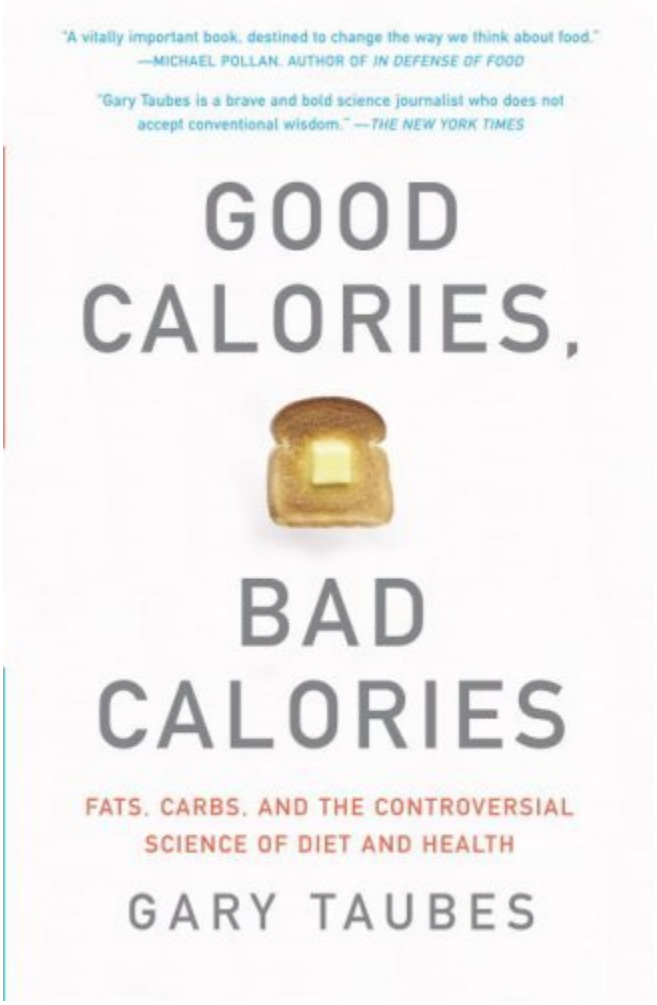
Complete Notes to *Good Calories, Bad Calories* by Gary Taubes



******These notes are ideal as a quick reference for those who have already read the book. For those who haven't read it, there is much information here, but this no substitute for the real thing. I strongly recommend reading it cover to cover (more than once), it's an incredibly important and astounding book. Buy it on Amazon: Good Calories, Bad Calories: Fats, Carbs, and the Controversial Science of Diet and Health******

Summary

- Underlying theme: Good Science, Bad Science
    - recurring pattern: unproven hypothesis becomes conventional wisdom, then all research is interpreted to fit the hypothesis (confirmation bias, often due to government's selective funding)
    - heavily distorted by government — three words capture it: "public health authority"
    - hyperspecialization of researchers has impeded the science; more cross-disciplinary work would quickly reveal flaws in the established wisdom
- Myth: dietary fat and especially saturated fat cause disease and obesity
- Reality: fat is good for you, especially animal fats; carbs, especially sugar and refined grains (via their effect on insulin), cause all the diseases of civilization: heart disease, diabetes, cancer, obesity, etc...
- Myth: obesity is a problem of the will (psychological) caused by caloric excess — overeating and/or underactivity
- Reality: obesity is a hormonal problem (physiological) caused by high-carb diets via their effect on insulin, which triggers metabolic changes that cause one to eat more and expend less energy. ***Obesity is caused by carbohydrates, not by gluttony and sloth!***
    - Insulin problems (hyperinsulinemia or insulin resistance) from a chronic high-carbohydrate diet cause your body to store away more energy in the fat tissue, and prevent the fat from being released and burned. With less energy available to the body, you get hungry and/or your metabolism slows down to compensate. Hence, gluttony and sloth are symptoms of an underlying insulin disorder.

Taubes's "inescapable" conclusions (p.454):

1. Dietary fat, whether saturated or not, is not a cause of obesity, heart disease or any other chronic disease of civilization.
2. The problem is the carbohydrates in the diet, their effect on insulin secretion, and thus the hormonal regulation of homeostasis—the entire harmonic ensemble of the human body. The more easily digestible and refined the carbohydrates, the greater the effect on your health, weight and well-being.
3. Sugars—sucrose and high-fructose corn syrup specifically—are particularly harmful, probably because the combination of fructose and glucose simultaneously elevates insulin levels while overloading the liver with carbohydrates.
4. Through their direct effect on insulin and blood sugar, refined carbohydrates, starches and sugars are the dietary cause of coronary heart disease and diabetes. They are most likely dietary causes of cancer, Alzheimer's disease, and the other chronic diseases of civilization.
5. Obesity is a disorder of excess fat accumulation, not overeating, and not sedentary behavior.
6. Consuming excess calories does not *cause* us to grow fatter, any more than it causes a child to grow taller. Expending more energy than we consume does not lead to long-term weight loss; it leads to hunger.
7. Fattening and obesity are caused by an imbalance—a disequilibrium—in the hormonal regulation of adipose tissue and fat metabolism. Fat synthesis and storage exceed the mobilization of fat from the adipose tissue and its subsequent oxidation. We become leaner when the hormonal regulation of fat tissue reverses this balance.
8. Insulin is the primary regulator of fat storage. When insulin levels are elevated—either chronically or after a meal—we accumulate fat in our fat tissue. When insulin levels fall, we release fat from our fat tissue and use it for fuel.
9. By stimulating insulin secretion, carbohydrates make us fat and ultimately cause obesity. The fewer carbohydrates we consume, the leaner we will be.
10. By driving fat accumulation, carbohydrates also increase hunger and decrease the amount of energy we expend in metabolism and physical activity.

Part One — The Fat-Cholesterol Hypothesis

The Eisenhower Paradox

- Eisenhower became obsessed about his cholesterol because of his heart attacks. Despite following a strict low-fat diet, his cholesterol and weight kept rising (his doctor eventually started lying to him)
- Heart Disease Mythology: 2 main myths
    - 1. The heart disease epidemic post-WW2
        - "coronary heart disease was rare until it emerged in the '20s and became the biggest killer"
            - complete myth: the apparent epidemic was the result of new diagnosis technology and increased attention
                - infectious diseases had been conquered, meaning more people were living long enough to get diseases
    - 2. The changing American diet story
        - "during first half of 20th century, the American diet has shifted away from plant-based foods to animal foods (high in saturated fat)"
            - complete myth: based on very sketchy data and guesswork
            - as historians know, Americans have traditionally been big meat-eaters
- Cholesterol starts to be blamed for heart disease after WW2
    - a natural assumption: it is the primary substance in atherosclerotic plaques
        - a silly hypothesis: circulatory system is like plumbing, and cholesterol is like rust that clogs arteries (this dumb "artery-clogging" hypothesis is now popular, making it seem like the fat you eat gets directly deposited in the arteries)
    - the cholesterol hypothesis was kept alive, despite no evidence, by the fact that it was an easy test that any physician could do
    - no link between cholesterol levels and clogged arteries: many get heart disease despite low cholesterol and many with high cholesterol never get the disease
    - Ancel Keys was the driving force behind the fat-cholesterol hypothesis
        - was convinced that dietary fat raises cholesterol and causes heart disease
        - the low-fat diet dogma was born, which developed into the low-fat-and-low-saturated fat version

The Inadequacy of Lesser Evidence

- the evidence simply didn't support the fat-cholesterol hypothesis
    - researchers were sharply divided on the issue
        - the skeptics took a rigorous scientific approach, not making public recommendations until the conclusions were dead certain
        - Keys's proponents felt it was best to give the public the latest info, even if it wasn't proven
            - got greater attention in the press, as recommendations make good news
- confirmation bias was common in the dietary-fat controversy: only looking at supporting evidence; dismissing any contradicting evidence
    - prime example: the massive Framingham Heart Study
        - evidence did not support Keys's hypothesis; NIH funders refused to allow publication of the results
    - virtually every study comparing diet, cholesterol, and heart disease within a single population failed to support the hypothesis
- Keys's Seven Countries Study was a landmark success for the hypothesis
    - but it was fatally flawed: he chose the 7 countries which he knew would have supporting data
- studies showed almost no evidence of benefits of low-fat or low-saturated-fat diets
    - Ivan Frantz's Minnesota trial went unpublished because of disappointing results (contradicted Keys)

Creation of Consensus

- by '77, though no new evidence showed that dietary fat causes heart disease, the idea gained acceptance in the public
    - anti-fat, anti-meat movement; spawned out of counter-culture 60s and concerns about famine in 3rd world (raising meat uses a lot of grain, which could feed more people than the meat could)
- January 14, 1977—the day when Keys's hypothesis decisively won
    - Senator George McGovern announced the publication of *Dietary Goals for the United States*
        - recommended caloric proportions of 55-60% carb, 30% fat (no more than a third of that saturated)
        - first time any government institution had taken a stance on dietary fat—turned it from a scientific into a political issue
            - led other government bodies to join in: USDA, NAS
        - McGovern's committee was up for renewal and fighting for its life
            - staff were total non-experts who read the stories in newspapers and thought the answer was simple
        - insisted that there was nothing to lose by going low-fat
            - "uproar" at press conference; lots of dissent
    - hard to overstate the impact, this was the major event that created the conventional wisdom consensus
- a dissenting view, *Toward Healthful Diets*, put out by the Food and Nutrition Board was excoriated in the press, discredited by accusation of conflicts-of-interests
    - back then, nutritionists in academia were encouraged to work closely with industry
    - you could only be seen as free of conflicts if the governments was your only source of funds
        - but your research had to support the government position or your funding would go to someone who's research did
- "Once politics, the public, and the press had decided on the benefits of low-fat diets, science was left to catch up."
    - now that the government had taken an official position, the low-fat researchers didn't feel obliged to test this hypothesis, they made their research fit the official position
    - further studies contradicted the conventional wisdom, but the results were often interpreted as though they supported it (the bias was that bad!)
- the NHLBI did 2 massive trials to resolve the heart-disease controversy:
    - MRFIT (Stamler): the subjects were advised to quit smoking, take blood pressure meds, and eat low-fat and cholesterol diet. They had slightly higher mortality than the control group.
    - LRC Coronary Primary Prevention Trial (Rifkind): tested the effects of cholesterol lowering drugs on heart disease. Trial showed a slight benefit.
        - this was taken as indisputable evidence that lowering cholesterol saved lives, even though the results were far from conclusive
        - took the leap of faith and extended the conclusion to low-cholesterol diets as well, with no evidence that such a diet could lower cholesterol levels

