Importance of the Glycemic Index for Obesity & Diabetes

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Children’s Hospital Boston

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Prevalence of Obesity in US Adults

Centers for Disease Control (BMI ≥ 30 kg/m²)

Men

Women

Flegal. JAMA 2002, Ogden JAMA 2006
Prevalence of Obesity in Boys 6 - 11 Years

Age-adjusted BMI > 95th percentile

Flegal. JAMA 2002, Ogden JAMA 2006
Prevalence of Obesity in Girls 6 - 11 Years

Age-adjusted BMI > 95th percentile

Flegal. JAMA 2002, Ogden JAMA 2006
Prevalence of Obesity in Boys 12 - 17 Years

Age-adjusted BMI > 95th percentile

Prevalence of obesity in boys 12-17 years by age group and ethnicity. The graph shows the percentage of the population with age-adjusted BMI greater than the 95th percentile for boys by age group and ethnicity from 1966-70 to 2003-04.

- **White Population**
  - 1966-70: 
  - 1971-74: 
  - 1976-80: 
  - 1988-94: 
  - 2003-04: 

- **Black Population**
  - 1966-70: 
  - 1971-74: 
  - 1976-80: 
  - 1988-94: 
  - 2003-04: 

- **Hispanic Population**
  - 1966-70: 
  - 1971-74: 
  - 1976-80: 
  - 1988-94: 
  - 2003-04: 

Flegal. JAMA 2002, Ogden JAMA 2006
Prevalence of Obesity in Girls 12 - 17 Years

Age-adjusted BMI > 95th percentile

Flegal. JAMA 2002, Ogden JAMA 2006
Worldwide Epidemic of Obesity in Children
Anticipated Trends

A plateau or a pause in prevalence rates?

• No significant changes in BMI among children and adults in the last decade
  Flegal. JAMA 2010, 303:235-41

• Between 2003 to 2007, obesity rates continued to rise in 23 states, and did not decrease in any state
  Trust for America, RWJF, July 2009
The Childhood Obesity Epidemic

A four-phase model

<table>
<thead>
<tr>
<th>Year</th>
<th>Prevalence</th>
<th>Obesity-related complications</th>
<th>Life-threatening events</th>
<th>Trans-generational propagation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1970</td>
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<td>1980</td>
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<td>2010</td>
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<td>2020</td>
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<td>2030</td>
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<tr>
<td>2040</td>
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</tr>
</tbody>
</table>

Ludwig. NEJM 2007, 357:2325-2327
Serious Warning Signs

Rates of ischemic stroke in adults vs. youth

METHODS

• Nationwide survey of hospitalizations from 1994 to 2007
• Ischemic stroke was identified by ICD 9 codes

RESULTS

• Prevalence decreased for older adults ≥ 45 years
  likely due to improved medical prevention
• Prevalence increased markedly for children and young adults
  – 35% for boys and girls 5 to 14 years
  – 51% for males 15 to 34 years
  likely due to increased obesity prevalence

Tong. American Stroke Association, Annual Meeting 2011 (abs)
Serious Warning Signs

Life-threatening complications of type 2 DM in adolescents

Individuals diagnosed with type 2 diabetes in adolescence have suffered, by age 30:

• renal failure requiring dialysis
• amputations
• increased mortality

The Childhood Obesity Epidemic

A four-phase model

Onset

Year


Prevalence

Obesity-related complications

Life-threatening events

Trans-generational propagation

Ludwig. NEJM 2007, 357:2325-2327
METHODS

• Diet-sensitive rats placed on standard or high energy diets prior to and during gestation

RESULTS

• *Mothers* fed the high energy diet became obese (as intended)
• *Offspring* of mothers fed the high energy were fatter than offspring of mothers fed the standard diet
Impact of Obesity on Society

*Life-expectancy*

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

Olshansky, Ludwig. NEJM 2005, 352:1138-45
Impact of Obesity on Society

Increasing economic costs

• Direct costs (2005 dollars) for treating obesity among US adults is $168 billion annually, or 16.5% of total spending on medical care

• By 2020, >50% of the US adult population will have diabetes or prediabetes, with annual costs approaching $500 billion
  Center for Health Reform & Modernization. UnitedHealth 2010

