Dietary Macronutrient Content and Metabolic Health

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A Case

MG is a 48 yo Hispanic man followed for hypertension. He has a family history of DM and CAD. He has a BMI = 31 kg/m², and wants to start the Atkins Diet to lose weight.

On exam his BP is 145/85 and his waist circumference is 42”

On laboratory exam his fasting glucose is 115 mg/dl, LDL is 150, Tg=210, HDL=35
What Feature of the Diet is Most Important for “Health”?

- Total calories?
- Macronutrient Composition?
- Macronutrient Subtypes?
- Energy Density?
- Specific Foods?

How would we know?

What is the burden of proof on someone making health claims for one of these?
What do we mean by ‘health’?

- Insulin resistance/Diabetes
- Coronary artery disease
- Cancer
- Weight per se
- ‘Optimizing Health’/wellness
Evolutionary History of Diets

► Hunter/Gatherer
  - 50% of calories from meat, high protein diet
  - meat was lean, low in fat especially saturated fat
  - Fish higher in omega 3 fat
  - High fiber

► Agrarian
  - Less meat = lower in protein
  - Grains = Higher in carb, lower in fat
Evolution of Diets

- Hunter/gatherers: 30% protein, 30% fat low saturated fat, 40% carb, low calories
- Native Greenlanders: 60% fat mostly seal fat, 15% carbohydrate
- Native Africans: 10% fat, 80% carbohydrate
- Japanese: 15% fat (mostly fish fat), 20% protein (mostly vegetable protein), 65% carbohydrate (mostly rice)
Evolution of Diets

► **American Diet:** 37%-33% fat, 50% of that is saturated fat, 15% protein mostly animal protein, 48%-52% carbohydrate, almost 1/3 from simple sugars. *The biggest changes in the modern diet are:*

- Increased omega-6 fat (Corn Oil)
- Trans fat
- Reduced whole grains and fiber
- Increased total energy intake (calories), no fasting
What Features of the Diet Might Predispose to Insulin Resistance?

- Relative amounts of fat or carbohydrate
- Type of Carbohydrate:
  - Sucrose, fructose
  - Glycemic Index and Glycemic Load
  - Amylose, Resistant Starch and Fiber
  - Whole grains, vegetables, legumes
- Total calories, positive energy balance
Types of Studies

► Animal or In Vitro Studies
  - Can provide the most detailed mechanistic information

► Epidemiological Studies
  - Population based Intake Data
  - Nurses Health Study and Health Professionals Follow Up Study, Iowa Women’s Health Study
  - Issues: Validity of intake data, reliability of IR diagnosis, interrelationship of factors
Types of Studies

► Short-Term Intervention Studies
  - More definitive than Epidemiological Studies
  - Problems with Power, Diet Control and Endpoint

► Long-Term Intervention Studies
  - Most definitive type of study
  - Da Quing, Finnish Diabetes Prevention, DPP
  - Once done will likely not be repeated with different dietary intervention
  - Multiple interventions
High Fat Diets cause insulin resistance

- Effect partly mediated by increase in body fat
- Worst with high n-6 polyunsaturated fat and saturated fat
- Fish oils have a protective effect
Insulin Resistance

- Saturated fat probably produces the most profound deterioration in insulin action
- PUFA (omega 6) almost as bad
- Mono unsaturated fat neutral or perhaps protective. Moderate data in diabetes, less in normal.
- Fish oils neutral or perhaps protective
- Trans fat less conclusive data
Epidemiological Studies: Dietary Fat and Diabetes Development

- SLVDS: Development of diabetes positively related to total fat and Sat fat
- Nurses Health Study and Health Professionals study: Emphasize role of Trans fat, downplay total fat and sat fat
- Iowa Women’s Health Study: Here again the effects of dietary fat on body weight are controlled for no effect of total fat on incidence of diabetes
- Fish Oils: A number of studies in special populations suggest Fish consumption is protective
Short Term Intervention Studies

- Increased dietary Saturated Fat causes deterioration in insulin sensitivity
  - KANWU Study Diabetologia 44:312-319 2001
  - Oxford Study Diabetologia 45:369-77 2002

- Increased Trans Fat no effect
  - Metabolism 48:870-5, 1999

- Increased Fish Oils no effect
  - KANWU Study Diabetologia 44:312-319 2001
Carbohydrate Intake Data

**FIGURE 3.** Increasing prevalence of type 2 diabetes (vertical bars) in the United States between 1933 and 1997 with increasing per capita percentage of carbohydrate intake from corn syrup (●) (14, 17).