The Greater Good

- diet debate went from whether we should eat low-fat or not to whether we should eat low-fat or very-low-fat (skeptics had vanished from the public debate)
- the evidence showed at best tiny benefits to lowering cholesterol (extremely tiny—nowhere close to being worth enduring a low-fat diet)
    - e.g., live 1-4 months longer by avoiding saturated fat your entire life
- Mass prevention philosophy of Geoffrey Rose:
    - though evidence showed little benefit of lower cholesterol for the individual, it was then rationalized that it had a paradoxically large effect for the total population
    - Rose: mass approach is the only answer to mass disease (e.g., 600 immunizations to save one life)
        - to overcome the individual's rational apathy, create social pressure to be healthy

        - problem: it becomes effectively impossible to challenge the science once it's become public policy. Policy and public belief are often set in early stages of scientific controversy when the topic is most newsworthy. If the conventional wisdom is revealed to be wrong, it's exceedingly difficult to change public belief (e.g., saccharine is widely considered unhealthy—it was determined to be safe over 20 years ago).
            - this mass-prevention philosophy implies that skepticism isn't in the interest of public health—a campaign to convince the public requires unconditional unanimity about the promised benefits
                - to fund further studies would imply that there is still uncertainty
            - and so, the science was horribly disfigured in the interests of public health politics
        - great example of this: "dietary fat causes breast cancer"
            - became popular belief based on mere speculation (no body of evidence yet)
            - studies were then done, but *all* the evidence showed the opposite: lower fat intake correlated with more cancer!
                - yet these studies were all interpreted as not refuting the hypothesis! It was always noted that the diet recommendations still held.
                - even the biased WHI trial got negative results
            - to this day it remains popular belief, as a result of Rose's philosophy of picking a hypothesis early on and sticking to it no matter what
- the "dietary fat, cholesterol, heart disease" hypothesis has also been a mess of bad science
    - plenty of contradicting evidence
        - mentality among researchers that contradicting evidence is not in the interest of public health, should be kept quiet
        - publication-confirmation bias: you publish results that correlate perfectly with a theory, but have less confidence in contradicting results
- Keys's hypothesis persists because any disconfirming evidence was consistently disregarded from the beginning.
    - the *totality of evidence* was defined as only the confirming data
    - self-fulfilling: any opposing evidence could not call the hypothesis into question because it would be immediately discarded as being inconsistent with the totality of the evidence.

Part Two — The Carbohydrate Hypothesis

Diseases of Civilization

- chapter is about the appearance of "diseases of civilization" among primitive populations as they adopt the western lifestyle
    - these diseases are: cavities (first symptom), obesity, diabetes, cardiovascular disease, hypertension and stroke, cancers, periodontal disease, appendicitis, peptic ulcers, diverticulitis, gallstones, hemorrhoids, varicose veins, constipation, and more
    - when one disease appears in a population, they all eventually appear
        - indicates a common cause
- low-fat proponents' view: updated version of the changing-American-diet story—eating less carbs and more meat and fat is the cause of the diseases
    - can't explain meat-eating American Indians, Inuits, etc.
- isolated populations eating traditional diets essentially never got diseases of civilization
    - grains were eaten wholemeal, very little sugar in diet
    - diseases appeared with introduction of white flour and sugar into diets

Diabetes and the Carbohydrate Hypothesis

- Diabetes: disease in which the body is unable to use carbs for fuel, and the blood glucose is expelled in the urine (glycosuria)
- prime suspects: sugar and white flour (easily digestible carbs that spike blood sugar and strain the pancreas)
    - strong correlation: diabetes rates dropped sharply in line with WW1 and 2 sugar rationing
- Joslin (king of diabetes research) refused to believe the refined carb hypothesis, insisting that all carbs are equal (refined or not)
    - this killed the hypothesis
    - went instead with the idea that high-fat low-carb diet was the cause, which became the conventional wisdom
        - can't explain healthy traditional meat eating populations
        - meat-fat intake correlated with diabetes rates, but so did sugar/white flour
            - consistent error in reading the data: as people become affluent, they eat more meat and less grain and carbs, but more of the carbs are white flour and sugar. Disease rates correlate with both, but the data was always interpreted in terms of Keys's fat-is-evil hypothesis, and refined carbs were overlooked
- ... loads of evidence that diabetes is not caused by dietary fat, but refined carbs and especially sugar
    - this also applies to the other diseases
- Cleave & Yudkin vs Keys
    - Since Keys's hypothesis dominated in the U.S., and Keys attacked Yudkin, the refined carb hypothesis was discarded
- this stupidity continues today, with diabetics advised to eat low-fat high-carb diets

Fiber

- the refined carb hypothesis morphed into the fiber hypothesis
    - this fit better with Keys's hypothesis, much easier to promote than dissing sugar
- led to the idea that lack of fiber causes obesity
    - less available energy in fiber-rich diets (fiber is zero-calorie bulk)
- fiber hypothesis took off in the media, had to be paired with the anti-fat message to get traction (i.e., fat is causative, fiber is protective)
    - became part of the conventional wisdom; its benefits were overstated
    - another example of Rose's mass prevention philosophy
- however, the evidence refuting the fiber hypothesis steadily piled up

    - since it was part of the conventional wisdom, it just wouldn't die
        - proponents completely disregarded the evidence or rationalized away the data, saying fiber has other benefits
            - fiber became detached from the original hypothesis and was promoted based on what was yet untested (staying alive by staying one step ahead of the science)

The Science of the Carbohydrate Hypothesis

- Tokelau Island Migration Study: monitored health of a native population that partly migrated to western society
    - traditional diet: coconuts and fish—high in fat, 90% of which was saturated
        - no disease, despite all that saturated fat
    - their new westernized diet: way less fat, much more carbs (bread, potatoes)
        - diseases of civilization struck
    - the researchers tried to explain it away, suggesting that each disease had an individual cause (salt, stress, obesity, red meat, allergens), rather than one cause triggering interrelated diseases
- mainstream view: diseases of civilization are only coincidentally related, each disease has unique causes
- alternative view: these interrelated diseases have a single underlying cause (simplest possible explanation)
- Syndrome X: elevated triglycerides, low HDL, dense LDL, high levels of fibrinogen, elevated uric-acid levels in blood, state of chronic inflammation, hypertension, hyperinsulinemia, insulin resistance, glucose intolerance
    - Reaven's term. AKA: insulin resistance syndrome or (most common) **metabolic syndrome**
    - the carb hypothesis was rejected in the 50s because it contradicted Keys, but metabolic syndrome has been accepted as a minor modification of Keys, even though it implies Keys is wrong
        - the science is impeded by the assumption that saturated fat is the primary evil
        - the science was contorted to accommodate both hypotheses
- Homeostasis: the parts of the body are interdependent, maintaining a dynamic equilibrium
    - insulin plays a huge role: nutrient storage hormone
        - primary role: store away blood sugar (too much is toxic)
        - other roles: primary regulator of fat, carb, and protein metabolism; glycogen synthesis; fat synthesis and storage in cells and liver, and inhibiting the release of that fat; and more...
    - evolutionary logic: this fantastically complex homeostasis system hasn't evolved to handle the huge blood sugar spikes from sugar and refined carbs
        - causes metabolic syndrome and diseases of civilization
- Salt-Hypertension Hypothesis: an example of bad science—looking at parts in isolation rather than the integrated whole (homeostasis)
    - hypothesis: salt intake causes body to retain water to maintain the sodium concentration in the blood, so chronic high-salt intake could cause hypertension
    - evidence: nothing worthwhile
        - cutting salt intake in half would have a minor impact on blood pressure (4-5mm Hg in hypertensives)
    - Rose's mass prevention philosophy at work: low-salt has become conventional wisdom, despite the fact that the evidence couldn't be found
    - hypertension is a disease of civilization
        - westernization brings refined carbs, meat, fat, and salt
            - this time they went after salt
        - carbs cause water retention: the insulin prompts the kidneys to retain salt, so the body retains water to maintain sodium concentration
            - cutting carbs works just like diuretics
        - insulin also stimulates the nervous system and the fight-or-flight response, which raises blood pressure

            - hypertension is accompanied by abnormally high insulin levels, and commonly referred to as an "insulin-resistant state"
- bad science has kept the carb hypothesis from acceptance
    - they accept the effects of insulin on chronic diseases, but interpret the evidence as saying nothing about the unique insulin-elevating properties of refined carbs.

