The truth is rarely pure and never simple.

Oscar Wilde
Overview of Today!

- Our Big Fat Mess
- The Perfect Storm
- Food as Medicine: The Matrix and Fat
- Biology of Obesity
- Slippery Science of Fat
- Fat and Heart Disease
- Saturated Fat and Heart Disease
- Cholesterol and Statins
- Understanding PUFA’s
  - Omega 6 and Omega 3 fat
Overview of Today

• Meat? To Eat or Not to Eat
• Areas of Agreement – Olive oil, Nuts, Trans Fats
• Controversies: Eggs, Meat, Coconut Oil
• What Should I Eat? The Pegan Diet
75% of Americans

40% of children
DIABESITY
Age-adjusted Prevalence of Obesity and Diagnosed Diabetes Among US Adults

Obesity (BMI $\geq 30$ kg/m$^2$)

1994

2000

2013

Diabetes

1994

2000

2013

No Data       <14.0%       14.0%–17.9%       18.0%–21.9%      22.0%–25.9%      > 26.0%

No Data         <4.5%         4.5%–5.9%           6.0%–7.4%        7.5%–8.9%            > 9.0%

Origins of Diet-Heart & Dietary Fat – Obesity Hypothesis

• The Perfect Storm
  • Scientists: Ancel Keys – 7 Countries Study
    – Professional Associations: AHA, ADA, AND
  – USDA Dietary Guidelines
    • McGovern Report: 1977 Diet Guidelines
    • 1992 Food Pyramid
    • My Plate
    • 2015 Dietary Guidelines = 180 degree turn!
  – Food Industry
    • 600,000 food products mostly low fat with added sugar
Current View of Obesity: Lack of Willpower

- Energy Balance: Fact or Fiction?
  - Calories In/Calories Out?
  - Global Energy Balance Network?
- Food Industry/Government Policy
  - Eat More, Exercise Less?
- Moderation
  - No Good or Bad Calories?
- Exercise?
  - Is it a viable weight loss strategy
= Walk 4.5 miles
4 miles a day for one week
TIME
THE WEEKLY NEWSMAGAZINE

Diet & Health

PHYSIOLOGIST
ANCEL KEYS

TIME
CHOLESTEROL
And Now the Bad News

©2011 The Institute for Functional Medicine
Ancel Keys on the cover of Time Magazine in 1961. He claimed that saturated fats in the diet clogged arteries and caused heart disease.

Time Magazine cover story in 2014. Scientists were wrong about saturated fats. They don’t cause heart disease after all.
Pure, White and Deadly

How Sugar is Killing Us and What We Can Do to Stop It

John Yudkin
The McGovern Report

Dietary Goals For The United States

Prepared By The Staff Of The Select Committee On Nutrition And Human Needs
United States Senate
February 1977

Original Document Printed for the use of the Select Committee on Nutrition and Human Needs

U.S. Government Printing Office
Washington : 1977
Sugar, Fat and CVD

• Large meta-analysis of 72 studies on fat show no link with CVD except trans fats

• Large meta-analysis on sugar found significant link to CVD
  – HR for CVD 1.3 for lowest and 2.75 for highest sugar consumption

• Large meta-analysis found sugar CVD risk factor independent of weight gain
  – *American Journal Clinical Nutrition* 2014 May 7
146 LBS FLOUR
152 LBS SUGAR
Sugar Facts and Diabesity

• Sugar consumption: 152 lbs/yr up
• Flour consumption: 146 lbs/yr (GI 100)
• Added sugars:
  – 600,000 products and 80% with added sugar
  – 8-15% calories from soda
  – HFCS biggest source of calories in diet
• Children sugar consumption facts: 34 tsp a day
“In a well balanced diet we need two liters of liquids a day. Soft drinks can be a healthy part of that intake. I would reject any argument that they are in any way harmful.”

Chair of American Beverage Association in testimony to Congress
Sugary Drinks: 184,000 deaths/year

- 133,000 deaths from diabetes
- 45,000 deaths from cardiovascular disease
- 6,450 deaths from cancer

The Biology of Obesity

What drives controls weight gain and weight loss?
Does EATING MAKE you FAT?
CARBS ARE KILLING YOU!
WHY EATING FAT DOESN'T MAKE YOU FAT

FAT'S GOT A BAD RAP. WE'VE HEARD THAT CURBING OUR CONSUMPTION OF FATTY FOODS WILL HELP US LOSE WEIGHT. WE'VE REDUCED OUR FAT INTAKE, BUT OBESITY IS THRIVING.

SO WHAT GIVES? THE ANSWER: IT'S NOT FAT'S FAULT.

INSTEAD, DIETS RICH IN CARBOHYDRATES HAVE BEEN SECRETLY STORING FAT, SLOWLY GROWING OUR WAISTLINES AND OUR OBESITY EPIDEMIC.
DON'T BELIEVE IT? HERE'S HOW IT HAPPENS.
EAT FAT, GET THIN

Why the Fat We Eat Is the Key to Sustained Weight Loss and Vibrant Health

"Finally we can all kick that low-fat muffin to the curb. And get our slim, healthy bodies back!"
—CHRISTIANE NORTHROP, MD

Mark Hyman, MD
#1 BESTSELLING AUTHOR OF The Blood Sugar Solution
Increasing Adiposity Consequence or Cause of Overeating?

Ninety years ago, an editorial in JAMA questioned the prevailing approach to obesity treatment. “When we read that the fat woman has the remedy in her own hands—or rather between her own teeth”... there is an implication that obesity is usually merely the result of unsatisfactory dietary bookkeeping... [Although logic suggests the body fat] may be decreased by altering the balance sheet through diminished intake, or increased output, or both... [the problem is not really so simple and uncomplicated as it appeared].” Since then, billions of dollars have been spent on research into the biological factors affecting body weight, but the near-universal remedy remains virtually the same: to eat less and move more. According to an alternative view, chronic overeating represents a manifestation rather than the primary cause of increasing adiposity. Attempts to lower body weight without addressing the biological drivers of weight gain, including the quality of the diet, will inevitably fail for most individuals. This viewpoint summarizes the evidence for this seemingly counterintuitive hypothesis, versions of which have been debated for more than a century.

