Disclosures
Objectives

1. Identify Clinical Relevance

2. Define the Physiology of the Ketogenic Diet

3. Explore Efficacy and Safety of the Ketogenic Diet

4. Determine the Clinical Utility of the Ketogenic Diet
Obesity in America

1. Obesity is a major cause of **morbidity** and **mortality**

2. > **2.8 million** adults die globally from obesity-related diseases
   
   a. ~ **400,000 preventable deaths annually** in America

3. Estimated **$210 billion** in healthcare costs annually (21%)


Cawley, J. J Health Econ (2012)
Figure 1: Obesity among adults, 2015 or nearest year
15% of people maintain weight loss in the long term

Why is it so hard to lose weight?

The Metabolic Set Point
Body Weight Homeostasis

- **Decrease** in basal metabolic rate
- **Increase** in exercise efficiency
- **Neuro-hormonal** regulation of satiety

In addition, there is no magic pill...
So, what do we recommend?

Healthy, Low Fat Diets
U.S. FOOD CONSUMPTION AS A % OF CALORIES

PLANT FOOD: 12%

ANIMAL FOOD: 25%

PROCESSED FOOD: 63%

Added Fats & Oils, Sugars, Refined Grains


New York Coalition for Healthy School Food * www.healthychoolfood.org
Special thanks to Joel Fuhrman, MD, author of Disease Proof Your Child: Feeding Kids Right * Graphics by MicheleBando.com
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US Sugar Consumption, 1822-2005

Sugary Consumption (lb/year/person)

1820 1840 1860 1880 1900 1920 1940 1960 1980 2000
Potential Problems with Low Fat Diets

1. Americans consume a lot of processed food
   a. High in Refined Sugar
      i. High glycemic index
      ii. Weight gain
      iii. Metabolic syndrome

How does sugar cause weight gain?
Insulin and Glucagon:

Blood sugar regulation
Insulin

1. Shifts glucose into cells
2. Promotes weight gain and anabolic metabolism
3. Suppresses glucagon and catabolism

Blood Sugar Regulation
1. Large portion of our population trying to lose weight

2. American diet is very high in refined carbohydrates

3. Foods with high glycemic index trigger insulin release

4. Insulin release = anabolism

5. Weight gain leads to metabolic syndrome
More importantly...

I gained **50** pounds in residency...
Reversing a 50 pound weight gain = Intense Clinical Relevance
Can I use this knowledge to facilitate weight loss?
Objectives

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3. **Explore Efficacy and Safety of the Ketogenic Diet**
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The Ketogenic Diet

1. **Very low** carbohydrate diet

   a. Typically \(< 20 \text{ g}\) of carbohydrates daily or \(<10\%\) of total caloric intake from carbs
Carbs

FAT

Protein
Protein
1 g/kg

Carbohydrate
<20 g

FAT
Why would this make you lose weight?

1. Depletion of glycogen stores → diuresis
2. Glucagon release leads to fat metabolism
3. Oxidation of fatty acids in the liver and release of ketones bodies

How are ketones utilized?

\[ \text{Beta-hydroxybutyrate} \rightarrow \text{Acetoacetate} \rightarrow \]

\[ \text{Acetoacetyl-CoA} \rightarrow 2 \text{ molecules of Acetyl-CoA} \]
The Krebs Cycle:
How is this different than DKA?
1. **Dietary ketosis is a** controlled process

2. **Ketone concentration of** ~8 mmol/L (vs 30)

3. **Body buffers the ketones, pH remains** normal

1. Low carb diets lead to **depletion of glycogen**

2. A conversion to **fat metabolism** occurs

3. Ketone bodies are an **effective** energy source

4. Clinically **different** entity than DKA
Objectives

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Is the ketogenic diet effective for weight loss?
Weight Loss with a Low-Carbohydrate, Mediterranean, or Low-Fat Diet

DIRECT Trial

Dietary Intervention Randomized Control Trial
Design

1. Randomized 322 individuals by diet
   a. Mean age of 52
   b. Mean BMI of 31

Design

2. 3 Study Groups

a. Low carb diet → Atkins

b. Mediterranean diet

c. Traditional low fat diet (based on AHA guidelines)

3. Primary end point was weight loss

1. Low carb diet was **not** calorie restricted

   a. <20 g carbs daily

2. Low fat and Mediterranean diets were calorie limited

   a. 1500 for women, 1800 for men

3. Subjects were predominantly **male** (86%)

Figure 2

P < 0.001 for both comparisons with the low-fat diet

Mean Weight Change (kg)

Months of Intervention

Low-fat diet
Mediterranean diet
Low-carbohydrate diet
Figure 3

A. HDL Cholesterol

B. Triglycerides

C. LDL Cholesterol

D. Ratio of Total Cholesterol to HDL Cholesterol

Conclusions

Low carb diets are as safe as low fat diets and more effective for weight loss.

