Metabolical

The Lure and the Lies of Processed Food, Nutrition, and Modern Medicine

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CHAPTER 1

“Treatment” Is Not “Cure”—It’s Not Even Treatment

We’re Number 1!—in Morbidity, Mortality, and Expense

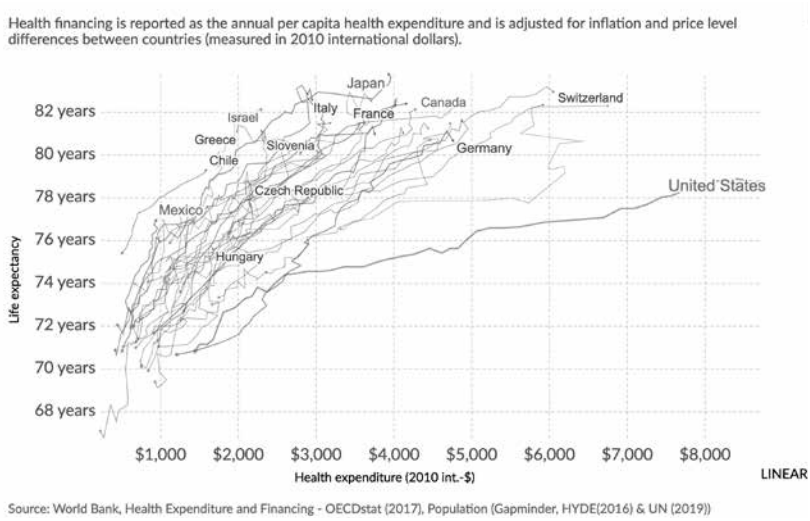


Figure 1–1: Comparison between healthcare expenditures versus life expectancy for Organisation for Economic Co-operation and Development (OECD) countries over forty-five years, 1970–2015. The US spends the most but gets the least.

CHAPTER 2

“Modern Medicine” Treats Symptoms, Not Disease

Just a Spoonful of Sugar Helps the Blood Pressure Go Up

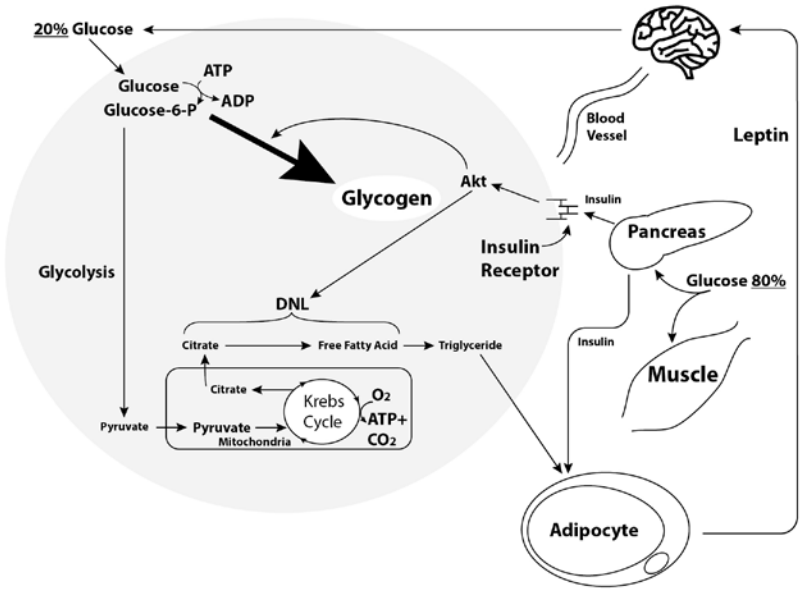
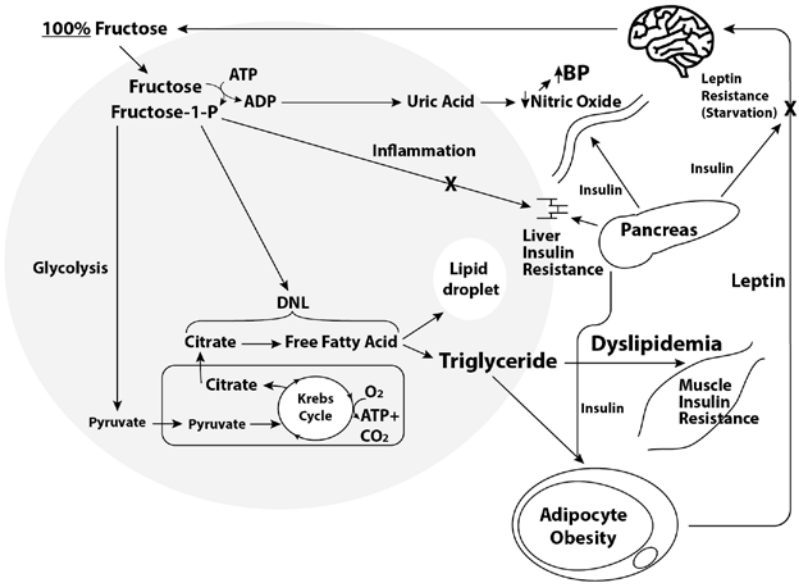