Triglycerides and the Complications of Cholesterol

- theme of the chapter: oversimplification of the science
- 1950: Gofman launched the modern era of cholesterol research
    - studied the different types of lipoproteins (molecules that transport cholesterol and triglycerides in the blood): HDL (high-density lipoprotein), LDL (low-), VLDL (very low-)
    - LDL cholesterol was found to correlate with heart disease, but not with total cholesterol
        - total cholesterol was found to be a poor indicator, LDL and VLDL combined were much better
        - Gofman found that while saturated fat raised LDL, carbohydrates raised VLDL
            - since lowering VLDL was usually the more important of the two, he recommended carb restriction (and opposed the general 'eat less fat' message)
- 1955: Pete Ahrens came to same conclusions while studying triglycerides
    - triglycerides rise on low-fat diets and fall on high-fat diets
    - low calorie diets also lower triglycerides, explaining the low triglycerides of impoverished populations (e.g., in Asia)
    - he questioned the Keys hypothesis: maybe carbs and trigs cause heart disease
- Margaret Albrink found evidence supporting Ahrens: triglycerides correlated with heart disease far better than total cholesterol, and low-fat high-carb diets raise triglycerides
    - her presentation caused an uproar at the meeting, people got angry
    - her interpretation of the evidence was confirmed independently by Peter Kuo, by Lars Carlson, and by Joseph Goldstein
        - prompted a JAMA editorial criticizing the 'cholesterol bandwagon' for overlooking other factors
- the triglyceride-carbohydrate hypothesis was buried by Key's hypothesis, which dominated the research
- Frederickson and Levy of the NIH did the first large-scale test of the hypothesis
    - found that the most common lipoprotein disorder was high triglycerides carried in VLDL
    - thus, they warned against low-fat dieting for fear of carbs raising trigs
- this prompted the NIH to fund more studies to measure LDL cholesterol and VLDL trigs
    - confirmed Gofman's argument that total cholesterol was irrelevant, and that measuring trigs and cholesterol in the different lipoproteins was more revealing
    - LDL cholesterol was a "marginal" risk factor
    - HDL was the surprise: the higher the HDL cholesterol the lower the trigs and the risk of heart disease
        - HDL had the largest impact on risk and was the only reliable predictor of risk
        - low-carb was recommended to increase HDL cholesterol
- the success of HDL paradoxically directed attention away from triglycerides
    - due to the low-fat bias, raising HDL was downplayed in favor of lowering LDL or total cholesterol (even though raising HDL is much more effective against heart disease)
        - In the press: Orwellian twisting of the HDL evidence to support Keys (this was happening right as McGovern was announcing *Dietary Goals* in 1977)
        - the low-carb implications prevented it from getting the attention it would have got in a scientific (not political) atmosphere: hardly any research was done (funding bias)
            - this lack of research would then be used to discredit the hypothesis as unproven and unsupported
- mainstream discussion shifted from benefits of lowering total cholesterol to lowering LDL
    - making LDL the "bad cholesterol" oversimplified considerably, was more about saving face (salvaging two decades of research)
- mainstream research focused on dangers of lowering HDL, rather than the dangers of carbs and high triglycerides

        - low-fat diets recommended (even though they lower HDL), dangers of carbs not mentioned
        - Grundy and Mattson, in 1985, found that monounsaturated fat (i.e., olive oil) lowers LDL and raises HDL cholesterol. (Saturated fat raises both; carbs lower both)
            - reignited the popularity of the Mediterranean Diet
            - Ironic: animal fat is is primarily monounsaturated
                - porterhouse steak: 51% of the fat is monounsaturated (of which 90% is oleic acid), 45% is saturated (a third of which is stearic acid which is metabolized into oleic acid), 4% is polyunsaturated (which lowers LDL but doesn't affect HDL). So 70% of the fat content will improve your HDL:LDL ratio; the other 30% will raise both. Should be promoted to reduce heart disease risk, but no nutritional authority will say so publicly.
- the non-simplified picture:
    - LDL is different than LDL cholesterol: the former is the lipoprotein (carrier molecule) and the latter is the cholesterol content carried by the LDL molecules
    - LDL is heterogeneous: ranges from small, dense LDL to large, fluffy LDL
        - a low-density lipoprotein is analogous to a balloon: a protein backbone—apo B—, an outer membrane of phospholipids, and inside are the triglycerides and cholesterol inflating it
    - small, dense LDL is bad: strong negative correlation with HDL,
        - a high number of LDL particles (the # of apo B proteins) strongly correlates with heart disease (reflecting elevated small, dense LDL)
            - many small LDL is bad, but the same amount of cholesterol in fluffy LDL is fine
            - small, dense LDL can more easily get through damaged artery walls to form plaques; they oxidize more readily (must oxidize to become plaque forming)
        - small dense LDL is invariably accompanied by high trigs and low HDL (fluffy LDL is not)
            - low-fat, high-carb diets promote the bad dense LDL (promote heart disease)
                - the reverse is true: high-fat, low-carb promotes fluffy LDL
                - funny: researchers who firmly believe that dense LDL is atherogenic refuse to comment on the dietary implications!
- the LDL mechanism:
    - LDL begins life as VLDL: liver transforms glucose into triglycerides for temporary storage and loads them onto VLDLs; as the trigs are unloaded the VLDL becomes smaller and denser and ends life as a LDL
        - any factor that increases the synthesis of VLDL will increase the number of LDL particles
        - process is well established:
            - if there are few trigs (low-carb or low-calorie diets), they get packaged on IDLs (intermediate-) which end life as fluffy LDL
            - if there are abundant trigs (high-carb diets), the lipoprotein is loaded with a large amount of trigs (which are lighter than cholesterol or apo B) resulting in VLDLs. They end life as dense LDL.

The Role of Insulin

- high triglycerides, high-carb diets, heart disease, obesity — all appear together and can be explained by the **twin phenomena of insulin resistance and hyperinsulinemia** (chronic high insulin levels)
    - Yalow and Berson showed that prediabetics have high insulin. It was previously thought that a lack of insulin was the root of diabetes.
        - the obese also have high insulin
    - insulin is produced to get glucose to the cells, but it also prompts the liver to synthesize triglycerides for storage as fat
        - high-carb diet = more insulin = more triglycerides
            - thus, carbs increase risk of heart disease

            - trigs, insulin levels, and insulin resistance are linked: they all move together
    - cognitive dissonance: researchers accepted the science of metabolic syndrome but resisted the dietary implications — they directly contradicted Keys
        - metabolic syndrome was integrated into the mainstream but the idea that carbs are the cause disappeared
            - dietary fat and cholesterol are still demonized; carbs are still harmless
    - metabolic syndrome also includes: small, dense LDL; insulin resistance; hyperinsulinemia; high blood sugar; hypertension; low HDL
        - triglycerides and HDL are the best predictors of insulin resistance and dense LDL

The Significance of Diabetes

- Chapter theme: Diabetes is a disease further along the continuum of metabolic syndrome. What we learn about diabetes also applies to the earlier stages of metabolic syndrome (is relevant for everyone).
- diabetics have an extraordinarily high incidence of heart disease (as well as the other diseases of civilization)
    - it was thought that this was because they ate more saturated fat than non-diabetics
        - so diabetics were advised to eat low-fat diets
    - makes much more sense in the context of metabolic syndrome
        - diabetics have a more severe form of the syndrome; healthy people have varying degrees of the syndrome
            - thus, what happens in diabetics happens to a lesser degree in the rest of us
            - if the incidence of a disease increases with diabetes in a population, then it's probably an insulin problem, caused by sugars and refined carbs (in both diabetics and non-diabetics)
    - insulin has a direct effect on heart disease, in addition to the indirect effect through elevating trigs
- blood sugar and AGEs
    - the normal burning of glucose for fuel in cells creates free radicals (oxidants)
    - advanced glycation end-products (AGEs) can take years to form
        - process: a sugar attaches haphazardly to a protein (glycation) without the help of an enzyme, which would normally connect them in a particular position
            - if blood sugar is high, the process of forming an AGE proceeds (otherwise the sugar and protein will disengage) — a series of transformations yields and AGE
        - AGEs bind easily to one another (cross-linking) — this linking causes aging: loss of skin elasticity, hardening of arteries, stiffness of heart, lungs, joints, etc.
            - diabetics have high levels — they cause cataracts and common diabetic problems with kidney membranes, nerve endings, artery lining.
            - diabetes is a form of accelerated aging
        - AGEs play a direct role in heart disease: they cause oxidation of LDL, which causes LDL to become trapped in the artery wall
            - oxidized LDL is quite elevated in diabetics, and commonly found in atherosclerotic lesions

Sugar

- glycemic index: measures the rate at which a food elevates blood sugar
    - misleading: doesn't account for fructose
        - sugar (sucrose) molecule = a glucose bonded to a fructose
        - only half (glucose) of sugar raises blood sugar, the other half (fructose) goes to the liver to be metabolized and has little immediate effect on blood sugar
            - fructose is still very harmful
- the introduction of high-fructose corn syrup (HFCS, which is 55% fructose and 45% glucose) led to a significant increase in sugar consumption

    - public didn't consider it as sugar, it was marketed as a healthy additive ("fruit sugar"), and it has a low glycemic index (because fructose doesn't register)
- fructose does it's damage through the liver, where it's converted into trigs and shipped out on lipoproteins for storage
    - fructose blocks the metabolism of glucose in the liver — the pancreas responds by producing more insulin to handle this glucose
    - fructose elevates blood pressure more than glucose does
- sugar = double whammy!
    - fructose stimulates production of trigs; glucose stimulates insulin response, which in turn prompts the liver to secrete even more trigs; the insulin also raises blood pressure in addition to the fructose
- fructose is much more reactive and forms AGEs more easily, and it's AGEs are more resistant and damaging (better at cross-linking)
- once the research on the effects of fructose came out, it was hard to change the official opinion that fructose was harmless because of its low glycemic index
    - the same old rationalization: "not sufficient evidence" (because they didn't do the research!)

