increased their energy consumption by about 15% without increasing weight gain. Macor, et al. (1990) found that glucose caused a smaller increase in metabolic rate in obese people than in normal weight people, but that fructose increased their metabolic rate as much as it did that of the normal weight people. Tappy, et al. (1993) saw a similar increase in heat production in obese people, relative to the effect of glucose. Brundin, et al. (1993) compared the effects of glucose and fructose in healthy people, and saw a greater oxygen consumption with fructose, and also an increase in the temperature of the blood, and a greater increase in carbon dioxide production.

These metabolic effects have led several groups to recommend the use of fructose for treating shock, the stress of surgery, or infection (e.g., Adolph, et al., 1995).

The commonly recommended alternative to sugar in the diet is starch, but many studies show that it produces all of the effects that are commonly ascribed to sucrose and fructose, for example hyperglycemia (Villaume, et al., 1984) and increased weight gain. The addition of fructose to glucose "can markedly reduce hyperglycemia during intraportal glucose infusion by increasing net hepatic glucose uptake even when insulin secretion is compromised" (Shiota, et al., 2005). "Fructose appears most effective in those normal individuals who have the poorest glucose tolerance" (Moore, et al., 2000).

Lipid peroxidation is involved in the degenerative diseases, and many publications argue that fructose increases it, despite the fact that it can increase the production of uric acid, which is a major component of our endogenous antioxidant system (e.g., Waring, et al., 2003). When rats were fed for 8 weeks on a diet with 18% fructose and 11% saturated fatty acids, the content of polyunsatured fats in the blood decreased, as they had in the Brown, et al., experiment, and their total antioxidant status was increased (Girard, et al., 2005). When stroke-prone spontaneously hypertensive rats were given 60% fructose, superoxide dismutase in their liver was increased, and the authors suggest that this "may constitute an early protective mechanism" (Brosnan and Carkner, 2008). When people were given a 300 calorie drink containing glucose, or fructose, or orange juice, those receiving the glucose had a large increase in oxidative and inflammatory stress (reactive oxygen species, and NF-kappaB binding), and those changes were absent in those receiving the fructose or orange juice (Ghanim, et al., 2007).

One of the observations in Brown, et al., was that the level of phosphate in the serum decreased during the experimental diet. Several later studies show that fructose increases the excretion of phosphate in the urine, while decreasing the level in the serum. However, a common opinion is that it's only the phosphorylation of fructose, increasing the amount in cells, that causes the decrease in the serum; that could account for the momentary drop in serum phosphate during a fructose load, but--since there is only so much phosphate that can be bound to intracellular fructose--it can't account for the chronic depression of the serum phosphate on a continuing diet of fructose or sucrose.

There are many reasons to think that a slight reduction of serum phosphate would be beneficial. It has been suggested that eating fruit is protective against prostate cancer, by lowering serum phosphate (Kapur, 2000). The aging suppressing gene discovered in 1997, named after the Greek life-promoting goddess Klotho, suppresses the reabsorption of phosphate by the kidney (which is also a function of the parathyroid

hormone), and inhibits the formation of the activated form of vitamin D, opposing the effect of the parathyroid hormone. In the absence of the gene, serum phosphate is high, and the animal ages and dies prematurely. In humans, in recent years a very close association has been has been documented between increased phosphate levels, within the normal range, and increased risk of cardiovascular disease. Serum phosphate is increased in people with osteoporosis (Gallagher, et al., 1980), and various treatments that lower serum phosphate improve bone mineralization, with the retention of calcium phosphate (Ma and Fu, 2010; Batista, et al., 2010; Kelly, et al., 1967; Parfitt, 1965; Kim, et al., 2003).

At high altitude, or when taking a carbonic anhydrase inhibitor, there is more carbon dioxide in the blood, and the serum phosphate is lower; sucrose and fructose increase the respiratory quotient and carbon dioxide production, and this is probably a factor in lowering the serum phosphate.

