Childhood Obesity: Novel Treatment for an Emerging Public Health Crisis

David S. Ludwig, MD, PhD
Associate Director, General Clinical Research Center
Director, Obesity Program
Children’s Hospital Boston

Associate Professor, Pediatrics
Harvard Medical School

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Charles H. Hood Foundation
Children’s Hospital League
The Iacocca Foundation
Boston Obesity Nutrition Research Center
WHAT REALLY MAKES YOU FAT?

The latest science on how your body handles CARBS vs. FATS
Prevalence of Obesity in US Adults

Centers for Disease Control (BMI $\geq 30$ kg/m$^2$)

Flegal. JAMA 2002, 288: 1728
Prevalence of Obesity in Boys 6 - 11 Years

Age-adjusted BMI > 95th percentile

Ogden. JAMA 2002, 288: 1728
Prevalence of Obesity in Girls 6 - 11 Years

Age-adjusted BMI > 95th percentile

Percent of Population

White
Black
Hispanic

Ogden. JAMA 2002, 288: 1728
Prevalence of Obesity in Boys 12-17 Years

Age-adjusted BMI > 95th percentile

Ogden. JAMA 2002, 288: 1728
Prevalence of Obesity in Girls 12-17 Years

Age-adjusted BMI > 95th percentile

Percent of Population

White  Black  Hispanic

Ogden. JAMA 2002, 288: 1728
Worldwide Epidemic of Obesity in Children


USA
- 6–11 years
  - 1971–74 to 1999: 4–13% (3-3)
  - 12–19 years: 6–14% (2-3)
  - BMI >95th percentile

England
- 4–11 years
  - 1984 to 1994: Boys: 0–6–1–7% (2–8)
  - Girls: 1–3–2–6% (2–0)
- Age-adjusted BMI cutoff linked to the adult value of 30 kg/m²

Scotland
- 4–11 years
  - 1984 to 1994: Boys: 0–9–2–1% (2–3)
  - Girls: 1–8–3–2% (1–8)
- Age-adjusted BMI cutoff linked to the adult value of 25 kg/m²

China
- 6–9 years
  - 1991 to 1997: Boys: <4% to about 10% (2–5)
  - Girls: about 4% to about 9% (2–3)
  - >120% of standard weight

Japan
- 10 years
  - 1970 to 1996: Boys: <4% to about 10% (2–5)
  - Girls: about 4% to about 9% (2–3)

Costa Rica
- 0–6 years (1982), 1–7 years (1996): 2–3–6–2% (2–7)
- Weight-for-height >2 SD from median

Chile
- 0–6 years
  - 1985 to 1995: 4–6–7–2% (1–6)
- Weight-for-height >2 SD from median

Brazil
- 0–5 years
  - 1974 to 1992: 2–7–6–8% (2–5)
- Weight-for-height >2 SD from median

Morocco
- 0–3 years
  - 1988 to 1993–94: 0–5–1–9% (3–8)
- Weight-for-height >2 SD from median

Ghana
- 0–3 years
  - 1985 to 1995: 1–4–4–7% (3–4)
- Girls: 1–2–5–5% (4–6)
- Age-adjusted BMI cutoff linked to the adult value of 30 kg/m²

Egypt
- 0–5 years
  - 1978 to 1995–96: 2–2–8–6% (3–9)
- Weight-for-height >2 SD from median

Australia
- 7–15 years
  - 1985 to 1995: 4–6–7–2% (1–6)
- Weight-for-height >2 SD from median

Age-adjusted BMI cutoff linked to the adult value of 25 kg/m²
Health Risks of Obesity in Adults
Nurses’ Health Study (women 30 to 55 yr)
Health Professionals Follow-up Study (men 45-60 yr)

Body Mass Index

<table>
<thead>
<tr>
<th>Relative Risk</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
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<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Type 2 diabetes
- Hypertension
- Heart Disease
- Cholelithiasis
Effects on Life Expectancy in Adulthood

Allison et al. JAMA 1999;282:1530-1538
- Excessive weight causes over 300,000 deaths per year