Physiological Mechanisms

Voluntary changes in calorie intake predictably produce short-term weight change, suggesting the possibility of conscious control of body weight over the long term. However, feeding studies demonstrate that changes in energy balance produce biological adaptations that antagonize ongoing weight loss or gain. For instance, in a study in which 41 lean or obese research participants were underfed or overfed to achieve 10% to 20% weight change, energy expenditure decreased or increased, respectively. These metabolic responses and reciprocal changes in hunger serve to defend baseline body weight. Indeed, only a small proportion of over- and obese people in the United States report ever having maintained weight loss of at least 10% for 1 year.

Metabolic Fuel Concentration, Hunger, Body Weight

The body has a continuous energy requirement, and for this reason, the concentration of major metabolic fuels—glucose, nonesterified fatty acids, and ketones—is tightly controlled, with their combined total ranging in the plasma between 4 and 6 mM, according to one study of 8 obese young adults. An acute decrease in the circulating concentration or oxidation of these fuels provokes intense hunger and food intake. Conversely, pharmacological manipulations that increase metabolic fuel availability, such as fatty acid synthase inhibition or β3 agonist administration, lower food intake.

Disorders involving the anabolic hormone insulin highlight the potential influence of metabolic fuel concentration on body-weight regulation. Insulin drives glucose and nonesterified fatty acids into storage forms through coordinated effects on carbohydrate and fat metabolism. States of increased insulin action, such as excessive insulin treatment in diabetes and insulinomas, predictably cause weight gain, whereas decreased insulin action (eg, insulin omission in type 1 diabetes) results in weight loss.

Metabolic Defects May Precede Overeating in Obesity

In experimental models, obesity may arise from genetic manipulation of energy homeostasis pathways throughout the body that do not affect food intake, including muscle-specific insulin receptor ablation, adipose-specific overexpression of FIH hydroxysteroid dehydrogenase type 1 (an enzyme involved in glucocorticoid metabolism), and liver-specific overexpression of sterol regulatory element binding protein-4c (a transcription factor regulating de novo lipogenesis). Of particular relevance, changes in dietary composition can produce obesity in genetically normal animals, independent of an increase in calorie intake. Rats fed a high vs low glycemic index diets developed hyperinsulinemia, increased expression of fatty acid synthase in fat tissue, and greater incorporation of glucose into lipids—metabolic abnormalities that predispose to excessive fat deposition. When the high glycemic index animals were food-restricted to prevent excessive weight gain, they still gained substantially more fat (70%) than the low glycemic index animals and also exhibited adverse changes in cardiovascular disease risk factors.

This combination of increased adiposity despite reduced energy intake cannot be explained by the calorie-centric view of obesity but may be understood by the alternative model. Various genetic or environmental factors, including the quality of the diet (Figure), induce an excessively anabolic state that favors storage rather than oxidation of ingested calories (ie, increased lipogenesis, and uptake of glucose/palmitate into fat cells, and lower fasting lipolytic and insulin resistance in muscle). Subsequently, hunger increases and energy expenditure decreases, reflecting the body’s attempt to compensate for the loss of circulating metabolic fuels sequestered into adipose tissue and therefore unavailable for other metabolic requirements.

A Focus on Diet Composition, Not Total Calories, May Best Facilitate Weight Loss

If anabolic metabolic defects precede and promote overeating, then conventional calorie-restricted diets would comprise symptomatic treatment, destructive failure over the long term for most people in an environment of unlimited food availability. Such diets could exacerbate the underlying metabolic dysfunction by further limiting metabolic fuel availability, lowering energy expenditure, and increasing hunger (recapturing the starvation response amid apparent nutritional adequacy). However, qualitative aspects of diet may improve metabolic function and increase...
Hypothesis:

Obesity driven by dietary composition not calories
Energy Intake

Calories Consumed (eating)

Energy Expenditure

Resting Calories

Activity

Exercise

Energy Balance

IFM
“Eat less and exercise more? That’s the most ridiculous fad diet I’ve heard of yet!”
Energy Balance?

• First Law of Thermodynamics
• Energy is conserved in a **SYSTEM**
• Is it true for human metabolism?
Energy Balance
Useful Concept or Not?

• Changes in metabolic rate, fat storage, hunger depends on dietary composition

• FOOD AS INFORMATION!
  – Food quality and dietary composition
  – Triggers shifts in catabolism/anabolism
  – Hormones (insulin, adiponectin, resistin), neurotransmitters, cytokines (IL-1, IL-6)
  – Schoeller DA. The energy balance equation: looking back and looking forward are two very different views. Nutr Rev. 2009 May;67(5):249-54.
Dopamine effects

nucleus accumbens

Opioid effects

gluteomorphins
Systems Approach to Obesity

The Functional Medicine Matrix
What are drivers of obesity?

• Nutrition
  – Surfeit of calories (500 kcal increase per person since 1970, mostly HFCS)
  – Increase in sugar and CHO consumption–
    • Sugar: 10 lb to 152 lbs per person/year since 1800
    • Flour: 146 lbs per person/year
  – Nutrient deficiencies (n3, vitamin D, Mg, etc.)
  – Changes in dietary composition (low fiber, low fat, high CHO, trans fat, processed foods, etc.)
What are drivers of obesity?

• **Assimilation (Gut)**
  – Changes in *microbiome* (diet, medications, birth methods, breast feeding trends, toxins, GMO)
  – Leaky Gut – metabolic endotoxemia

• **Defense and Repair**
  – Inflammation: food sensitivities, hybridization, GMO, infections, toxins

• **Detoxification**
  – Environmental toxins “*obesogens*”, POP’s, metals
What are drivers of obesity?