Gross AJ CN 79:774 2004
Putative Contributors to the Secular Increase in Obesity


[Graph showing various factors and their impacts on obesity prevalence over time.]
Carbohydrate Subtypes

- Sucrose and fructose
- Fiber, whole grains
- Glycemic Index, Glycemic Load
Sucrose and Fructose

*Mixed data*

- Fructose is not glucose and so doesn’t raise ‘glucose levels’
- However, has unique metabolic effects on the liver.
- Clearly causes hepatic insulin resistance in rodents independent of weight gain.
- Growing evidence of adverse effects in humans.
Effects of Dietary Fructose on Body Fat in Humans

Figure 1
Changes of BW and abdominal fat. (A) Changes of BW during the 2-week inpatient baseline, 8-week outpatient intervention, and 2-week inpatient intervention periods. **P < 0.01; ****P < 0.0001, day 56 outpatient:intervention vs. day 1 outpatient:intervention; paired Student’s t test. Glucose, n = 15; fructose, n = 17. (B) Changes of total abdominal adipose tissue, SAT, and VAT volume in subjects after consuming glucose- or fructose-sweetened beverages for 10 weeks. *P < 0.05; **P < 0.01, 10 weeks vs. 0 weeks; paired Student’s t test. Glucose, n = 14; fructose, n = 17. Data represent mean ± SEM.

### Table 5

Baseline levels and percentage changes in fasting glucose and insulin and indices of insulin sensitivity after consumption of glucose- or fructose-sweetened beverages for 10 weeks

<table>
<thead>
<tr>
<th>Outcome variable</th>
<th>Glucose (0 weeks)</th>
<th>Glucose (% change 10 weeks)</th>
<th>Fructose (0 weeks)</th>
<th>Fructose (% change 10 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td>87.6 ± 1.5</td>
<td>−1.4 ± 0.6^A</td>
<td>88.7 ± 1.0</td>
<td>+5.3 ± 1.0^B</td>
</tr>
<tr>
<td>Fasting insulin (µU/ml)</td>
<td>15.0 ± 1.9</td>
<td>+2.9 ± 4.0</td>
<td>14.0 ± 1.5</td>
<td>+10.2 ± 4.2^C</td>
</tr>
<tr>
<td>Glucose 3-h AUC OGGT (mg/dl × 3 h)</td>
<td>129.4 ± 16.2</td>
<td>+31.4 ± 16.5^D</td>
<td>107.7 ± 18.5</td>
<td>+60.2 ± 23.8^E</td>
</tr>
<tr>
<td>Insulin 3-h AUC OGGT (µU/ml × 3 h)</td>
<td>232.9 ± 33.0</td>
<td>+13.9 ± 9.2</td>
<td>273.1 ± 44.4</td>
<td>+20.9 ± 5.9^D</td>
</tr>
<tr>
<td>Insulin sensitivity index (mmoles H2O/4-h insulin AUC)</td>
<td>0.236 ± 0.036</td>
<td>+1.1 ± 8.6</td>
<td>0.254 ± 0.049</td>
<td>−17.3 ± 3.8^E</td>
</tr>
</tbody>
</table>

^A^P < 0.05; ^B^P < 0.001; ^C^P < 0.01, PROC MIXED 3-factor (time, sexual phenotype, MSRF) RM ANOVA, effect of time. ^D^P < 0.05; ^E^P < 0.01, paired Student’s t test, 10 weeks vs. 0 weeks. Data represent mean ± SEM.
Epidemiological Studies: Fiber, GI and GL

► Increased fiber intake associated with lower insulin levels and less diabetes

  ▪ CARDIA study: JAMA 282:1539-46, 1999
  ▪ SLVDS: Diabetologia 40:430-8, 1997

► Glycemic Load: GI times Carbohydrate load

  ▪ Nurses Health Study and Health Professionals Follow Up Study
Glycemic Load, Cereal Fiber and Diabetes Development
Health Professionals Follow Up Study

Salmeron Diabetes Care 20:545, 1997
Issues with GI, Fiber, Whole Grains, Vegetables

- High fat/sucrose/fructose foods have a low GI
- GI Information not on labels, fiber is
- Complexity with sugar alcohols, amylose and resistant starch
- GI altered by method of preparation and time of day
4 Month Interventional Trial in Subjects with IGT

Wolever AJ CN 77:612, 2003

34 subjects with IGT, no change in HbA1C
Positive Energy Balance

► No question that this is the most powerful determinant of diabetes development.
► Obesity/body fat associated with development of diabetes.
► Weight gain independently associated with the development of diabetes.
► Cluster analysis suggests weight gain causally related.
Long Term Intervention Trials:

*High carb low calorie diets prevent diabetes*

- Gold Standard
- Used a range of lifestyle interventions including reduced total fat, reduced saturated fat, increased fiber, increased physical activity
- Finnish Diabetes Prevention Study, DPP, Da Quing, New Zealand Workforce Diabetes Study, and others.
Finnish Diabetes Prevention Study

► 522 subjects randomized to lifestyle intervention or control

► Goals
  ▪ Weight reduction >5%
  ▪ Fat intake <30% of energy
  ▪ Saturated fat <10% of energy
  ▪ Fiber >15 g/1000 kcal
  ▪ Exercise > 4hr/wk

NEJM 344:1343-50, 2001
Finnish Diabetes Prevention Study

Each aspect of the intervention was important in the observed effect.

