The Low-Fat Lie

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Rise of Obesity, Diabetes and Inflammation

Glen D. Lawrence

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List of Abbreviations

2AG	2-arachidonylglycerol
5-HETE	5-hydroxyeicosatetraenoic acid
5-HEPE	5-hydroxyeicosapentaenoic acid
AA	arachidonic acid
ACE	angiotensin converting enzyme
ACTH	adrenocorticotropic hormone
ADA	American Diabetes Association
ADHD	attention deficit hyperactivity disorder
ADP	adenosine diphosphate
AGE	advanced glycation end-products
AHA	American Heart Association
AMP	adenosine monophosphate
ATGL	adipose triglyceride lipase
ATP	adenosine triphosphate
BAT	brown adipose tissue
BMI	body mass index
CB1/CB2	cannabinoid 1 receptor/cannabinoid 2 receptor
CBD	cannabidiol
CCK	cholecystokinin
CDC	United States Centers for Disease Control and Prevention
CLA	conjugated linoleic acid

cm	centimeter
COX1/COX2	cyclooxygenase 1/cyclooxygenase 2
CPPT	Coronary Primary Prevention Trial
CRH	corticotropin-releasing hormone
CRP	C-reactive protein
DHA	docosahexaenoic acid
DHEA	docosahexaenoyl ethanolamide
DGLA	dihomo-gamma-linolenic acid
dL	deciliter (0.1 liter)
DNA	deoxyribonucleic acid
EC	endocannabinoid
EPA	eicosapentaenoic acid
EPEA	eicosapentaenoyl ethanolamide
FDA	United States Food and Drug Administration
ft	foot (12 inches or 30.5 cm)
g	gram
GABA	gamma-aminobutyric acid
gal	gallon (3.79 L)
GI	gastrointestinal
GLUT2	glucose transporter 2
GLUT4	glucose transporter 4
GLUT5	glucose transporter 5
HbA1c	hemoglobin A1c (glycated hemoglobin)
HDL	high-density lipoprotein
HFCS	high-fructose corn syrup
HMW	high-molecular-weight (adiponectin)
in	inch (2.54 cm)
kcal	kilocalorie

kg	kilogram
L	liter
lb	pound (454 g)
LDL	low-density lipoprotein
LPS	lipopolysaccharide
LT	leukotriene (such as LTB_4)
LX	lipoxin (such as LXA_4)
MaR	maresin (such as MaR1)
mcg	microgram
mg	milligram
mL	milliliter
MRFIT	Multiple Risk Factor Intervention Trial
NAFLD	nonalcoholic fatty liver disease
nM	nanomolar (10^{-9} molar)
NO	nitric oxide
OEA	oleoyl ethanolamide
oz	ounce (28.3 g)
PEA	palmitoyl ethanolamide
PG	prostaglandin (such as PGE_2)
PLA_2	phospholipase A2
PTSD	post-traumatic stress disorder
PUFA	polyunsaturated fatty acid
RNA	ribonucleic acid
ROS	reactive oxygen species
Rv	resolvin (such as RvD1)
T1R2/T1R3	protein components of sweet taste receptors
T1R1/T1R3	protein components of umami taste receptors
tbsp	tablespoon (12.5 g to 17 g depending on substance)

THC	tetrahydrocannabinol
TLR4	toll-like receptor 4 (LPS receptor)
tsp	teaspoon (4.2 g to 4.8 g depending on substance)
TX	thromboxane (such as TXA_2)
USDA	United States Department of Agriculture
VLDL	very low-density lipoprotein
WAT	white adipose tissue
yr	year

Preface

I have been fascinated with the biochemical and physiological phenomena that constitute life, especially the workings of the human body, for most of my adult life. Some of my early professional work involved research into how different types of fats—specifically, fatty acids—can influence certain diseases and disorders. Much of my early research at Mt. Sinai School of Medicine and the Institute of Human Nutrition at Columbia University focused on oxidation of polyunsaturated fatty acids, which can lead to premature aging, cancer, inflammation, and neurological diseases. At both of those institutions, I attended lectures by renowned researchers who presented their studies on cholesterol and heart disease. I looked into the basis of the saturated fat–cholesterol hypothesis and the recommendation that the public reduce its saturated fat consumption by substituting polyunsaturated vegetable oils. Such dietary recommendations seemed to have, at best, modest effects on the risk of heart disease and conflicted with my own observations that polyunsaturated vegetable oils would increase the incidence of cancer, inflammation, and aging related diseases.

