

METABOLICAL, by Dr. Robert H. Lustig, MD, MSL
A Book Report by David G. Schwartz, MD, Part I
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This book puts it all together, better than any other I reviewed so far, regarding nutrition, metabolism, and chronic diseases' causes and their reversal. Dr. Lustig outlines 8 major sub-cellular pathologies that encapsulate the underlying processes that result in chronic disease, all related to processed food. It comes up with the same recurring advice we have been hearing from multiple sources: Eat real food. This clinches the evidence in a way it cannot be missed.

Many other books on which I have reported present partial aspects of the whole picture regarding nutrition: Food Rules, Farmacology, Fiber Fueled, Dr. Lustig's book, Fat Chance, the movie documentary Fed Up, Clean, Green, and Lean, the textbook, Clinical Environmental Medicine, The Disease Delusion, and the naturopaths' panel discussion on obesity. They all present aspects of how our food is our medicine.

Dr. Lustig has practiced pediatric endocrinology for several decades and is now Emeritus Professor of Pediatrics and Endocrinology at UCSF. He has done a most thorough examination of multiple aspects of food, food politics, and chronic disease. The title brings to mind "diabolical," with which one could describe the "food" industry in its major aspects, after reading his scathing denunciation of the industry's practices. Although "Eat real food" sounds simple, covering this topic may take 2 articles, as his discussion unveils in great detail the complexities of how chronic disease comes down to one thing: *processed* food. Furthermore, he describes the complexities of food politics and economics, and asserts that it's not what's *in* the food, but what's *been done to* the food that causes problems. I would add that what's *in* the food is majorly important also, that food pollution plays a large role in causing illness. Nonetheless, environmental toxicants often go hand in hand with processed food.

He warns that the health care system is collapsing because of the enormous burden of chronic disease. In 1980, 30% of the adult US population had at least one chronic condition. Now it's 60%. He doesn't let the doctors off the hook. It is a moral hazard to have the doctors and the insurance industry making money off people's suffering, with no financial incentive for people to be well. He goes on to say it is an *immoral* hazard for doctors to treat people's symptoms, knowing full well that what they do will mostly not cure the maladies but keep them alive longer to make a bigger market for medical treatments. We are also starting to see a decrease in *lifespan* in the last few years, but more important is the decrease in *health-span*, people getting sicker at younger ages. Medical treatment puts off *death*, but it is not very good at putting off *disease progression*. Modern medicine has achieved better screening, diagnostics, and treatments, but *preventing and reversing* disease is not what it does. Treating is after the fact. It is like going after a wasp-infested attic with a fly swatter. By the time you've killed one, the others have stung you into submission. Most of the dramatic historical increase in life expectancy has been through sanitation and refrigeration, not through modern medicine. Health professionals need to get on board with nutrition. The solution to this medical and economic Armageddon is safe, simple, cheap, and green. Its called Real Food. (I would argue with the cheap part if we want clean food.)

Cancer, autoimmune disease, dementia, and psychiatric illness are all driven by processed food. As one example, cancer *initiation* may be caused by mutations from environmental toxicants, but the immune system usually takes care of those mutations. The next phase in cancer development is *promotion*, largely driven by processed food. This same effect applies to all these chronic diseases.

Obesity is a “red herring.” It is thought of usually as eating too much for the calories expended. This is a much oversimplified concept. Processed food, especially sugar, causes insulin resistance. When insulin is working properly, the hunger hormone, ghrelin, and the satiety hormone, leptin, are in balance. With insulin resistance, the body has to make more insulin to keep the blood glucose in control. Too high insulin leads to leptin resistance, and the ghrelin takes over. This is one aspect of a complex issue leading to obesity.

Obesity is a symptom. Eighty per cent of obese people were metabolically sick before they became obese. The other 20% are metabolically healthy. Subcutaneous fat is usually not a cause for problems, up to a certain point. It is the intra-abdominal fat that causes insulin resistance. Forty per cent of normal weight people have insulin resistance, sometimes termed “TOFI,” thin on the outside, fat on the inside. Much of the fat is in the muscle and the liver, where they should not be. When people reduce their insulin resistance first, they protect the liver, the diabetes comes down, and the weight comes off. Just calorie restriction and exercise to lose weight will reduce diabetes a little. It takes 25 people on such a regimen for one person to get benefit, because they are not dealing with the metabolic problem first. I repeat, *feed the gut, protect the liver*. Stop the processed food and sugar, and eat fiber. Soluble fiber feeds the gut bacteria. Insoluble fiber provides a protective network in the gut lining to protect against things leaking out of the gut to the liver.