Flegel et al. JAMA 2005;293:1861-1867
- Obesity causes 100,000 deaths per year
- Potential methodological problems
  - Reverse causation (chronic disease causes weight loss)
  - Survivor effects
Funding:
Coca-Cola
Cargill
Monsanto
Tyson Foods
Wendy’s
Outback Steakhouse
Perdue Farms
Applebee’s
Nat’l Steak & Poultry
Sugar Foods Corp

Source:
Center for Media & Democracy
Effects on Life Expectancy in Childhood

Childhood obesity may decrease life expectancy 2 - 5 years or more by mid-century (ie, more than all cancers combined).
Complications of Childhood Obesity


Psychosocial \cite{17-20}
- Poor self-esteem
- Depression
- Eating disorders

Neurological \cite{21}
- Pseudotumor cerebri

Pulmonary \cite{22-24}
- Sleep apnoea
- Asthma
- Exercise intolerance

Cardiovascular \cite{25-29}
- Dyslipidaemia
- Hypertension
- Coagulopathy
- Chronic inflammation
- Endothelial dysfunction

Gastrointestinal \cite{30,31}
- Gallstones
- Steatohepatitis

Renal \cite{36}
- Glomerulosclerosis

Musculoskeletal \cite{37-40}
- Slipped capital femoral epiphysis
- Blount’s disease
- Forearm fracture
- Flat feet

Endocrine \cite{32-35}
- Type 2 diabetes
- Precocious puberty
- Polycystic ovary syndrome (girls)
- Hypogonadism (boys)
Adults who were overweight during adolescence:
  * Complete fewer years of school -- women
  * Have higher poverty rates -- women
  * Are less likely to be married -- women & men

Other chronic medical conditions (e.g., epilepsy, cerebral palsy, physical deformities) were NOT associated with these consequences.
What is the Cause of the Obesity Epidemic?
Obesity: a Weakness of Character?

• Anger, Avarice, Envy, **Gluttony**, Lust, Pride, Sloth
  -- “Seven Deadly Sins”

• “Obese people . . . should perform hard work . . . eat only once a day, take no baths, sleep on a hard bed, and walk naked as long as possible.”
  -- Hippocrates
Obesity: a Genetic Disorder?

(1) Controlled feeding studies suggest an apparent body weight “set-point.”
   -- Leibel et al.  NEJM 1995; 332:673

(2) Heritability accounts for about 70% of the variability in BMI among identical twins raised apart.
   -- Stunkard et al.  NEJM 1990, 322:1483

(3) Numerous single-gene mutations known to cause obesity in rodents and humans.
However, our genes haven’t changed much in the last several decades

Thus, environmental factors must underlie the obesity epidemic

Weight Gain = Energy Intake - Energy Expenditure
When informed by his doctor of the correlation between fat dogs and their masters, Brian set out immediately to rectify his weight problem.

Courtesy of Garry Egger MPH, PHD
### Is Obesity Caused by Inadequate Physical Activity?

*Leisure-time Activity Level (BRFSS, CDC)*

<table>
<thead>
<tr>
<th>Activity Level</th>
<th>1991</th>
<th>1998</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactive</td>
<td>29.7%</td>
<td>28.6%</td>
</tr>
<tr>
<td>Irregularly active</td>
<td>28.4%</td>
<td>28.2%</td>
</tr>
<tr>
<td>Regular, not intense</td>
<td>33.2%</td>
<td>29.6%</td>
</tr>
<tr>
<td>Regular, intense</td>
<td>8.7%</td>
<td>13.6%</td>
</tr>
</tbody>
</table>

Mokdad et al. *JAMA* 1999, 282:1519
Is Obesity Caused by Inadequate Physical Activity?

Meta-analysis of 14 studies involving patients with type 2 diabetes

Body Weight (Kg)

Exercise

Control

83 kg

82.5 kg

p = .76

Boule et al. JAMA 2001, 286:1218-27
Thus, dietary factors appear to play a critical role in the obesity epidemic.
Conventional Dietary Treatment for Obesity

- Dietary fat is widely believed to cause weight gain

- Low-fat diets constitute the most common approach to the prevention and treatment of obesity and diabetes.
Fat
Nutrients
Carbohydrate
What if Fat Doesn’t Make You Fat?