• By 2030, total annual economic costs of cardiovascular disease in the US predicted to exceed $1 trillion
Brain
Increased intracranial pressure
(causing headache and double vision)

Heart and blood vessels
- High LDL (bad) cholesterol
- Low HDL (good) cholesterol
- High triglycerides
- High blood pressure
- Abnormal blood clotting tendency
- Blood vessel inflammation

Lungs
- Sleep apnea
- Asthma
- Shortness of breath with exertion

Digestive track
- Acid reflux
- Constipation
- Gallstones
- Fatty liver

Bones & Joints
- Dislocated growth plate in hip socket (slipped capital femoral epiphysis)
- Bowel knees (Blount’s disease)
- Flat feet
- Pain in weight-bearing areas

Hormones
- Type 2 diabetes
- Early puberty (girls & boys)
- Delayed puberty (boys)
- Polycystic ovarian syndrome (girls)

Well-being
- Poor self-esteem
- Depression
- Eating disorders

Complications of Childhood Obesity
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?

• Numerous genes affect body weight (e.g., leptin)

• Controlled feeding studies suggest an apparent body weight “set-point”

  -- Leibel et al. NEJM 1995; 332:673
Obesity: a Genetic Disorder?

• Human populations have maintained relatively stable body weight over time amidst an abundance of food

• Our genes haven’t changed much in the last several decades
Thus, environmental factors must be responsible for the observed “calorie gap”
Calories in Versus Calorie Out
Magnitude of the “energy gap” driving the obesity epidemic

calorie intake > calorie expenditure

15 – 50 kcal/d

Typical individual

Assumes a linear relationship between calories and weight gain

Calories in Versus Calorie Out

Magnitude of the “energy gap” driving the obesity epidemic

Calorie intake > calorie expenditure

250 – 350 kcal/d  Typical adult

Based on models that consider calorie compensation

Katan, Ludwig JAMA 2010, 303:65-66
Calories in Versus Calorie Out

Magnitude of the “energy gap” driving the obesity epidemic

Based on models that consider calorie compensation

Katan, Ludwig JAMA 2010, 303:65-66
Calories in Versus Calorie Out
Magnitude of the “energy gap” driving the obesity epidemic

Massive changes in diet and/or physical activity level

+ \[ \text{calorie intake} > \text{calorie expenditure} \]

- \[ \text{calorie intake} < \text{calorie expenditure} \]

\[ 250 - 350 \text{ kcal/d} \] Typical adult

\[ 500 - 1000 \text{ kcal/d} \] Obese adolescents

Based on models that consider calorie compensation

Katan, Ludwig JAMA 2010, 303:65-66
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
Exercise in the Treatment of Obese Adults

Meta-analysis of 14 studies involving type 2 diabetes

Body Weight (Kg)

<table>
<thead>
<tr>
<th></th>
<th>Exercise</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>83 kg</td>
<td>82.5 kg</td>
</tr>
<tr>
<td>p</td>
<td>.76</td>
<td></td>
</tr>
</tbody>
</table>

Boule et al. JAMA 2001, 286:1218-27
Exercise in the Treatment of Childhood Obesity

• **Design**
  – 100 overweight boys and girls, ages 7 to 11 years
  – Randomly assigned for 3 months to:
    • control
    • low dose exercise (20 min/day)
    • high dose exercise (40 min/day)

• **Results**
  – No difference in BMI
Thus, dietary factors appear to play a critical role in the obesity epidemic.
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
Relationship Between Dietary Fat & Obesity

- Calories from fat
- Obesity prevalence

Year:
- 1960
- 1970
- 1980
- 1990
- 2000
- 2010

Percent Dietary Fat:
- 0
- 10
- 20
- 30
- 40
- 50
- 60
A 7-Year Clinical Trial of Diet & Weight

The Women’s Health Initiative

- 48,835 women ages 50 to 79 years
- Intervention: counseling sessions to promote a low fat diet
- Control: written education materials
- Dietary fat decreased from 39% to < 30% in the intervention group

What if Fat Doesn’t Make You Fat?
High Fat vs Low Fat Diets

Greater weight loss at 6 months on an Atkins’-type very low carbohydrate compared to a low fat diet in adolescents and adults