Dementia, Cancer, and Aging

- Alzheimer's disease appears to be another disease of civilization (a product of metabolic syndrome)
    - diabetics are twice as likely to get Alzheimer's
        - diabetics on insulin therapy are four times more likely to get it
    - may be caused by accumulation of AGEs, which are found in the amyloid plaques (characteristic of Alzheimer's)
    - insulin is the simplest explanation
        - insulin-degrading enzyme (IDE) normally clears both amyloid and insulin from around the neurons
            - the more insulin in the brain, the less IDEs to clean up amyloid (insulin monopolizes IDE activity)
            - carbs raise insulin, which reduces the cleanup of amyloid, resulting in Alzheimer's
- Cancer also appears to be a result of metabolic syndrome
    - population studies indicate that cancer occurs along with other diseases of civilization, and very rarely in primitives
        - 1981: Doll and Peto concluded that 75-80% of cancers in the US may be avoidable with lifestyle and diet changes
            - **pollution, food additives (i.e., man-made chemicals) play a minimal role; diet plays largest role in cancer**
        - Yudkin had noted that the top five nations for breast cancer mortality also had the highest sugar consumption; those with the lowest rates had the lowest sugar consumption
    - the pattern of cancer incidence is similar to the other diseases of civilization
        - diet related cancers hit the gastrointestinal tract and the endocrine-dependent organs (breast, uterus, ovaries, prostate — whose functions are regulated by hormones). This strongly suggests the implication of estrogen.
    - calorie-restriction dramatically inhibits tumor growth
        - insulin stimulates tumor growth; tumors have more insulin receptors, conferring a selective growth advantage
            - to become malignant, a cell must undergo a series of successive mutations (timespan of a few years). Any selective advantage will increase the population of mutated cells, increasing the probability of successive mutations.
            - mutations occur during cell division: average person will have ten quadrillion cell divisions in their life
                - mutations are unavoidable; but cells have mechanisms to repair or destroy bad cells

        - IGF (insulin-like growth factor): a growth factor that can mimic the effects of insulin. Acts locally, and concentrations change slowly over days or weeks, reflecting long-term food supply.
            - likely the key player in cancer; shutting down IGF receptors strongly (if not totally) suppresses tumor growth
            - IGF is mostly bound to proteins in the bloodstream, and inactive; only a small percentage is unbound and active
                - insulin reduces the amount of binding proteins, freeing up more IGF
                - carbs raise insulin, which raises IGF, which promotes cancer
            - tumor cells have 2-3 times as many IGF receptors
            - IGF may even inhibit or override the programmed cell death mechanism (fail-safe mechanism to prevent damaged cells from multiplying)
        - extra insulin receptors provide the extra glucose for fuel, extra IGF receptors provide the strong stimulus to proliferate.
            - **cancer is caused by the internal conditions that nurture cancerous cells (not by mutations, which are inevitable)**
                - problem is with the endocrine and growth factor environment, not "carcinogens"

- Longevity
    - caloric restriction dramatically increases the lifespans of rodents, worms, fruit flies, and more
        - not because they have less fat or weigh less — genetically obese mice live as long as normal lean mice when both are calorie restricted (even though they're 4 times fatter)
            - longevity correlates with food consumption, not the degree of adiposity
        - caloric restriction reduces oxidative stress (from free radicals), but this is only a secondary phenomena
    - insulin and IGF: primary role in longevity
        - long-lived organisms in the lab (due to caloric restriction) all have reduced insulin resistance; very low blood sugar, insulin and IGF.
            - low blood sugar also means less AGE formation
            - genetic studies have found that mutations to the genes that control insulin and IGF signaling bestow extreme longevity
        - insulin and IGF respond to food availability, regulating metabolism, fat storage, and reproduction
            - IGF regulates cell division and growth; insulin regulates metabolism by partitioning fuel for use or storage
            - **longevity implications: when food is abundant, insulin and IGF activity increases and stimulates growth, maturity and reproduction; when food is scarce, such activity is reduced and long-term survival is favored over immediate reproduction.**
                - evolutionary logic: if food is abundant, organisms can successfully multiply; if food is scarce, reproduction will be useless as parent and offspring will die of starvation. The food-sensing mechanism extends lifespan to increase the chances of being alive and fertile when food returns.
        - Cynthia Kenyon found that feeding worms glucose shortened their lives
            - she personally went low-carb with great results: weight loss; lower blood pressure, trigs, and blood sugar; HDL increased
    - the mainstream accepts the insulin-IGF research, but avoids any possible dietary implications, instead focusing solely on drug or gene therapies
        - another common approach accepts the insulin-disease connection, but then assumes that hyperinsulinemia is caused by insulin resistance which is caused by a combination of high-fat, high-calorie diets, physical inactivity and excess weight

Part Three — Obesity and the Regulation of Weight

The Mythology of Obesity

- obesity research hardly deserves to be called science; based on the assumption that excess weight results from excess calorie consumption and/or physical inactivity ("gluttony-sloth hypothesis")
    - the attitude is that this assumption cannot be questioned, doing so makes one an extreme skeptic
    - the evidence all points to different causes, and contradicts the gluttony-sloth hypothesis over and over
- mainstream explanation of obesity epidemic: prosperity leads to overeating and higher-fat diets, and less physically demanding work
    - a few major problems with this explanation:
        - the increase in calories since the 70s has been primarily from carbs; fat intake has fallen
        - the exercise mania started in the 70s
        - obesity is most prevalent among the poor and hard-working (commonly co-existing with childhood malnutrition)
- case study: the Pima Indians
    - hit very hard by diseases of civilization (obesity, diabetes) after taking up western foods (beans, sugar, flour, soft drinks)
    - low-fat diet: only 24% of calories from fat
    - very high soft drink consumption
    - very physically demanding labor
- thrifty gene hypothesis: humans evolved under an unpredictable food supply, hence our propensity to store fat
    - problems:
        - no evidence that the paleolithic food supply was unpredictable or alternated between abundance and scarcity
            - on the contrary, evidence suggests that much of the planet was a "paradise for hunting" before the last two centuries
            - hunter-gatherers have multiple food sources (hunting and gathering), so famine is rare
        - survival may have been aided by some fat storage, but not the excessive obesity that hinders mobility (hunting, fleeing from predators, or even gathering)
        - wild animals are very lean, even when food is abundant. (The thrifty gene hypothesis presupposes that to remain lean, we must be hungry — that consumption is limited by food supply rather than appetite)
            - thrifty gene proponents invoke the Israeli sand rat as an example, even though the initial experiments showed that it was carbs and not total calories that caused obesity
        - hibernators regulate their fat stores very consistently on a schedule: it's very hard to prevent them from gaining and losing weight
            - even if you surgically remove some fat, the animal will compensate and restore the fat or conserve it's remaining fat

Hunger

- Two main semi-starvation studies: Benedict's in 1917 and Keys's in 1944
    - Parameters: 1400-2100 calories/day
    - Results: some weight loss, but dramatic decreases in metabolism and other negative/ dangerous effects
        - metabolism adjusted so that any consumption greater than normal led to weight gain
            - subjects were always cold, and couldn't keep warm

            - lowered pulse and blood pressure, slowed movements, weakness
        - psychological havoc: loss of ambition, irritability, depression, neurosis
            - several of Keys's subjects cracked and binged
            - constant complaints of hunger
        - post-restriction, subjects ate enormous amounts (8000 cal), still felt hungry but physically incapable of ingesting more
            - rapidly gained back the weight, usually ending up fatter than before
                - Keys's subjects ended up 5% heavier; with 50% more body fat!
    - Conclusions:
        - obese and lean subjects get the same effects
        - energy expenditure decreased dramatically with intake restriction
            - adding calories brought energy expenditure back up, but any lost fat would be regained
                - thus, **weight loss via calorie restriction can only be maintained by permanent calorie restriction**
- Hirsch did a similar experiment in 1995 on obese subjects
    - concluded that calorie restriction resulted in a disproportionate decrease in energy expenditure and metabolism
        - the body resists changes in adiposity
- Positive energy balance hypothesis: weight gain is a result of energy intake exceeding expenditure
    - just doesn't work that way; calorie restriction has been remarkably ineffective for weight loss in obese patients
    - low-fat, calorie-restricted diets are no better than balanced calorie-restricted diets
    - long-term calorie-restriction studies even show slight fat gain
- Conventional wisdom sticks with calorie restriction, despite the evidence
- Exercise: the other side of the equation
    - since calorie restriction is ineffective, then by the process of isolation, energy expenditure must be the key to weight control
    - problem: exercise burns insignificant amounts of energy and increases appetite
        - e.g., lumberjacks eat 5000 cal/day vs tailors at 2500 cal/day
    - Mayer's evangelism overcame the prevailing attitude that exercise was ineffective or counterproductive
        - he noticed that obesity correlates with inactivity, then assumed that inactivity causes obesity (it's really obesity that causes inactivity)
            - problem: obesity correlates with poverty — more likely physical laborers
        - Mayer's hypothesis: there is a loophole in the relation between appetite and activity; hunger and activity are proportional only to a certain point — below that, hunger remains even if you don't exercise
            - based on two of his own studies, both of which are prime examples of bad science
        - public figure: wrote in NYT and had a syndicated column
    - ultimately, the evidence has shown that exercise is ineffective for weight loss
        - "underwhelming" support of Mayer's hypothesis in the scientific literature
- Flawed assumption: hunger is a psychological phenomenon, a question of will power
    - No, it's a physiological drive to get enough calories; that's why we get hungrier after exercise (or after not eating for a few hours)