Influential researchers are beginning to embrace the medical heresy that maybe Dr. Atkins was right.

By Gary Taubes
Dietary Fat and Obesity

Arguments Against a Relationship

- Prevalence of obesity has continued to rise despite a **DECREASE** in fat consumption since the 1960s
- Longitudinal studies do not consistently show an association between dietary fat and body fat
- Low fat diets have poor clinical effectiveness
Relationship Between Fat & Carbohydrate

- Calories from fat
- Obesity prevalence

<table>
<thead>
<tr>
<th>Year</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>60</td>
</tr>
<tr>
<td>1990</td>
<td>50</td>
</tr>
<tr>
<td>1980</td>
<td>40</td>
</tr>
<tr>
<td>1970</td>
<td>30</td>
</tr>
<tr>
<td>1960</td>
<td>20</td>
</tr>
</tbody>
</table>
Dietary Fat and Obesity

Arguments Against a Relationship

• Prevalence of obesity has continued to rise despite a **DECREASE** in fat consumption since the 1960s

• Longitudinal studies do not consistently show an association between dietary fat and body fat

• Low fat diets have poor clinical effectiveness
**Relationship Between Dietary Fat and Weight**

10-year weight change among young adult subjects in CARDIA 
(n = 1602 Whites, 1307 Blacks)

<table>
<thead>
<tr>
<th>QUINTILES OF INTAKE</th>
<th>&lt; 30</th>
<th>30-34</th>
<th>34-38</th>
<th>38-42</th>
<th>&gt; 42</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total fat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(%) energy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whites</td>
<td>168.6</td>
<td>169.1</td>
<td>168.2</td>
<td>171.1</td>
<td>169.4</td>
<td>.324</td>
</tr>
<tr>
<td>Blacks</td>
<td>182.1</td>
<td>182.2</td>
<td>185.2</td>
<td>185.4</td>
<td>185.7</td>
<td>.028*</td>
</tr>
</tbody>
</table>

*p = ns after adjustment for dietary fiber*
Dietary Fat and Obesity
Arguments Against a Relationship

• Prevalence of obesity has continued to rise despite a **DECREASE** in fat consumption since the 1960s

• Longitudinal studies do not consistently show an association between dietary fat and body fat

• Low fat diets have poor clinical effectiveness
Meta-analysis of Low Fat Diets

Pirozzo et al, Cochrane Review, Issue 2, 2002

Methods

• Included all available randomized trials comparing low fat to control diets (n=6)
• Free living overweight/obese adults given dietary advice

Results

• No significant differences between diets at 6, 12 & 18 months
A Massive RCT of Dietary Fat Reduction

• **Protocol**
  – 7.5 year RCT of approximately 50,000 women
  – Intervention: individual and group sessions to promote decreased dietary fat, increased vegetables, fruits and grain consumption (control group received education materials only)

• **Results**
  – Dietary fat 8% lower in intervention group (30 vs 38%)
  – Weight differed by < 0.5 kg between groups at end of study
High Fat vs Low Fat Diets

Greater weight loss at 6 months on an Atkins-type diet compared to a low fat diet

-- Brehm et al. JCEM 2003, 88:1617-1623
-- Samaha et al. NEJM 2003, 348:2074-81
-- Foster et al. NEJM 2003, 348:2082-90
Relationship Between Fat & Carbohydrate

- Calories from fat
- Obesity prevalence


Percent

- 0
- 10
- 20
- 30
- 40
- 50
- 60
Relationship Between Fat & Carbohydrate

![Graph showing the relationship between obesity prevalence, calories from fat, and calories from CHO over the years. The graph indicates an increase in obesity prevalence and calories from CHO, while a decrease in calories from fat is observed.](image-url)
Trends in Food Intake 1971-2000, NHANES