Fructose affects the body's ability to retain other nutrients, including magnesium, copper, calcium, and other minerals. Comparing diets with 20% of the calories from fructose or from cornstarch, Holbrook, et al. (1989) concluded "The results indicate that dietary fructose enhances mineral balance." Ordinarily, things (such as thyroid and vitamin D) which improve the retention of magnesium and other nutrients are considered good, but the fructose mythology allows researchers to conclude, after finding an increased magnesium balance, with either 4% or 20% of energy from fructose (compared to cornstarch, bread, and rice), "that dietary fructose adversely affects macromineral homeostasis in humans." (Milne and Nielsen, 2000).

Another study compared the effects of a diet with plain water, or water containing 13% glucose, or sucrose, or fructose, or high fructose corn syrup on the properties of rats' bones: Bone mineral density and mineral content, and bone strength, and mineral balance. The largest differences were between animals drinking the glucose and the fructose solutions. The rats getting the glucose had reduced phosphorus in their bones, and more calcium in their urine, than the rats that got fructose. "The results suggested that glucose rather than fructose exerted more deleterious effects on mineral balance and bone" (Tsanzi, et al., 2008).

An older experiment compared two groups with an otherwise well balanced diet, lacking vitamin D, containing either 68% starch or 68% sucrose. A third group got the starch diet, but with added vitamin D. The rats on the vitamin D deficient starch diet had very low levels of calcium in their blood, and the calcium content of their bones was low, exactly what is expected with the vitamin D deficiency. However, the rats on the sucrose diet, also vitamin D deficient, had normal levels of calcium in their blood. The sucrose, unlike the starch, maintained claim homeostasis. A radioactive calcium tracer showed normal uptake by the bone, and also apparently normal bone development, although their bones were lighter than those receiving vitamin D.

People have told me that when they looked for articles on fructose in PubMed they couldn't find anything except articles about its bad effects. There are two reasons for that. PubMed, like the earlier Index Medicus, represents the material in the National Library of Medicine, and is a medical, rather than a scientific, database, and there is a large amount of important research that it ignores. And because of the authoritarian and conformist nature of the medical profession, when a researcher observes something that is contrary to majority opinion, the title of the publication is unlikely to focus on that. In too many articles in medical journals, the title and conclusions positively misrepresent the data reported in the article.

When the idea of "glycemic index" was being popularized by dietitians, it

was already known that starch, consisting of chains of glucose molecules, had a much higher index than fructose and sucrose. The more rapid appearance of glucose in the blood stimulates more insulin, and insulin stimulates fat synthesis, when there is more glucose than can be oxidized immediately. If starch or glucose is eaten at the same time as polyunsaturated fats, which inhibit its oxidation, it will produce more fat. Many animal experiments show this, even when they are intending to show the dangers of fructose and sucrose.

For example (Thresher, et al., 2000), rats were fed diets with 68% carbohydrate, 12% fat (corn oil), and 20% protein. In one group the carbohydrate was starch (cornstarch and maltodextrin, with a glucose equivalence of 10%), and in other groups it was either 68% sucrose, or 34% fructose and 34% glucose, or 34% fructose and 34% starch. (An interesting oddity, fasting triglycerides were highest in the fructose+starch group.)

The weight of their fat pads (epididymal, retroperitoneal, and mesenteric) was greatest in the fructose+starch group, and least in the sucrose group. The starch group's fat was intermediate in weight between those of the sucrose and the fructose+glucose groups.

At the beginning of the experimental diet, the average weight of the animals was 213.1 grams. After five weeks, the animals in the fructose+glucose group gained 164 grams, those in the sucrose group gained 177 grams, and those in the starch group gained 199.2 grams. The animals ate as much of the diet as they wanted, and those in the sucrose group ate the least.

The purpose of their study was to see whether fructose causes "glucose intolerance" and "insulin resistance." Since insulin stimulates appetite (Chance, et al, 1986; Dulloo and Girardier, 1989; Czech, 1988; DiBattista, 1983; Sonoda, 1983; Godbole and York, 1978), and fat synthesis, the reduced food consumption and reduced weight gain show that fructose was protecting against these potentially harmful effects of insulin.

Much of the current concern about the dangers of fructose is focussed on the cornstarch-derived high fructose corn syrup, HFCS. Many studies assume that its composition is nearly all fructose and glucose. However, Wahjudi, et al. (2010) analyzed samples of it before and after hydrolyzing it in acid, to break down other carbohydrates present in it. They found that the carbohydrate content was several times higher than the listed values. "The underestimation of carbohydrate content in beverages may be a contributing factor in the development of obesity in children," and it's especially interesting that so much of it is present in the form of starch-like materials.

