The Slippery Science of Fat
Separating Fat From Fiction

Mark Hyman, MD
Director, Cleveland Clinic Center for Functional Medicine
Pritzker Foundation Chair in Functional Medicine,
Cleveland Clinic Lerner College of Medicine
Chairman, Institute for Functional Medicine
March 12, 2015
Outline

- Our Big Fat Mess
- The Perfect Storm
- Food as Medicine: The Matrix and Fat
- Biology of Obesity
- Fat and Heart Disease
- Slippery Science of Fat
- Saturated Fat and Heart Disease
- Cholesterol and Statins
- Understanding PUFA’s
  - Omega 6 and Omega 3 fat
- Meat? To Eat or Not to Eat
- Areas of Agreement – Olive oil, Nuts, Trans Fats
- Controversies: Eggs, Butter, Meat
- What Should I Eat? The Pegan Diet
75% of Americans

40% of children
DIABESITY

HEALTHY  BELLY FAT  PRE-DIABETES  TYPE 2 DIABETES
Age-adjusted Prevalence of Obesity and Diagnosed Diabetes Among US Adults

**Obesity (BMI ≥30 kg/m²)**

1994

2000

2013

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

**Diabetes**

1994

2000

2013

- 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, Government and Food Industry
  – Ancel Keys – 7 Countries Study
• McGovern Report – 1977 Diet Guidelines
• 1992 Food Pyramid
• Revision of Guidelines 2015
Current View of Obesity: Lack of Willpower

• Energy Balance: Fact or Fiction?
• Calories In/Calories Out?
• 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
Epidemiology of Obesity and Chronic Disease

• Role of sugar in chronic disease
  – CVD, type 2 DM, stroke dementia, cancer, etc.

• Fat or Sick: Biology of Obesity

• TOFI or Skinny Fat:
  • 21% type 2 DM normal weight
  • Twice morality of obese diabetics
  • *JAMA.* 2012;308(6):581-590

• New Definition of Obesity?
  – BMI, W/H ratio, Body composition, metabolic obesity (biomarkers- insulin, lipid size)
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.
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 from 40 lbs in 1980
• Flour consumption: 146 lbs/yr (GI 100)
• Added sugars:
  – 600,00 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
Dopamine effects
*nucleus accumbens*

Opioid effects
*gluteomorphins*
“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?
Hypothesis:

Obesity driven by dietary composition not calories
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 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.
“Eat less and exercise more? That’s the most ridiculous fad diet I’ve heard of yet!”
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 consumption – 10 lb to 152 lbs per person/year since 1800 and flour to 146 lbs per person/year.
  – Nutrient deficiencies (n3, vitamin D, Mg, etc.)
  – Changes in dietary composition
What are drivers of obesity?

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

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

- **Detoxification**
  - Environmental toxins “obesogens”
What are drivers of obesity?

- **Energy**
  - Mitochondrial dysfunction

- **Communication**
  - Stress & cortisol, insulin, appetite regulation, anabolic/catabolic states

- **Antecedents**
  - Genetics (DR2, thrifty gene)

- **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 Fats as 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
  - Transcription Factors
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
  - Hibblen: n6 increase and n3 decrease increases depression, suicide, homicide and violence
  - EFA: Role in depression, bipolar, dementia, ADHD, schizophrenia
Immune Modulation

• Cytokine and eicosonoid pathways regulated by fatty acids including ALA, EPA/DHA, GLA, arachidonic acid, linolenic acid
• Omega 6 GLA – role as anti-inflammatory in autoimmune, eczema, etc.
• Omega 3 – anti-inflammatory eicosinoids
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 increase fatty liver, and LFT’s
- MCT 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 TNFalpha on insulin signaling
• High n3 oils reduce inflammation and do not create endotoxemia
Energy and Mitochondrial Function

- MCT’s and fatty acid oxidation
- Increases metabolism and energy expenditure
- MCT absorbed directly from portal system without having and directly metabolized
- Associated with improved body composition and weight loss
- Increase sports performance
Structural Integrity

- Cell membranes composition
- Essential fatty acids
- Phospholipids
- Eicosinoid metabolism
All calories are NOT created equal
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
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
• Treatment of tissue insulin resistance (omega 3 fatty acids, nutrients, exercise, interval training)
• Mitochondrial support
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
Are all calories equal?
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

It is time to stop counting calories, and time instead to promote dietary changes that substantially and rapidly reduce cardiovascular morbidity and mortality.