- **Energy**
  - Mitochondrial dysfunction (sugar, toxins, inflammation)
- **Communication**
  - Stress & cortisol, insulin, appetite regulation, anabolic/catabolic states
- **Antecedents**
  - Genetics (DRD2, thrifty gene, etc.)
- **Social trends**
  - Food convenience, outsourcing cooking to corporations, demise of home cooking
- **Others?**
New Weight Loss Drug
How does food influence human biology?

Beyond Calories

Food as Information

Dietary Composition
Properties of Food

• Energy – Calories
• Macronutrients (protein, fat, CHO)
• Micronutrients (vitamins and minerals)
• Fiber
• Phytonutrients
• Plant genome
• “Anti-nutrients”
Food as Medicine
Through the Lens of the Matrix
The Role of Fat as Medicine
The Patient’s Story Retold: Organizing the Patient’s Clinical Imbalances

**Physiology and Function**

**Antecedents** (Predisposing Factors - Genetic/Environmental)
- Assimilation (e.g., Digestion, Absorption, Microbiota/GI, Respiration)
- Defense & Repair (e.g., Immune, Inflammation, Infection/Microbiota)

**Triggering Events** (Activators)
- Structural Integrity (e.g., from Subcellular Membranes to Musculoskeletal Structure)

**Mediators/Perpetuators** (Contributors)
- Communication (e.g., Endocrine, Neurotransmitters, Immune messengers)
- Biotransformation & Elimination (e.g., Toxicity, Detoxification)
- Transport (e.g., Cardiovascular, Lymphatic System)
- Energy (e.g., Energy Regulation, Mitochondrial Function)
- Spiritual (e.g., meaning & purpose, relationship with something greater)
- Mental (e.g., cognitive function, perceptual patterns)
- Emotional (e.g., emotional regulation, grief, sadness, anger, etc.)

**Personalizing Lifestyle Factors**

- Sleep & Relaxation
- Exercise & Movement
- Nutrition & Hydration
- Stress & Resilience
- Relationships & Networks

Name: ___________________  Date: ______________  CC: ___________________  © Copyright 2011 Institute for Functional Medicine
Nutrigenomics

- Nutrigenomics
  - PPAR signaling EPA (n3) vs. Trans fat (TFA)
    - EPA improves insulin signaling, increases fatty acid oxidation and reduces inflammation
    - TFA impairs insulin signaling, slows fatty acid oxidation and increases inflammation
  - Sterol Regulatory Element Binding Proteins (SREPB): fatty acid & cholesterol metabolism
  - Gene transcription factors (NK-kB, FOXO, etc.)

Am J Clin Nutr June 2006 vol. 83 no. 6 S1520-1525S
Examples of the different gene families regulated by n-3 fatty acids and their interaction.
Nutrient Status

• Essential fatty acid deficiency
  – Heart disease, dyslipidemia, hypertension, arrhythmia
  – Metabolic disease: diabetes, obesity
  – Neurocognitive disorders: dementia, depression, bipolar disease, ADHD, intelligence (breast milk and IQ), schizophrenia
  – Immune disorders: autoimmune disorders, skin disorders (eczema), asthma, cancer (prostate, breast, colon, etc.)
Communication

• Communication (hormones, neurotransmitters and cell signaling)
  – Sex hormones: building block is cholesterol
  – High fat diets increase testosterone and reduce estrogen in men
  – High fat, low CHO diets reduce insulin, increase lean body mass, reduce fat mass and increase total T4
    • *Metabolism* 2002 Jul;51(7):864-70.
  – Hibblen: n6 increase and n3 decrease increases depression, suicide, homicide and violence
    • *Lipids* 2004;39:1207–13
  – EFA: Role in depression, bipolar, dementia, ADHD, schizophrenia
Immune Modulation

- Cytokine and eicosanoid pathways regulated by fatty acids including ALA, EPA/DHA, GLA, arachidonic acid, linolenic acid
- Omega 6 – inflammatory eicosanoids
- Omega 6 GLA – role as anti-inflammatory in autoimmune, eczema, etc.
- Omega 3 – anti-inflammatory eicosanoids
Metabolic Pathways of Omega-3 and Omega-6 Fatty Acids

**Omega-6**
- Linoleic Acid (LA)
  - Polyunsaturated oils, including flax, corn and safflower
  - Delta-6-desaturase
  - Gamma-Linolenic Acid (GLA)
    - Black Currant, EPO, Borage (18-24% GLA)
  - Dihomo-Gamma-Linolenic Acid (DGLA)
    - Delta-5-desaturase
      - Arachidonic Acid (AA)
        - Lipoxigenase
        - Cylooxygenase (COX2)
        - LBT-4 Pro-inflammatory
        - PGE-2 Pro-inflammatory

**Omega-3**
- Alpha-Linolenic Acid (ALA)
  - Black Currant (15%) Flax (85%)
  - Delta-6-desaturase
    - Delta-5-desaturase
      - Steridonic Acid (SDA)
        - Eicosatetiaenoic Acid (ETA)
          - Delta-5-desaturase
            - EPA/DHA
              - Fish Oil & Cod Liver Oil

**DGLA and EPA block Omega 6 AA buildup and downstream conversion**

- Tear Specific Anti-inflammatory
  - PGE1
  - BioTears Curcumin inhibits COX2

**LBT-5 Anti-inflammatory**
Detoxification

• NAFLD (fatty liver) affects 90 million in US
• Result of metabolic syndrome (high CHO and sugar diet)
• Dietary intervention with 70% corn oil (n6 PUFA) or 65% MCT oil (saturated fat)
  – n6 PUFA increased fatty liver, and LFT’s
  – MCT oil reversed fatty liver, reduced free radicals, increased fatty acid oxidation and PPAR activation and mitochondrial function
Assimilation (Gut & Microbiome)

• High n6 oils increase metabolic endotoxemia through increase LPS and effects of TNF alpha on insulin signaling

