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BARRY SEARS, PH.D.

WITH BILL LAWREN

THE ZONE

A Dietary Road Map

Barry Sears, Ph.D.

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THE ZONE

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PREFACE

A sword of Damocles hangs over my head, something I've known since my early twenties. You see, I'm a walking genetic time bomb. I'm genetically programmed by nature to die of heart disease within the next ten years. My early death seems all but inevitable: my grandfather, father, and every one of my three uncles were killed by heart attacks before they reached the age of fifty-four.

As I write this, I'm forty-seven.

The genes that are killing the men in my family are insidious. To look at us, no one could imagine that we are—or were—anything but healthy and hearty. My father, Dale Sears, was a great athlete in the 1940s. At only six feet two inches tall, he was an All-American basketball center at the University of Southern California, as he liked to say, "the last of the six-foot centers." He was chosen to play on the U.S. Olympic basketball team in 1940, but World War II robbed him of his Olympic opportunity. (I myself played college basketball, and continued playing volleyball at the national level for some time after receiving my Ph.D.)

After the war, my dad went into the floor-covering business with one of my uncles. He gained about twenty pounds and he smoked, but he was still active and in reasonably good shape. He continued to play basketball, and took up volleyball on the side.

When he was just forty-three, he had his first heart attack. I was thirteen at the time, and all I remember is that he spent a few days in the hospital. The doctors said it was a relatively mild attack, and he recuperated at home for another six weeks. Like all teen-agers, I wasn't much inclined to worry about health problems, even my father's. And he didn't seem too concerned either.

The next ten years brought more danger signs: two of my uncles had heart attacks. Then, when he was only fifty-three, my father had a second, fatal attack. There was no warning. He died in his sleep. During the next few years, my three uncles all died of heart attacks. They were all in their early fifties.

By then I could hear a clear message. If I didn't do something, I'd become an early victim too. So I did the normal things: tried to stay in shape by maintaining a highly athletic lifestyle, kept my weight under control, and ate what I thought was a healthy diet. But with my unfortunate genetics, I suspected that even that would not be enough.

I realized that to save my own life I would have to know much more. I needed to know what made the difference between a healthy heart and a heart so genetically flawed it would only last two-thirds of a normal lifetime.

By then I had already earned a Ph.D. in biochemistry from Indiana University. I was doing postdoctoral work at the University of Virginia, looking at the molecular structure of lipids, the medical name for the class of compounds that includes, among others, cholesterol and the so-called lipoproteins: HDL, LDL, and VLDL.

Up to then, my research had been pure basic science. I wanted to see how these complex molecules were put together. But my father's death (and my own sense of impending doom) shifted my direction. Instead of just looking at the molecular architecture of cholesterol and its relatives, I decided to look at their role in heart disease. It was the early 1970s and, scientifically speaking, the study of cholesterol and its relationship to heart trouble was just getting off the ground. Still, it was already a hot and emerging medical field.

I knew a lot about lipids, but virtually nothing about heart disease. So I moved on to Boston University School of Medicine to work with Don Small, who was performing ground-breaking research on how the structure of lipids might be contributing to cardiovascular disease. I ensconced myself in the university medical library, reading anything I could find on the subject. I had no preconceptions, no base of knowledge to work from, so I read everything.

I eventually came across an obscure report. At San Francisco's Mount Zion Hospital, two researchers, Sanford Byers and Meyer Friedman, had induced atherosclerosis—the clogging and hardening of the arteries that often leads to heart attacks—in rabbits by feeding the animals a diet high in saturated fat. Then half the animals were injected with the same phospholipids I had studied for my Ph.D. dissertation. The results were astonishing. The phospholipid injections acted like a biological Roto-Rooter, completely clearing most of the animals' clogged arteries, in effect erasing all traces of heart disease.

My interest was already starting to be rewarded. But this report appeared in a very obscure journal, so I continued reading. Soon I found an equally obscure report in which Jonas Maurukas and Robert Thomas had replicated the earlier work with phospholipids—not to see if it was right, but to prove it wrong. (In fact, almost all the noted researchers seemed to think the earlier work was idiotic. How could you eliminate heart disease simply by injecting phospholipids into animals?) These investigators were going to use a better animal model and better techniques to prove how wrong this early report was. Much to their surprise, they got the same results—elimination of all traces of atherosclerotic lesions.