Figure 2–1: a) Pathway of liver glucose metabolism. More information can be found in Chapter 7, under “Cell Bio 101.” Only 20 percent of a glucose load enters the liver, and the majority is turned into glycogen (liver starch) for storage. A small amount of glucose will undergo glycolysis (the first step of glucose metabolism, which doesn’t need oxygen) to the breakdown product pyruvate. Pyruvate can then enter the mitochondria to be burned via the Krebs cycle all the way to carbon dioxide and water, capturing energy in the form of the chemical adenosine triphosphate (ATP)—the energy is in the phosphates. b) Pathway of liver fructose metabolism. 100 percent of a fructose load enters the liver. Fructose leads to loss of phosphates from ATP, generating of uric acid, which reduces nitric oxide, your blood vessels’ relaxing agent, which leads to hypertension. Most of the fructose is turned into pyruvate, the mitochondria become overwhelmed, and the excess generates liver fat, which causes insulin resistance. High insulin interferes with satiety, driving further consumption.


100% Fructose
Fructose
ATP
ADP
Fructose-1-P
Uric Acid
BP
Nitric Oxide
Leptin Resistance (Starvation)
Inflammation
Insulin
Insulin
Liver Insulin Resistance
Pancreas
Glycolysis
Lipid droplet
Leptin
DNL
Citrate
Free Fatty Acid
Triglyceride
Dyslipidemia
Citrate
Krebs Cycle
O2
ATP+
CO2
Pyruvate
Pyruvate
Insulin
Muscle Insulin Resistance
Adipocyte Obesity

CHAPTER 7

The "Diseases" That Aren't Diseases

Cell Bio 101

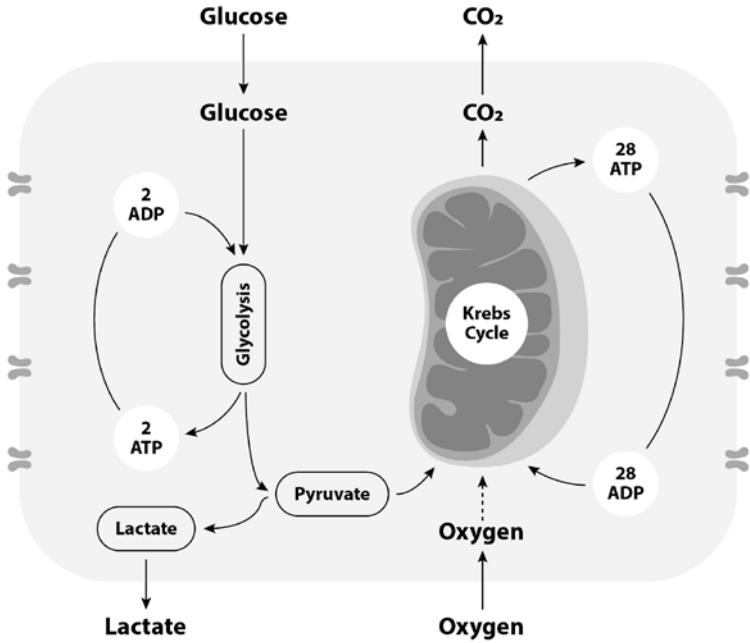


Figure 7–1: Energy metabolism 101. The cell imports glucose and converts it into pyruvic acid (glycolysis, left side), yielding two ATPs. If the mitochondria are functioning, the pyruvic acid is metabolized by the Krebs cycle (right side), yielding twenty-eight ATPs and carbon dioxide.

