

## The Health Implications of Sucrose, High-Fructose Corn Syrup, and Fructose: What Do We Really Know?

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### Abstract

The epidemic of obesity and related metabolic diseases continues to extract an enormous health toll. Multiple potential causes for obesity have been suggested, including increased fat consumption, increased carbohydrate consumption, decreased physical activity, and, most recently, increased fructose consumption. Most literature cited in support of arguments suggesting a link between obesity and fructose consumption is epidemiologic and does not establish cause and effect. The causes of obesity are well-known and involve the overconsumption of calories from all sources. Research employing a pure fructose model distorts the real-world situation of fructose consumption, which predominantly comes from sweeteners containing roughly equal proportions of glucose and fructose. The fructose hypothesis has the potential to distract us from further exploration and amelioration of known causes of obesity. Randomized prospective trials of metabolic consequences of fructose consumption at normal population levels and from sources typically found in the human diet such as sucrose and high-fructose corn syrup are urgently needed.

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### Introduction

The epidemic of obesity and related metabolic diseases continues to extract an enormous health toll around the world. In the United States alone, over 68% of the adult population is now considered to be overweight or obese.<sup>1</sup> The prevalence of adult obesity in the United States has grown at an alarming rate since 1995.<sup>2</sup> Unfortunately, this epidemic is not confined to adults. The prevalence of childhood obesity in the United States has doubled since 1990.<sup>3</sup> The epidemic of obesity is not confined only to the United States. Obesity rates are continuing to rise worldwide, making it a global health challenge.<sup>4</sup>

Obesity has clearly established links to coronary heart disease,<sup>5,6</sup> type 2 diabetes,<sup>7</sup> glucose intolerance,<sup>8</sup> metabolic

syndrome,<sup>9</sup> sleep apnea and other sleep disorders,<sup>10</sup> and many other chronic conditions and diseases. It has been suggested that, unless we get the obesity epidemic under control, many of the public health gains in leading causes of morbidity and mortality such as coronary heart disease achieved since 1990 may be wiped out.<sup>11</sup> Furthermore, the current generation of children in the United States may be the first generation of Americans to have a shorter life expectancy than their parents.<sup>12</sup>

With all this as background, it is not surprising, and entirely appropriate, that the search for underlying causes of obesity has assumed a prominent place in our national health dialogue. Over the years, a variety of potential

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causes for obesity have been suggested, including increased fat consumption,<sup>13</sup> increased carbohydrate consumption,<sup>14</sup> increased consumption of high-fructose corn syrup,<sup>15</sup> genetic and hormonal etiologies,<sup>16</sup> and an inactive lifestyle.<sup>17</sup> The newest potential “culprit” to be blamed for causing obesity is the consumption of fructose.<sup>18</sup> While many arguments have been proffered attempting to link fructose consumption to obesity and related metabolic conditions, what do we really know and what is the quality of the evidence?

## The Perfect Storm for Potential Mischaracterization of Fructose

All the elements are in place to create the potential for the “perfect storm” to mischaracterize the relationship of fructose to obesity. First, obesity is not only a significant health issue, it is also a deeply emotional one for many people. Second, making headway on the complex issue of obesity has been frustratingly difficult—in fact, we appear to be moving steadily in the wrong direction. Third, some research teams have focused their efforts in both human and animals on studies employing consumption of large amounts of pure fructose (rarely consumed in the human diet).<sup>19–25</sup> Further confusion has resulted from the erroneous extrapolation of these results to high-fructose corn syrup, which is a very different ingredient consisting of roughly equal proportions of glucose and fructose as opposed to pure fructose, which, as the name implies, consists of 100% fructose. Fourth, there is a general desire, particularly in the media and public, to seek simple solutions to complex, multifactorial conditions such as obesity. For all these reasons, there has been a tendency, premature in my estimation, to link fructose consumption as a major contributor to obesity and related metabolic conditions.