Lipids and cholesterol, given so much attention and much profitability for pharmaceutical companies, play a more minor role than *metabolic syndrome*, which is the complex derangement of metabolism related to insulin resistance, glucose intolerance, diabetes, fatty liver, and truncal obesity. It is the small oxidized LDL cholesterol particles that are most toxic to the arteries. The large LDL particles are more neutral, and they comprise 80% of the LDL. Statins and low fat diets mostly lower the large LDL, and have very little effect on the small LDL. The small LDL is correlated with high triglycerides, high glucose, low HDL, insulin resistance, metabolic syndrome, etc. Little attention is paid to triglycerides, but they are a much better predictor of heart disease than LDL. Of people who have had a heart attack, 60% had metabolic syndrome. Statin drugs help people who have already had a heart attack, probably by decreasing inflammation, rather than the effect on lipids. For healthy people at low risk for cardiovascular disease, statins increase life expectancy on average by about 4 days. Fewer people now are dying from heart attacks, due to better emergency treatment, but more are living with heart disease, many with low levels of LDL cholesterol.

High blood pressure (HBP) also is a symptom of vascular disease, and if it is high enough, it is also a cause of vascular disease. Mild HBP treated with drugs brings the BP down but doesn't reduce the risk of cardiovascular disease significantly. Treatment with natural means does. (My comment). Drug treatment for severe HBP has a more significant effect. Is salt the culprit? Well, in people with insulin resistance, the high insulin causes the kidneys to retain salt. So people with metabolic syndrome need to restrict salt. But the real culprit is dietary sugar, that causes insulin resistance. Restricting sugar lowers BP better than restricting salt intake. Dietary indiscretions cause dysregulation of insulin. Insulin has a good effect of keeping the blood sugar down, but it has many other effects on other organs and tissues that is not so beneficial. Good diet can reduce the need for insulin, so that the glucose is regulated with less insulin. Too much insulin causes the muscular walls in the arteries to thicken, leading to HBP and vascular disease. So hypertension, like cholesterol, often comes back to the same metabolic imbalances we have been talking about. And with type II diabetes, it is mostly the insulin rather than the glucose that causes the most damage. When glucose starts going up, treat the insulin resistance, and the sugar comes down.

How did we get here? Doctors need to relearn nutrition. In fact they (we) never were taught much in medical school about real nutrition, and medical schools still don't teach much about it. The wrong concepts we did pick up need to be unlearned. The author himself had to relearn nutrition. Then after 26 years as an endocrinologist, 14 of those years studying insulin and its role in chronic disease, he was kicked out of the UCSF Pediatrics Diabetes Clinic mostly at the urging of the clinic dietitian, who told parents that kids could eat all the carbohydrates they wanted, just up the insulin dose, which caused them to gain weight. In 2015 the head of the Joslin Diabetes Center was still saying that "a calorie is a calorie," and "insulin is good." Even the non-profit diabetes associations get large donations from Big Pharma, Big Food, Big Sugar, and Big Soft Drinks, so that they that would stand to lose a lot of income if they told the truth about processed food, and these sponsors would lose a lot of profits if people got well by eating healthfully. So the diabetes associations in various countries stick to the old dogmas. The doctors are subordinated by their academic societies and universities that get funded by Big Pharma. If you don't stay with the orthodoxy, you can be booted off the hospital medical board and get lousy evaluation on Healthgrades. Talking to patients about lifestyle changes takes time, and doctors don't listen to their patients adequately when the insurance companies limit their time with each patient. Then the patients won't follow lifestyle advice if they don't understand why, with inadequate discussion with their health professionals, and also if they are addicted to sugar.

The author launches into the "diabolical" part of the problem. "The Dietitians Lost Their Mind." is one of the chapter heads. The AND (Academy of Nutrition and Dietetics) gets 90% of its operating budget from "Big Food." One of the founders of AND was trained by John Harvey Kellogg, proponent of high carbohydrate diets, especially Kellogg corn flakes. In order to be registered with the CDR (Commission on Dietetic Registration), dietitians have to conform to the policies of the AND. Dallas dietitian Neva Cochran, RD, representing the processed food industry, tried to discredit Dr. Lustig in public for saying that "A calorie is not a calorie," and that it depends on what has been done to the source of the calories. At a meeting of the AND, Dr. Lustig debated Connie Diekman, AND's spokesperson, who upheld the Sugar Association's stand on Energy Balance. Foods provided to schools and hospitals are highly processed, conforming to AND standards, and the School Nutrition Association is a big proponent of processed food, sponsored by the food industry.

