Industrialized Food Components and Obesity Risk

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Department of Pathology
Overview

- Role of science in policy development
- Components versus calories
- Past lessons (trans fat)
- Present issue (added sugars)
- Future challenges (??)
Public Health Models
Obese Primates
Obese Primates

Schmidt et al., Int J Obesity 2017
Study Goals

The problem with cohort studies of people:
• Conflicting evidence
• Need to evaluate effects that are independent of variability in body weight.

Our objectives:
• Evaluate the effect of dietary ingredients on health in the absence of weight gain
Individual Determinants of Obesity

• **Nutrition**
• **Behavior**
• **Environment**
• **Genes**
Individual Determinants of Obesity

- Nutrition
- Behavior
- Environment
- Genes

*Jorgensen and Kavanagh, unpublished data*
Individual Determinants of Obesity

- Nutrition
- Behavior
- Environment
- Genes

Althoff et al., Nature 2017
Individual Determinants of Obesity

- Nutrition
- Behavior
- Environment
- Genes
Nutritional history
Industrialization of food

1985

1995

2005

2014

CDC March 2018  Wake Forest Baptist Medical Center
The obesity epidemic

- ≈5% obesity before 1960
- Fast food industry uses trans-fat 1985
- High Fructose Corn syrup process derived and implemented 1975-85
- Trans fat GRAS revoked 2015
**Trans Fatty Acids**

Sources of TFAs:

- **Natural sources**
  - milk, butter, beef fat
- **Made from industrial processing:**
  - margarine, shortenings, and frying fat
Trans Fatty Acids

Shortening Use (High Source of Trans Fats)
US Per Capita Relative to 1909

Year

Animal products 21%
Candy 4%
Breakfast cereal 1%
Salad dressing 3%
Household shortening 4%
Potato chips, corn chips, popcorn 5%
Fried potatoes 8%
Margarine 17%
Cakes, cookies, crackers, pies, bread, etc 40%

Wake Forest Baptist Medical Center
Calorie controlled *Trans* fat intake

Kavanagh et al, *Obesity* 2007
Body Fat Distribution

Kavanagh et al, Obesity 2007
Body Fat Distribution

Kavanagh et al, Obesity 2007
Vulnerable periods

- **Pregnancy**
  - Gp 1: CIS
  - Gp 2: TRANS
  - Gp 3: CIS
  - Gp 4: TRANS

- **Lactation**
  - CIS

- **Adulthood**
  - CIS

**Graphs**

- % of Baseline Glucose

- Kavanagh et al, Nutr Res 2010
Controversy

<table>
<thead>
<tr>
<th>Fatty Acid Intake</th>
<th>Studies, n</th>
<th>Participants, n</th>
<th>Events, n</th>
<th>RR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total saturated fatty acids</td>
<td>20</td>
<td>276,763</td>
<td>10,155</td>
<td>1.03 (0.98–1.07)</td>
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<tr>
<td>Total monounsaturated fatty acids</td>
<td>9</td>
<td>144,219</td>
<td>6,031</td>
<td>1.00 (0.91–1.10)</td>
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<tr>
<td>Total n-3 fatty acids</td>
<td>7</td>
<td>157,258</td>
<td>7,431</td>
<td>0.99 (0.86–1.14)</td>
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<tr>
<td>α-Linolenic</td>
<td>16</td>
<td>422,786</td>
<td>9,089</td>
<td>0.87 (0.78–0.97)</td>
</tr>
<tr>
<td>Total long-chain n-3</td>
<td>8</td>
<td>206,376</td>
<td>8,155</td>
<td>0.98 (0.90–1.06)</td>
</tr>
<tr>
<td>Total n-6 fatty acids</td>
<td>5</td>
<td>155,270</td>
<td>4,662</td>
<td>1.16 (1.06–1.27)</td>
</tr>
</tbody>
</table>

Trans fat intake (% energy) for adults ≥20 years (2016)

RR (95% CI) Comparing Top vs. Bottom Thirds of Baseline Dietary Fatty Acid Intake

Chowdhury 2014, Ann Intern Med
Micha 2014, BMJ
Lessons learned from Trans-fat

• A natural product mimicked by industrialization
• Naïve motivation for development and dissemination
• Science converged 1996-2007 to document health effects
• Labeling required in 2003
• Safe status revoked in 2015
• WHO recommends global elimination by 2023
• A 20 year timeline
Fructose
Should we really be worried?
Fructose

- Syrup, made from corn – easy to use and make
- Intake is about 8-15% of total calories, 75% of products have added sugar
- Encouraged by farm subsidies for corn
- Currently supplies nearly half of the sweeteners in our diet

Duffey and Popkin, 2008 Am J Clin Nutr
Fructose controversy

- Is it the ingredient or just the excess calories?