• High n3 oils reduce inflammation and do not create endotoxemia

• Olive oil reverses increases in TMAO from meat consumption
Energy and Mitochondrial Function

- MCT’s (coconut oil) increase fatty acid oxidation
- Increases metabolism and energy expenditure
- MCT absorbed directly from portal system and directly metabolized
- Associated with improved body composition and weight loss
- Increased sports performance
Structural Integrity

- Cell membranes composition
- Essential fatty acids
- Phospholipids
- Eicosanoid metabolism
NOT ALL CALORIES ARE CREATED EQUAL
Failure of Current Treatment Models

• Calorie restriction – Failure of Model
• Why it fails: **Compensatory mechanisms** defend against weight loss by decreasing energy expenditure and increasing appetite
• Calorie hypothesis: Flaws
  – Multiple factors regulate metabolism
    • Dietary composition, microbiome, toxins, infections, allergens, nutrient status, mitochondrial dysfunction, hormonal and neurotransmitter dysregulation, social
Calories or Quality?

- Reductions in CVD with changes in fat composition
- DART, PREDIMED, GISSI trials
- Look Ahead – low fat, low calorie diet, no change in outcomes even with weight loss
- Diabetes reversal with high fat diets
- CHF reversal with high fat diets

Open Heart. 2015 Aug 10;2(1)
How does dietary composition affect hunger and metabolism?
Is Your Fat Hungry?
Hungry Fat?  
Chicken or Egg?  
Does being fat make you hungry or being hungry make you fat?
Does Overeating Make You Fat?

• Being fat makes you overeat
• Visceral fat as anabolic driver of behavior
• Visceral fat biology
  – Hormones and neurotransmitters
    • adiponectin, resistin, insulin, leptin, MSH
  – Cytokines
    • IL-6, IL-1, TNF alpha, etc.
Dietary Glycemic Index: Reward and Cravings

- Lennerz BS, et.al, Effects of dietary glycemic index on brain regions related to reward and craving in men.
Nucleus Accumbens
Overeating: Cause or Effect?
Increasing Adiposity
Consequence or Cause of Overeating?

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Opinion

Ninety years ago, an editorial in JAMA questioned the prevailing approach to obesity treatment: “When we read that the fat woman has then remedy in her own hands—or rather in her own teeth!... there is an implication that obesity is usually merely the result of unsatisfactory dietary bookkeeping...” (Although logic suggests that body fat may be decreased by altering the balance sheet through diminished intake, or increased output, or both... the problem is not really so simple and uncomplicated as it appears.) Since then, billions of dollars have been spent on research into the biological factors affecting body weight, but the near-universal remedy remains virtually the same: to eat less and move more. According to an alternative view, chronic overeating represents a manifestation rather than the primary cause of increasing adiposity. Attempts to lower body weight without addressing the biological drivers of weight gain, including the quality of the diet, will inevitably fail for most individuals. This Viewpoint summarizes the evidence for this seemingly counterintuitive hypothesis, versions of which have been debated for more than a century.

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Always Hungry?

Conquer Cravings, ☑
Retrain Your Fat Cells, ☑
& Lose Weight Permanently ☑

David Ludwig, MD, PhD
Overeating: Cause or Effect

• Problem with Weight Loss
  – Inability to voluntarily control food intake
  – Can you change voluntary intake by controlling dietary composition?
  – In environment of unrestricted refined sugar and CHO – partition toward fat deposition and excess hunger
  – Calorie restriction antagonizes weight loss through biological adaptations decrease energy expenditure
Dietary Composition
JAMA 2012; 307(24):2627-2634

• Cross over trial iso-caloric diets
• low fat/high glycemic (10% fat/60 carbs/30 protein)
• vs. low GL (40/40/20)
• vs. high fat VLCD (60% fat/20% carbs/20% protein)
Dietary Composition

- Decrease in REE (resting energy expenditure) greatest in low fat group
- Least decrease in REE in VLCD/high fat
- Overall difference of >300 kcal/day
- Low VLCD – most improvements in insulin resistance, HDL, TG, PAI-1 lower, but CRP higher (0.87 vs. 0.78)
Low-carb vs. low-fat diets

Results from a new study published Monday

- **Low-carbohydrate diet**
- **Low-fat diet**

**Change in body weight**

- 0 months: -5.7 pounds
- 3 months: -12.6 pounds
- 6 months: -11.7 pounds
- 12 months: -4 pounds

**Change in heart disease risk score**

- 0 months: 0.4%
- 3 months: -0.5
- 6 months: -1.0
- 12 months: 0.4

*Estimated 10-year risk for coronary heart disease, represented by Framingham risk score

Source: Annals of Internal Medicine
From: Increasing Adiposity: Consequence or Cause of Overeating?


**Figure Legend:**
Prevailing and Alternative Models of Obesity
Is your fat hungry?
Metabolic Fuels & Appetite

Availability of metabolic fuels regulates hunger and food intake

- Glucose, non-esterified fatty acids and ketones
- Tightly controlled at 4-6 kcal/L
- Insulin decreases metabolic fuel availability
Dietary Composition, Metabolic Fuels & Appetite

PloS ONE 2013;8:e58172

- Iso-caloric LF, LGI and VLC diets randomized crossover design for 4 weeks
- Measured energy availability (EA) (glucose, FFA, β-OH-butyrate or ketones)
- Low fat diet – lower EA and metabolic rate
- VLC had highest EA and metabolic rate
Role of Insulin

• Insulin is anabolic hormone
• Drives circulating fuel into storage
• Stimulates lipogenesis (fat storage)
• Inhibits lipolysis (fat burning)
• Insulin treatment increases weight gain in humans and animals
Dietary Composition vs. Calories
Lancet 2004;364:778-85