Aseem Malhotra, 1,2 James D Nicolantonio, 3 Simon Capewell 4

Most heart attacks and ischemic strokes are caused by complicated atheromas usually complicated by thrombus suddenly reducing blood flow in a critical artery. Extensive evidence suggests that the atheromas already build up over many decades. However, atrial fibrillation can be seen even in children who are obese, and fatty streaks are visible in teenagers and young adults. So most cardiovascular events do not manifest until after the age of 40 years. The general perception is that of a slow process that will therefore only reverse slowly if at all. However, this perception is wrong. Extensive experimental and trial evidence shows that substantial reductions in morbidity and mortality occur within months of quitting smoking, and making healthy dietary changes. These reductions apply to both individuals and to entire populations. In one American hospital, admissions for acute coronary syndromes decreased by 40% within 6 months of the introduction of a smoke-free legislation. When the law was enacted, coronary admissions rapidly returned to previous levels. The introduction of smoke-free legislation in Scotland in 2006 was followed by a 6% decrease in out of hospital cardiac arrests and a 17% decrease in hospital admissions within a year. Even 30 min of second-hand smoke exposure has been shown to increase plasma activity and enhance chronic cardiovascular risk.

Similarly, changes in diet can rapidly improve outcomes of cardiovascular disease (CVD), as demonstrated by several randomised trials. In the DART trial, HIV patients of myocardial infarction, who were advised to eat fish had a significant 19% reduction in all-cause mortality compared with control patients, with survival curves separating within months. Likewise, in the Gengo Italiano pluris the DART trial, 1 g of D-3 fatty acids significantly reduced all-cause mortality and cardiovascular mortality in II 948 sequential infarction survivors. Moreover, survival curves separated early, with a significant reduction in total mortality after just 3 months of treatment (p=0.05).

The PREMIER and DAPA-METFORMIN (PREMIER2) primary prevention randomised-controlled trial found that an energy unrestricted diet supplemented with extra virgin olive oil or nuts achieved an impressive 30% reduction in major cardiovascular events (NNH=60) in over 7500 high risk individuals initially free of CVD. This reduction occurred within 3 months. Furthermore, this solid RCT evidence builds on a wealth of existing data from observational, cohort and secondary prevention intervention studies. It also provides further strong causal evidence that simple diet interventions can rapidly and powerfully reduce CVD outcomes, in comparison with an American Heart Association recommended “low fat” diet. A Mediterranean diet, post myocardial infarction is a most powerful coronary intervention tool for morbidity than aspirin, statins, or coronary artery bypass without any significant difference in total cholesterol, triglycerides or HDL between the two groups. It is the abundant vilidic acid, polyphenols and D-3 fatty acids found in nuts, olive oil, fish and vegetables, that rapidly exert positive health effects by attenuating inflammation, atherosclerosis and thrombosis. Consequently, the consumption of trans fatty acids found in fast food can rapidly increase C reactive protein and other inflammatory markers within weeks. Strategies that promote excessive weight gain in children and adults through the consumption of the amounts of unhealthful foods should also be welcomed. However,
1000 CALORIES
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 (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.
EXTRA INGREDIENT
Nucleus Accumbens
Overeating: Cause or Effect?
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 diet is the answer, we should ask whether the answer is in the hands of the physician or in the hands of the patient," the editors wrote.