- Sondike. J Pediatr 2003, 142:253-8
- Brehm et al. JCEM 2003, 88:1617-1623
- Samaha et al. NEJM 2003, 348:2074-81
- Foster et al. NEJM 2003, 348:2082-90
- Gardner et al. JAMA 2007, 297:696-77
12-Weel Trial of the Atkins’ Diet in Adolescents

Evidence of short term effectiveness

- 30 obese adolescents treated for 12 weeks
- Randomly assigned to low fat vs very low carbohydrate diets
- Mean weight loss 4.1 vs. 9.9 kg, p < 0.05

Individual results

Sondike. J Pediatr 2003, 142:253-8
1-Year Clinical Trial of the Atkins’ Diet

Rapid weight regarding after 6 months

- 63 obese adults randomized to two diets for 1 year
- Intervention: subjects given a copy of Atkins’ New Diet Revolution or The LEARN Program (low fat)

Foster et al. NEJM 2003, 348:2082-90
What about dietary approaches based on carbohydrate quality?
Classification of Carbohydrate

Sugars:
- glucose
- fructose
- glucose
- fructose

Starch:
- glucose
- glucose
- glucose
- glucose
- glucose
- glucose
Carbohydrate

Sugars

Starchy Food
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
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
Glycemic Load as a Marker for Poor Food Quality

Characteristic of highly processed products

- High energy density
- High portion size
- Low nutrient and fiber content
- Poor dietary fat quality
- “Primordial” palatability
## Glycemic Index and Hunger

<table>
<thead>
<tr>
<th>Low GL</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 and Hunger

Blood glucose

![Graph showing the glycemic index and hunger over time for different GI levels.](attachment:image.png)

Glycemic Index and Hunger

Plasma epinephrine

Glycemic Index and Hunger

*Cumulative food intake*

Kilocalories Consumed

- **High GI**
- **Med GI**
- **Low GL**

Time (hr)

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
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
Effects of Glycemic Load on REE

Change from baseline to end of study

High GL

Low GL

Kcal/d

p < .05

• **Protocol**
  – 10 trained cyclists given low vs high GI meals 30 minutes before exercise
  – For 2 hr, subjects cycled at moderate effort (70% VO2 max)
  – Then subjects cycled at maximum effort until exhaustion

• **Results** (low vs high GI)
  – During the first 2 hours:
    • Perceived exertion lower
    • Fat oxidation was greater
  – At maximum effort, time to exhaustion 60% longer
Does glycemic index/load affect body weight over the long term?
• **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


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

• **Results**
  – 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: Epidemiology

Hare-Brunn et al AJCN 2006, 84:871-879

• **Protocol**
  – 6-year, prospective observational study of 375 Danish adults
  – Diet assessed by dietitian-conducted interviews

• **Results**
  – GI directly associated with body weight, body fat and waist circumference in women but not men.
  – Effect was strongest in sedentary women, per 10 GI units:
    • +3.8 kg body weight, p = 0.001
    • +3% body fat, p = 0.002
    • +4 cm waist circumference per 10 GI units; p = 0.008
GI & Body Weight: Epidemiology

Liese AD et al. Diabetes Care 2005, 28:2832-2838

• **Protocol**
  – Cross-sectional study of 979 adults with normal and impaired glucose tolerance in the Insulin Resistance & Atherosclerosis Study (1992-1994)
  – Diet assessed by FFQ, insulin resistance by FS-IVGTT

• **Results**
  – There were no associations between GI and BMI, waist circumference, insulin sensitivity or disposition index.
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 (dextra): -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)
GI & Body Weight: Chronic Effects

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
GI & Body Weight: Chronic Effects


Treatment x time effect: p = 0.05

[Graph showing time in months on the x-axis and change in BMI (kg/m²) on the y-axis, with two lines representing reduced fat and reduced glycemic load, indicating a statistically significant effect at p = 0.05]
GI & Body Weight: Chronic Effects
Maki et al. AJCN 2007, 85:724-34

- 86 adults ages 18 to 65 years, from the Chicago metropolitan area
- Intervention: ad libitum low GL diet vs energy restricted low fat diet
- Process measures showed significant differences in GI and GL