Van Horn L et al. Circulation 2010
Fructose Is Biologically Different

- Small intestine has a limited capacity for uptake
- Energy, insulin and sodium independent
- Does not stimulate insulin release
- Increases liver glucose output
Sugar Industry and Coronary Heart Disease Research: A Historical Analysis of Internal Industry Documents

Cristin E. Kearns, DDS, MBA; Laura A. Schmidt, PhD, MSW, MPH; Stanton A. Glantz, PhD

Early warning signals of the coronary heart disease (CHD) risk of sugar (sucrose) emerged in the 1950s. We examined Sugar Research Foundation (SRF) internal documents, historical reports, and statements relevant to early debates about the dietary causes of CHD and assembled findings chronologically into a narrative case study. The SRF sponsored its first CHD research project in 1965, a literature review published in the *New England Journal of Medicine*, which singled out fat and cholesterol as the dietary causes of CHD and downplayed evidence that sucrose consumption was also a risk factor. The SRF set the review’s objective, contributed articles for inclusion, and received drafts. The SRF’s funding and role was not disclosed. Together with other recent analyses of sugar industry documents, our findings suggest the industry sponsored a research program in the 1960s and 1970s that successfully cast doubt about the hazards of sucrose while promoting fat as the dietary culprit in CHD. Policymaking committees should consider giving less weight to food industry-funded studies and include mechanistic and animal studies as well as studies appraising the effect of added sugars on multiple CHD biomarkers and disease development.

Published online September 12, 2016. Corrected on October 3, 2016.
Fructose in Monkeys

- High fructose diets fed for < 7yrs
- 15% develop Type 2 diabetes after a median of 3.7 years
- 55% less calories fed to maintain weight stability

<table>
<thead>
<tr>
<th></th>
<th>High Fructose % of calories in diet</th>
<th>Control % of calories in diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHO</td>
<td>69</td>
<td>69</td>
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<tr>
<td>Sucrose</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>Fructose</td>
<td>24</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Fat</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Protein</td>
<td>14</td>
<td>18</td>
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</table>
# Liver Injury With Fructose

## Calories fed to maintain weight stability

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6-weeks</th>
<th>% Change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>62</td>
<td>71</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>High Fructose</td>
<td>75</td>
<td>286</td>
<td><strong>281%</strong></td>
<td>0.006</td>
</tr>
<tr>
<td><strong>ALP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>99</td>
<td>99</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>High Fructose</td>
<td>91</td>
<td>149</td>
<td><strong>64%</strong></td>
<td>0.002</td>
</tr>
<tr>
<td><strong>GGT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>37</td>
<td>32</td>
<td>-14%</td>
<td></td>
</tr>
<tr>
<td>High Fructose</td>
<td>36</td>
<td>84</td>
<td><strong>133%</strong></td>
<td>0.0002</td>
</tr>
</tbody>
</table>

*Kavanagh et al, 2013 Am J Clin Nutr*
Liver Injury With Fructose

Kavanagh et al, 2013 Am J Clin Nutr
Intestinal bacterial circulate with fructose diets

Portal sampling for bacteria was 31% higher with high fructose feeding

*Kavanagh et al, 2013 Am J Clin Nutr*
Fecal Bacterial Analysis

No differences – BUT it was only 6 weeks

Kavanagh et al, 2013 Am J Clin Nutr
Fructose → fat AND fibrosis

\[ fructose \rightarrow \text{fat AND fibrosis} \]

\begin{align*}
\text{Steatosis Score} & \quad (\log \text{# lipid droplets}) \\
\text{Fibrosis Score} & \quad (\text{# area collagen}) \\
\end{align*}

\[ r=0.68, \ p<0.001 \]

\[ r=0.48, \ p=0.02 \]

\[ r=0.68, \ p<0.001 \]

\textit{Cydylo..Kavanagh, Obesity 2017}
Why does the liver matter?

Naukkarinen et al, 2015 Diabetologia
Take home message…

- Trans-fat makes you abdominally obese and insulin resistant
- Fructose induces microbial translocation (inflammation) and promotes fatty/fibrotic liver
- Neither ingredient is ‘necessary’
Science and the fructose environment

• Added sugars labeling is under debate
• Public pressure needs to continue
• No forecast GRAS status on fructose-syrups
• The science is clear but only really implicated fructose 1990 onwards
The future

Many things... but
Dietary Emulsifiers

- Theme - not a required ingredient
- Carboxymethocellulose and polysorbate-80
- FDA safe, used < 2% by weight in food products as a stabilizer
- Used in packaged, ready to eat foods, beverages

Cani and Everard, Trends Endocrinol Metab 2015
Chassaing et al. Nature 2015
“Emulsification” of the intestinal surface

- Replicates what is seen in older adults and those with increased risk for colon cancer
“Emulsification” of the intestinal surface

- Graph: Comparison of Fasting Glucose (mg/dL) between different diets (Old - Chow Diet, Old - Western Diet, Young - Western Diet) at Baseline and 8-Week. Significant difference marked with * (p=0.03).

- Sub-graph: Scatter plot showing the correlation between Ln Mucosal 16s Gene Count (AU) and Goblet Cells (#/100 μm) with a correlation coefficient of r=-0.46, p<0.05.
Please ask questions and
THANK YOU for your interest and support