1. Glycation

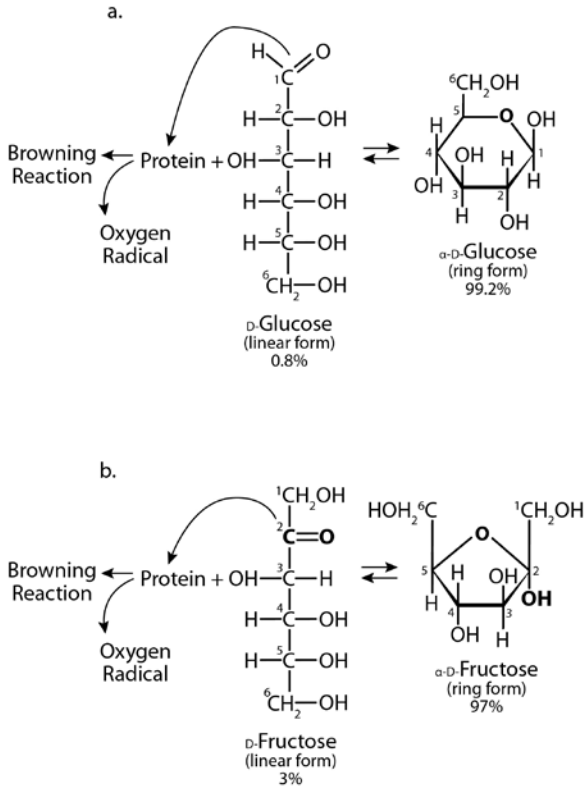
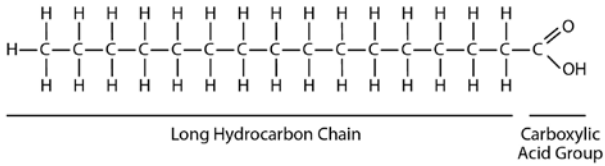
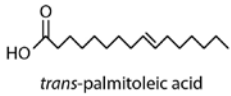


Figure 7–2: Structures of a) glucose and b) fructose, in the linear form and the ring form. This figure demonstrates that a sugar is not a sugar. Glucose is a six-membered ring and is more stable than the five-membered ring of fructose, which breaks down more easily to the linear form. Only the linear form can engage in the Maillard reaction. Therefore, fructose drives the Maillard reaction seven times faster than glucose, causing seven times the damage.

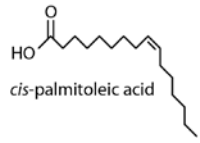
5. Membrane Integrity



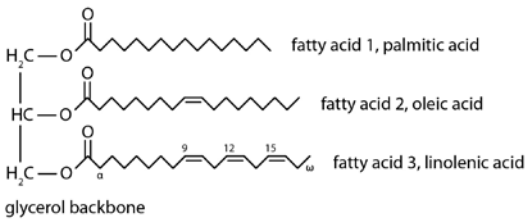
Features of a Saturated Fatty Acid (palmitic acid, 16-carbon)



trans-palmitoleic acid



cis-palmitoleic acid



Features of a Triglyceride

Figure 7–3: a-c) Structures of free fatty acids. a) palmitic acid (16-carbon saturated), b) *trans*-palmitoleic acid (16-carbon *trans*-unsaturated), and c) *cis*-palmitoleic acid (16-carbon *cis*-unsaturated). Note that the COOH carboxyl group (which is inflammatory) is free. d: Structure of a triglyceride, which is composed of three different free fatty acids (at least one of which must be unsaturated), linked to a glycerol backbone, so that the inflammatory COOH carboxyl groups are not free and available to do damage.

CHAPTER 8

Checkpoints Alpha, Bravo, Charlie: Nutrient-Sensing and Chronic Disease

Nutrient-Sensing, Kinases, and the Setup for Chronic Disease

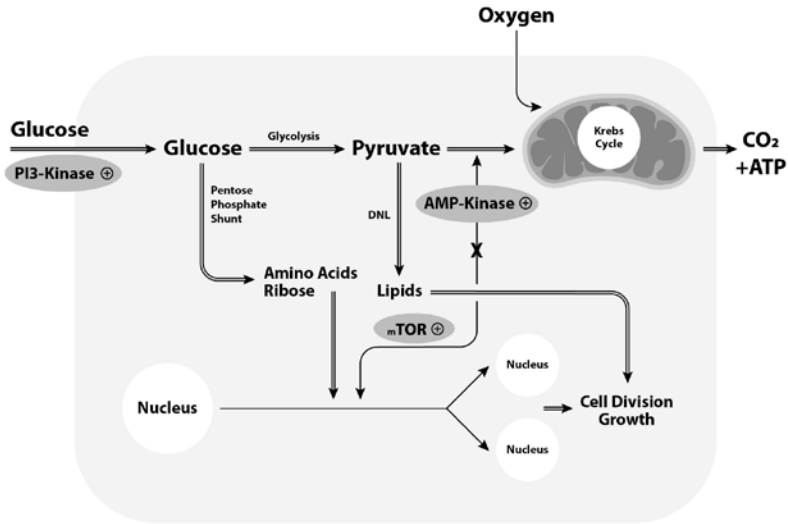


Figure 8–1: The three enzymes that determine cell fate. PI3-kinase lets glucose into the cell; AMP-kinase directs that energy either to produce structural components for the cell or to enter the mitochondria to burn all the way to carbon dioxide; and mTOR determines whether the cell lives or dies.