Schwartzfuchs D. NEJM (2012)
4 Years Later

1. Serum CVD biomarkers remained **favorable**

2. Weight loss remained **significant**

Schwartzfuchs D. NEJM (2012)
Have these results been replicated in women?
Comparison of the Atkins, Zone, Ornish, and LEARN Diets for Change in Weight and Related Risk Factors Among Overweight Premenopausal Women
The A TO Z Weight Loss Study: A Randomized Trial

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THE ONGOING OBESITY EPIDEMIC, along with its health costs and consequences and the health benefits of weight loss, have been well established. National dietary weight loss guidelines (ie.

Context Popular diets, particularly those low in carbohydrates, have challenged current recommendations advising a low-fat, high-carbohydrate diet for weight loss. Potential benefits and risks have not been tested adequately.

Objective To compare 4 weight-loss diets representing a spectrum of low to high carbohydrate intake for effects on weight loss and related metabolic variables.


Intervention Participants were randomly assigned to follow the Atkins (n=77), Zone (n=79), LEARN (n=79), or Ornish (n=76) diets and received weekly instruction for 2 months, then an additional 10-month follow-up.

Main Outcome Measures Weight loss at 12 months was the primary outcome. Secondary outcomes included lipid profile (low-density lipoprotein, high-density lipoprotein, and non-high-density lipoprotein cholesterol, and triglyceride levels), percentage of body fat, waist-hip ratio, fasting insulin and glucose levels, and blood pressure. Outcomes were assessed at months 0, 2, 6, and 12. The Tukey studentized range test was used to adjust for multiple testing.
The A TO Z Weight Loss Study

1. Randomized **311** women to diet
   a. Mean age **40**
   b. Mean BMI > **30**

2. Primary endpoint was **weight loss** at 1 year

Gardner et al.  JAMA (2007)
Figure 2

Gardner et al. JAMA (2007)
Secondary Outcomes

1. No adverse effect of Atkins on lipid variables

2. Atkins had greatest reduction in triglycerides (P = 0.01)

3. Atkins had greatest reduction in BP (P = <0.01)

4. Atkins had greatest reduction in BMI (P = 0.01)

Gardner et al. JAMA (2007)
Conclusions

1. The ketogenic diet is also **efficacious** for weight loss in a large population of women

2. CVD risk modification **as encouraging** as DIRECT Trial

Gardner et al. JAMA (2007)
How does ketogenic diet affect lean muscle mass?
Body Composition Changes After Very-Low-Calorie Ketogenic Diet in Obesity Evaluated by 3 Standardized Methods

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Author Notes


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Design

1. 20 patients
   a. Given 800 calories per day
   b. < 50 g carbs daily
   c. All achieved a 20 kg weight loss

2. Ketosis confirmed by capillary blood

3. Body composition evaluated by 3 validated tools

Change in Fat Mass

Figure 2.

Change in Lean Mass

Figure 3.

Conclusions

Low carb diets cause weight loss predominantly from visceral fat and preserve lean muscle

How could anyone comply with this diet?
Study participants who are in ketosis spontaneously restrict caloric intake...
ORIGINAL ARTICLE

Ketosis and appetite-mediating nutrients and hormones after weight loss

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BACKGROUND/OBJECTIVES: Diet-induced weight loss is accompanied by compensatory changes, which increase appetite and encourage weight regain. There is some evidence that ketogenic diets suppress appetite. The objective is to examine the effect of ketosis on a number of circulating factors involved in appetite regulation, following diet-induced weight loss.

SUBJECTS/METHODS: Of 50 non-diabetic overweight or obese subjects who began the study, 39 completed an 8-week ketogenic very-low-energy diet (VLED), followed by 2 weeks of reintroduction of foods. Following weight loss, circulating concentrations of glucose, insulin, non-esterified fatty acids (NEFA), β-hydroxybutyrate (BHB), leptin, gastrointestinal hormones and subjective ratings of appetite were compared when subjects were ketogenic, and after refeeding.