MMWR 2004, 53:80-82

• Total energy intake increased
  -men 168 kcal/day
  -women 270 kcal/day
• Fat intake in grams unchanged
• Carbohydrate increased by 65 g/d

Increase in energy entirely attributed to carbohydrate
Is Obesity Caused by Consumption of Certain Types of Carbohydrate?
Classification of Carbohydrate

Sugars:
- glucose
- fructose
- glucose
- fructose
- glucose
- glucose

Starch:
- glucose
- glucose
- glucose
- glucose
- glucose
- glucose
Biologic Significance of Saccharide Chain Length Questioned

- Consumption of glucose as monomer or polysaccharide (starch) produces similar changes in BG and insulin levels.
- No difference in BG response to meals with sucrose compared to meals with wheat among normal and diabetic subjects.

Bantle et al. NEJM 1983, 309:7
Consumption of Unprocessed Grain

Glucose

Fiber

Digestive Enzymes

Glucose

Fiber
Processed Grain

![Diagram showing the relationship between fiber and glucose](image-url)
Processed Grain

(glucose) → (glucose) → (glucose) → (glucose)
(glucose) → (glucose) → (glucose) → (glucose)
(glucose) → (glucose) → (glucose) → (glucose)
Refined Starch
Consumption of Refined Starch

Digestive Enzymes

glucose → glucose → glucose → glucose

Digestive Enzymes

glucose → glucose → glucose → glucose

Digestive Enzymes

glucose → glucose → glucose → glucose
Consumption of Refined Starch

Digestive Enzymes

glucose → glucose → glucose → glucose → glucose

glucose → glucose → glucose → glucose → glucose

Digestive Enzymes
Consumption of Refined Starch

<table>
<thead>
<tr>
<th>glucose</th>
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<tbody>
<tr>
<td>glucose</td>
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<td>glucose</td>
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<td>glucose</td>
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</tbody>
</table>
Thus, the distinction between “simple sugar” and “complex carbohydrate” has little biological significance.
The Glycemic Index

A measure of carbohydrate digestion rate

Area under the glycemic curve after consumption of 50 g CHO from test food divided by area under curve after 50 g CHO from control food
Glycemic Load
Proposed to characterize the impact of dietary patterns differing in macronutrient composition on glycemic response

Average Dietary GI (weighted) X Amount of Carbohydrate Consumed
<table>
<thead>
<tr>
<th>Food</th>
<th>Glycemic Index</th>
<th>Glycemic Load</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corn flakes</td>
<td>84</td>
<td>21.0 (1 cup)</td>
</tr>
<tr>
<td>White bread</td>
<td>70</td>
<td>21.0 (2 slices)</td>
</tr>
<tr>
<td>Rye bread</td>
<td>65</td>
<td>19.5 (2 slices)</td>
</tr>
<tr>
<td>Muesli</td>
<td>56</td>
<td>16.8 (1/2 cup)</td>
</tr>
<tr>
<td>Banana</td>
<td>53</td>
<td>13.3 (6 oz)</td>
</tr>
<tr>
<td>Spaghetti</td>
<td>41</td>
<td>16.4 (2 oz)</td>
</tr>
<tr>
<td>Apple</td>
<td>36</td>
<td>8.1 (6 oz)</td>
</tr>
<tr>
<td>Lentil beans</td>
<td>29</td>
<td>5.7 (1/2 cup)</td>
</tr>
<tr>
<td>Milk</td>
<td>27</td>
<td>3.2 (1 cup)</td>
</tr>
<tr>
<td>Peanuts</td>
<td>14</td>
<td>0.7 (1 oz)</td>
</tr>
<tr>
<td>Broccoli</td>
<td>***</td>
<td>***</td>
</tr>
</tbody>
</table>
Does Glycemic Index Affect Regulation of Appetite Over 1 Day?
# GI & Regulation of Food Intake