Many people are claiming that fructose consumption has increased greatly in the last 30 or 40 years, and that this is responsible for the epidemic of obesity and diabetes. According to the USDA Economic Research Service, the 2007 calorie consumption as flour and cereal products increased 3% from 1970, while added sugar calories decreased 1%. Calories from meats, eggs, and nuts decreased 4%, from dairy foods decreased 3%, and calories from added fats increased 7%. The percentage of calories from fruits and vegetables stayed the same. The average person consumed 603 calories per day more in 2007 than in 1970. If changes in the national diet are responsible for the increase of obesity, diabetes, and the diseases associated with them, then it would seem that the increased consumption of fat and starch is responsible, and that would be consistent with the known effects of starches and polyunsaturated fats.

In monkeys living in the wild, when their diet is mainly fruit, their cortisol is low, and it rises when they eat a diet with less sugar (Behie, et al., 2010). Sucrose consumption lowers ACTH, the main pituitary stress

hormone (Klement, et al., 2009; Ulrich-Lai, et al., 2007), and stress promotes increased sugar and fat consumption (Pecoraro, et al., 2004). If animals' adrenal glands are removed, so that they lack the adrenal steroids, they choose to consume more sucrose (Laugero, et al., 2001). Stress seems to be perceived as a need for sugar. In the absence of sucrose, satisfying this need with starch and fat is more likely to lead to obesity.

The glucocorticoid hormones inhibit the metabolism of sugar. Sugar is essential for brain development and maintenance. The effects of environmental stimulation and deprivation-stress can be detected in the thickness of the brain cortex in as little as 4 days in growing rats (Diamond, et al., 1976). These effects can persist through a lifetime, and are even passed on transgenerationally. Experimental evidence shows that polyunsaturated (omega-3) fats retard fetal brain development, and that sugar promotes it. These facts argue against some of the currently popular ideas of the evolution of the human brain based on ancestral diets of fish or meat, which only matters as far as those anthropological theories are used to argue against fruits and other sugars in the present diet.

Honey has been used therapeutically for thousands of years, and recently there has been some research documenting a variety of uses, including treatment of ulcers and colitis, and other inflammatory conditions. Obesity increases mediators of inflammation, including the C-reactive protein (CRP) and homocysteine. Honey, which contains free fructose and free glucose, lowers CRP and homocysteine, as well as triglycerides, glucose, and cholesterol, while it increased insulin more than sucrose did (Al-Waili, 2004). Hypoglycemia intensifies inflammatory reactions, and insulin can reduce inflammation if sugar is available. Obesity, like diabetes, seems to involve a cellular energy deficiency, resulting from the inability to metabolize sugar.

Sucrose (and sometimes honey) is increasingly being used to reduce pain in newborns, for minor things such as injections (Guala, et al., 2001; Okan, et al., 2007; Anand, et al., 2005; Schoen and Fischell, 1991). It's also effective in adults. It acts by influencing a variety of nerve systems, and also reduces stress. Insulin is probably involved in sugar analgesia, as it is in inflammation, since it promotes entry of endorphins into the brain (Witt, et al., 2000).

An extracellular phosphorylated fructose metabolite, diphosphoglycerate, has an essential regulatory effect in the blood; another fructose metabolite, fructose diphosphate, can reduce mast cell histamine release and protect against oxidative and hypoxic injury and endotoxic shock, and it reduces the expression of the inflammation mediators TNF-alpha, IL-6, nitric oxide synthase, and the activation of NF-kappaB, among other protective effects, and its therapeutic value is known, but its relation to dietary sugars hasn't been investigated.

A daily diet that includes two quarts of milk and a quart of orange juice provides enough fructose and other sugars for general resistance to stress, but larger amounts of fruit juice, honey, or other sugars can protect against increased stress, and can reverse some of the established degenerative conditions.

Refined granulated sugar is extremely pure, but it lacks all of the essential nutrients, so it should be considered as a temporary therapeutic material, or as an occasional substitute when good fruit isn't available, or when available honey is allergenic.

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