**Graph:**
- Treatment x time, p < 0.001
- Change in Weight (kg)
- Low Fat
- Low Glycemic Load
GI & Body Weight: Chronic Effects

*Sloth et al. AJCN 2004, 80:337-47*

- **Protocol**
  - 10 week study parallel study, 45 overweight women
  - Low vs high GI CHO substituted on outpatient basis
  - No significant difference in weight

**Limitations:** underpowered to see significant effect
Effects of Glycemic Load on Body Weight

*Diogenes Adult Study, NEJM 2010, 363:2102-13*

- 773 adults from 8 European countries who initially lost >7% body weight
- Diet: Low vs high protein; low vs high GI for 26 weeks – *ad libitum*
- Intervention: family counseling

![Graph showing change in body weight over weeks for different dietary groups.]

- **High GL**: (low protein, high GI)
- **Medium GL**: (high protein, high GI)
- **Medium GL**: (low protein, low GI)
- **Low GL**: (high protein, low GI)
Effects of Glycemic Load on Body Weight

Diogenes Child Study, Pediatrics 2010, 126:e1143

METHODS

• 800 children from 8 European countries whose parents were participating in a weight loss maintenance study

• Diet: Low vs high protein; low vs high GI for 26 weeks – *ad libitum*

• Intervention: family counseling

RESULTS:

• High glycemic load diet showed greatest increase in adiposity

• Low glycemic load diet showed greatest decrease overweight/obesity prevalence
Translational research
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
Effects of Glycemic Index in an Animal Model

At identical mean body wt, 548 vs 549 g

Adiposity (%)  
\[ p < .01 \]

Effects of Glycemic Index in an Animal Model

Prediction of body weight by baseline insulin

High GI

Low GI
An 18-month Randomized Controlled Trial

*Ebbeling, Ludwig.* JAMA 2007, 297:2092-2102

**Methods**

- 73 obese young adults, mean BMI 37 kg/m$^2$
- Diets: Low Glycemic Load vs Low Fat (outpatient counseling)
- Intervention controlled for treatment intensity, fidelity, behavioral methods and physical activity prescriptions
- Serum insulin measured 30 minutes after OGTT at baseline
- Dietary process measures: repeat 24-hr food recalls
- Completion rate: 90% at 6 months, 70% at 18 months
An 18-month Randomized Controlled Trial

Change in diet at 6 months

<table>
<thead>
<tr>
<th></th>
<th>Low Glycemic Load Diet</th>
<th>Low Fat Diet</th>
<th>(P)</th>
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<tr>
<td><strong>Glycemic load, g/1000 kcal</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>63.8 ± 2.6</td>
<td>62.8 ± 1.8</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>40.0 ± 2.8</td>
<td>70.4 ± 2.3</td>
<td>&lt;0.0001</td>
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<tr>
<td><strong>Total fat, % energy</strong></td>
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<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>34.3 ± 1.4</td>
<td>34.8 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>37.5 ± 1.4</td>
<td>23.6 ± 1.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Protein, % energy</strong></td>
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<tr>
<td>Baseline</td>
<td>17.3 ± 0.8</td>
<td>17.3 ± 0.8</td>
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<tr>
<td>6 months</td>
<td>21.2 ± 0.9</td>
<td>20.5 ± 0.9</td>
<td>0.61</td>
</tr>
<tr>
<td><strong>Fiber, g/1000 kcal</strong></td>
<td></td>
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<tr>
<td>Baseline</td>
<td>8.1 ± 0.5</td>
<td>7.6 ± 0.4</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>13.1 ± 0.8</td>
<td>11.5 ± 0.7</td>
<td>0.15</td>
</tr>
</tbody>
</table>
An 18-month Randomized Controlled Trial

Change in weight throughout study

Full cohort, n = 73

P = 0.02 for interaction

High insulin response, n = 28

Full cohort, n = 73
Chronic Disease
Postprandial Glycemia

Effects in subjects with diabetes

![Graph showing the effect of different carbohydrates on blood glucose levels over time. The graph compares Placebo, Rosiglitazone, White Bread, and Spaghetti (al dente) on blood glucose levels post-prandially.]
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