When I moved from those research institutions to a teaching-oriented institution, my opportunities to pursue research regarding manipulation of dietary fats and its consequences on various diseases were limited due to lack of funding for projects that carried big price tags. I continued to follow the research being done in those areas, and by the early 2000s, I decided to write a book about my perspective on dietary fats. That book, *The Fats of Life: Essential Fatty Acids in Health and Disease*, presented many of the biochemical and physiological aspects of polyunsaturated fatty acids, which are essential fatty acids. In that book, I challenged the basic tenets of the saturated fat–cholesterol hypothesis and I presented a body of evidence

showing that when men considered to be at high risk for a heart attack replaced saturated fat with vegetable oil, no significant reduction in cardiac events or death resulted. I also described how the omega-3 fatty acids found in fish oil could suppress not only several factors that increase risk of heart disease but also cancers, inflammation, and some neurological diseases when compared with omega-6 fatty acids from vegetable oils.

The Fats of Life was written for a professional audience with a moderate academic understanding of biochemistry and physiology. Several friends encouraged me to write another book for a more general audience. My research, both in the library and in the laboratory, turned to sugar, its toxic degradation products, and its adverse health effects. I was appalled that mainstream nutrition and health experts were blaming saturated fats for numerous maladies that, in my estimation, were really being caused by sugar, especially the fructose component of sugar. I decided to write a book describing the scientific evidence to implicate sugar rather than fat as the root cause of obesity and its associated diseases.

The most abundant saturated fatty acid in nature, palmitic acid, was being denounced for numerous adverse health effects, which did not make sense considering nature has a tendency to select substances that assure survival. The short-chain saturated fatty acids in milk represented another case where nature had selected substances that were advantageous for survival. I collected numerous reports regarding the health effects of saturated fatty acids from various sources and realized there was no rational reason to implicate saturated fats for any unhealthy condition. I found reports indicating how countries that consumed primarily coconut oil as their main dietary vegetable oil had some of the lowest rates of heart disease in the world, which shattered the idea that coconut oil should be avoided because it was shown in early studies to raise serum cholesterol of confined subjects.

As an educator, I opted to give scientific explanations for phenomena rather than just saying, "It is so, and you have to believe me." I also felt that giving the scientific evidence to support my arguments would make it more difficult for my detractors to refute my conclusions. As I gathered more

information on the adverse effects of fructose and read books by Gary Taubes, Richard Johnson, Robert Lustig, and others on the topic, I realized I had things to add to what those authors were saying. I must admit I have repeated some of their work in this book, but I feel I have taken a different angle by describing the common factors behind the obesity epidemic and diabetes, with inflammation being a major factor. I describe how omega-6 polyunsaturated oils, which were recommended to replace saturated fat in the diet, can actually exacerbate inflammation, as I saw firsthand in my own studies with rats. The low-fat, low-saturated fat dietary recommendations led to an increase in both sugar and omega-6 vegetable oils in the American diet, which in turn led to obesity and its associated adverse health conditions.

I received a lot of positive feedback on a paper I published in *Advances in Nutrition* in 2013 questioning the wisdom of the low-fat, low-saturated fat diet recommendations. I became interested in the gut microbiome and the fascinating research that demonstrated the influence microorganisms in the digestive tract have on not only obesity but also systemic inflammation and the numerous consequences the latter can have. Research into the microbiome then led to the role of endocannabinoids in communications between the microbes and the various organs of the body where they were exerting their influence. I decided to devote a chapter to the gut microbiota and another chapter to the endocannabinoids. The endocannabinoids had piqued my interest years earlier because they are made from polyunsaturated fatty acids.

Although this book describes a substantial number of biochemical and physiological phenomena, I feel that a reasonably well-informed reader of nutrition and health issues should be able to follow the text without too much difficulty. When the science gets a little complex, please bear with it. I give a summary at the end of each chapter that avoids most of the scientific terms and should help you understand the main points I am trying to get across. I am hoping this book will help readers understand why the low-fat, low-saturated fat doctrine did not work in terms of improving health or helping people to live longer. In fact, this recommendation contributed

to the dramatic increase in sugar in the diet, which has had dire consequences on the health of not only Americans but also populations around the world that try to emulate what the Americans do. The food-processing and beverage industries have a powerful influence over people's perceptions of what is healthy or not healthy through their massive, worldwide advertising. This book is an attempt to give the public, as well as policymakers, a better understanding of the scientific facts that call into question the mainstream dietary guidelines.

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Public Enemy Number One

Obesity, diabetes, high blood pressure, heart disease—these health problems afflicted a very small portion of the population 100 years ago. To be fair, these are problems associated with age, and life expectancy was about 50 years in the United States in 1910, compared with 78 or more years today. More importantly, these diseases have been afflicting younger and younger people at an alarming rate over the past 40 years. These chronic diseases are not confined to the American population but are spreading throughout the world, along with globalization and the processed-food industry's quest for greater markets. There is abundant scientific evidence to implicate the so-called Western diet in these startling statistics, although scientists and policy experts cannot agree on which dietary factors are responsible.