Paradoxes

- obesity: psychological or biological (physiological)?
    - fat deposition is very specific (men: above waist, women: below waist)
        - suggests a role for sex hormones
    - obesity is hereditary
        - babies of diabetic mothers are born fatter and more likely to become obese
    - a starved endomorph doesn't become an ecto or mesomorph
    - different people fatten differently when they overeat: some gain weight easily, others not at all
        - one study overfed sedentary men (getting up to 10,000 cal/day)
            - a minority gained weight easily (large differences in degree of fattening)

            - all lost weight readily afterward (just as starved subjects gained it)
            - what happens to all the extra calories in those who don't fatten when overfed?
        - farmers breed livestock to be more or less fatty: genetic component
    - experiments on Zucker rats (one gene is changed, resulting in major obesity) demonstrate that the rats will store fat even when half-starved
        - this suggests the cause of obesity is biological (hormonal or genetic)
- Why does the "gluttony-sloth" hypothesis (caloric balance) persist?
    - Hilde Bruch found that fat children always overate; ~focus on psychological factors
    - Louis Newburgh: published the seminal article on the subject
        - strongly advocated the gluttony-sloth hypothesis (psychological; failure of will)
    - problem: "obesity is caused by overeating and/or deficient activity" - this is both an assumption and a tautology
        - assumption: that the correlated phenomenon is the cause (and not effect)
        - tautology: overeating and inactivity are defined in terms of the degree to which they cause obesity
            - we never say that a lean person with a big appetite overeats
            - a fat person has overeaten by definition
            - like saying that alcoholism is caused by chronic overdrinking
            - vague terms, relative to whether the person is obese or not
    - obese people don't gain weight endlessly, they stabilize at a certain weight
        - someone at a stable weight is not overeating (calories in = calories out)
- other hypotheses like "gradual weight gain from consistent small caloric excess" and "toxic environment" also fail
    - the first doesn't explain why the person doesn't notice the fat gain and cut back
    - the second doesn't explain why we all don't get fat, despite sharing the same toxic environment
        - deeply immersed in moral and class judgments: cheap fast-food is vilified while equally high calorie Starbucks drinks are never blamed; if we watch too much tv then we're couch potatoes bound to get fat, but if we sit around reading or studying then we're not accused
- if obesity is a result of a psychological defect (willpower problem), why don't all other defective individuals (drug addicts, gamblers, criminals) get fat?
- Hilde Bruch later re-evaluated her hypothesis, revising which was cause and which was effect, coming to the view that overeating is the symptom of obesity, not the cause

Conservation of Energy

- conventional wisdom is founded on two misinterpretations of thermodynamic law (caloric balance equation)
    - first misconception: association implies cause and effect
        - law of energy conservation: *Change in energy stores = Energy intake - Energy expenditure*
            - the equation doesn't indicate which is cause and which is effect
            - it's possible that a change in energy stores could cause changes in intake and/or expenditure
                - evidence supports this interpretation (metabolic/hormonal changes that drive us to change adiposity by adjusting intake/expenditure)
        - in children, a positive caloric balance is associated with physical growth
            - evidently, they eat a lot because they're growing (not growing because they eat a lot)
            - hormonal drive to grow causes increased appetite
            - positive caloric balance is a result, not a cause, of growth
        - pregnant women fatten due to hormonal changes
            - hormones induce hunger and lethargy to create the positive caloric balance necessary for fat accumulation
        - fattening is the cause, gluttony and sloth are the effects
            - to understand what causes obesity, we need to understand what causes the hormonal changes that induce fattening

        - studies on obese people's behavior only find associations, not causes
            - don't explain *why* they eat more, are less active, have slower metabolism
            - actually, the obese don't eat more than the lean (both are in caloric balance)
        - prospective studies show that pre-obese people expend less energy
            - doesn't imply causation; only an association
        - obesity is associated with metabolic syndrome (diseases of civilization)
            - conventional interpretation: obesity causes/contributes to the diseases
            - alternative logic: the underlying disorder causes both obesity and the other diseases
    - second misconception: energy intake and expenditure are independent variables (a change in one doesn't affect the other)
        - the popular notion that obesity comes gradually over the years from small daily caloric excesses is a gross oversimplification of biology
            - 2700 cal/day = about 1 million cal/year. To maintain a constant weight over a couple decades would be a feat of remarkable accuracy
            - rather, the body balances intake with expenditure. They are dependent variables.
                - explains how people maintain constant body weights under varied intake and activity levels
- if energy intake and expenditure are dependent variables, then the conventional practice of creating a negative caloric balance can't work
    - **any attempt to change energy stores by changing intake or expenditure will be compensated for by the body's regulatory system: intake and expenditure are adjusted to achieve the desired amount of energy storage**
        - an attempt to force a caloric deficit (by dieting or exercising) will be foiled by increased hunger and/or lethargy and lowered metabolism (e.g., always feeling cold)
        - an attempt to force a caloric surplus will be foiled by reduced appetite and/or increased physical energy and metabolism (e.g., increased body heat)
    - this phenomenon confounds the caloric balance crowd; a very inconvenient fact
    - researchers of malnutrition (not obesity) take this for granted
        - caloric deprivation is compensated for by lowering expenditure
    - ***no wonder dieting is so difficult: it is a fight against mechanisms which evolved precisely to to minimize fat loss when caloric intake is reduced***
        - traditional response to failure of dieting is to blame the victim for lack of willpower; the real problem is that you can't force a caloric deficit
        - any weight lost from caloric restriction can only be kept off by continuous restriction; a return to natural eating will bring the weight back
            - an extreme masochistic challenge: to fight hunger and lethargy for a lifetime
            - a child's growth can be stunted by starvation; fat accumulation can be offset by starvation. But in neither case will starvation address the root causes.
    - **obesity is a symptom of an underlying disorder; caloric restriction attempts to treat the symptom, but doesn't address the root cause**
    - lean people are more active because they have more energy made available to their cells; obese people have less available (more goes into storage)
        - lean people are active because they're lean
        - fat people are lazy because they're fat
            - doing more exercise doesn't address the cause of the lethargy (it just fights it); hunger and metabolism will adjust to maintain fat stores
    - hunger is like thirst, a physiological drive to get more energy (or fluids); not a psychologically controlled desire
        - the impulse to physical activity is also physiological, not psychological: depends on availability of energy to the cells
- the crucial factor is not intake or expenditure, but distribution: how much the body stores and how much is available to the cells
    - so the left side of the equation is fundamental (energy stores = intake - expenditure)

Fattening Diets

- no reason to believe that fattening a lean person is any easier than leaning a fat person
    - to fatten, extra calories (beyond expenditures) must be consumed *and* stored as fat and not expended via increased metabolism/physical activity
- intentional fattening
    - Massa tribe male fattening ritual: 1000+ extra calories from milk and porridge made from sorghum (like sugarcane)
    - Japanese sumo wrestlers eat a high calorie, high carb, and very low fat diet
        - seems that if obesity is the goal, then carbs, not fat, is the means
- conventional wisdom: "dietary fat causes obesity"; rests on 4 weak pieces of evidence
    - 1. since they assume that dietary fat causes heart disease, and since heart disease, obesity and diabetes are linked, then dietary fat causes obesity and diabetes
        - but as we've seen, dietary fat is *not* responsible for heart disease
    - 2. certain strains of rats get fattest by eating fat
        - key word: certain strains; the rest fatten on carbs
        - pigs — which have similar digestive systems to humans — fatten on carbs
            - as do other animals, including cows and monkeys
        - rats given unlimited amounts of all foods get super obese, eating mostly sweets; they didn't eat high-fat, low-carb foods to excess
    - 3. fat is twice as calorically dense as carbs and protein, fools people into overeating
        - this is the volume hypothesis: intake is limited by stomach capacity
        - this idea was blown apart by Edward Adolph's rat experiments in the 40s
            - diluted rat diets with water, fiber, and even clay
            - rats would keep eating until they got enough calories
            - if calories were injected directly into stomach, they would eat less by that amount, but injecting water had no such effect
        - thus, intake is regulated by caloric need, not volume, mass, or even taste
    - 4. lower metabolic cost of storing fat than carbs (carbs must be converted to fat first)
        - this neglects the effect of carbs on the desire to overeat
        - **it's impossible to fatten people on high-fat, high-protein diets: they just can't eat enough**
            - in one experiment, the volunteers would sit staring at "plates of pork chops a mile high" and refuse to eat enough to get an excess thousand cal/day
            - Elliot Danforth (University of Vermont obesity researcher): "The bottom line is that you cannot gain weight on the Atkins diet. It's just too hard. I challenge anyone to do an overfeeding study with just meat. You can't do it. I think it's a physical impossibility."
        - but, people do fatten readily when overfed on fat *and* carbs
            - while people lose their appetite with an excess thousand fat calories, they can eat 6-7 thousand excess calories of fat and carbs and still feel hungry
            - suggests something unique about carbohydrates to allow such enormous overconsumption/appetite
    - hunger, satiety, and physical activity are physiologically regulated (not psychological)
        - imagine if diabetologists attributed the ravenous hunger that accompanies uncontrolled diabetes to a behavioral disorder, to be treated by psychotherapy or behavior modification!
        - the nutrient composition of the diet has a fundamental effect on eating behavior and energy expenditure

Reducing Diets

- before the low-fat craze, conventional obesity treatment was low-carb, low-fat, high-protein (to maintain muscle mass)
    - some diets only allowed for a little bit of carbs for brain glucose (only from non-starchy vegetables)
    - some were also very low calorie (360-600)
        - raises the question: is it calories or carbs?