Similar results continued to appear in scientific literature about every three to five years. Then in 1975 researchers at Upjohn published definitive research confirming these isolated reports. In essence, heart disease could be reduced, if not eradicated, through a simple injection of the natural lipids that are the basis of every cell in the body. This was real biotechnology! Since I was one of the few scientists studying phospholipids at that time, I thought I was going to go to the head of the class—not to mention save my own life.

When the Upjohn scientists published their research, it should have been big news. It should have touched off a furious race among the giant drug companies to develop and market phospholipids as a treatment for heart disease in humans. But it didn't. The drug manufacturers had a business problem: phospholipids are natural substances, and it's impossible to get a patent for something that occurs in nature. Without the possibility of the exclusive rights a patent confers, the drug companies, including Upjohn, were not interested.

But I was. Younger and more naïve then, I thought the only thing I needed to cure atherosclerosis was to develop a patentable phospholipid. This newly created substance would act like a chemical Roto-Rooter (just like a natural phospholipid), sucking the cholesterol from artery-clogging plaques and carrying it to the liver, where it would be metabolized like garbage in an incinerator. If I could turn this trick, I realized, it might not only save my own life, it could also help lengthen the lives of millions of heart-disease patients. And, of course, in the process I would become a pharmaceutical tycoon.

As I would soon discover, life is never quite that easy or straightforward.

Through my research background, I already knew quite a bit about how to change the molecular structure of phospholipids. Making small changes in that structure, I could produce a phospholipid-like substance that could be patented. That, I thought, should prove interesting to the big drug companies, which had the money and the facilities to take a phospholipid drug to the public. I went to my funding partners—my mother, my father-in-law, and my aunts and uncles—and in 1976 started one of the first biotech companies: Lipid Specialties, Inc. I rented lab space in downtown Boston and started working with a single technician to eradicate heart disease.

By tweaking the phospholipid molecule—adding a carbon atom here, a methyl group there—I soon created a series of "new" phospholipids. These molecules were at least slightly unlike anything seen in nature, and therefore patentable.

Sure that I was on the brink of a cure for heart disease, I patented the new molecules and took them to Upjohn. The drug-company researchers tested these phospholipids on the same atherosclerotic Japanese quails that they had used in their own studies. My phospholipids had virtually the same effect as the natural variety: they reduced the amount of plaque on the animals' artery walls.

But a slight complication was occurring—some of the animals were dying. It turned out that the patentable phospholipids I had made were too good. They were pulling cholesterol from the atherosclerotic lesions, but they were also pulling the cholesterol from the red blood cells. These cells then ruptured and leaked hemoglobin—the substance that carries oxygen to the cells. This was killing some of the animals. Once I saw the results, I knew immediately how to solve the problem. Only two things stood in my way. One was that I had run out of money, the second was Upjohn.

Upjohn wasn't interested in any further work. Why? Because our new phospholipids had to be injected in order to remove the cholesterol from the atherosclerotic lesion, and Upjohn's upper management didn't want to deal with any potential cardiovascular drug that couldn't be made into a pill.

So much for my dreams of being financially solvent, let alone a pharmaceutical tycoon. And, of course, my own biological time bomb was still ticking.

Still, I had learned a valuable lesson: when it comes to treating heart disease, think of something you can swallow or eat.

All was not lost. I still had all this new and patentable phospholipid technology. What I needed was a partner. As luck would have it, I came across my mentor in drug-delivery technology, David Yesair. David was a vice president at Arthur D. Little, a major consulting company in Boston. He was uninterested in heart disease, but was passionate about cancer treatment.

David's cancer-fighting drugs at the time were great antitumor agents in the test tube, but because they were so water-insoluble, they could never be injected into humans. No problem: I now had a patentable technology to solve this dilemma. So rather than sucking cholesterol from atherosclerotic lesions, I used this phospholipid technology to deliver new and unusual anticancer drugs with greater specificity and less toxicity than ever before imagined. (One of these drugs, by the way, was AZT, now among the only drugs approved to treat people with AIDS.)