With all the technology available today, and our understanding of many physiological processes on the molecular level, one has to wonder why we cannot get a handle on these problems. How did the nutritional recommendations turn out to be so wrong? But more remarkably, why are the "experts" so hesitant to revise them? Indeed, when Nina Teicholz, author of *The Big Fat Surprise*, published a feature article in the *British Medical Journal* (*BMJ*) (Teicholz 2015) exposing flaws in the most recent *Dietary Guidelines for Americans*, she was vehemently attacked by members of the Guidelines Committee and like-minded colleagues around the world for daring to criticize the "established experts." Instead of allowing discussion of the flaws, these so-called experts chose to demand a retraction of

Teicholz's article. The *BMJ* appears to have let reason prevail and did not print the letter written by these detractors, nor did they retract the article.

We were led to believe that nutrition and health experts had it all figured out in the 1970s with regard to the types of foods we should be eating in order to live longer and healthier lives. Although a majority of people strove to adopt the dietary recommendations of the authorities—some more avidly than others—our overall health did not seem to show much improvement. Average life span did improve, but that was due more to advances in medical technology than to improved nutrition and health. People who would have died of heart attacks and cancer in the 1970s are now able to get treatments to prolong their lives, often for many years.

In terms of abiding by those dietary recommendations, the proportion of fat in the American diet has decreased from more than 40% in the 1960s and 1970s to about 33% or less today. However, if the percentage of fat in the diet decreases, the percentage of another macronutrient must increase. That something else has been carbohydrates, with sugars showing the biggest increase. Although the number of calories derived from a gram of fat is more than twice as much as those from a gram of carbohydrate, the total number of calories consumed by the average American has increased quite substantially (see Table 1.1). In other words, people are eating more, probably because of less satisfaction with what they are eating.

The data for Table 1.1 was selected for the years in which nutrient intakes changed the most: from 1970 to 2000. Per capita consumption of total carbohydrates and refined sweeteners reached a maximum around the year 2000 and decreased substantially by 2010. The obesity epidemic also seemed to reach a plateau after 2000, as did the incidence of diabetes and other health issues associated with obesity. Table 1.1 is intended to emphasize the relative consumption of nutrients by Americans during the period in which obesity rates were skyrocketing and associated health problems were increasing dramatically.

The first source in Table 1.1 is a report from the USDA Economic Research Service, "Nutrients and Other Components of the U.S. Food Supply," which provides data from 1909 to 2010. It is interesting to note that the estimated total calories consumed daily by Americans from 1909

Table 1.1 Statistics on daily per capita consumption of carbohydrates, fat, and protein.[†]

Nutrient consumption	1970	2000	% Change 1970–2000	2010	% Change 2000–2010
Total carbohydrate[a]	401 g	505 g	26	474 g	–6
Refined sweeteners[b]	148 g	185 g	25	164 g	–11
Sugar (sucrose)[b]	127 g	82 g	–35	82 g	0
High-fructose corn syrup[b]	0.6 g	78 g	([e])	60 g	–23
Total protein[a]	98 g	124 g	26	120 g	–3
Total fat[a]	147 g	191 g 165 g[d]	30 6	190 g	–<1 +15
Total calories[a] (kcal)	3,300[c]	4,200[c]	27	4,000	–5

[†]*Sources*: [a]USDA, Economic Research Service, Nutrients and Other Components of the U.S. Food Supply, calculated by USDA/Center for Nutrition Policy and Promotion, updated May 13, 2014.
[b]USDA, Economic Research Service, Sugar and Sweeteners Outlook, Table 50: U.S. per capita caloric sweeteners estimated deliveries for domestic food and beverage use, by calendar year, updated July 25, 2017.
[c]Total calories (kcal) are based on food available for consumption and not the actual amount consumed; much of the food available is often discarded as waste.
[d]Note: Total fat data for 1997 in Statistical Abstract of the United States, 120th Ed., U.S. Census Bureau, Washington, DC (2000), Table No. 235 based on ERS estimates. ERS data for 1990 to 1999 varied from 164 to 173, then jumped to 191 and greater after 2000, indicating there may be some change in how the data was calculated from 2000 onward. Total carbohydrate rose steadily from 468 to 506 between 1990 and 1999, while protein varied from 118 to 124 during that time; these figures are in reasonably good agreement with data published in the Statistical Abstracts for respective years.
[e]High-fructose corn syrup was introduced in 1970, so the percentage of change is meaningless.

to 1975 did not change much, varying from about 3,100 to 3,400 for every year during that period. However, the total calories steadily increased after 1975, reaching a maximum of 4,200 during the years 2000 to 2004. The per capita consumption data is for the total amount purchased and does not consider uneaten food discarded as waste, which may have increased as well during those time frames.