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.1 These metabolic responses and reciprocal changes in hunger serve to defend baseline body weight. Indeed, only a small proportion of overweight and obese people in the United States report having maintained weight loss of at least 10% for 6 years.2

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 0.6 and 5.6 mmol/L. According to a study of 8 obese young adults,3 an acute decrease in the circulating concentration of oxidation of these fuels provokes intense hunger and food intake.4 Conversely, pharmacological manipulations that increase metabolic fuel availability, such as fatty acid synthesis inhibition or β-hydroxybutyrate administration, lower food intake.5 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 insulin resistance, such as in obesity and diabetes, predispose to weight gain, whereas decreased insulin action (eg, insulin resistance in type 2 diabetes) results in weight loss.

Metabolic Deficits May Precipitate 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 expression of receptor ablation, adipose-specific overexpression of epihypoxichloroide hydrolase (a lipolytic enzyme involved in lipolysis), and liver-specific overexpression of IGF-1 (a transcription factor regulating glucose metabolism). Of particular relevance, changes in dietary composition can cause obesity in genetically normal animals, independent of an increase in caloric intake. Rats fed high vs low glycemic index diets developed hyperinsulinemia, increased expression of fatty acid synthase in fat tissue, and greater incorporation of glucose into lipogenic metabolic pathways that predispose to excessive fat deposition.5 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.6

This combination of increased adiposity despite reduced energy intake cannot be explained by the caloric deficit theory, and may be understood by the alternative model. Various genetic or environmental factors, including the quality of the diet (Figure), induce an excessive anabolic state that favors storage rather than oxidation of ingested substrates (ie, increased triglycerides, increases in platelets, and increase uptake of glucose 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 sequenced 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 deficits precede and promote overeating, then conventional calorie-restricted diets would be ineffective. In contrast, Weight Watchers, the longest-term study in a group of people of limited food availability. This diet did not compromise the underlying deficits of the diet. It is likely that limiting metabolic fuel availability, lowering energy expenditure, and increasing hunger (by exploiting the starvation response and appetite regulation) would have greater potential to treat and prevent obesity in the obesity population.7 This study suggests that diet-induced weight loss increases the body's ability to produce metabolic fuels, which is consistent with the above hypothesis.
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 low fat/high glycemic (60/20/20) vs. low GL (40/40/20) vs high fat VLCD (10/60/30)
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)
**Figure Legend:**
Prevailing and Alternative Models of Obesity
Is your fat hungry?
• 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
Insulin Resistance

Eat Food → Make Insulin → Sugar Stores As Fat → Cells Resist Insulin → Feel Tired & Hungry → Eat Food
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 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
• Palatability of food?
  – Quality of food or your biochemistry?
• 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
Fat and Heart Disease

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

- **PREDIMED study**
  - 7000 people RCT at risk for MI
  - Control group low fat
  - 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 after 4.8 years

- **Lyon Heart Study - RCT**
  - Higher omega 3 and lower omega 6 fats
  - 73% reduction in MI

- **WHI – RCT 49,000 women**
  - No evidence of CVD risk reduction on low fat diet despite reductions in LDL cholesterol

- **MRFIT Trial - largest RCT**
  - 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 fat and CVD

• Physicians Health Study 1996:
  – observational study 43,000 men no link between total or saturated fat and CVD
  – link to high sugar and low fiber diets and low omega 3 fat
  – If controlled for fiber no link with saturated fat
2015 US Dietary Guidelines

• No restriction on total fat
• Cholesterol: no longer nutrient of concern
• Reduce sugar to 25 grams (6 teaspoons)
Saturated Fat?

Villain?
Benign?
Health promoting?
Evidence on Saturated Fat

- small controlled trial of 264 men who had heart attacks no benefit reducing heart attacks or death
- the low fat group ate less 1/3 less fat, 500 less calorie per day and achieved a 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 saturated fats.*
Saturated Fat?

