Discussions of Obesity in the US and its causes are heard daily

"Obesity, which leads to chronic ailments, such as diabetes and heart disease, was twice as high among boys and three times as high for girls in families whose head of household lacked a degree compared with more educated households"
Bloomberg Business Week (5/17/2012)
What Role Does Sugar(s) Play in Obesity and its Major Health Concern for US Citizens regardless of age.

Mysteries of Carbohydrate
Vast majority of carbohydrates that we consume
Glucose (~85%)
Forms: Simple glucose, ½ of sucrose and lactose, maltose, limit dextrin, large starch molecules
Galactose (0 – 5%) (50% if an infant)
No real natural source as galactose alone
>99% from milk
Disaccharide of glucose and galactose---Lactose
Fructose (~10%)
Free fructose in fruits
Most consumed as
• disaccharide as sucrose
• “high fructose corn syrup”

Primary Carbohydrate Molecules
Monosaccharides

<table>
<thead>
<tr>
<th>Mole Wt</th>
<th>Formula</th>
<th>Sweetness</th>
<th>Calories/gm</th>
</tr>
</thead>
<tbody>
<tr>
<td>180</td>
<td>C₆H₁₂O₆</td>
<td>74</td>
<td>4</td>
</tr>
<tr>
<td>180</td>
<td>C₆H₁₂O₆</td>
<td>173</td>
<td>4</td>
</tr>
<tr>
<td>180</td>
<td>C₆H₁₂O₆</td>
<td>33</td>
<td>4</td>
</tr>
</tbody>
</table>
**Similar Molecules BUT not the Same**

Same Molecular Weight
Same number of Carbon, Hydrogen and Oxygen atoms

**Disaccharides**

<table>
<thead>
<tr>
<th></th>
<th>Sweetness</th>
<th>Calories/gm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maltose</td>
<td>33</td>
<td>4</td>
</tr>
<tr>
<td>Sucrose</td>
<td>100</td>
<td>4</td>
</tr>
<tr>
<td>Lactose</td>
<td>33</td>
<td>4</td>
</tr>
</tbody>
</table>

**Polysaccharides**

Starch: Corn, wheat, rice and glycogen

- Maltodextrin
- Dextrin
Sucrose vs High Fructose Corn Syrup

Sucrose (Disaccharide of glucose and fructose)
- 50% fructose 50% Glucose

High Fructose Corn Sweeteners (mixture of monosaccharides of glucose & fructose)
- Corn starch
- Hydrolysed to glucose (Corn Syrup)
- Enzymatically treated
  - HFCS 55 55% fructose 42% glucose (soft drink)
  - HFCS 42 42% fructose 53% glucose (drinks & processed food)
  - HFCS 90 90% fructose 10% glucose (special applications)

Digestion of CHO

- Mastication
- Salivary Amylase
- Pancreatic Amylase
- Disaccharidases
- Bacterial digestion
- Osmotic effects
- Gas formation
- Gastric acid inhibits amylase

Carbohydrate Absorption

- Normally
  - All Carbohydrates are absorbed as monosaccharides
  - Enterocytes & the blood draining the gut only see
    - Glucose
    - Galactose
    - Fructose
- With damaged intestine
  - (severe diarrhea, Crohn’s disease or ulcerative colitis)
  - Disaccharides can be absorbed
  - They are toxic to the kidney
  - Dissacharidase deficiency
  - Gas & bloating
  - Osmotic diarrhea
Simple Sugars absorbed via Portal Vein

Hepatic Metabolism of Carbohydrates

Glucose

- Liver
- Glycogen
- Glucose
- Insulin
- Tissue Metabolism
- Lactate
- Triose Phosphates
- TCA Cycle
- Glycogen
- Fructose
- Lactate
- Triglycerides

Portal Blood
Peripheral Blood
Hepatic Metabolism of Carbohydrates

So How Much Fructose Do We Consume

<table>
<thead>
<tr>
<th>Source</th>
<th>% Kcal</th>
<th>g/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHANES 1999-2004</td>
<td>9</td>
<td>49</td>
</tr>
<tr>
<td>Populations Mean*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subpopulation means</td>
<td>7-12</td>
<td>32-75</td>
</tr>
<tr>
<td>90th %tile</td>
<td>11-16</td>
<td>52-117</td>
</tr>
<tr>
<td>95th %tile</td>
<td>13-18</td>
<td>60-134</td>
</tr>
</tbody>
</table>