<table>
<thead>
<tr>
<th>Low GI</th>
<th>Medium GI</th>
<th>High GI</th>
</tr>
</thead>
<tbody>
<tr>
<td>55 g whole egg</td>
<td>63.9 g steel-cut oats</td>
<td>60.9 g instant oatmeal</td>
</tr>
<tr>
<td>45 g egg white</td>
<td>160 g 2% milk</td>
<td>160 g 2% milk</td>
</tr>
<tr>
<td>40 g lowfat cheese</td>
<td>15 g H &amp; H cream</td>
<td>15 g H &amp; H cream</td>
</tr>
<tr>
<td>200 g spinach</td>
<td>16.0 g fructose</td>
<td>19.0 g dextrose</td>
</tr>
<tr>
<td>30 g tomato</td>
<td>0.0 g saccharine</td>
<td>0.2 g saccharine</td>
</tr>
<tr>
<td>185 g grapefruit</td>
<td>397 g water</td>
<td>397 g water</td>
</tr>
<tr>
<td>115 g apple slices</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Macronutrients (% carbohydrate/protein/fat):**

- Low GL: 40/30/30
- Medium GI: 64/16/20
- High GI: 64/16/20

**Energy density (KJ/g):**

- Low GL: 2.46
- Medium GI: 2.52
- High GI: 2.52
Glycemic Index & Appetite

Blood Glucose

Glycemic Index & Appetite

Plasma Epinephrine

GI & Regulation of Food Intake

Kilocalories Consumed

Time (hr)

High GI
Med GI
Low GL

Voluntary Food Intake After High vs Low GI Meals

Studies controlling for macronutrients, of > 3hr duration

- Favored Low GI
- Trend favoring Low GI
- No difference
- Trend favoring High GI

Spitzer & Rodin, 1987
Rodin et al, 1998
Rodin, 1988
Holt & Miller, 1995
Rigaud et al, 1998
Ludwig et al, 1999
Holt et al, 1999
Guss et al, 1994
Lavin & Read, 1995
Barkeling et al, 1995
Holt & Miller, 1995
Raben et al, 2000

(%) Difference In Energy Intake
Does Glycemic Index/Load Affect Metabolism?
Body Weight Set-Point

- Poor long-term outcome of conventional diets gives rise to concept of a “Body Weight Set-Point”

- Changes in body weight elicit physiologic adaptations that antagonize further weight change

- Genetic factors specify Set-Point

However, environmental factors must also affect body weight Set-Point e.g., increasing prevalence of obesity
Body Weight Set-Point

Methods

• 39 obese young adults, age 18 - 40, weight stable ≥ 6 months

• Randomly assigned, parallel design

• Energy restricted Low or High GL diets intended to produce 10% weight loss over 8 to 12 weeks

• Subjects studied before and after weight loss in GCRC

• 1° endpoint:
  – REE by indirect calorimetry > 10 hr after last meal (no TEF)
  – body composition by DXA scan
Body Weight Set-Point

Glycemic responses to diet

![Graph showing glycemic responses to diet with low and high GL diets compared over time.](image-url)
Body Weight Set-Point

Insulinemic responses to diet

[Graph showing changes in insulin levels over time for Low GL and Low Fat diets.]
Effects of Glycemic Load on REE

Change from baseline to end of study

High GL  Low GL

-220  -170  -120
-70  -20

Kcal/d

p < .05

# Effects of Glycemic Load on CVD Risk Factors

*Percent change from baseline*

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>Low Fat</th>
<th>Low Glycemic</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOMA Insulin Resist.</td>
<td>-15.8</td>
<td>-33.9</td>
<td>.01</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>16.2</td>
<td>-3.5</td>
<td>.01</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>-8.1</td>
<td>-8.9</td>
<td>.87</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>-15</td>
<td>-16.1</td>
<td>.84</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>-5.1</td>
<td>-47.7</td>
<td>.03</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>-3.1</td>
<td>-6.4</td>
<td>.07</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>-2.5</td>
<td>-6.5</td>
<td>.07</td>
</tr>
<tr>
<td>Mean BP (mm Hg)</td>
<td>-3.0</td>
<td>-6.5</td>
<td>.04</td>
</tr>
</tbody>
</table>