Human nature has not changed much over the ages. Those who speak loudest seem to get the most attention, and the message that gets repeated most often tends to be believed. Or as Lewis Carroll's Bellman claims in *The Hunting of the Snark*, "What I say three times is true." Perhaps the most effective publicity campaign in the history of nutrition claimed that saturated fats and cholesterol were killing us and were to be eliminated from

our diets. Today, growing numbers of scientists and medical experts are questioning or refuting the saturated fat–cholesterol hypothesis, yet many people still cling to this flawed idea. Persuasive arguments a half-century ago were the basis for the saturated fat–cholesterol hypothesis, before our understanding of human physiology had advanced to its current status.

I must admit that I accepted much of the rationale behind this hypothesis for heart disease in my early scientific career, when I was just beginning to look at relationships between dietary fats and various diseases. Much of the scientific literature I read showed that feeding humans a high-saturated fat diet did increase their serum cholesterol,[1] with the increases quite large in some individuals yet not much at all in others (Hegsted et al. 1965). I also considered the data from the Framingham Heart Study, which indicated that men with the highest levels of cholesterol (greater than 244 mg/dL) were at greater risk of developing heart disease than men in the lowest cholesterol group; the data for women was not as convincing (Kannel et al. 1961). However, the Seven Countries Study by Ancel Keys and his coworkers showed that heart disease risk tended to increase at relatively high levels of total serum cholesterol (greater than about 275 mg/dL), with little correlation between cholesterol and heart disease at lower levels within cohorts (Keys 1980). In other words, increases in total cholesterol from 180 mg/dL to 240 mg/dL had little or no impact on longevity or even heart disease. In these early studies, serum cholesterol was not yet being separated into different lipoprotein fractions, such as very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL).

I could see that although eating a diet containing mostly saturated fat raised a person's serum cholesterol, such a diet did not condemn them to a heart attack or premature death. In fact, my research seemed to show that

[1] The term *serum cholesterol* refers to the amount of cholesterol in the blood after the blood is allowed to clot. Clotting removes all the clotting proteins as well as most of the cells and platelets that may interfere with some measurements of blood constituents. *Total cholesterol* is the same as *serum cholesterol* and *cholesterol,* which will all be used in this book to refer to serum total cholesterol. Total cholesterol consists of the cholesterol found in several lipoprotein fractions that circulate in the blood, including VLDL, LDL, and HDL.

substituting polyunsaturated oils for saturated fats in the diet should cause people to age faster and increase their risk of dying prematurely from cancer or other ailments—even from coronary thrombosis, or blood clots in the heart. I was studying how polyunsaturated fatty acids (PUFA) undergo free-radical reactions, known as *lipid peroxidation*, which promote cancer, aging, and a wide range of detrimental effects. Peroxidation of PUFA was also found to be the underlying cause of atherosclerosis, yet the cholesterol–heart disease advocates were claiming PUFA to be "healthy" fats. Something was amiss!

It will be instructive to review some history of the development of the saturated fat–cholesterol hypothesis in order to see how it became so firmly entrenched in our modern nutritional lore, even though there was little or no proof to support such a hypothesis. This is not to say there was no proof of the connection between high serum cholesterol and heart disease, but that is quite different from a connection between dietary saturated fat and heart disease, as we will see. Nevertheless, the role of cholesterol in heart disease became extremely overstated, and once drugs were developed to lower cholesterol, the pharmacomedical establishment never looked back. Indeed, the vast global market for statins became the driving force behind perpetuating the cholesterol doctrine, and the saturated fat–cholesterol hypothesis simply remained a fixture in the policy.

My research interests were focused not on heart disease, but rather on several other life-threatening and disabling diseases, such as cancer, arthritis, neurological diseases, and aging in general. In nearly all cases, we found that polyunsaturated oils, particularly vegetable oils, could exacerbate these diseases and were often implicated as an underlying cause of the given disease. I remember hearing cholesterol–heart disease researchers begin their presentations with the claim that one in every two Americans was dying of heart disease—the leading killer in America. These researchers went on to describe some of their findings in the early 1980s. The differences they were seeing in cholesterol and heart disease with changes in diet were minuscule relative to the effects being reported for polyunsaturated oils promoting certain cancers. Later, I observed that dietary polyunsaturated oils exacerbated inflammation in a model for arthritis in lab rats (Lawrence 1990).