• Changes in dietary composition produce obesity in genetically normal animals independent of calorie intake
• Rats fed to maintain identical body weight developed 70% more body fat on high GL vs. low GL diet
• High GL diet results in lower muscle mass despite lower calorie intake
• High GL fed animals develop hyperphagia after onset of hyperinsulinemia
Effects of Glycemic Index in Rodents

Differences in body composition

Low GI

High GI

Dietary Composition: Ketogenic Diet

• Body weight decreased on rats with isocaloric diets that were low GL – improved hepatic gene expression that favors catabolism

• Excessive fat deposition driven by high GL diet precedes and promotes hyperphagia

• Overeating driven by loss of metabolic fuels sequestered in adipose tissue
Dietary Composition vs. Calories

• High GL Food - Intensifies reward value of food leading to hedonic eating
• Mild low blood sugar triggers craving
• Anabolic changes in adipose tissue precede overeating
Calorie Restriction: Effects

- Calorie restricted diets exacerbate metabolic dysfunction leading to more overeating
- Decline in energy expenditure and increase in hunger – triggers starvation response
Weight Loss: Solution?

Negative Energy Balance
or
Lower Anabolic Drive
Lower Anabolic Drive
Automatic WEIGHT LOSS!

Automatically Increases
Energy Expenditure

Automatically Decreases
Voluntary Food Intake
People have more control over WHAT they eat than HOW much they eat.
Willpower?
Why do we crave?
Willpower or Metabolic State of Fat
Treatment Implications
Treatment Implications

• Reduce **anabolic drive** of visceral fat
• Reset neuro-hormonal responses to food
• Normalize brain chemistry and dopamine receptor status to regulate appetite
Chicken or Egg? New Hypothesis

• Diet quality (GL) affects fat storage availability of metabolic fuels (high GL drives sequestration of energy in fat)

• Leading to perceived deficit of metabolic fuels to lower energy expenditure and increase in energy intake
Reduce Anabolic Drive

• **Dietary composition** that favors oxidation vs. substrate storage

• Diet composition vs. calorie or energy balance

• Low glycemic, high micronutrient, phytonutrient content, high fiber
Reduce Anabolic Drive

• Omega 3 to trans fat ratios
• Saturated fat: are all created equal?
• Protein content (quality, nature of protein – plant, animal, which animals)
• Lower inflammation (allergens, obesogens, infections)
Reduce Anabolic Drive

• Microbiome treatments (pre and probiotics) – fecal transplants, HDC’s?
• Treatment of tissue insulin resistance (omega 3 fatty acids, nutrients, exercise, interval training)
• Mitochondrial support
Fat & Heart Disease
Fat and Heart Disease

Saturated Fats?
Omega 6 PUFA’s
Omega 3 PUFA’s
Evidence on Total Fat

• **PREDIMED Study**  N Engl J Med. 2013 Apr 4;368(14):1279-90
  – 7000+ people RCT at risk for MI
  – Low fat control group
  – Treatment group: 1 L or 4 TBSP (500 calories of olive oil or 30 grams of nuts daily)
  – 30% risk reduction in MI independent of calories or weight loss
  – Study ended by IRB after 4.8 years

• **Lyon Heart Study**  – RCT  Circulation 1999;99:77.
  – Higher omega 3 and lower omega 6 fats
  – 73% reduction in MI
Evidence on Total Fat

- Women’s Health Initiative – RCT 49,000 women
  - No evidence of CVD risk reduction on low fat diet despite reductions in LDL cholesterol

- MRFIT Trial - largest RCT *JAMA.* 1976 Feb 23;235(8): 825-7
  - No evidence of CVD risk reduction with lower total fat or saturated fat.

- Nurses Health Study – Observational 80,000 women over 20 years
  - No link between total or saturated fat consumption
Evidence on Fat and CVD

• Cochrane Collaborative:
  – no correlation with total fat and CVD
    • Cochrane Database Syst Rev. 2011 Jul 6;(7)

• Physicians Health Study 1996:
  – observational study 43,000 men no link between total or saturated fat and CVD
  – link to high sugar, low fiber diets and low omega 3 fats
  – If controlled for fiber no link with saturated fat
    • BMJ. 1996 Jul 13;313(7049):84-90.
2015 US Dietary Guidelines

• Advisory Committee:
  – Reduce sugar to 25 grams (6 teaspoons)
  – Reduce sugar sweetened beverages

• Final Guidelines:
  – Reduced added sugars to less than 10% of calories (about 45 grams for 1800 calorie diet)
  – No restriction on total fat
  – Cholesterol: “no longer nutrient of concern”

• Limitations: “added sugars”, low fat, limits on saturated fats, environmental impact of meat, disconnect between polices and guidelines.

• Revision of guidelines process underway
  – http://health.gov/dietaryguidelines/2015/
FDA BAN

Trans Fat 0g

Saturated Fat 0g

Cholesterol 0mg
Saturated Fat?

- Villain?
- Benign?
- Health promoting?
Evidence on Saturated Fat

• Small controlled trial 264 men who had heart attacks no benefit reducing heart attacks or death

• Low fat group ate less 1/3 less fat, 500 less calories per day -- had lower cholesterol and weight than the control group.
Saturated Fat and CVD

- Meta-analysis 72 studies, > 600,000 people from 19 countries
- RCT’s, observational studies, measurement of plasma fatty acids
- Blood saturated fats
  - Even chain palmitic and stearic associated with CVD
  - Produced from CHO and sugar through lipogenesis and not impacted by dietary saturated fat
  - Odd chain margaric (from dairy) associated with reduction in CVD
- Omega 6 PUFA’s
  - No benefit and trend toward increased risk of CVD
  - AA (arachidonic acid) from eggs, poultry and beef showed reduced risk
- Omega 3 fats were protective
- Trans Fats increased risk
- Conclusions: *Current evidence does not clearly support cardiovascular guidelines that encourage high consumption of polyunsaturated fatty acids and low consumption of total or saturated fats.*
Saturated Fat?