The author says the dentists have lost their way. They used to promote sugar restriction to reduce decay. Before the increase in dietary sugar, the mouth had a much more diverse microbiome, but since the increase in sugar intake, it is much less diverse, with one predominant one, streptococcus mutans, which can turn sugar into substances that decay teeth. Then the dentists got on the fluoride bandwagon, but the result of fluoridation on cavities was less than phenomenal. The American Dental Association still doesn't emphasize sugar restriction, but pays more attention to treatment, which is big business. In contrast, the World Dental Federation's number one strategy to fight cavities is sugar restriction. There aren't enough dentists to fill all the cavities in the world, so the goal is to prevent them. Follow the money.

Doctors are educated by Big Pharma, so they know treatment with drugs, and so Big Pharma is glad to provide the treatments. The 8 metabolic conditions described in this book have no drug to target them, so doctors don't talk about them. "If there's no treatment, there's no problem."

Big Pharma contributes to 2/3 of the FDA's budget and has 1,378 lobbyists on Capitol Hill. For every \$1 spent on basic research, \$19 is spent on promotion and advertising. Now 70% of the US population take at least one prescription medication. About 88% are metabolically sick, but the metabolic disorder is not "druggable". It is "foodable." Much of the research on drugs is sponsored by

pharmaceutical companies, with interpretation of the results more favorable toward the drug than the analysis of research on the same drug by an independent entity.

Dr. Lustig says that metabolic dysfunction is a “disease without a name.” This reminds me of Jeffrey Bland’s book, The Disease Delusion, a report on which is in the archives. Dr. Bland points out that by focusing on taxonomy, naming *diseases*, we look at and treat the symptoms that result from many imbalances in the body, when we should be paying more attention to correcting those imbalances in many body systems. These are the real conditions that are occurring, and the disease concept is a fictitious entity. We are really dealing with a complex system out of balance. The resulting symptom complex has a name, and can be treated with a drug, but it does not correct the underlying problem.

The author goes into a discussion of the 8 basic imbalances, called “cell biology 101.” He says that if this part is too technical or “wonky,” the reader can skip it. I think it is important to understand the basis for the premise that sugar and processed food are at the basis of this problem. I will try to summarize, hopefully without getting bogged down in the technical details. The 8 areas of dysfunction are: Glycation, Oxidative Stress, Mitochondrial Dysfunction, Insulin Resistance, Membrane Integrity, Inflammation, Epigenetics, and Autophagy.

The glycation, sometimes called the *browning* or *caramelization* effect, or the *Maillard* reaction, is when sugar gets latched onto proteins in a way that results baked goods turning brown, and in faster aging in the body or general deterioration of many systems. The more sugars we have around, the more glycation occurs. People with diabetes have a lot of it, but dietary sugar drives it. Fructose drives it faster than glucose, (250x faster), and glucose does it faster than starches. The hemoglobin A₁C is a measure of how much the proteins are being damaged by sugars. The main problem with glycation is that it creates oxidative stress.

Oxidative stress is the production of oxygen radicals as the result of glycation, inflammation, iron metabolism (rusting), and as a waste product of normal mitochondrial function. We need oxygen to live, and some oxidative stress is an inevitable part of that. Our cells have organelles inside them that make antioxidants to quench the oxygen radicals. We need highly colored real food to give us more antioxidants for when the endogenous antioxidants need help. When normal mitochondrial function gets overwhelmed, it becomes dysfunctional.

If more glucose comes into the mitochondria faster than they can process it, the burning of pyruvate from the breakdown of glucose shuts down, and it goes into fat. At that point the energy production breaks down. Sick mitochondria are involved in most chronic diseases. The brain, endocrine organs, and muscle have a lot of mitochondria because they require a lot of energy. So, for example, neurological conditions have a lot of sick mitochondria. When the diversion of the pyruvate to fat occurs in the liver, we get fatty liver, which leads to insulin resistance.

When organs and tissues become resistant to insulin, that is, not being able to utilize insulin to bring glucose in, the insulin has to rise in order to force the process, then the high insulin levels make inflammation and all sorts of dysfunction and disease, especially cardiovascular disease. Things that make more insulin resistance besides too much sugar and unprocessed food are environmental toxicants, obesity, and chronic stress.

When oxidative stress, toxins, and the wrong kinds of fats damage cell membranes, the cells break down and die, and then inflammation results from the clean up of the mess. Saturated fatty acids come from saturated fats, and because they are so fluid, they layer and clump up in the cell membranes.

Unsaturated fatty acids are better for the structure of the cell membrane, but toxins and oxidative stress can easily oxidize the polyunsaturated fatty acids to make oxygen radicals and lipid peroxides. Monounsaturated fats are less vulnerable (i.e. olive oil, etc.) So cell membrane integrity is vital to staying healthy.