Conclusions:

• Dietary composition can modify the metabolic adaptations to weight loss

• Differences in REE are too small to cause much variance in body weight over the short term (weeks to months)

• Smaller fall in REE following weight loss on the low GL diet may be a marker of lower risk of weight regain

• Low glycemic index/load diets may be useful in the long-term treatment of obesity
Does glycemic index/load affect body weight over the long term?
GI & Body Weight: Epidemiology


• Eurodiab Study
  – Cross-sectional, n = 2868 subjects with type 1 diabetes
  – Diet assessed by 3-day record
  – GI was independently and directly associated with WHR
GI & Body Weight: Epidemiology

Murakami et al.  AJCN 2006, 83:1161-9

• **Protocol**
  – Cross-sectional study of 1354 Japanese adult farmers
  – Diet assessed by self-administered questionnaire

• **Results:** (comparing highest to lowest quintiles of GI)
  – BMI was 0.7 kg/m² greater (p = 0.017)
  – Triglycerides were 16 mg/dL higher (p = 0.001)
  – Fasting glucose was 6 mg/dL higher (p = 0.022)
  – HgA1c was 0.2% higher (p = 0.038)
GI & Body Weight: Epidemiology


• **Protocol**
  – Observational study of 572 adults in Massachusetts
  – Diet assessed by 7-day recalls

• **Results** (low vs high GI)
  – BMI directly associated with GI in both cross-sectional and longitudinal analyses (.75 BMI per 5 units GI, p=.01)
  – BMI not associated with total carbohydrate
GI & Body Weight: Chronic Effects


• Protocol
  – 5 week cross-over design, 11 overweight men
  – Intervention: substitution of high or low GI CHO, outpatient
  – Diets with similar energy, macronutrients

• Results (low vs high GI)
  – Similar changes in body weight
  – Lower fat mass (dxa): -500 g (p < .05)
  – Lower lipoprotein lipase and hormone sensitive lipase (p < .05)
GI & Body Weight: Chronic Effects

Slabber. AJCN 1994, 60:48

• **Protocol**
  – 3 month parallel & cross-over design, 15 obese females
  – Intervention: Exchange list meal planning, outpatient
  – Dietary prescriptions similar in energy, macronutrients

• **Results** (low vs high GI)
  – Body Weight: -7.4 vs -4.6 kg, p = .04 (cross-over limb)
  – Fasting insulin: -91 vs -21 pmol/L, p = .01 (parallel limb)
Effects of Glycemic Load on Body Weight
A 12-month Pilot Study

Methods

• 16 obese adolescents, age 13 - 21 years

• Intervention:
  – *Ad lib* low GL vs energy-restricted reduced-fat diet
  – Total of 14 treatment visits with a dietitian

• Treatment intensity, behavioral approaches, physical activity prescription identical between groups

• Changes in diet assessed by 3 and 7 day food records

• > 85% completion rate at 12 months (7 of 8 per group)
## Change in Diet During Treatment

<table>
<thead>
<tr>
<th></th>
<th>Low Glycemic Load</th>
<th>Reduced Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glycemic Load (g/1000 kcal)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>86 ± 5</td>
<td>79± 2</td>
</tr>
<tr>
<td>Intervention</td>
<td>68 ± 7 *</td>
<td>77± 5</td>
</tr>
<tr>
<td>Follow-up</td>
<td>69 ± 6 *</td>
<td>79± 7</td>
</tr>
<tr>
<td><strong>Fat (% energy)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>27 ± 2</td>
<td>33± 1</td>
</tr>
<tr>
<td>Intervention</td>
<td>31 ± 2 *</td>
<td>28± 1 *</td>
</tr>
<tr>
<td>Follow-up</td>
<td>29 ± 3</td>
<td>29± 3 *</td>
</tr>
</tbody>
</table>

* Significant change from baseline
Change in BMI


Treatment x time effect: p = 0.05

Change in BMI (kg/m²)

Time (months)