*2148 Kcal/day

1. 12 oz soft drink contains 40 gm of "sugar" or 20 gm of fructose
2. 12 oz soft drink would be the 60 to 120 gm of fructose but total Kcals 480 to 960 Kcal

Inherent Difficulties in Measuring Eating Behaviors of Human

Compliance with the dietary intervention is transient:
  - Interest in the study
  - Duration of the study
  - But mostly how much they might be paid to participate

Long term studies dietary changes will be small

Fidelity to study design is inverse to the duration

Dietary recall methodology is severely flawed
Concerned about Fructose:

Fructose Ingestion → ↑ Serum Lipids
Fructose Ingestion → ↑ Body Weight
Fructose Ingestion → ↑ Uric Acid
Fructose Ingestion → ↑ Glycemia
Fructose Ingestion → ↑ Blood Pressure

Meta Analysis or Systematic Review

Meaningful Extrapolations are difficult from any single study

Identify all potential publications & collectively analyze the results

Methods section describes
- How all relevant trials were found & included or excluded
- Assessing: a) the validity of found trials and b) were the results consistent from study to study

Example of a Meta Analysis Result
Effects of Fructose on Plasma Lipids

Screened: 1251
Isocaloric trials: 30 trials, N=549
Hypercaloric trials: 7 trials, N=127

Isocaloric diets in T2DM or non-diabetics:
No effect on TAG, TC, LDL-C, HDL-C

Hypercaloric
Hypercaloric fructose feeding (+18-35%E) at extreme doses (median dose = +182-g/d) CAUSED increased TG (0.32 mM)

Excess energy
May be a more important consideration than substrate
Majority of the trials were <12-weeks and of poor quality.
Need for larger, longer & higher quality trials and at "real world" doses

Effects of Fructose on Weight & Glycemia

Body Weight (Sievenpiper Ann Intern Med, 2012; 156:291)
Screened: 1984
Isocaloric trials: 31 trials, N=635
Hypercaloric trials: 10 trials, N=119
Isocaloric fructose did not increased body weight
Hypercaloric fructose (+18-97%E) (104-250g/d) increase body weight by ~0.330-kg over 12 weeks.

Glycemia (Cozma et al. Diabetes Care, submitted)
Screened: 4312
Isocaloric trials: 18 trials, N=209
Isocaloric exchange of fructose for other carbohydrate (median dose: 62-g/d [25-120-g/d]) improved longterm glycemic control in people with diabetes

Effects of Fructose on Blood Pressure & Uric acid

Blood Pressure (Ha et al. Hypertension, 2012;59:787-95)
Screened: 316
Isocaloric trials: 13 trials, N=352
Hypercaloric trials: 2 trials, n=24
No evidence for a BP effect of added fructose in either isocaloric or hypercaloric diets

Uric Acid (Yang et al. J Nutr, 2012 May;142:916-23)
Screened: 375
Isocaloric trials: 18 trials, N=390
Hypercaloric trials: 3 trials, N=35
Isocaloric exchange of fructose for other carbohydrate
No Effect
Hypercaloric exchange (+35%E)
Increased uric acid (+30-µmol/L) raising Extreme doses of fructose (213-220g/d)
New Stories about the dangers of Fructose

There are no scientifically valid or reproduced results in humans that would support any of these communications. Should there be dietary intake guidelines or not?? The rare syst... My Answer is NO.

Examine carefully the source information and make your own conclusions.

Summary and Conclusions

Simple sugars (including fructose) consumed in reasonable dietary amounts (in an isocaloric diet) have no adverse affects on human health.

Chronic consumption of increased fructose content in the presence of excess to caloric intake contributes to:
- Weight gain
- Hypertriglyceridemia
- Hyperuricemia

Consumption of excess fructose with or without excess calories has little effect on BP or Glycemia.