Growth Versus Burning, and Everything in Between—the Eight Combinations

Kinase	1	2	3	4	5	6	7	8
PI3K	+	—	+	—	—	+	+	—
AMPK	—	+	—	—	—	+	+	+
mTOR	+	—	—	+	—	—	+ —> —	+ —> —
	Normal Growth	Normal Burning	Metabolic Syndrome	Early Aging	Early Cell Death	Low-level Inflammation	Becomes #6	Becomes #2

Table 8–1: The activity of three enzymes (PI3-kinase, AMP-kinase, and mTOR), in two different states (on [+] or off [–]), leads to eight separate permutations. In any given cell at any given time, each enzyme can either be (+) or (–), although AMP-kinase (+) activation automatically results in mTOR (–) inactivation; thus combinations 7 and 8 are theoretical.

CHAPTER 9

Assembling the Clues to Diagnose Yourself

Assembling the Clues

	Laboratory
Fatty liver disease	ALT >25 in Caucasians, >20 in African Americans, >30 in Latinos
	GGT >35
	Uric acid > 5.5
Glucose intolerance	Fasting glucose > 100 or 2-hour glucose > 140; HbA_{1c} > 6.0 percent
Type 2 diabetes mellitus	Fasting glucose > 125 or 2-hour glucose > 200; HbA_{1c} > 6.5 percent
Dyslipidemia and heart disease	Lipid profile: TG > 150, HDL < 40, TG:HDL > 2.5, LDL-C >300, LDL-P >1000
	Homocysteine > 15
Insulin resistance	Fasting insulin > 15
Insulin hypersecretion	3-hour OGTT with insulin levels; measure insulin secretion and resistance indices

Table 9–1: Lab tests for chronic metabolic disease and normal ranges

CHAPTER 12

Nutrition "Unwrapped"

A Fiber Is Not a Fiber

Figure 12–1: Two kinds of whole grain bread. Each weighs one pound. The one on the left is and remains whole grain, while the one on the right started as whole grain but was then milled and processed.

CHAPTER 14

What and How Adults Eat

The "Secret" to Weight Loss

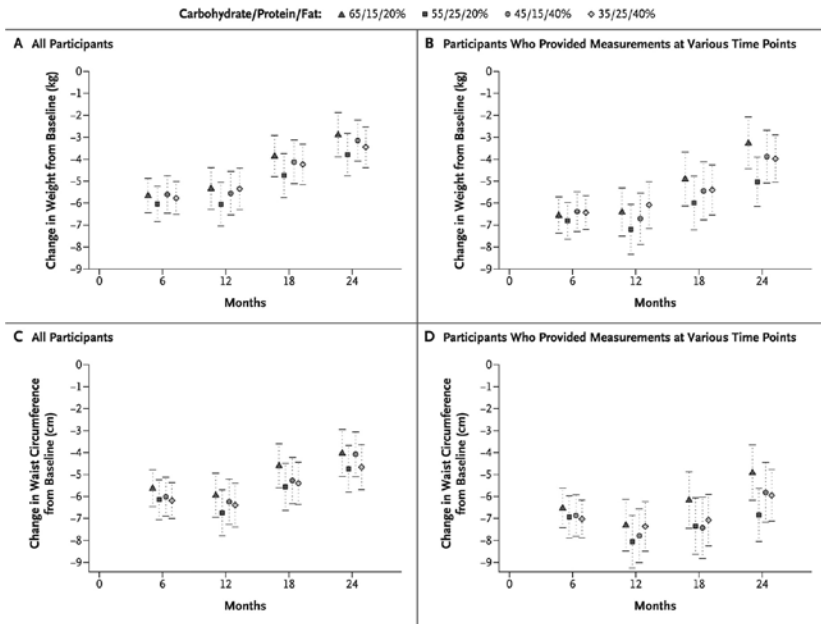


Figure 14–1: Weight and waist circumference loss on various diets with differing macronutrient composition, from 35 percent to 65 percent carbohydrate 3. The a) mean change in weight and b) mean change in waist circumference for each diet at each time point is essentially the same, suggesting that all four diets were equivalent. However, the standard errors of the mean (SEM, the "I-bars") demonstrate a wide distribution of response to each diet, suggesting that some subjects responded well to each diet, while others did not. This suggests that the authors' interpretation that all diets are the same is incorrect; rather that different diets work for different people.