Since that time, I have continued to evolve my drug-delivery technology to solve many of the inherent problems associated with cancer drugs (I now hold most of the major patents in the world for intravenous cancer-drug delivery).

But all this still did nothing for my heart, which was not getting any younger. To make things worse, in 1984 I had a personal wake-up call: I was hospitalized for a week with cardiac arrhythmias. Needless to say, my interest in treating heart disease was intensifying.

But I could see the light at the end of the tunnel. In 1982 news came from Oslo that would change both the direction of my research and the course of my life. That year's Nobel Prize for Physiology and Medicine was awarded to Sune Bergstrom and Bengt Samuelsson of the Karolinska Institute in Stockholm and John Vane of the Royal College of Surgeons in England for research on the powerful class of hormones called *eicosanoids.* (Remember this word. You'll hear it again and again in the course of this book. It's pronounced eye-KAH-sah-noids.) Actually, Vane's part of the Nobel Prize was based on his research on aspirin—that's right, plain old garden-variety aspirin.

At the time, virtually no one outside the world of lipid research (and that's a very small world) had ever heard of their work. Before the three prize-winning scientists came along, everyone knew at least some of the things that aspirin does—it reduces pain, controls fever, etc.—but no one really knew how it works its magic in the body. Bergstrom, Samuelsson, and Vane's award-winning work solved the mystery: aspirin works its wonders by affecting eicosanoids.

These hormones—there are hundreds of them—are among the most powerful and important substances in the body. They act as "master switches" that control virtually all human body functions—including the cardiovascular system, the immune system, and the systems that govern how much fat we store (and therefore how much we weigh). Eicosanoids are so crucial to our health and well-being that I came to think of them as the "molecular glue" that holds the human body together.

I first became aware of eicosanoids during my research on lipids. Certain fatty acids associated with natural lipids are also the building blocks of eicosanoids. But Bergstrom, Samuelsson, and Vane's Nobel Prize–winning research opened my eyes to how important eicosanoids really are. It occurred to me that if someone could control eicosanoids, they would actually control virtually every aspect of human physiology, including the cardiovascular system.

It also occurred to me that since eicosanoids are involved in virtually everything the body does, controlling them might represent a new paradigm for health and illness. It seemed to make sense that many of our disease states—heart disease, diabetes, arthritis, and cancer, to name just a few—might be the result of imbalances among the eicosanoid hormones.

If that were true, restoring and maintaining a proper balance of eicosanoids might help prevent or even become the primary treatment for these diseases. Even better, it might help maintain a state of nearly perpetual good health: a molecular definition of "wellness" that would lead to a better quality of life. As an ultimate payoff, keeping eicosanoids in balance might help all of us reach that near-euphoric state of maximum physical, mental, and psychological performance that athletes call "the Zone."

Now everyone knows that in the athletic context the Zone is a fleeting thing—it's extremely hard to reach. Even when an athlete gets there, it rarely lasts longer than a few minutes. (I found it myself a few times when I played at the national volleyball championships, but my time in the Zone was usually measured in seconds.) The key to reaching the Zone and staying in it, I realized, might lie in controlling the balance of eicosanoid hormones. I began to wonder if it might even be possible to stretch the duration of the Zone—to reach it whenever we wanted and then to *stay* in it, not just for a few minutes (or a few games), but twenty-four hours a day for the rest of our lives.

In cancer-drug delivery there is a Zone too, known as the therapeutic zone. When a concentration of cancer drug is too low, it is ineffective. If the concentration is too high, it is toxic. At the right level, it is therapeutic. Like the Zone in athletics, the therapeutic zone for a cancer drug can be exceedingly narrow. So I figured that this eicosanoid Zone I was searching for would probably combine properties of the Zone taken from both the athletic context (optimum performance) and the context of cancer-drug delivery (defined mathematical limits).

The question, of course, was how to accomplish all this? I knew that eicosanoids couldn't just be injected into the bloodstream like cancer drugs. They're so powerful they would simply overwhelm the body, throwing all its important physiological systems dangerously haywire. This is why major drug companies like Upjohn, Burroughs Wellcome, and Ono had spent billions of dollars on eicosanoid research but had no drugs to show for it.