- obese people tend to eat the same amount of calories as lean people, but a greater proportion is carbohydrate
    - common finding is that obese people consume excessive starches and sweets
- calorie restriction successes may be the result of carb restriction (you can't significantly restrict calories without restricting carbs)
    - Per Hanssen compared a low-carb, high-fat 1850 calorie diet (25% carb, 60% fat calories) with a high-carb 950 calorie diet (50% carb calories)
        - the low carb diet was just as effective, even though it had double the calories
            - patients never felt hungry, their fatigue rapidly improved
            - a much more humane treatment than semi-starvation
- nutritionists say that 130 grams of carbs is the minimum safe amount — to provide glucose for brain and nervous system
    - glucose can be synthesized from protein
    - glucose is not the only fuel, ketone bodies are the backup
        - common error: "ketosis is pathological"
            - ketoacidosis is bad (~200 mg/dl of ketone bodies)
            - ketosis is normal (overnight fasting levels: 5 mg/dl; extreme low-carb diet: 5-20 mg/dl)
- All-meat diets: pioneered by anthropologist Vilhjalmur Stefansson, who lived with the Inuit for a decade eating nothing but meat (early 1900s)
    - Inuits ate no plant food, they considered vegetables and fruit "not proper human food"
    - controversial in the face of the reigning idea that a healthy diet had to be balanced
    - myth: high-protein diets are bad for the kidneys
        - belief based on early research by Newburgh on rabbits — herbivores that don't naturally eat animal protein!
    - Stefansson and Anderson were subjects in a closely supervised yearlong experiment
        - only cooked meat, about 2 lbs/day: 79% fat, 19% protein, 2% carb
        - they remained perfectly healthy: slight weight loss, improved blood pressure, no vitamin or mineral deficiencies
            - calcium is interesting: they only ate a quarter of the calcium usually found in mixed diets, and the acidity of the meat supposedly depletes calcium!
    - why don't the Inuits get deficiency diseases (scurvy, pellagra, beriberi, rickets, etc)?
        - deficiency diseases only appear on high-carb diets
        - meat contains all the essential amino acids in the optimal proportions, and all the essential vitamins in large quantities (except vitamin C)
            - vitamin C competes with glucose for cellular uptake, but glucose is heavily favored (glucose crowds out vitamin C)
                - the more glucose in the blood, the less C is absorbed into the cells, and the less C reabsorbed by the kidney (so it gets excreted in urine)
                    - vitamin C deficiency is associated with metabolic syndrome, so it is likely a disease of civilization
                - so, carbs cause excretion of vitamin C, while inhibiting the use of what is present
    - thus, **deficiency diseases are not necessarily caused by insufficient intake, but by wastage caused by refined carbs**

Unconventional Diets

- obesity experts have looked down on first-hand observation and treatment
    - the clinicians who regularly treat obese patients and have first-hand experience don't get much attention in the field
- Blake Donaldson treated obese patients with a fatty-meat paleo-style diet (1920's)
    - got the idea from anthropologists who informed him that prehistoric humans lived almost exclusively on the fattest meat they could kill
    - low-carb, high-fat, high-protein: 1.5 lbs of meat per day (75% fat calories)
    - great success, treating 17,000 patients over 4 decades
    - the main difficulty was "bread addiction" (aka carb cravings)
- Alfred Pennington heard about Donaldson's method and started using it

        - he worked at DuPont, where they were trying to improve the health of executives
            - calorie counting and exercise failed, so they tried Donaldson's meat diet
            - great results: significant weight loss, absence of hunger, increased energy and sense of well-being
                - no calorie restriction
        - he got some attention in the press and in an academic journal, but this prompted competing journals to address it: they rejected it as absurd
            - clinicians who were actually treating people successfully with the method put pressure on the journals, with some success
                - they backed down from the claim that Pennington's diet would increase weight, now arguing that it was dangerous for health
- Pennington's Dupont experience would be confirmed repeatedly in the literature
    - Margaret Ohlson and Charlotte Young tested a low-calorie version
        - subjects lost weight and never reported hunger as they did on balanced low-calorie diets
        - compared low-fat vs low-carb
            - 1200 cal low-fat didn't bring about the expected weight loss (from calorie deficit): only 0.5 lb/week
                - subjects were always hungry and lacked 'pep'
            - 1400 cal Pennington-style diet: almost 3 lb/week — 6 times more effective and higher in calories
                - no hunger, felt well
        - Ohlson then tested different dietary compositions for this diet
            - subjects found low-fat versions bland, uninteresting and hard to eat
            - hunger levels were proportional to carbohydrate intake
            - high-protein diet increased muscle mass while burning fat
                - balanced calorie-restriction causes muscle and fat loss
        - Young had the same results: remarkable weight loss without hunger
            - subjects were remarkably healthy on the diet
            - in every case, the weight lost exceeded what would be expected from caloric deficit
- the experts didn't bother testing weight reducing diets (until recently)
    - since they already knew that obesity was caused by caloric excess, it would have been a waste of time
    - clinical investigators who did test diets reported consistent results for low-carb diets
        - 1-5 lbs/week of weight loss, none of the nasty symptoms of semi-starvation or food deprivation
            - the patients loved it: the food and the results
        - more effective than caloric restriction, even compared to balanced diets with half the calories of the low-carb diets
    - in the past decade, renewed interest has led to several trials to test low-fat semi-starvation diets against all-you-can-eat Pennington diets (aka Atkins)
        - in every case, low-carb diets resulted in 2-3 times the weight lost compared to low-fat semi-starvation diets
        - a survey of low-carb diet trials found they averaged 37 lbs lost in total vs. 4 lbs for higher-carb diets
- this evidence overturns some fundamental assumptions
    - "a calorie is a calorie"; weight gain is the result of overeating
        - Bistrian and Blackburn: 650-800 cal meat-only diet; 50% of subjects lost 40 lbs each (no hunger)
            - had they added 400 cal of carbs to balance the diet, only 1% would be likely to lose 40 lbs
                - would cause hunger and semi-starvation
            - but if they added 400 cal of protein and fat, they would still get considerable weight loss
                - still no hunger
            - somehow, adding extra carbs to the meat-only diet made it less filling
                - how can people eat 10,000 cal (Sims) and still be hungry, but not feel hungry on very-low-calorie, zero-carb diets?
- fasting produces the same metabolic response as carb-restriction

    - the body relies on protein and fat for fuel, whether from diet or from internal sources
    - hunger disappears after a few days of total starvation
        - but low-calorie diets induce hunger and suffering
    - if you break a fast with protein or fat, you still won't feel hungry, but with carbs the hunger returns with full force (along with the symptoms of food deprivation)
- mainstream rationalizations of low-carb effectiveness:
    - "low-carb is really low-calorie in disguise" or "no bread, no butter"
        - yes, low-carb reduces appetite in obese people and thus intake (not due to monotony of the diet or other psychological reasons)
            - just like you drink less when you're not thirsty
            - why is it that low-carbers don't feel hungry with reduced caloric intake, whereas regular semi-starvation causes gnawing hunger?
        - the deficit is not the cause of the weight loss: trials of normal calorie low-carb still result in considerable weight loss
    - "ketosis suppresses appetite"
        - it does not: people reduce their intake before ketones show up
    - "fat and protein are particularly satiating"
        - so, why are carbs less satiating?
- **Paradox: weight loss and hunger can be largely independent of calories**
- the mainstream insistence on the laws of thermodynamics is based on a misinterpretation: they've got cause and effect backward
- Pennington's hypothesis: fuel supply and demand at the cellular level determines hunger and expenditure
    - obese people are in energy balance (while they are maintaining a steady weight), and when they reduce intake, expenditures fall in compensation
    - the metabolic defect of obesity is that fat is readily stored in the cells, but not released fast enough when needed
        - this theory explains all the paradoxical observations by applying the same law of energy conservation with the proper direction of causation
        - fat mobilization is the key: cells get their energy from dietary intake and from fat released from cells
        - explains hunger and expenditure: the defect starves the cells (by storing nutrients away), so they demand more energy and reduce their expenditure
            - when the defect is cured, fat is released (lots of energy available) so demand is reduced (reduced appetite) and energy expenditure rises
        - calorie restriction just starves the cells further: the defect has not been addressed. Hence, the hunger, lethargy and suffering.
        - explains how obesity and malnutrition can coexist in the same populations
    - it must be carbs that cause the defect of fat mobilization
    - fat loss causes reduced appetite and increased energy expenditure (not the other way around, which is still the dominant view)
        - likewise, fat gain (due to the metabolic defect) causes hunger and lethargy

The Carbohydrate Hypothesis, I: Fat Metabolism

- the debate: caloric-excess hypothesis vs. hormonal/metabolic defect hypothesis
    - must explain the facts: prevalence of obesity among the poor, the recent obesity epidemic
        - defect hypothesis: genetic defect being triggered by environmental condition
            - ironically, this hypothesis disappeared in the low-fat craze of the 80s, just as the details had been worked out
- Germans and Austrians researched lipophilia in early 1900s
    - localization of fat deposition: male (abdomen) and female (hips, thighs) patterns
    - evidence contradicted caloric balance hypothesis:
        - in one case, a girl had skin transplanted from her abdomen to her hand. When she became obese, that skin also became inflated with fat
        - fatty tumors are unaffected by weight loss
        - progressive lipodystrophy: inability to store fat in certain areas (e.g., emaciated upper body, obese lower body)