- Reduced Glycemic Load (n=7)
- Reduced Fat (n=7)
• **Protocol**
  – 10 week study parallel study, 45 overweight women
  – Low vs high GI CHO substituted on outpatient basis
  – No significant difference in weight (low v high): -1.9 v -1.3 kg
Can effects observed in clinical trials be attributed, at least in part, to glycemic index *per se*?
Effects of Glycemic Index in an Animal Model

- Sprague-Dawley rats identical diets
  - high GI (amylopectin starch), $n = 11$
  - low GI (high amylose starch), $n = 10$
- Energy intake controlled to maintain identical mean body weight between groups
- Body composition measured after 18 weeks
Animal Study

Body weight & food intake

Animal Study: Body Composition

At identical mean body wt, 548 vs 549 g

Adiposity (%)

$p < .01$

Animal Study

Low GI

High GI

Animal Study

Prediction of body weight by baseline insulin

High GI

Low GI

Body weight (g)

Insulin 30 min (ng/ml)

R=0.91
p<0.0001

R<0.01
P=NS
GI & Body Weight: Chronic Effects

Interim 6-month analysis of an 18-month RCT

- 58 obese young adults, mean BMI 37 kg/m²
- Intervention: dietary counseling, low fat vs low GL diets
- Serum insulin measured 30 minutes after OGTT

![Graph showing % decrease in body fat for low insulin and high insulin responders, with P values 0.45 and 0.005.]

Low Fat
Low GL
Glycemic Index and Diabetes
Mechanisms Relating GI to Diabetes Risk

- High-Glycemic Index Meal
  - Postprandial Hyperglycemia
  - Counterregulatory Hormone Secretion
  - Increase in Free Fatty Acids

- Hyperinsulinemia
  - Beta Cell Demand
  - Insulin Resistance

- Glucotoxicity
- Lipotoxicity

- Chronic Oxidative Stress
  - Beta Cell Failure
  - Type 2 Diabetes Mellitus

- Genetic Factors
- Lifestyle Factors
GI and Risk for Type 2 Diabetes
Observational studies show a direct association

• **Nurses’ Health Study** *JAMA 1997, 277:472*
  – Prospective study, 6 year follow-up (n = 65,173)
  – Diet assessed by FFQ
  – Controlled for age, BMI, physical activity, etc
  – 37% (9-71%) increased risk of diabetes in highest quintile of GI
Animal Study: Islet Abnormalities

Low GI  

High GI
GI and Cardiovascular Disease
GI & CVD: Clinical Studies

Reviewed in: JAMA 2002, 287:2414

Triglyceride
- Jenkins 1985
- Jenkins 1987
- Jenkins 1987
- Jenkins 1988
- Collier 1988
- Fontvieille 1988
- Brand 1991
- Wolever 1992
- Wolever 1992
- Fontvieille 1992
- Luscombe 1999
- Jarvi 1999
- Giacco 2000

LDL Cholesterol

Total: HDL Chol

Percent Change (After Low Compared to High GI)
GI & CVD: Epidemiology

Observational studies show a direct association

• Nurses’ Health Study *Liu et al. AJCN 2000, 71:1455*
  – Prospective study, 10 year follow-up (n = 75,521)
  – Diet assessed by FFQ
  – Controlled for age, smoking, and other risk factors
  – Individuals in the highest quintile of glycemic load had a 2-fold greater relative risk of myocardial infarction
Glycemic Load to the Extreme

Fast Food & Soda, American Style

“Super-size”
“Palatability”
Energy density
Trans/sat fats
Low fiber
Micronutrients
Fast Food

Fast food increased from 2% to 15% of calories in children’s diets since 1970s.

Fast food is intensively marketed to young children.