## Epidemiologic Studies Do Not Establish Cause and Effect

Most of the studies being cited to support the proposed linkages between fructose consumption and obesity and other metabolic conditions employ epidemiologic data that establishes associations rather than cause and effect.<sup>26–29</sup>

Numerous examples exist to demonstrate the dangers of this approach. The recommendation to consume antioxidant supplements to lower the risk of heart disease and cancer was widely followed until prospective studies demonstrated their lack of efficacy.<sup>30</sup> Hormone replacement therapy for postmenopausal women was prescribed by a generation of physicians until the Women’s Health

Initiative demonstrated its lack of efficacy in most segments of this population.<sup>31</sup> A unique linkage between high-fructose corn syrup and obesity postulated by Bray and colleagues<sup>15</sup> in 2004 based on epidemiologic data has now been widely discounted by the scientific community based on prospective data. Major professional groups such as the American Medical Association<sup>32</sup> and the American Dietetic Association<sup>33</sup> have issued statements refuting a unique linkage between high-fructose corn syrup and obesity. An unfortunate aftermath of this saga is that, while the debate on this issue is over in the scientific community, serious misperceptions persist in the public domain and nonrefereed vehicles such as the Internet.

## The Causes of Obesity Are Well-Known

According to the U.S. Department of Agriculture Economic Research Service, there was a *per capita* increase of 24% in the number of calories consumed in the United States between 1970 and 2005.<sup>34</sup> This represents an average *per capita* increase of 605 Kcal/day. An analysis by Swinburn and associates<sup>35</sup> concluded that this caloric increase could entirely account for the increased prevalence of obesity in the United States since 1975. During this period of time, the increase of calories from all fructose-containing sweeteners combined rose by only 52 Kcal/day and, as a percentage of total calories consumed, actually declined.<sup>34</sup> Fructose consumption has declined in the United States since 1999<sup>36</sup> while obesity levels have increased or stayed stable in all population groups.<sup>1</sup> There is widespread agreement in the obesity research community that overconsumption of calories from all sources is the major driving force behind the obesity epidemic.

## Studies on How Pure Fructose May Distort Metabolic Pathways

Studies performed employing a model comparing 25% of calories from either pure fructose or pure glucose (neither found in large quantities in the human diet) suggested differences in energy-regulating hormones such as insulin, leptin, and ghrelin, which could theoretically lead to increased appetite and caloric consumption.<sup>37</sup> However, when these studies were repeated in a laboratory<sup>38</sup> employing the “real-world” comparison of sucrose and high-fructose corn syrup, all differences in insulin, leptin, ghrelin, appetite, and caloric consumption at the next meal disappeared. Other laboratories have generated similar findings.<sup>20,39</sup> It is important to emphasize that sucrose, the leading source

of fructose in the American diet and overwhelmingly the leading source of fructose consumption<sup>40</sup> worldwide, and high-fructose corn syrup, as well as virtually all of the nutritive sweeteners commonly found in the American diet, are combinations of glucose and fructose in roughly equal proportions and are nutritionally interchangeable.

## Summary/Conclusions

While the fructose hypothesis is an interesting one, it poses the danger of distracting us from further exploration and amelioration of the known causes of obesity and related metabolic conditions. It is important to remember that many of the metabolic abnormalities currently being postulated as attributable to fructose consumption may also be ascribed to obesity itself.

The epidemiologic evidence being cited to support metabolic abnormalities related to fructose consumption leaves many questions unanswered. There are compelling data to support excessive caloric consumption as the major dietary driver of obesity. The fructose hypothesis is based largely on epidemiologic data that do not establish cause and effect. All too often, we have been led astray by confusing associations with cause and effect. With the fructose argument, we are in danger of repeating mistakes frequently made in the past by basing judgments on insufficient evidence. Perhaps the American poet and philosopher George Santayana<sup>41</sup> summed up this danger most succinctly when he stated "Those who do not learn from history are doomed to repeat it."

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