JAMA. 2002;287:2414-2423. © American Medical Association
Translational Study: Islet Abnormalities

Low GI

High GI
GI & Risk for Type 2 Diabetes

Salmeron et al. JAMA 1997, 277:472-7

• **Design**
  – Prospective study, 6 year follow-up (n = 65,173)
  – Diet assessed by FFQ
  – Controlled for age, BMI, physical activity, etc

• **Results**
  – The odds ratio for diabetes was 1.37 (1.09-1.71) comparing highest to lowest quintiles of GI
GI/GL & Gestational Diabetes
Zhang et al. Diabetes Care 2006, 2223-2230

• **Design**
  – Prospective analyses of 13,000 women in the NHS II
  – Diets assessed by FFQ, data adjusted for pre-pregnancy BMI, etc

• **Results**
  – Individuals in the highest vs lowest quintiles of glycemic load had a 61% increased risk of developing gestational diabetes (p = .03)
GI/GL & Pregnancy

• **Design**
  – 46 pregnant obese woman randomized to low GL vs. low fat diets
  – Provided dietary counseling and home deliveries of food

• **Results** *(low GL vs low fat)*
  – Improved CRP, triglycerides, total cholesterol
  – Gestational duration 39.3 vs 37.9 wk (p=0.05)
  – Head circumference (adjusted for GA): 35.0 vs 34.2 cm p=0.01)
Acute elevation in blood glucose causes a burst of reactive oxygen species that can:

- increase blood pressure
- promote blood clot formation
- reduce endothelium-dependent blood flow
- diminish baroreceptor reflex
- increase concentrations of inflammatory mediators

Similar changes have been observed after consumption of high GI meals.

Antioxidant vitamins can prevent these changes.
GI/GL & Cardiovascular Disease

Hu Y et al. AJCN 2006, 84:70-6

• **Design**
  – 292 healthy adults
  – Diet assessed by a food frequency questionnaire
  – Plasma markers of oxidative stress measured

• **Results**
  – Comparing highest to lowest quartile of GI
    • Malondialdehyde increased by 33%
    • F2-isoprostanes increased by 18%
  – Total carbohydrate was not associated with oxidative stress
GI & Cardiovascular Disease

Liu et al. AJCN 2000, 71:1455-61

• Design
  – Prospective study, 10 year follow-up (n = 75,521)
  – Diet assessed by FFQ
  – Controlled for age, smoking, and other risk factors

• Results
  – Relative risk for myocardial infarction was 1.98 (1.41 - 2.77) comparing Individuals in the highest vs. lowest quintiles of GI
  – GI was a better predictor of risk than other systems of classifying carbohydrate (e.g., simple vs complex)
GL & Liver Disease

• **Design**
  – Male 129vPas mice studied for 25 weeks
  – Diets: amylose (low GI) vs amylopectin (high GI)
  – No difference in body weight

Low GI: Triglyceride 9.6%  High GI: triglyceride 20.7%
GI & Liver Disease
Valtuena et al. AJCN 2006, 84:136-42

• **Design**
  – Cross-sectional study of 247 healthy Italian adults
  – Diet assessed by 3-day food record; liver steatosis graded by ultrasound

• **Results**
  – The prevalence of high-grade steatosis was 2-fold greater comparing individuals in the highest vs lowest quartiles of GI
  – Effect especially pronounced among those with insulin resistance
  – No association with total carbohydrate or dietary fiber
GI/GL and Cancer: Mechanisms

- Insulin is a potent growth, promoting hormone, affecting dozens of genes in tissues throughout the body.

- Higher levels of insulin produced by a high GL diet could initiate or propagate uncontrolled cell growth in susceptible individuals.
GI/GL & Cancer: Breast

  - Prospective study, 16 year follow-up (n = 49,693)
  - Diet assessed by FFQ
  - Controlled for BMI, physical activity, hormone usage
  - Among post-menopausal women, risk of developing breast cancer increased by 87% in the highest vs lowest quintile of glycemic index
What is the Optimal Diet for the Treatment of Obesity and Related Disease?
FOOD GUIDE PYRAMID
A Guide to Daily Food Choices
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