CHAPTER 18

Food Adulterations

Toxins and Heavy Metals

Fig 18–1: Cuts of Italian, Argentinean, and US beef. Picture taken through a restaurant window in Rome, Italy, 2016. The Italian and Argentinean beef is homogeneous, while the US beef is marbled, a sign of fat deposition in the muscle, insulin resistance, and metabolic syndrome.

CHAPTER 19

Food Subtractions

Grass and Omega-3s

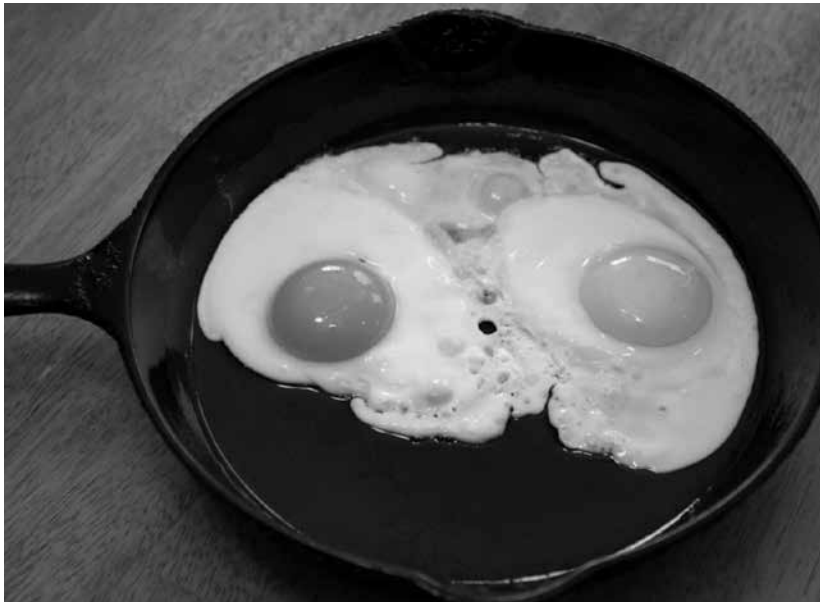


Figure 19–1: An egg from a pasture-raised chicken with high omega-3s (left) has a deep orange–colored yolk vs. a standard feedlot chicken with low omega-3s (right) has a pale yellow–colored yolk.

CHAPTER 26

Real Food Is Good for the Wallet

Food and Farm—Two Four-Letter Words Beginning with "F"

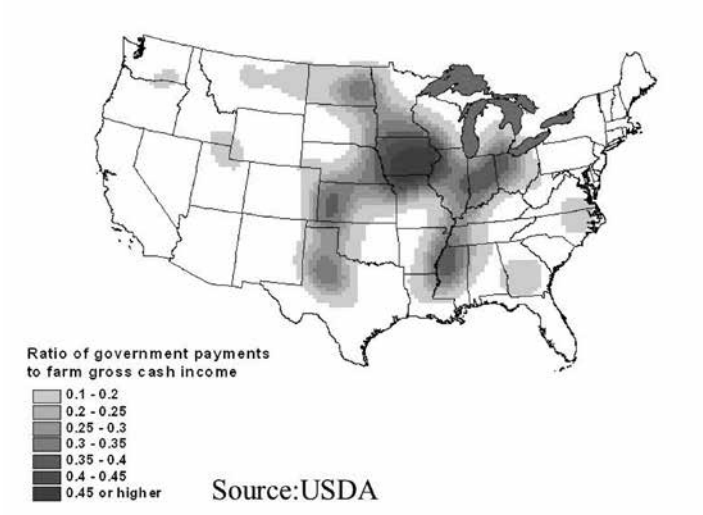


Figure 26–1: Ratio of US government payments to farm gross income, 2007. Iowa receives the lion's share of government subsidies, produces corn but receives little revenue for it, and Iowans have more than double the representation in the U.S. Senate based on state population.

Glossary

ACE2: angiotensin-converting enzyme-2, a receptor on cells that regulates water balance and which the coronavirus uses to inject its RNA into a cell to infect it.