I decided to approach eicosanoids from a different perspective—at the level of the individual cell, where the eicosanoids are manufactured in the first place. My goal was to learn how to tip the balance of the molecular building blocks of eicosanoids in the cell membranes so that the cells would manufacture the right types of eicosanoids to reach the Zone.

How could I do this? By applying the drug-delivery principles I was already using for cancer drugs to the ideal oral drug-delivery system for eicosanoids: food. That's it in a nutshell, and that's what this book is all about—using food to manipulate eicosanoid balance, and using that balance as a passport to the Zone. In the following chapters I'll explain in detail how I learned to break this nutritional code, and how I've continued to refine it until it's now finally ready for public consumption.

How do I know it's ready? Because I've now spent almost six years developing this dietary program, testing it on the only species that counts: human beings. From my first human "guinea pigs" (myself, my brother, Doug, and my wife), I've gone on to test and refine this eicosanoid-favorable nutritional system on world-class athletes—including the Stanford University swim teams, elite triathletes, and various NFL, NBA, and professional baseball players. I've also tested it on people with some of our nastiest killer diseases, including diabetes, heart disease, and AIDS. In addition, the program has been tried by hundreds of ordinary people who simply wanted to lose weight and feel their best.

My results have convinced me that this dietary technology is the most powerful means ever discovered to help people achieve that state of optimal good health, physical performance, and mental alertness that's called the Zone.

I'm now convinced that reaching the Zone and staying in it can help prevent heart disease. It should even help reverse heart disease when it does occur. Staying in the Zone is your best defense to ward off cancer, and has a positive impact on a host of other diseases, including diabetes, arthritis, "mental" diseases like depression and alcoholism, even chronic fatigue.

In fact, reaching the Zone and maintaining it should ultimately help us reach that most universal of personal goals: to live longer, healthier, and more satisfying lives. In the bargain, staying in the Zone will keep us performing at our absolute best—hour after hour, day after day, month after month—for the rest of our lives.

These are not unique claims. The proponents of every new diet that comes along say essentially the same thing. But if you're reading this book, you probably already know that these diets don't really work. You may have already tried one of today's trendy, low-fat, low-protein, high-carbohydrate diets and been disappointed with the results. Well, the fact is that for a number of reasons these diets can't possibly work. They can't help you lose weight in a permanent way, and they can't boost your physical performance—even if that's exactly what they're designed to do.

In fact, I'm now firmly convinced that these high-carb diets can actually be dangerous, that they can actually help bring on the diseases they're supposed to prevent. Why? Because they violate the basic biochemical laws required to enter the Zone.

The beauty of the dietary system presented in this book is that it's doable. It doesn't require that you eat anything weird, and it doesn't call for a great deal of the kind of unrealistic self-sacrifice that causes many people to fall off the diet wagon. It doesn't rob food of most of its flavor, as do many of the extremely low-fat diets. In fact, I can even show you how to stay within these dietary guidelines while eating at fast-food restaurants. And yes, you can still have your Häagen-Dazs.

Think of this book as having two distinct parts. The first portion gives you the rules and dietary tools to reach the Zone. The second part goes into greater detail on the health-care implications for living in the Zone, specifically with regard to chronic disease states such as heart disease, cancer, and others.

I hope this book serves as a wake-up call for both health-care professionals and the general public. I hope it will help reverse the growing health-care disaster stemming from the high-carbohydrate diets now being pushed on the American public.

Understanding the implications of the Zone can completely change your life. All you have to do is read this book, follow the simple dietary guidelines it recommends, and put them to work for you in your own life.

You'll be glad you did.

This book is not intended to replace medical advice or be a substitute for a physician. If you are sick or suspect you are sick, you should see a physician. If you are taking a prescription medication, you should never change your diet (for better or worse) without consulting your physician as any dietary change will affect the metabolism of that prescription drug. As powerful as modern medicine is, it remains a poor substitute for prevention.

Prevention will always be the best medicine. However, prevention can only be undertaken by the individual and that includes eating correctly. This is the foundation of a healthy lifestyle. You have to eat, so you might as well eat wisely.

Although this book is about food, the Authors and the Publisher expressly disclaim responsibility for any adverse effects arising from the use of nutritional supplements to your diet without appropriate medical supervision.

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