- Meta-analysis 21 studies of 350,000 people over 23 years
- 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
- Risk only found with omega 3 deficiency
- Post prandial lipids only adversely affected in face of low omega 3’s
Saturated Fat Feeding Studies

- VLCD (12%), High fat (either high n6 PUFA or saturated fats 86 grams)
- 8 men over 6 weeks
- Assessed plasma lipids, cholesterol profile, inflammation
- 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
CHO and Saturated 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) reverse fibrotic fatty liver in rats (n6 PUFA did not show same results)
• Reversal occurred despite continued ethanol intake
Cholesterol and Heart Disease
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

- 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
- 75% had normal LDL (under 130 mg/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 161 mg/dl
- 54% had HDL under 40 mg/dl and only 10% had HDL levels over 60 mg/dl
Statins: Primary Prevention?

• Primary Prevention? Cochrane Data 2011
• 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”
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.
- 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.
- Countries with higher average cholesterol than Americans such as the Swiss or Spanish have less heart disease.
Statins?

- Evidence shows statins ability to lower inflammation accounts for the benefits of statins, not their ability to lower cholesterol.
- 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 (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
- Homocysteine
- Environmental toxins (metals, POP’s)
- Oxidative Stress
- 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?

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

(LA) n-6 FA

GLA

DGLA

Stim: Insulin & Statins
Inhib: Glucagon, EPA

PGE1

TXA1

PGE2

TXA2

LTB4

Anti-inflammatory

2004-09 Dr. David Seaman.


(ALA) n-3 FA

Green veg, chia, flax, hemp

Fish, n3 meat, wild game, n3 eggs

EPA

DHA

Resolvins
Neuroprotectins
Docosatrienes

PGE3

LTB5

TXA3

Anti-inflammatory
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
Ramsden & Hibblen

- Two large investigative reviews
- 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 double 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
Omega 6: Other Risks

- OXLAMs – Oxidized LDL
- Heat damage
- Solvents
- Dysbiosis – metabolic endotoxemia
- GMO soybeans: Glyphosate residue
Opposing View

- Review by Willet, et. Al found benefit to replacing SFA with PUFA’s
- Not clear if combination or just n6
Food Controversies

- Eggs
- Butter
- Coconut Oil
Meat: To Eat or Not To Eat?
Quality of Research

• Mostly limited to observational studies
• Multiple confounding factors
• Biological plausibility? TMAO
• Historical context:
  • Plains Indians: highest per capital centenarians in history
  • Seventh Day Adventists?
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
- 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
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
TMAO and Heart Disease

- Trimethylamine-N-oxide (TMAO)
- Produced by dysbiotic bacteria from carnitine (meat), choline (eggs) and lecithin (soy)
- Highest concentrations of TMAO in fish (with lower risks of CVD?)
- Vegetarians who ate steak showed no increase in TMAO
- Antibiotic use prevented TMAO increase after meat consumption
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
• Cooking techniques: PAH, HCA, AGE’s
Grass Fed vs. CAFO Meat

• CAFO
  – Antibiotics, hormones, pesticides
  – Ethical 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?
Coconut Oil?
Meat Issues

- Saturated fat
- Inflammation
- Cancer risk?
- Diabetes risk?
- TMAO production (dysbiosis)
- Polycyclic aromatic hydrocarbons and heterocyclic amines, advanced glycation end products
Fat: Other Health Benefits
What to Eat?

The Pegan Diet?
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 fish
Areas of Controversy

- Dairy
- Grains
- Beans
- Meat
- Eggs
GOOD FATS
PHYTONUTRIENTS & ANTIOXIDANTS
Daniel and Rebecca

- Daniel’s Story: 340 lbs
- Rheumatoid arthritis, chronic fatigue & pain, muscle pain, headaches, allergies, high blood pressure & cholesterol, low testosterone
- Perocet & 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

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

- **Rebecca** lost 58 lbs
THE FUTURE OF HEALTH
If you want to travel swiftly, travel alone.

If you want to travel far, travel together.

African Proverb