ACLM: American College of Lifestyle Medicine, a physician-based vegan advocacy group.

ADA: American Dental Association or American Diabetes Association (also, formerly the American Dietetic Association, now called the Academy of Nutrition and Dietetics, or AND).

Addiction: a strong and harmful need to regularly have something (such as a drug) or engage in a specific behavior (such as gambling), due to an overwhelming biochemical drive, and which cannot be controlled by behavioral restraint.

AGE: advanced glycation end product, the result of the Maillard reaction either in the food or in the body.

ALEC: American Legislative Exchange Council, a nonprofit that crafts legislation and lobbies governmental entities on behalf of industry clients.

ALT: alanine aminotransferase, a blood test that tells about liver function and is sensitive but not specific for the amount of fat in the liver.

AMP-kinase: adenosine monophosphate-kinase, an enzyme that routes energy to mitochondria for burning.

Amygdala: part of the stress-fear-memory pathway. This walnut-sized area of the brain generates the feelings of fear and stress, which tells the hypothalamus to tell the adrenal glands to make extra cortisol.

Anandamide: a naturally occurring neurotransmitter that binds to the CB_1 endocannabinoid receptor and reduces levels of anxiety.
AND: Academy of Nutrition and Dietetics (formerly the American Dietetic Association).
Apoptosis: Programmed cell death, in which proteins in the cell are activated to cause self-destruction.
ARDS: acute respiratory disease syndrome, a lung disease due to an overwhelming inflammatory cytokine response.
ATP: adenosine triphosphate, the chemical in which energy is stored inside the cell.
Autonomic nervous system: the part of the nervous system that controls unconscious functions of the body. It consists of two parts: the sympathetic system controls heart rate, blood pressure, and temperature; while the parasympathetic system (the vagus nerve) controls eating, digestion, and absorption, slows the heart rate, and lowers blood pressure. The two together control energy balance.
Autophagy: the process of clearing away and resorbing old and dysfunctional cellular debris to keep cells functioning optimally—in the brain, this occurs during sleep.
BCAA: branched-chain amino acid, either leucine, isoleucine, or valine, necessary for muscle growth, but can be metabolized in the liver into energy.
BMI: body mass index, an index of excess adiposity, computed from the weight and height.
BP: Blood pressure.
BPA: bisphenol A, a chemical found in food and household goods that acts like an estrogen.
CAFO: concentrated animal feeding operation (animals confined specifically for food production).
CDR: Commission on Dietetic Registration, the entity that certifies and protects clinical dietitians.
CGM: continuous glucose monitor.
Cortisol: the stress hormone released from the adrenal glands, which

acutely mobilizes sugar for use, but which chronically lays down visceral fat.

COVID-19: coronavirus disease 2019, the disease caused by the virus SARS-CoV-2.

CVD: cardiovascular disease.

Cytokine: a protein made by one cell that travels elsewhere and leads to inflammation.

Depression: a mental condition characterized by feelings of severe despondency and dejection, inadequacy, and guilt, often accompanied by lack of energy and disturbance of appetite and sleep often needing medical treatment.

Developmental programming: alterations in brain or body functioning due to alterations in the environment that occur in the fetus prior to birth.

DGAC: Dietary Guidelines Advisory Committee, convened every five years to advise the USDA on population dietary recommendations.

DNA: deoxyribonucleic acid, the molecule inside the cell that carries genetic information.

DNL: *de novo* lipogenesis, or the process of turning carbohydrate into fatty acids, occurring in the liver.

DO: doctor of osteopathy, a medical degree conferred by schools of osteopathy.

Dopamine: a neurotransmitter that when released acutely can cause feelings of reward, but when released chronically reduces the number of its receptors, leading to tolerance.

Dopamine receptor: the protein that binds dopamine to generate the reward signal, and when reduced in number leads to tolerance.

EC: endocannabinoid, a kind of neurotransmitter (e.g., anandamide) that binds to brain receptors and acts like marijuana, driving reward and reducing anxiety.

EDC: endocrine-disrupting chemical, a chemical that binds and either activates or inhibits a cellular hormone receptor.

EFSA: European Food Safety Authority.

Endogenous opioid peptide (EOP): a neurotransmitter made in the brain

that binds to its receptor to signal the consummation of reward or euphoria.

Endogenous opioid peptide (EOP) receptor: part of the reward pathway. A protein that binds either opiates (e.g., heroin) or endogenous opioid peptides (e.g., beta-endorphin) to signal the consummation of reward or euphoria.