- Meta-analysis of 21 studies of 350,000 people over 23 years showed no increased risk of CVD from saturated fat.
- RCTs: Review of all data up to 1983 before dietary guidelines established on fat found no link between saturated fat and CVD.
  - Open Heart. 2015 Jan 29;2(1)
- Risk only found with omega 3 deficiency.
- Post prandial lipids only adversely affected in face of low omega 3’s.
  - Lipids. 2015 Apr;50(4):339-47
Saturated Fat Feeding Studies

• VLCD (12% carbs), high fat diet
  – Either high n6 PUFA or saturated fats 86 grams (774 cals)
  – 8 men over 6 weeks

• Assessed plasma lipids, cholesterol profile, inflammation (CRP)

• Doubling dietary intake of saturated fat had no impact on plasma saturated fat

• Lowest inflammation in the high saturated fat group and lower oxidative stress

• Lower insulin, triglycerides and more large LDL particles
  – Lipids. 2010 Oct;45(10):947-62
CHO and Saturated Fat
“Sweet Fat”

• Adverse effects of “Sweet Fat”
• Promotes atherogenic lipids profile in context of a high CHO diet
Saturated Fat and Inflammation

- Inflammation occurs only in the context of refined CHO and sugar (sweet fat)
- And in context of low omega 3 fats
- With adequate omega 3’s saturated fats lower triglycerides, increase HDL and increase large LDL particles
- High fat diet 55% with 25% saturated fat no impact on inflammatory markers or oxidative stress
Fatty Liver & Inflammation

• Dietary saturated fats (MCT oil) reverses fibrotic fatty liver in rats (n6 PUFA did not show same results)

• Reversal occurred despite continued ethanol intake
  – J Pharmacol Exp Ther. 2001 Nov;299(2):638-44
Cholesterol and Heart Disease

But is it really cholesterol?
Statins: When Are They Indicated?
Men occasionally stumble over the truth, but most of them pick themselves up and hurry off as if nothing ever happened.

--Winston Churchill
Statins: Is LDL Cholesterol the Problem?

- 1998 to 2002 statin use tripled in Sweden
  - No impact on CVD
- 541 hospitals, 231,836 admissions for heart attack equaled 59% of all MI’s in the USA over 6 years
- 75% had normal LDL (under 130mg/dl) and 50% had optimal levels (under 100 mg/dl) and 17% had levels under 70 mg/dl
- Average HDL was 39 mg/dl and average triglycerides 161mg/dl
- 54% had HDL under 40 mg/dl and only 10% had HDL levels over 60 mg/dl
Statins: Primary Prevention?

• Primary Prevention Data Review
  – Selective reporting and not reporting bad outcomes or side effects
  – Included those who had heart attacks
• “Caution should be taken in prescribing statins for primary prevention”
  – Cochrane Database Syst Rev. 2011 Jan 19; (1)
  – Lancet. 2007 Jan 20;369(9557):168-9
Statins: NTT  
www.thennt.com

- **Primary prevention**
  - 1 in 104 prevented heart attack
  - 1 in 154 prevented stroke
  - 0 benefit in preventing death
  - Risks: 1 in 10 had myopathy and 1 in 50 developed diabetes

- **Secondary prevention**
  - 1 in 83 prevented death (1.2%)
  - 1 in 39 prevented no fatal heart attack (2.6%)
  - 1 in 125 prevented stroke (0.8%)
  - Risks: 1 in 10 had myopathy and 1 in 50 developed diabetes
“Virtually all of the major statin studies were paid for and conducted by their respective pharmaceutical company. A long history of misrepresentation of data and occasionally fraudulent reporting of data suggests that these results are often much more optimistic than subsequent data produced by researchers and parties that do not have a financial stake in the results. Also, harm from these drugs is difficult to predict, partly because harms are often difficult to anticipate and are often poorly tracked. Such findings often come up years after new drugs have been on the market.”
Shaky Evidence: Statins

- Low (LDL) with low HDL (good cholesterol) no benefit to statins.
- Lower (LDL) without reduction in inflammation (C-reactive protein), no benefit to statins.
- Healthy women with high cholesterol, no evidence statins reduces risk of heart attack or death.
- Men or women over 69 years old with high cholesterol, there is no proof statins reduce risk of heart attack or death.
  - Lancet. 2007 Jan 20;369(9557):168-9
Statins: Shaky Evidence

- Aggressive cholesterol treatment with two medications (Zocor and Zetia) lowered cholesterol much more than one drug alone, but led to more plaque build up in the arteries and no fewer heart attacks.
- Older patients with lower cholesterol higher risks of death than those with higher cholesterol.
  - N Engl J Med 352:1685, April 21, 2005
- Countries with higher average cholesterol than Americans such as the Swiss or Spanish have less heart disease.
Statins: Common Side Effects?

- 20 percent of people who take statins have side effects including muscle damage and pain, neurologic problems, memory issues, sexual dysfunction and more.

- Statins linked to higher risk of diabetes.
- 26,000 healthy people, statins users had an 87 percent increased risk of getting type 2 diabetes.

- In RCT WHI, 153,840 women, statins users had 48% increased risk of type 2 diabetes.
True Causes of CVD

• Insulin resistance (75% of admissions for MI)
  – Atherogenic lipid profile (low HDL, high TG, small LDL particles)
  – NMR (Labcorp) or Ion Mobility/Cardio IQ (Quest)
  – 2 hour insulin/glucose tolerance test and HbA1c
• Inflammation (elevated CRP): Jupiter Trial
  – All those at risk were those with small LDL and inflammation (liked by insulin resistance)
  – Large LDL (even when elevated in absence of inflammation) didn’t lead to CVD
• Oxidative Stress
• Homocysteine
• Environmental toxins (metals, POP’s)
• Smoking
• Sedentary lifestyle
• Hypertension (secondary to insulin resistance and OSA)
Omega 6 PUFA’s Friend or Foe?
FIGURE 2. Coronary heart disease mortality is proportional to n-6 HUFA in plasma HUFA. Available at <http://efaeducation.nih.gov/sig/personal.html>.
Omega 6 Fat Facts

• 20 percent of calories from soybean oil
  – 10% linoleic acid

• 18 billion pounds per year consumed

• GMO (Round Up Ready and Glyphosate)
Linoleic Acid Data?
Evidence Based or Biased Evidence?