Fast food has penetrated all aspects of society, including schools, playgrounds and hospitals.
Fast Food and Obesity in Young Adults


• 3000 young adults ages 18 to 30 years, followed for 15 years

• Individuals with the highest intakes of FF gained an extra 10 lbs compared to those with the lowest intakes

• Insulin resistance increased twice as fast among individuals in the highest category of FF
Soft Drinks

- Per capita soda consumption in the US has increased by 500% since the 1950s.
- Soda comprise $\geq 10\%$ of total calories for the average adolescent.
- Sweetened beverages are the leading contributor of added sugar in children’s diets.
Among 500 middle school children in Cambridge, MA, the risk of becoming obese increased by 60% for every additional serving of sugar-sweetened drink per day.

Humans appear to compensate poorly for calories consumed in liquid form

Mattes. Physiol Behav 1996, 59:179-87
Summary

• Short-term studies show decreased food intake or increased satiety following consumption of low GI vs high GI meals

• Medium term studies suggest beneficial effects of low GI diets on body weight or central body fatness

• Animal studies demonstrate improvements in adiposity and related metabolic variables on a diet of low vs high GI starch

• Low GI diets may reduce risk for other chronic diseases, including cardiovascular disease and type 2 diabetes

• GI can be related to disease processes through plausible physiological hypotheses
Is the Glycemic Index Practical?

**Concern:** GI is too complex (influenced by many dietary factors: ripeness of a banana, cooking time of pasta, nutrient interactions)

- Other important dietary factors are complex (e.g., palatability)
- *Key concepts* can be presented in a simple manner (e.g., increase intake of non-starchy vegetables, fruits, and unrefined grains)
- Meaningful effects have been obtained numerous clinical studies in which outpatients consumed self-selected diets
- Consistent with current nutritional recommendations to increase consumption of vegetables, fruits and whole grains
- No known side-effects (in contrast with drugs, low-fat diets)
- Inexpensive
Effects of GI in an Outpatient Setting

**Methods**

- Retrospective analysis, clinical obesity program (n = 107)
- Intervention: dietary counseling, outpatient setting
- *Ad lib* low GI diet vs energy-restricted reduced-fat diets
- Mean treatment intensity: 3.3 visits over 4 months
- Data adjustment for confounding factors (eg, age, sex, race).
Effects of GI in an Outpatient Setting

Baseline BMI tertiles (kg/m²)

- < 28.3
- 28.3 - 34.9
- > 34.9

Change in BMI (kg/m²)

Low GI versus Reduced-fat

* p < 0.01

What is the Optimal Diet for the Treatment of Obesity and Related Disease?
Low Glycemic Load Pyramid
Low Fat

Not effective long-term
Higher trigs, lower HDLC

Low CHO

Highly restrictive
Long-term safety unknown
Low Fat

Low GI

Low CHO

The Perfect Compromise
The Toxic Environment

*Profit Over Public Health*

- $12 billion spent each year to influence the eating habits of children, overwhelmingly for high calorie, low quality products.

- Marketing campaigns specifically target children, linking brand names with toys, games, movies, education tools, and baby bottles.

- Food industry has extensive political influence, close relationships with scientists, and ties to professional associations, producing a corrosive effect on nutrition-related research and public policy.

- Fast food & soda pervade all regions of the country, public schools and even Children’s Hospitals.
Coke is like family.

You can never have enough.

Always.
GOOD! YOU'VE EATEN ALL YOUR CANDY BARS!
BUT YOU HAVEN'T TOUCHED YOUR POTATO CHIPS,
AND IF YOU EAT YOUR FRIED PUFFED CHEESE
SNACKS AND DRINK YOUR SODA, I HAVE A SPECIAL
DESSERT FOR YOU!
DON'T GO AWAY,
I'LL BE RIGHT BACK...

Epidemic childhood obesity baffles researchers.
A Common Sense Approach

- **Home**
  - Set aside time for family meals
  - Limit TV viewing

- **Media**
  - Restrict food advertising directed at children

- **Policy**
  - Tax fast food and sugar-sweetened soft drinks
  - Subsidize fruits and vegetables

- **Schools**
  - Improve quality of school lunch program
  - Fund mandatory physical education classes
  - Ban fast food and soda from schools (hospitals?)

- **Insurance**
  - Improve reimbursement for obesity treatment

- **Politics**
  - Regulate political contributions from food industry
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