NEJM 344:1343-50, 2001
Diabetes Prevention Program

► 3234 subjects randomized to metformin, lifestyle or control

► Lifestyle
  ▪ Fat gram budget 25% of calories from fat
  ▪ 7% weight loss, with caloric restriction -500 kcal
  ▪ 150 min/wk physical activity
  ▪ individualized program
Diabetes Prevention Program

Conclusions From RCTs

► High carbohydrate/fat and calorie restricted diets prevent diabetes in those at risk

► Confounded by other aspects of interventions such as fiber, sat fat restriction and physical activity

► Low carbohydrate diets work as well as low fat (perhaps even better than) in producing weight loss.
My Biases/Opinions

- Positive energy balance is the most potent dietary cause of diabetes.
- Reversing this positive energy balance has a strong protective effect.
- It may not matter what dietary approach is used to reverse this positive energy balance.
- The ‘gold standard’ is a fat restricted modest caloric restriction
Health Effects of High Fat Diets

- High fat diets are often high calorie (positive energy balance) diets

- Epidemiology suggests that not all fats are created equal, that it may not be the % fat in the diet, but rather the kind of fat in the diet
  - Examples: Eskimos, Mediterranean Diet
Dietary Fat and Atherosclerosis

- In Vivo animal data
- Epidemiology
- Effects on Lipids
- Clinical trials in Humans

While the data on different fats is somewhat variable, the best data on the relationship between dietary fat types and health effects comes from long term controlled interventional trials in humans.
Dietary Fatty Acids and Coronary Artery Stenosis in African Green Monkeys

Dietary Fat Intake and the Risk for CHD in Women

Hu, F.B. *et al* NEJM 337:1497, 1997
Traditional Mediterranean Diet

- Abundance of plant foods
- Minimally processed, locally grown foods
- Fresh fruit as typical dessert, limited sugar
- Olive oil as the principal source of fat
- Cheese and yogurt daily, limited amounts
- Fish and poultry in low to mod amounts
- Zero to four eggs/week
- Red meat in low amounts
- Wine daily with meals
Cardiovascular Events in the Lyon Heart Study

Fish and/or Omega-3 Fatty Acids

- Although controversial, evidence for decreased
  - Sudden death
  - Arrhythmias
  - Triglycerides
  - Thrombosis
  - Coronary morbidity and mortality in patients with CHD
Robert C. Atkins, M.D.

DR. ATKINS' NEW DIET REVOLUTION

THE AMAZING NO-HUNGER WEIGHT-LOSS PLAN THAT HAS HELPED MILLIONS LOSE WEIGHT AND KEEP IT OFF
Ad Libitum Low-Fat Diets Decrease Daily Energy Intake

Meta-analysis of 12 Intervention Trials; n = 1910

Change in Energy Intake on Low-fat Diet (kJ/d)

Lee-Han, 1988
Boyd, 1990
Sheppard, 1991
Kasim, 1993
Pritchard, 1996
Siggaard, 1996
Simon, 1997
Weststate, 1998
Stefanick (M), 1998
Stefanick (F), 1998
Saris SCHO, 2000
Saris CCHO, 2000

Weighted sum

Decreasing Dietary Fat is Associated with a Decrease in Body Weight

Analysis of 37 Diet Intervention Studies

n = 9276 subjects

Which Foods Cause Weight Gain?

Health Effects of High, Low and “Good” Fat Diets

► Atkins Diet: 20 grams carbohydrate per day in “induction phase”
► Ornish Diet: 10% fat vegetarian diet with yoga based exercise and stress reduction
► Zone Diet: 30% fat, 30% protein, 40% carbohydrate
► Mediterranean Diet: High monounsaturated fat.
A to Z Trial

Gardner, CD JAMA 2007; 297: 269-277
Effectiveness of Popular Diets

Dietary Intervention Randomized Controlled Trial (DIRECT)

104-109 subjects
In each diet group
95% retention at 1 year and 85% Retention at 2 yrs

Shai I, NEJM 359:229-241 2008
Macronutrient Content and Weight Loss
Sacks FM, NEJM 2009 Feb 26;360(9):859-73
Macronutrient Content and Weight Loss
Sacks FM, NEJM 2009 Feb 26;360(9):859-73
Low Carb, Low Fat: No Difference in Weight Loss at 2 Years

Summary of weight effects

► Diet composition probably doesn’t matter much for weight loss
► Adherence with treatment plan is the most important
► Low carb and Mediterranean diet are reasonable options, may be better in some.
Summary

► Overall macronutrient composition of the diet is not the critical parameter
► Subtypes of macronutrients are probably more important to focus on.
► Positive energy balance may be the most important factor
► It is hard to be dogmatic about any of this as there is likely large inter-individual variability