• Lowers LDL
• Increases LDL oxidation (OXLAM’s)
• Increases inflammation
• Cancer promotion?
Eicosanoid synthesis - made ridiculously simple

(LA) n-6 FA

(GLA)

(DGLA)

Stim: Insulin & Statins
Inhib: Glucagon, EPA

(Farmed-raised tilapia & catfish

Arachidonic acid

NSAIDS
Aspirin
Singular

PGE1
TNFA1

PGE2

TXA2
LTB4

Pro-inflammatory

Anti-inflammatory

(ALA) n-3 FA

(EPA)

(DHA)

Resolvins
Neuroprotectins
Docosatrienes

PGE3
LTB5
TXA3

Anti-inflammatory

2004-09 Dr. David Seaman.
Joseph Hibblen (NIH)

- Excess omega 6 and reduction in omega 3 lead to increases in CVD, type 2 DM, obesity, IBS and IBD, psychiatric disorders, autoimmune disease and cancer
Psychiatric Effects
High Omega 6 and Low Omega 3

• 1960 to 1999 increase of LA (from soybean oil) predicted 100 fold increase in homicide deaths.

• Also linked to aggression, depression, suicide

Omega 6: Ramsden & Hibblen

- Two large investigative reviews
  - *World Rev Nutr Diet.* 2011;102:30-43
- In studies that included n3 and n6 there was 27% reduction in CVD events and mortality
- In studies with only omega 6 fats there was a 13% increase in mortality
- RCT’s that used n6 alone while reducing saturated fat and trans fat also showed increase in death
- Most studies didn’t distinguish different PUFA’s (n6 or n3)
- Previous analyses omitted key data
Holes in Omega 6 PUFA Story

• Lyon Heart Study
  – Reduction in n6 with increase in n3
  – 70+% reduction in CVD

• Oslo Heart Study
  – Substituted meat and eggs for fish, shellfish and whalebeef (all rich sources of omega 3)
  – Bread spread (sardines) (equiv of 16 fish oil pills or 5 X GISSI trial with 40% reduction in CVD and 20% reduction in total deaths

• Minnesota Coronary Survey
  – 4393 men and 4663 women
  – Only increased n6 not n3
  – Women doubled risk of MI in first year

• Other data shows at 4.64 increase risk of MI with n6
Sydney Heart Trial

- RCT 1966 to 1973
- Safflower increase to 15% of calories (including soft margarine with some trans fats which both groups had)
- Reduction in saturated fat to less than 10% and cholesterol less than 300 mg a day
- n6 group had 37% increase in heart attacks despite lowering cholesterol
  - BMJ. 2013 Feb4;346
Omega 6: Other Risks

- OXLAMs – Oxidized LDL
- Heat damage
- Solvents
- Dysbiosis – metabolic endotoxemia
- GMO soybeans: Glyphosate residue
  - Agricultural Sciences, 2015, 6, 630-662
Opposing View

- Review by Willet, et. Al found benefit to replacing SFA with PUFA’s
- Not clear if combination or just n6
Food Controversies
Meat: To Eat or Not To Eat?
You Wouldn’t Let Your Child Smoke.

Like smoking, eating meat increases the risk of heart disease and cancer.

Go vegan!

IFM
Meat Issues

- Saturated fat
- Inflammation
- Cancer risk?
- Diabetes risk?
- TMAO production (dysbiosis)
- Polycyclic aromatic hydrocarbons and heterocyclic amines, advanced glycation end products (AGE’s)
Quality of Research

• Mostly limited to observational studies
• Multiple confounding factors
• Biological plausibility? TMAO
• Historical context:
  – Plains Indians: highest per capita centenarians in history
  – Seventh Day Adventists: Blue Zones
Meat Research

- Observational nutritional studies
- Food frequency questionnaires
- Nature of population: Meat eater characteristics – unhealthy habits
- Healthy user effect (meat seen as bad so health conscious people at less)

Healthy Meat Eaters?

• Healthy meat eaters vs. vegetarians
• 11,000 people (57% omnivores and 43% vegetarians who shopped at health food stores)
• Overall death rates cut in half
• No difference between meat eaters or vegetarians
Meat Studies

• NIH-AARP Diet and Health Study
  – *Archives of Internal Medicine*, 169(6), 562–571.
• 500,000 people higher risk of CVD, cancer and death
• Meat eaters: smoked more, weight more, consumed 800 more calories/day, exercised less, ate more sugar, drank more alcohol and ate fewer fruits and veggies and took fewer vitamins
• CAFO meat’s vs. grass fed meat
  – Antibiotics, hormones, pesticides, more omega 6
  – More omega 3 in grass fed beef
Negative Meat Studies

- EPIC study of 500,000 found no association with unprocessed fresh meat and heart disease cancer or death, but association found with processed meat
- 1.2 million meta-analysis: no link between red meat and CVD, diabetes or stroke.
- 65,000 meat eaters with overall healthy diet – no increase risk of CVD or death
- Asian study: 300,000 with increased meat in context of healthy baseline diet, **red meat associated with decrease in heart disease and cancer**
Meat Myths

- Saturated fat in meat does not raise blood cholesterol (mostly neutral stearic acid)
Paleolithic Diet RCT’s

• Australian Aboriginal Study
  – Converting to wild meat and wild diet from western diet reversed diabetes, HTN and lipids abnormalities

• Feeding Studies: Paleo diets better outcomes for weight, body fat, muscle mass, metabolic rate, triglycerides, HDL, large LDL, blood pressure
Diabetes and Meat