Epigenetics: modifications in DNA without changes in the DNA genetic sequence, usually occurring prior to birth.

ER stress: endoplasmic reticulum stress, a cell metabolic defect leading to abnormal production and misfolding of proteins.

Estrogen: female sex hormone, made either in the ovary or in fat tissue.

EWG: Environmental Working Group.

FDA: US Food and Drug Administration.

Fructose: a monosaccharide, half of dietary sugar or high-fructose corn syrup, the molecule that makes sugar taste sweet, causes the reward system to activate, and is the addictive component.

FTC: US Federal Trade Commission.

Galactose: a monosaccharide, half of lactose or milk sugar, a molecule that contributes to brain structural components.

GGT: gamma-glutamyl transpeptidase, a liver function test that signifies liver damage.

GHGs: greenhouse gases, specifically methane, nitrous oxide, and carbon dioxide.

Ghrelin: a hormone made by the stomach that conveys a signal of hunger to the hypothalamus.

Glucose: a monosaccharide, half of dietary sugar or high-fructose corn syrup; also the molecule found in starch, the molecule that every cell on the planet burns to liberate energy.

Glycogen: starch stored in cells; a string of glucose molecules that are easily cleaved to liberate glucose.

HbA_{1c}: hemoglobin A_{1c}, a blood test of glucose control in diabetes management.

Hcy: homocysteine, a metabolic by-product of the Krebs cycle, whose excess is associated with heart disease.

HFCS: high-fructose corn syrup, isolated from corn, which has undergone enzymatic reaction with glucose oxidase, converting some of the glucose into fructose, so that the product contains varying amounts of fructose and glucose.
Hippocampus: part of the stress-fear-memory pathway. The part of the brain where memories are housed, and which exerts influences on the amygdala and prefrontal cortex.
HOMA-IR: homeostatic model of insulin resistance, an index computed based on the fasting glucose and insulin level.
Hypothalamus: the area at the base of the brain that controls hormones of the body, particularly cortisol.
IEA: UK Institute of Economic Affairs, a political action group.
ILSI: International Life Sciences Institute, a nonprofit representing the food and drug industries.
Insulin: a hormone made in the pancreas that tells fat cells to store energy, and interferes with the leptin signal to increase food intake.
Insulin resistance: the state in which insulin signaling is reduced, requiring the beta-cells of the pancreas to make more insulin, which drives both obesity and chronic disease.
Insulin secretion: the process of insulin release in response to both rising blood glucose and the firing of the vagus nerve.
IRKO: insulin receptor knockout, an animal model of insulin resistance in different tissues.
Ketogenic diet: a diet in which little to no carbohydrate is consumed, so the body will generate ketones as an energy source instead of using glucose.
LCHF: low-carbohydrate, high-fat diet, also known as the low-carb diet.
LDL-C: low-density lipoprotein cholesterol concentration.
LDL-P: low-density lipoprotein particle number.
LDL: low-density lipoprotein, a blood lipid that contributes to heart disease.
Leptin: a hormone released from fat cells that travels in the bloodstream to the hypothalamus to report on peripheral energy stores.
Leptin resistance: the state where the leptin signal is dampened, leading to the hypothalamus interpreting starvation.

Maillard reaction: the naturally occurring binding of a simple sugar (glucose or fructose) to a protein, making the protein less flexible and generating oxygen radicals in the process.
Metabolic syndrome: a cluster of chronic metabolic diseases characterized by energy overload of the mitochondria.
Micronutrient: vitamin or mineral found in Real Food, usually isolated with the fiber fraction.
Mitochondria: subcellular organelles specialized to burn either fat or carbohydrate for energy.
mTOR: mammalian target of rapamycin, an enzyme that controls cell survival vs. cell death.
NAFLD: nonalcoholic fatty liver disease.
NCD: noncommunicable disease.
Necrosis: cell death due to exposure to a toxin or lack of blood or oxygen.
Neurotransmitter: a chemical in the brain made in one nerve cell, which when released causes other nerve cells to fire or stop firing.
NNT: number needed to treat, a measure of the population efficacy of a given treatment.
NSLP: National School Lunch Program, an entitlement program sponsored by the USDA.
Nucleus accumbens (NAc): the area of the brain that receives the dopamine signal and interprets the feeling as reward.
Obesity: excess body fat deposition.
Obesogen: a chemical that increases the amount of fat stored, to a greater extent than the calories released when it is burned.
OECD: Organisation for Economic Co-operation and Development, the thirty-seven richest countries.
OGTT: oral glucose tolerance test, a test to screen for diabetes and hyperinsulinemia.
Omega-3 fatty acids: a fatty acid found in wild fish and flax that is an important component of neuronal membranes, and which reduces inflammation.