        - there's more to the story of obesity than just calories: lipophilic tissues store fat regardless of energy balance
    - sex hormones play a role:
        - males without testosterone (boys, castrated men) have feminine fat patterns
        - female sex hormones influence the quantity, but not the pattern
- In the 1920s, lipophilia research was confined to the German and Austrian researchers
    - Hitler doomed their hypothesis: the anti-German sentiment hurt them
    - English became the universal language of science and the German literature rapidly disappeared from the field
- experiments generated the two hypotheses:
    - animal experiments: obesity interpreted as result of hormonal/metabolic defect
        - genetically obese rats fattened even with caloric intake held constant (ruling out overeating as the cause)
        - when starved, the rats consumed muscle and organ and conserved their fat
    - human experiments: obesity interpreted as result of overeating (caloric excess)
        - contradictory animal evidence was rejected as not applicable to humans
- hypothalamus lesion experiments: effects included increased appetite and obesity
    - overeating hypothesis came to dominate: hypothalamus as "feeding and satiety center" — behavioral hypothesis
        - obesity research became the domain of psychologists and psychiatrists
    - Stephen Ranson, a top neurologist, studied the hypothalamus, but held the metabolic defect view
        - lesioned rats grew obese even without overeating — the overeating hypothesis couldn't explain this
        - the hypothesis of a fat storage defect causing increased appetite and reduced energy expenditure fit the evidence best
            - lesioned rats gained 6 times as much weight per calorie consumed
            - hibernating ground squirrels fatten seasonally, no matter what — even if they aren't allowed to eat any more than at other times of the year
            - after fasting, animals gain back weight regardless of amount eaten
            - female rats without estrogen (ovaries removed) will rapidly grow obese, and they get just as obese if their intake is not allowed to rise
- evolutionary logic: reproduction depends on food availability
    - fat accumulation, energy balance, and reproduction are closely linked (regulated by the hypothalamus): homeostatic balance
    - food deprivation suppresses ovulation: offspring need food for survival
    - hormones regulate fuel partitioning and usage
- with WW2 there was a changing of the guard as many researchers retired and a new generation took over and started from scratch, embracing the (psychological) overeating hypothesis
    - and with this, bad science took over

The Carbohydrate Hypothesis, II: Insulin

- like heart disease, obesity research saw the "truth" declared based on incomplete evidence, and all further research was then interpreted in support of it
    - in 1955, JAMA completely ruled out the possibility that obesity was caused by a hormonal disorder
        - but the evidence piled up in support of the roles of hormones such as insulin and adrenaline
- Carl von Noorden speculated in 1905 on a link between insulin, obesity, and diabetes
    - with obesity, the ability to use blood sugar is impaired, but the conversion to and storage of fat is not
    - with diabetes, both the usage and storage of blood sugar are impaired, and glycosuria results
- insulin discovered in 1921
    - used very effectively to therapeutically fatten people (e.g., anorexics)
    - Wilhelm Falta: the only way to gain fat is to increase insulin
        - he noted that injecting insulin increased the appetite specifically for carbs

        - diabetic's dilemma: a) take insulin to control blood sugar, but get fat; or b) slack off on the insulin to avoid fattening
- insulin-obesity research was doing well in prewar Europe, but in America it started out on the wrong foot
    - Newburgh set the conventional wisdom: insulin causes overeating by reducing blood sugar to the point where the patient eats to remain conscious
        - directly contradicted by the fact that the obese tend to have high blood sugar
    - unfortunately, only the American research community (Newburgh's hypothesis) survived the war years
- research on insulin and fat metabolism from '20s to '60s made great progress, but would have effectively no influence on mainstream though about obesity
    - "fat tissue is inert, like a garbage can"
        - fat tissue is remarkably dynamic: fatty acids are in constant flux in and out of fat tissues (more like a coin purse for daily expenditures than a long-term savings account)
            - fattening occurs when the rate of deposition exceeds the rate of mobilization
            - controlled by hormones, not by quantity of fatty acids in the blood
    - "carbs are the primary fuel for muscles"
        - fat tissues provide a steady supply of fatty acids to fuel the body
            - fat is like ready cash for covering expenditures
        - when fasting, fat provides 85% of energy, with protein converted to glucose for the rest
            - inversely, the presence of glucose or insulin removes fatty acids from circulation (control mechanism: cells burn glucose when it's available, otherwise fat)
- the mechanism of fat metabolism: body first burns available glucose, then fatty acids cover the rest; most carbs and all fat is stored in fat cells before use (50-70% of energy is supplied from fat cells)
    - free fatty acids vs triglycerides:
        - fat stored in adipose tissue = triglycerides
            - 3 fatty acids (tri) on a glycerol backbone (glyceride)
            - some trigs in fat cells come from dietary fat, the rest from carbs (converted in the liver)
        - fat can only enter and exit cells as free fatty acids—trigs are too large to pass through the cell membrane, they must be broken down first
            - triglyceride/fatty-acid cycle: inside fat cells, trigs are continuously broken down and recomposed; any fatty acids not immediately repackaged into trigs will escape into the bloodstream
            - fatty acids in the blood will be used as needed for fuel, and the rest are converted to trigs by the liver, loaded on VLDL and shipped back to fat cells
    - simple control mechanism: blood sugar
        - glycerol phosphate: byproduct of burning glucose, provides the glycerol molecule for trigs
            - the rate of trig formation (and so fat deposition) depends primarily on availability of glycerol phosphate
            - so: carbs = glucose = glycerol phosphate = trigs = fattening
        - triglyceride/fatty-acid cycle: regulated by amount of blood sugar available to fat tissue
            - if blood sugar low, less glucose available to fat cells to burn, and thus less glycerol phosphate to keep fatty acids bound up in the cell (and vice versa). Energy control system:
                - as blood sugar decreases, fatty acids are released to compensate
                - as blood sugar increases, fatty acids are bound up in fat cells
        - glucose/fatty-acid cycle (Randle cycle): blood sugar regulation
            - when blood sugar low, more fatty acids are released: this triggers the muscle cells to stop burning glucose in favor of fatty acids
                - fatty acid levels regulate whether the muscles burn glucose or fat
                - keeps blood sugar within safe limits

        - hormones orchestrate these control mechanisms to adjust for other factors (external environment, seasons, emergency energy requirements, etc)
            - insulin stimulates transport of glucose to fat cells, thus controlling trig formation and fattening — insulin is the master control of fat metabolism
                - fat tissue is very sensitive to insulin; even trace amounts have powerful effects
            - all other hormones act to mobilize fat from the tissues
                - can only do so if insulin levels are low
                    - virtually anything that increases insulin secretion will also suppress secretion of other hormones
            - explains the fattening of hypothalamus-lesioned animals: their insulin goes through the roof
                - while the evidence overwhelmingly supports this insulin view, the mainstream opinion remains the old psychological overeating one
- fructose is converted to glycerol phosphate more efficiently than glucose
    - this is another reason why fructose stimulates the liver so readily to convert it into trigs
    - most fattening carbohydrate
    - very deadly when paired with glucose, as in sugar or HFCS (fructose doesn't stimulate insulin secretion)
- fat tissues are extremely sensitive to insulin, much more so than other tissues
    - muscles become insulin resistant long before fat cells do
        - then, fat cells soak up all the excess blood sugar to prevent it from reaching toxic levels, while extra insulin is secreted to make it happen (compensating for muscle's resistance)
            - this in turn causes increased fat storage, and suppresses the release of fat
        - weight stabilizes once fat cells become resistant or fat cells can't hold any more
- by the mid-60s, four facts had been conclusively established:
    - carbs are singularly responsible for promoting insulin secretion
    - insulin is singularly responsible for inducing fat accumulation
    - dietary carbs are required for fattening
    - both type 2 diabetics and the obese have hyperinsulinemia and a greatly exaggerated insulin response to dietary carbs
- carbs actually increase insulin-sensitivity of fat cells
    - eating high-carb can mask diabetes by temporarily lowering blood sugar, but at the cost of fattening
- fat distribution mechanism: LPL (lipoprotein lipase) — the gatekeeper of fat accumulation
    - LPL: an enzyme that breaks trigs down into free fatty acids, enabling their absorption into cells
        - regulated primarily by insulin, which increases LPL activity in fat tissue and decreases it in muscles
            - high insulin levels promote fat storage and so muscles burn glucose
    - local concentrations of LPL determine the pattern of fat distribution
        - calorie-restriction increases LPL activity in fat tissue and decreases it in muscles: both resist fat loss!
        - exercise increases LPL activity in muscles during activity, but afterwards it increases them in fat tissue
            - the body restocks whatever fat it surrendered
        - carbs increase LPL activity in fat tissues (via insulin), fats do not
- none of this fat metabolism research is particularly controversial, yet it is rejected out-of-hand in the mainstream obesity field
    - they religiously insist on the law of energy conservation and caloric excess theory
- societal insulin problems are only going to get worse if not seriously addressed
    - babies develop insulin problems of their mothers in the womb
        - vicious cycle: more people each generation are born with predisposition to obesity and disease

The Fattening Carbohydrate Disappears

- between 1973 and the mid-'80s, the notion of the fattening carbohydrate was replaced by dietary fat
    - this is perplexing: it happened just as the science of fat metabolism had been worked out and low-carb diets were enjoying credibility among clinicians
        - obesity conferences were dominated by discussions of the efficacy of low-carb diets for weight loss
- Keys' hypothesis had a contagious effect on obesity research: since fat caused heart disease, that was a strong reason to think it couldn't be healthy for weight control
- Yudkin made low-carb politically acceptable by insisting that it is low-calorie in disguise
    - nutritionists rejected any low-carb diets that disagreed with Yudkin
        - they were seen as commercial quackery because of the popular diet books
        - low-carb completely fell out of the academic discourse, rejected out of hand as "nutritional nonsense"
- Atkins had great personal and clinical success with carb-restriction
    - *Diet Revolution* was a polemic — a revolution against the lies of conventional wisdom
        - unfortunately, it antagonized the establishment and ruined low-carb credibility
- the established wisdom in the field of obesity research was determined by the judgment of less than a dozen men (not by the scientific process)
    - from North-eastern academic corridor — Harvard, Yale, Columbia, Rockefeller, UPenn
        - Van Itallie, Bray, Cahill, Stare, Stunkard, Mayer, White, Hirsch
        - none did clinical treatment of obesity
    - Van Itallie and Bray did the most to eliminate the fattening carbohydrate
        - Van Itallie wrote the AMA-sponsored 'denunciation' of Atkins (an unscientific rejection)
            - big name in debunking low-carb diets
        - Bray became the leading proponent of the dietary fat-obesity hypothesis
    - low-carb was dismissed for its commercial motives (many popular diet books)
        - this critique also applied to them: Harvard got big funding from General Foods (Post cereals, Kool-Aid, Tang)
            - in the following decade, Stare became the most public defender of sugar and food additives, and his department received funds from Oscar Mayer, Coca-Cola, National Soft Drinks Assoc.
        - another example: when *Science* dedicated special issues to obesity, James Hill wrote the review article both times
            - Hill had received funds from the Sugar Association, Mars, Kraft, Coca-Cola, Proctor & Gamble, as well as government grants to test the Atkins diet