Disclosures

Advisory Board for the Patton Medical Devices
Scientific Advisory Committee for Xeris Pharmaceuticals, Inc (Glucagon Rescue Pen) Daiichi-Sankyo Pharmaceuticals (Cialisovelam)
Medical Advisory Committee Merck Pharmaceuticals (Sitagliptin)
Data Safety Committee Meyer Squibb (Saxagliptin for pediatrics)
Consultant Kellog Company on healthy eating Corn Growers Association on high fructose corn syrup

None relevant to the substance of this discussion.
"It is the position of the Academy of Nutrition and Dietetics that consumers can safely enjoy a range of nutritive sweeteners and nonnutritive sweeteners (NNS) when consumed within an eating plan that is guided by current federal nutrition recommendations, such as the Dietary Guidelines for Americans and the Dietary Reference Intakes, as well as individual health goals and personal preference."

Nutritive sweeteners are those that provide calories. Nutritive sweeteners include sucrose, high fructose corn syrup, corn syrup, honey, fructose, molasses, and sugar alcohols.
ARE WE MINING, TORTURING, OR IGNORING THE DATA ON ADDED SUGARS?

Intake of Added Sugars in the U.S.

**Added Sugar Overall Results**

- 87% of the U.S. population: added sugars intake >0<25%
- 6.6% of the population: added sugars intake >25%<30% = 160 mean gram-equivalents (g-eq)
- 3% in each of >30<35% and >35% added sugar groups
- Only approximately 13% of the population with added sugars intakes > 25% of total energy
- Majority of individuals had an estimated added sugars intake >5<20% = 2,063 kcal to 2,138 kcal OR 45 to 92 (g-eq) added sugars/d (11-23 tsp) (total energy controlled in analysis)


Consumption of Added Sugars is Decreasing in the United States

* Linear trends for all subjects > 35y


Barclay AW, Brand-Miller J. The Australian paradox: a substantial decline in sugars intake over the same timeframe that overweight and obesity have increased. Nutrients. 2011 Apr;3:491-504.
2000 remains a popular—but—wrong endpoint in justifications

<table>
<thead>
<tr>
<th>Added Sources</th>
<th>Mean Total (% of DI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk and milk products</td>
<td>8.6</td>
</tr>
<tr>
<td>Grains and cereals</td>
<td>20.3</td>
</tr>
<tr>
<td>Nondairy beverages</td>
<td>12.1</td>
</tr>
<tr>
<td>Nonalcoholic beverages</td>
<td>54.3</td>
</tr>
<tr>
<td>Naturally occurring fructose</td>
<td></td>
</tr>
<tr>
<td>Grains and cereals</td>
<td>3.4</td>
</tr>
<tr>
<td>Fruits and fruit products</td>
<td>72.5</td>
</tr>
<tr>
<td>Vegetables and vegetable products</td>
<td>10.6</td>
</tr>
<tr>
<td>Sugars and sweets</td>
<td>12.1</td>
</tr>
<tr>
<td>Nonalcoholic beverages</td>
<td>6.6</td>
</tr>
<tr>
<td>Alcoholic beverages</td>
<td>3.8</td>
</tr>
<tr>
<td>Total fructose</td>
<td></td>
</tr>
<tr>
<td>Milk and milk products</td>
<td>7.1</td>
</tr>
<tr>
<td>Grains and cereals</td>
<td>17.3</td>
</tr>
<tr>
<td>Fruits and fruit products</td>
<td>13.4</td>
</tr>
<tr>
<td>Vegetables and vegetable products</td>
<td>2.7</td>
</tr>
<tr>
<td>Sugars and sweets</td>
<td>10.3</td>
</tr>
<tr>
<td>Nonalcoholic beverages</td>
<td>46.0</td>
</tr>
</tbody>
</table>

Table shows the percentage of fructose intake contributed by each food group, for each category of fructose. Food groups were defined according to the first or 2 digits of the USDA food code. Twelve USDA food groups were examined. Food groups listed under each category of fructose accounted for at least 3% of fructose intake for at least 1 age group.

2 The analysis excluded pregnant and lactating women and infants.

3 The gender and age groups presented here were used by the comparison study (2) and are the age groups used in the 9th edition of the Recommended Dietary Allowances (16) with the exception that we did not include children less than 1 year of age. This information is also presented for the Dietary Reference Intake gender/age groups (26) in Supplemental Table 6.

4 Source: NHANES 1999–2004 24-h dietary recall. Estimates are based on a single dietary recall per person.

Review Articles
Sweetened Beverages and Weight Status

Strong Evidence 1, 2


Inconclusive Evidence 3, 4

Review Articles
Sweetened Beverages and Weight Status

Where is the weight of the evidence?