• Observational data: 400,000
• 50 gram serving of processed meat (hot dogs, deli meat) increased risk by 51%
• 50 gram serving fresh meat increased risk by 20%
• Relative vs. absolute risk
  – Fresh meat: absolute risk 7% to 8.4% risk of diabetes
• Meat eater: unhealthy group
• Paleo Diet intervention trials reverse type 2 diabetes
  – Cardiovasc Diabetol. 2009 Jul 16;8:35.
TMAO and Heart Disease

- Trimethylamine-N-oxide (TMAO)
- Produced by dysbiotic bacteria from carnitine (meat), choline (eggs) and lecithin (soy)
- Vegetarians who ate steak showed no increase in TMAO
- Antibiotic use prevented TMAO increase after meat consumption
- Highest concentrations of TMAO in fish (with lower risks of CVD?)
- Olive oil, red wine and balsamic vinegar and TMAO
  - Cell, Volume 163, Issue 7, 1585-1595
Red Meat and Cancer

- WHO Review IARC?
  - Processed meat yes
  - Red meat: maybe – dissent on committee (where usually consensus)
  - Degree of risk base line risk calculator
    - i.e. 2.4% risk to 3.2% risk with intake
    - Absolute vs. relative risk?

- Review of 35 prospective studies on colon cancer and meat little risk
  - Am J Clin Nutr. 2014 Sep;100(3):924-9
  - Obes Rev. 2011 May;12(5):e472-93

- Cooking techniques: PAH, HCA, AGE’s
  - Cancer Science, 95: 290–299, Mutat Res. 1999 Jul 15;443(1-2)
Grass Fed vs. CAFO Meat

• CAFO
  – Antibiotics, hormones, pesticides
  – unethical treatment of animals
  – 1/5 of greenhouse gases (methane)
• Grass fed beef
  – Environmental factors: restorative grazing
  – Health benefits: lower omega 6 fats, 2-5x omega 3 fats (ratio 7.5:1 vs. 1.5 to 1), more stearic acid, more antioxidants, CLA (conjugated linoleic acid) with CVD, weight and cancer benefits
  – More vitamin E, beta carotene, vitamin A, zinc, iron, phosphorous and potassium
Eggs?
Eggs: The Data

- Physician’s Health Study: no link to heart disease
- Meta-analysis 16 studies, 90,000 people no link to heart disease
- Prevent LDL oxidation and increase LDL and HDL particle size
- Nutrient dense: B vitamins, A, E, D, minerals (Cu, Fe, Mn, K, Se, Zn), choline, lutein, zeaxanthin
Coconut Oil?
Coconut Oil: The Data

• South Pacific up to 40% of calories from coconut oil (90% saturated fat)

• Increased LDL particle size and increases HDL but lower TC/HDL ratio, lower triglycerides, lower insulin

• Some Pacific Islanders 63% calories from coconut oil without heart disease, obesity or stroke

• Other benefits: immune boosting, antimicrobial, sports performance, brain function
  – Journal of Medicinal Food. 2007 Jun. 10(2)384-7.)
MCT Oil Benefits

• MCT oil benefits
  – Thermic effects (increase metabolism)
  – Decreases visceral fat
  – Weight loss
  – Enhanced cognitive function

• *Lipids.* 2009 Jul. 44(7):593-601
Fat: Other Health Benefits

• High fat diets for treatment of type 1 and type 2 diabetes

• Brain aging and dementia
Fat: Brain Health Benefits

- **Neurologic benefits:**
  - Seizures, depression
  - ADHD, autism
  - trauma, ALS, brain cancer

  - Cancer Metab. 2015 Mar 25;3:3.
  - Expert Opin Investig Drugs. 2013 Dec;22(12):1519-34.
  - Neuropsychopharmacology. 2015 Mar 19.
  - Neurosci Biobehav Rev. 2014 Sep;45:369-78.
Fat: Other Health Benefits

• Autoimmune disease

• Sports performance

• Hair, skin and nails

• Sexual function
What to Eat?
WHAT IS THE PEGAN DIET?

VEGAN + PALEO

Unlimited fruit and vegetables

Small amounts of gluten-free grains, legumes, nuts and seeds

Small amounts of meat and eggs

No dairy
No gluten
No added sugar

YAHOO! HEALTH
The Pegan Diet

- Very low glycemic load
- Very high in vegetables and fruit
- Low or no pesticides, antibiotics or hormones
- Very few to no chemicals, additives, preservatives and GMO foods
- Higher in good quality fats: omega 3, olive oil, nuts and seeds
- Low in refined omega 6 oils (soy, safflower, etc.)
- Adequate protein (vegetable or animal?)
- Ideally organic, whole, fresh, local
- Animal food: sustainably and humanely raised (grass fed, etc.)
- Fish: low mercury fish, sustainable fisheries and farmed
Areas of Controversy

• Dairy
• Grains
• Beans
• Meat
• Eggs
GOOD FATS
GOOD PROTEINS
PHYTONUTRIENTS & ANTIOXIDANTS
SOCIOgenomics
THE DANIEL PLAN
40 DAYS to a Healthier Life

Rick Warren D.Min.
Daniel Amen M.D.
Mark Hyman M.D.
Daniel and Rebecca

- Daniel’s Story: 340 lbs
- Rheumatoid arthritis, chronic fatigue & pain, muscle pain, headaches, allergies, high blood pressure & cholesterol, low testosterone
- Percocet & Energy Drinks
- 15 medications
- Toxicity Score: 152
Daniel and Rebecca

- Rebecca’s Story
- 232 lbs
- Yo-yo diets
- South Beach, Weight Watcher’s, Liquid fasts, diet pills
Daniel and Rebecca

- **Daniel** lost 110 lbs
- FLC Score from 152 to 52 in 40 days
- Lab tests all normal!
- NO medications except preventive aspirin and vitamins

- **Rebecca** lost 58 lbs
If you want to travel swiftly, travel alone.

If you want to travel far, travel together.

African Proverb