OSA: obstructive sleep apnea, a lack of oxygenation during sleep due to obstruction of the airway either due to obesity or tongue placement within the pharynx, often leading to metabolic dysfunction.
PAH: polycyclic aromatic hydrocarbon, a cancer-causing chemical that is a product of burning coal, petroleum, tobacco, wood, or meat.
PBDE: polybrominated diphenyl ether, a chemical added to mattresses and pajamas as a flame retardant, and which causes insulin resistance.
PCRM: Physicians Committee for Responsible Medicine, an anti-meat advocacy group.
Peptide $YY_{(3-36)}$: a hormone made by the small intestine in response to food that signals satiety to the hypothalamus.
Peroxisome: an area of the cell that contains antioxidants to detoxify reactive oxygen species.
Phenylalanine: a dietary amino acid that can be converted into dopamine.
PI3-kinase: phosphatidylinositol-3-kinase, an enzyme that increases glucose transport into the cell.
Prefrontal cortex (PFC): part of the stress-fear-memory pathway. The part of the brain, located in the front (above the eyes), that inhibits impulsive and socially unacceptable and potentially dangerous behaviors and actions.
Pyruvate: a metabolic breakdown product of glucose, which can be further broken down by mitochondria to carbon dioxide and water, generating ATP.
Reactive oxygen species: chemicals generated from cellular metabolism that can cause protein or lipid damage and can lead to cell dysfunction or death if not detoxified by antioxidants.
RNA: ribonucleic acid, the molecule that codes for specific protein synthesis inside the cell.
ROS: reactive oxygen species or oxygen radical, a metabolic by-product of cell metabolism or inflammation, which can inflict damage if it is not quenched by an antioxidant.
SARS: severe acute respiratory syndrome, caused by a coronavirus, first noted in 2002.

Satiety: the feeling of fullness that stops further eating.
SDA: Seventh-day Adventists, a Christian sect advocating vegetarianism or veganism.
Serotonin: part of the contentment pathway. A neurotransmitter made from the amino acid tryptophan, which, when it binds to its 1a receptor on neurons, transmits feelings of contentment; and when it binds to its 2a receptor, evokes the mystical or psychedelic experience.
Stress: an uncomfortable state of mental or emotional strain or tension resulting from adverse or demanding circumstances. Accompanied by neural output from the amygdala, which tells the hypothalamus to signal the adrenal glands to make the hormone cortisol.
Subcutaneous fat: the fat outside of the abdomen, which is a storehouse of extra energy, but which does not signify an increased risk for metabolic syndrome.
Sympathetic nervous system: the part of the autonomic nervous system that raises heart rate, increases blood pressure, and burns energy.
TEF: thermic effect of food, the energy released from the process of digestion and metabolism.
Telomere: the ends of chromosomes, which confer stability and shorten as the cell ages.
TG: triglyceride, a blood lipid that contributes to heart disease.
THI: True Health Initiative, an anti-meat advocacy group.
TOFI: thin on the outside, fat on the inside, referring to increased visceral fat.
Tolerance: the state where the signal for reward is dampened and can only be generated by consuming more substrate (in the case of obesity, palatable food) or engaging in more behaviors (e.g., gambling).
Transcription factor: a protein in cells that turns on genes to make the cell change its function.
Tryptophan: the rarest dietary amino acid in the diet, which is converted into serotonin.
Type 1 diabetes: a disease of high blood sugar due to inadequate insulin production by the beta-cells of the pancreas.

Type 2 diabetes: a disease of high blood sugar due to defective insulin action on tissues.
Tyrosine: a dietary amino acid that is converted into dopamine.
Uric acid: a breakdown product of nucleic acids, which causes gout and is a contributor to high blood pressure, and is sensitive to sugar and meat consumption.
USDA: US Department of Agriculture.
Vagus nerve: the part of the autonomic nervous system that promotes food digestion, absorption, and energy storage, and slows heart rate.
Ventral tegmental area (VTA): part of the reward pathway; the area of the brain that sends the dopamine reward signal of signifying reward to the nucleus accumbens.
Ventromedial hypothalamus (VMH): the area of the hypothalamus that receives hormonal information from the body to regulate energy balance.
Visceral fat: the fat around the organs in the abdomen, which is a risk factor for diabetes, heart disease, and stroke, and a marker for metabolic syndrome.