THE HEALTH BEHAVIOR IN SCHOOL-AGED CHILDREN OBESITY WORKING GROUP.
COMPARISON OF OVERWEIGHT AND OBESITY PREVALENCE IN SCHOOL-AGED YOUTH FROM 34 COUNTRIES AND THEIR RELATIONSHIPS WITH PHYSICAL ACTIVITY AND DIETARY PATTERNS.
To present and compare prevalence of overweight and obesity in school-aged youth from 34 countries.

To examine associations between overweight and selected dietary patterns of 137,593 youth (2001-2002).

Conclusion

Overweight status was not associated with the intake of fruits, vegetables and soft drinks.

Reasons for Discrepancies

- Insufficient long-term interventions.
- Differing definitions of SSB*.
- Differing units for serving size and frequency.
- Unreliable methods for dietary assessment.
- Narrow focus on SSB with inadequate assessment of other diet components or energy.
- Weight and height self-reported, not measured.
- Poor or no measurement of physical activity.
- Inadequate exploration of confounders or effect modifiers in analysis (for example, baseline BMI, ethnicity, baseline diet, misreporting).
- Multi-collinearity in the diet.
- Inconsistent evidence between subgroups.
- Underpowered studies, no conclusions can be drawn.
- Possibility of publication bias towards positive studies.


* SSB = Sugar-sweetened Beverages

Relationship between Added Sugars and BMI Z-Score and Weight Categories: Adolescents 12-15 Years

<table>
<thead>
<tr>
<th>BMI Z-SCORE</th>
<th>WEIGHT CATEGORIES</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="BMI Z-score graph" /></td>
<td><img src="image2" alt="Weight categories graph" /></td>
</tr>
</tbody>
</table>

Notes: BMI = Body Mass Index; SSB = Sugar-sweetened Beverages; NHANES = National Health and Nutrition Examination Survey.
Relationship between soft drinks and BMI is not simple. Some who consume no soft drinks have very high BMI, some who consume a lot of soft drinks have low BMI.

Added Sugars Explains Virtually None of the Variance in Adolescents' BMI Z- Scores

Variance of Children’s BMI Explained by Regression Model
No Simple Answer to the Obesity Epidemic

- Food Industry
- Candy
- Genes
- Soft Drinks
- Pouring Contracts
- Junk Food
- Restaurants
- Fast Food
- Working Mothers
- Poverty
- Computers
- Poor Parenting
- School Feeding
- Decreased PE in Schools
- Energy Density
- Decreasing Physical Activity
- TV

Family

- Age
- Gender
- Income
- Education
- Parents' education
- Weight
- Height
- Family composition
- Poverty
- Household income
- School curriculum
- Time

Food Choice

- Fat
- Calories (fast foods)
- Quantity

Food Preparation

- Shiite Tiki

Activity

- Physical activity
- TV
- Video/computer
- Video games
- Walking
- School
- Uniforms
- Safety perceived risk

“SINCE OBESITY IS COMPLEX AND INVOLVES GENETICS, DIET AND LIFESTYLE, IT IS VITAL TO MAINTAIN AN INTEGRATED PERSPECTIVE ON ALL THE INFLUENCES (AND INTERACTIONS) RELEVANT TO WEIGHT GAIN.”

“One can hypothesize that the association between eating patterns and overweight status is not a result of a single eating pattern but from a combination of eating patterns that are interrelated and cumulative in their effect on overweight status.”


“If you eat more of one thing, you eat a lot less of something else. So for every theory saying this disease is caused by an excess in x, you can produce an alternative theory saying it’s a deficiency in y.”

~ Hugh Tunstall Pedoe

Should we be making policy recommendations based on……

- Intuition versus science
- Inconsistent findings
- Lack of consensus from systematic reviews
- Amount of variance explained in BMI is less than 1% for diet
“If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health.”

Hippocrates 460-377 BCE

The Energy Balance Equation

Dietary Intake – Energy Expenditure = Stores

(What you got – What you spent = What’s left)

Disclosures

- Egg Nutrition Board
- Juice Products Association
- Kellogg’s
- Kraft
- MARS
- National Cattlemen’s and Beef Association
- National Dairy Council
- National Institutes of Health
- Nutrition Impact (National Confectioners Association, International Tree Nut Council, Florida Citrus)
- The Sugar Association
- United States Department of Agriculture
Thank You!!!!