The Carbohydrate Hypothesis, III: Hunger and Satiety

- Sidbury (pediatrician) developed a low-carb, low-calorie diet for obese children
    - despite the low calories, children did not feel hungry nor was growth stunted
- any viable hypothesis of obesity must also be a hypothesis of hunger and satiety
    - what the law of energy conservation does tell us: anything that works to change body mass must affect energy intake and/or expenditure
- there are few scientific conceptions of hunger/satiety
    - common assumption: hunger is signaled by the contraction of the stomach as it empties; so fat is satiating because it digests slowly
    - another: hunger is psychological, unrelated to metabolic needs of the body
        - researchers will disagree with this, yet it's essential to the logic of calorie restriction
- study of hunger focuses almost exclusively on the brain: 2 main hypotheses
    - Mayer's glucostat hypothesis: low blood glucose triggers hunger in hypothalamus
    - lipostat hypothesis: the body defends a certain degree of adiposity (its "set point")
        - problem: little precedent—other biological systems maintain stability without a set point
- the physiological psychologists found a viable alternative (by rediscovering fat metabolism)

    - although, this alternative hypothesis is hardly known among researchers (due to hyper-specialization and fragmentation)
    - need drives taste: in rat experiments, rats prefer solutions containing minerals they are deficient in
        - dilution experiments: quantity eaten is regulated by calories, not volume or taste
- Le Magnen (physiological psychologist) developed a physiological hypothesis
    - animals overeat during the day and undereat while they sleep
        - fatty acids compensate for reduced glucose to maintain satiety overnight
        - insulin suppresses fat mobilization and induces immediate hunger
            - insulin response enhanced while awake, suppressed while asleep
        - insulin drives the diurnal cycle of hunger, satiety, and energy balance
    - the hypothesis is based on 3 fundamental propositions:
        - the supply of fuel to tissues must always remain adequate for their functioning
        - protein, fat, carbs are all equally capable of providing energy for the body
        - the body is unable to distinguish between internally and externally derived energy
    - simple conclusion: body maintains caloric homeostasis — a constant flow of energy to cells
    - fat tissue is an energy buffer: takes up excess energy and releases it as needed (dynamic tissue)
        - when fat mobilization slows, hunger returns
        - hormone-driven process (directed by hypothalamus)
        - anything favoring fat deposition and inhibiting fat mobilization will cause hunger and fat gain (and vice versa)
    - insulin suppresses fat mobilization, causing hunger and fat storage
- nutrition and fertility are closely linked
    - Le Magnen's hypothesis implies that fertility is mainly influenced by the immediate availability of fuel, not by body fat stores
        - experiments confirm: animals become infertile without food (regardless of body fat); the more food, the more fertile
        - insulin stores fuel (makes it unavailable): infusing insulin into animals shuts down their reproductive systems
    - thus, low-carb has clear implications for infertility treatment
- any weight loss technique must work via fat mobilization
    - drugs that reduce hunger or increase metabolism won't work—the body will adjust expenditure or intake to compensate
    - nicotine works because it acts on fat and muscle cells: affects LPL and fat cell insulin sensitivity
- Insulin: the master orchestrator of weight, hunger, and expenditure
    - circulating insulin is proportional to body fat (very strong correlation)
    - seasonal variations in weight match insulin variations (higher in fall/winter, lower in spring/summer)
- Taste: highly dependent on hunger ("hunger is the best sauce")
    - rats given solutions with sugar or artificial sweetener will come to prefer sugar because of the calories; if glucose is injected into their stomachs as they drink the artificial solution, they develop no such preference
    - insulin is secreted in waves:
        - first wave within seconds of eating, lasts ~20 min
        - second wave follows, gradually building; lasts several hours
    - insulin takes 10 mins to have an effect on blood sugar: the first wave primes the blood to handle the incoming glucose
        - first wave clears nutrients from the blood, increasing hunger and improving taste ("l'appetit vient en mangeant")
            - hunger/palatability decreases as nutrients enter circulation
    - sight, smell, thought of food triggers an insulin response
        - clears nutrients from the blood, stimulating hunger
        - it's possible that an exaggerated insulin response excessively increases hunger and is responsible for fattening
    - this hypothesis explains why we can eat so much more if the meal includes carbs
        - the insulin response stores away the nutrients, allowing further intake
        - thus, carbs are anti-satients
    - carb cravings of obesity: chronic hyperinsulinemia causes hunger

- high insulin between meals primes cells to burn glucose, but none is available
    - this results in cravings for glucose, akin to addiction
    - even eating fat and protein won't help: the insulin just stores them away
- sugar is especially addictive: creates an exaggerated response in the reward center of the brain
    - going low-carb can bring on withdrawal symptoms (can make low-carb seem unhealthy, but it's really the sugar addiction)

Epilogue

- mainstream obesity research is deeply entrenched in the idea that obesity is caused by caloric excess; so their solution is calorie counting
- the Mertonian ideal of functioning science is absent from the study of nutrition, chronic disease, and obesity
    - it's debatable whether they've been practicing science (Taubes avoided the term "scientist" throughout the book)
- good science was sacrificed for "public health" (the Rose philosophy)
    - they aimed at convincing the public that the science is settled instead of rigorously testing their hypotheses—a religion masquerading as a science
- "The science is uncertain, but we still have to eat." Two common conventional replies:
    - eat in moderation, play it safe—balanced diet
        - bad advice: balanced diets aren't very effective at preventing disease
    - follow all the reasonable hypotheses that accord with lipid hypothesis (e.g. fiber, MUFA & Omega-3, avoid trans and saturated fat, limit red meat, etc...)
        - politically correct, but probably not healthiest (especially when compared to a high meat & fat diet)
- the making of this book:
    - Taubes has spent much of the last 15 years writing on issues of public health and nutrition
        - 5 years of research and writing for this book alone
    - he followed the facts wherever they led
        - had no idea at the outset that he would come to these unconventional conclusions
- the evolutionary logic is the fundamental guide to understanding health
    - carbs are the major deviation from our natural diet: first grains, then processing, then sugar (fructose)
        - eliminating these carbs can only bring us closer to biological normality
- to shift scientific opinion, the carb hypothesis needs to be rigorously tested (as the lipid hypothesis should have been)
    - that would settle the debate between the lipid hypothesis and carb hypothesis
    - we also urgently need studies on the long-term health effects of sugar and HFCS
        - probably the main source of diseases
- unfortunately, funding only goes to test the conventional lipid hypothesis
    - studies are never directly structured to test the carb hypothesis
    - until carb hypothesis is tested, the fat-carb controversy will continue

Unpublished Chapter: Gout

http://www.fourhourworkweek.com/blog/2009/10/05/gout/

- gout is caused by uric acid accumulating to the point that it falls out of solution (hyperuricemia), forming sharp crystals that get lodged in soft tissues (typically the big toe)
    - since uric acid is a breakdown product of purines (building block of amino acids), excess meat consumption was blamed
        - but low-purine diets have a negligible effect on uric acid levels (just like low-cholesterol diets and serum cholesterol, or low-salt diets on blood pressure)
        - purine-free diets are no longer prescribed due to ineffectiveness (even vegetarians are still quite susceptible)
        - eating more protein increases excretion of uric acid from the kidney
- alternative hypothesis: metabolic syndrome/disease of civilization
    - gout follows the classic pattern of a disease of civilization
    - Reaven found that insulin resistance and hyperinsulinemia raised uric acid levels (by decreasing excretion)
- the unique contribution of fructose
    - the appearance of gout has paralleled the availability of sugar, and not all refined carbs
    - fructose increases serum levels of uric acid
        - fructose injections cause a "striking increase" in uric acid

        - it accelerates breakdown of ATP, which is loaded with purines
            - alcohol apparently does the same
        - it also stimulates the synthesis of purines directly, and fructose metabolism produces lactic acid which reduces uric acid excretion
    - strong hereditary component due to a defect in the fructose metabolism genes
    - Peter Mayes (he wrote the seminal article on the topic) reviewed the literature and concluded that high-fructose intake caused hyperuricemia
    - sugar and HFCS are most dangerous: the fructose increases uric acid, while the glucose (through insulin) reduces excretion
- the fructose hypothesis was ignored because of bad timing, and the meat-alcohol hypothesis reigns
    - nutrition was ignored in favor of drug treatment (allopurinol), and misunderstood
    - in the 80s, the researchers who discovered the fructose link had left the field
- Richard Johnson's research shows that fructose induced hyperuricemia damages blood vessels leading into the kidneys in such a way as to raise blood pressure
    - this would explain the common association of gout and hypertension (and even diabetes and hypertension)
    - (Johnson only realized in 2004 that sucrose was half fructose and that his research was even relevant to sugar!)