RESULTS: During the ketogenic VLED, subjects lost 13% of initial weight and fasting BHB increased from (mean ± s.e.m.) 0.07 ± 0.00 to 0.48 ± 0.07 mmol/l (P < 0.001). BHB fell to 0.19 ± 0.03 mmol/l after 2 weeks of refeeding (P < 0.001 compared with week 8). When participants were ketogenic, the weight loss induced increase in ghrelin was suppressed. Glucose and NEFA were higher, and amylin, leptin and subjective ratings of appetite were lower at week 8 than after refeeding.

CONCLUSIONS: The circulating concentrations of several hormones and nutrients which influence appetite were altered after weight loss induced by a ketogenic diet, compared with after refeeding. The increase in circulating ghrelin and subjective appetite which accompany dietary weight reduction were mitigated when weight-reduced participants were ketogenic.


Keywords: appetite; ketosis; very-low-energy diet; weight loss
Findings

1. Ghrelin levels were lower than expected.

2. Ketotic patients did not feel hungry.


What about the metabolic set point?

Does keto promote weight regain?
Effects of Dietary Composition on Energy Expenditure During Weight-Loss Maintenance

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Context  Reduced energy expenditure following weight loss is thought to contribute to weight gain. However, the effect of dietary composition on energy expenditure during weight-loss maintenance has not been studied.

Objective  To examine the effects of 3 diets differing widely in macronutrient composition and glycemic load on energy expenditure following weight loss.

Design, Setting, and Participants  A controlled 3-way crossover design involving 21 overweight and obese young adults conducted at Children's Hospital Boston and Brigham and Women's Hospital, Boston, Massachusetts, between June 16, 2006, and June 21, 2010, with recruitment by newspaper advertisements and postings.

Intervention  After achieving 10% to 15% weight loss while consuming a run-in diet, participants consumed an isocaloric low-fat diet (60% of energy from carbohydrate, 20% from fat, 20% from protein; high glycemic load), low-glycemic index diet (40% from carbohydrate, 40% from fat, and 20% from protein; moderate glycemic load), and high-glycemic index diet (60% from carbohydrate, 20% from fat, and 20% from protein; high glycemic load) for 2 months each, with a 2-week washout period.
Design

1. Enrolled 21 obese adults
2. Achieved a 10 - 15% weight reduction
3. Trialed 3 maintenance diets
4. Monitored basal and total energy expenditure

Ebbeling CB. JAMA Network (2012)
Design

**Figure 1. Study Design of the Run-in and Test Phases**

- **Run-in phase**
  - Weight monitoring
  - Weight loss
  - Weight stabilization

- **Test phase**
  - Weight loss maintenance
  - Test diet A
  - Test diet B
  - Test diet C

- **Randomization to diet sequence**

- **Assessment**
  - Body composition assessment
  - Assessment under free-living conditions
  - Inpatient hospital admission

Ebbeling CB. JAMA Network (2012)
Results

1. **Decrease in energy expenditure greatest for the low-fat diet**
   
   a. **REE:** -205 [-265 to -144] kcal/day
   
   b. **TEE:** -403 [-606 to -239] kcal/day

2. **Decrease in energy was the least for the very low carbohydrate diet**
   
   1. **REE:** -138 [-198 to -77] kcal/day
   
   2. **TEE:** -97 [-281 to 86] kcal/day

Ebbeling CB. JAMA Network (2012)
1. Ketogenic diet is **effective** for weight loss

2. CVD risk factors **appear to improve** with ketogenic diet

3. Rapid loss does not negatively impact **lean body mass**

4. Metabolism may be **preserved** on a very low carb diet

5. Ketosis modifies **appetite and satiety**
What about safety?
Objectives

1. Identify Clinical Relevance
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Why not find out for myself?
My Plan

✓ Buy a food scale
✓ Track my macronutrients
✓ Eat < 20 grams of carbs daily
✓ Monitor urine ketones
✓ Maintain an exercise plan
My Stats

✓ Starting weight of 236 lbs
✓ Averaged 1200 calories per day
✓ Averaged 100 gram of protein daily
✓ Averaged 22 grams of carbs daily
At the end of the day...

- I lost **38 pounds** in 15 weeks
- Roughly **0.4 pounds** per day
- Decreased blood pressure by **10 mmHg**
- Decreased waist size by **6 inches**
Conclusions
✓ The ketogenic can be safe and effective

✓ It offers certain advantages over traditional diets

✓ Keto may appeal to certain patients

✓ Likely an effective tool for rapid and potentially durable weight loss