Oxidative stress, toxins, hyperinsulinemia, cell membrane disruption, too much body fat, (especially visceral or abdominal fat), infections, *molecular mimicry*, (when body tissues are mistaken for infection causing microbes), and dysbiosis in the gut, all lead to inflammation. Due to lack of fiber, bad bacteria predominate and reduce diversity, resulting in leaky gut, that allows toxins and bacteria to enter the bloodstream. See my article on Fiber Fueled. All those factors lead to inflammation, characteristic of all chronic diseases. We see how these 8 sub-cellular pathologies are not so separate, all connected with each other in a web. If we mess up one of these areas, they all are affected.

The next major area is epigenetics, how the foods we eat and other lifestyle factors affect our genes, turning them on or off, having effects on the genes even to the next generation(s). See my article on Dirty Genes. An example could be that some people have inherited a deficiency in folate and folic acid metabolism, resulting in high homocysteine, leading to higher risk for cardiovascular disease. Supplementing with folate, B₁₂, betaine, B₂, and B₆ can lower the homocysteine by changing the metabolism. Another example is environmental toxicants that change how our hormones are metabolized, such as BPA and phthalates from canned and plastic wrapped foods affecting our endocrine organs.

The last of the 8 areas is autophagy, cleaning up of debris and clutter. Cells need to replace worn out organelles such as mitochondria. Sleep is an important time when the *glymphatic* system in the brain removes damaged cellular components, moving them to the blood for disposal. Vitamin D, vitamin B₁, intermittent fasting (increasing ketones, decreasing insulin) all promote autophagy.

The author discusses 2 major metabolic programs the cells have, one for growth, the other for burning energy, glycolysis for growth and the Krebs cycle for burning. Three enzymes regulate these 2 programs: PI3-kinase, AMP-kinase, and mTOR. PI3-kinase brings glucose into the cell, (with the help of insulin), so the more sugar and insulin we have, the more glucose gets into the cell. AMP-kinase looks at the fuel gauge to decide whether to burn the glucose for energy, or if it is too loaded with fuel (glucose), it will use it to grow more structures and fat. Then mTOR decides if a cell will grow, just hang out, or die (autophagy). There are 8 possible combinations of these 3 enzymes, and that determines whether the cells will burn energy, grow, or create disease. The point I think that the author is making, is that the more sugar and processed food in the diet, the more difficult for these enzymes to create a healthy balance between these processes, although I did not study thoroughly the complexities of these combinations. Specifically he mentions that sugar and processed food increase PI3-kinase, decrease AMP-kinase, and increase mTOR, all of these effects that drive cancer. That in itself should be a sufficient reason to raise a red flag.

How is a person to assess how one is doing with all this? Some measurements and tests are: Blood pressure, waist circumference, and blood tests, such as lipids, homocysteine, ALT and AST (liver enzymes), uric acid, hemoglobin A_{1C}, and fasting glucose and insulin. To best assess metabolic syndrome, triglycerides, HDL, small dense LDL, glucose, insulin, and HbA_{1C} are good blood tests. Among the liver tests, high ALT gives an indication of fatty liver, AST could indicate toxic effects. The liver produces uric acid when it processes sugar. Uric acid above 5.5 indicates mitochondrial dysfunction and insulin resistance, and leads to liver fat, gout, and HBP. A fasting glucose below 90 and fasting insulin below 15 is preferable. Also the HOMA-IR or *Homeostatic Model Assessment of*

Insulin Resistance takes fasting insulin x fasting glucose/405 to give a quotient of which 4.3 is average, 2.8 is excellent, and anything above average is trouble. A triglyceride/HDL ratio over 2.5 correlates with metabolic syndrome. If LDL is extremely high, a genetic variant is probable, and a low fat diet or maybe even a statin drug may be advisable. Body mass index, calculated by weight vs. height, is not an accurate indicator. Waist circumference is. For men, less than 40 inches, and for women less than 35 inches is desirable. A high waist circumference means high intra-abdominal or visceral fat, or liver fat, or both, and it suggests inflammation, mitochondrial dysfunction, insulin resistance, and oxidative stress, 4 of the 8 subcellular pathways mentioned before.

So most of the modern scourges, diabetes, heart disease, fatty liver, tooth decay and periodontitis, cancer, dementia, autoimmune disease, and depression, are all related to processed food. Insulin resistance has been shown to be a primary cause of depression. Exercise can repair 5 of the 8 subcellular pathologies, but won't improve glycation, oxidative stress, or membrane integrity. A bad diet can't be completely remedied by exercise.

This gives you a look at at the first half of the book. In the second half, the author looks at the foods adults and children eat and how it affects health, the many ways food is processed, food fraud, food politics, and how we could un-process our food supply. More on that next month.