Best Future You

Harnessing Your Body's Biochemistry to Achieve Balance in Body, Mind, and Spirit

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Introduction

Even though the title of this book is Best Future You – and its overall theme is to help you achieve your ultimate peak of health, vitality, and mental/physical performance, this book is really about how to achieve all that through balance. The one common theme that runs through every concept and each chapter is the idea that maintaining balance, specifically biochemical balance, in our body, mind, and spirit is the secret to feeling our best, looking our best, and performing our best. Unfortunately, this is not at all what we see in most of the popular "self-help" and health-improvement programs these days. In fact, most popular programs are the antithesis of balance because they focus on the complete exclusion of entire food groups (e.g. carbs or grains or meat or fat or gluten or whatever) – or the imperative that you "must" include one certain magical "superfood" that has miraculous medicinal properties. What these misguided approaches fail to understand, is that such limited approaches deliver limited results (and limited benefits for you). In contrast, Best Future You takes a more comprehensive approach, to focus on a holistic approach to reducing cellular stress, restoring both physiological strength and psychological vigor, and thus improving how we feel, look, and perform on every parameter imaginable.

Being "out" of balance is a type of stress, specifically a state of cellular stress that leads to dysfunction and eventually to disease. The list of stressors that cause biochemical imbalance and cellular stress is a long one – covered in detail in Chapter 1 – and chances are good that you're exposed to many of them on a daily basis.

As a lifestyle expert trained in the Western scientific disciplines of exercise physiology and nutritional biochemistry – as well as being a student of the Eastern concepts of Qi from traditional Chinese medicine (TCM) and Prana from Indian (Ayurvedic) medicine, my idea of "balance" is quite a bit different than the standard definition. For many of my colleagues, and especially among writers of popular health books, the idea of balance refers to an inexact and imprecise concept of eating better and exercising more – which is not very helpful for readers who are trying to improve themselves. Instead, my idea of balance is very precise and very focused on the concept of maintaining *biochemical* balance between myriad hormones, enzymes, neurotransmitters, and signaling molecules that course through our blood and brain and all parts of our body on a second-by-second basis. These molecules are responsible for one of my favorite sayings that, "biochemistry drives behaviors" which describes how our feelings of energy (or fatigue), or happiness (or depression), or mental clarity (or brain fog), or even feelings of success and achievement (or failure and defeat) are driven in large part by positive or negative changes in our underlying biochemistry.

I've been studying how to help people "feel/look/perform their best" for my entire career – more than 20 years now. As early as my first days of high school, I can remember being interested in the relationships between what we eat, how we look, and how we feel – even before I really understood that there were branches of science that studied these areas (nutrition, physiology, psychology, etc). Being interested in health and human performance led me to pursue undergraduate degrees in both sports medicine (BS) and fitness management (BA). While in college at a

small liberal arts school (Marietta College in Ohio), I tried my hand at a sport that was completely new to me – rowing, also known as crew. I had no idea what I was getting myself into as a member of the novice crew team, much of which was already populated by rowers with years of prep-school crew experience. My first few weeks of rowing were miserable – I didn't know how to properly hold an oar or balance a boat (called a crew shell) – so I got yelled at a lot by the coxswain (the person who steers the shell, guides the oarsmen, and commands the crew). Over time, and with the support and guidance of experienced rowers and patient coaches, I gradually learned both the proper technique of rowing and the important fact that being successful in crew hinges on a combination of hard individual work and coordinated teamwork. Thinking back to those four years as a collegiate rower, I'm convinced that my crew coaches are responsible for the way that I "coach" my readers and lecture audiences to harness scientific information for their own improvement. From my inauspicious beginnings, as a freshman who had never even seen a crew shell, I progressed steadily to become a member of a multi-championship boat, 2-time captain of my collegiate team, and member of the United States National Rowing Team.

After college and my short stint on the national team, I decided to study exercise physiology and human performance at the University of Massachusetts at Amherst, while paying my tuition as the coach of the novice rowing team (Go Minutemen!). Being a crew coach was one of my most personally and professionally satisfying experiences, because it allowed me to impart my knowledge to help a group of young men and women to improve themselves beyond their expectations (exactly

what I learned from my own crew coaches). My experience with the national team made me realize that there were plenty of better rowers than me, so needing a new exercise endeavor, I started riding as part of the UMASS Cycling Team. As a cyclist, I experienced the same steep learning curve, where I was initially terrible and was frequently "dropped" (left behind) by the group of experienced and talented collegiate cyclists. Eventually, I gained enough experience with team tactics, race strategy, and riding in a group at 30+ mph, to be invited to be part of a cycling development program at the US Olympic Training Center in Lake Placid, NY. Once again, I was able to rely on the guidance and advice of far more experienced cyclists and dedicated coaches to teach me how to improve my skills as a cyclist. As part of this elite group of cyclists, I realized as I did with rowing a few years prior, that there were plenty of riders with vastly superior cycling skills compared to mine. As such, after a couple of years as a dedicated cyclist, I decided to switch my sports focus again to a new and rapidly growing sport – triathlon (swim, bike, run).

Right around the same time, I graduated from UMASS with a master's degree in exercise physiology and took a job with a corporate wellness company. In this new role, I split my time between developing multi-million dollar corporate wellness programs for Fortune 500 companies and training for triathlons (eventually holding a professional license and getting trounced by some of the top triathletes in the world at the time, including a young Lance Armstrong). I loved designing corporate wellness programs and helping thousands of people become healthier and live fuller lives – and I enjoyed even more making myself a guinea pig for different training regimens and racing strategies that I would experiment with on the professional

triathlon circuit. However, after several years in both of these roles, corporate wellness and professional triathlon, I felt that something was missing in my knowledge base, so I decided to go back to school to study nutrition.

I studied nutritional biochemistry at Rutgers University, where my work was funded by competitive research grants from the American College of Sports Medicine, American Institute of Nutrition, Reebok, LifeFitness, and a variety of other public and private scientific grants. Studying the biochemistry of the body enabled me to delve into the "how and why" that various lifestyle interventions exerted their effects (including diet, exercise, stress management, and many others). For example, what molecules in the body are responsible for muscle growth, or bone loss, or appetite, or athletic performance, or energy levels, or any of the other aspects of health that we might be concerned with? Now I felt that I finally had the tools to help people get better from the inside out – right down to the cellular, molecular, and biochemical level.

Upon completing my PhD, I now had a broad educational background and lots of ideas that spanned many aspects of health (sports medicine, fitness management, exercise physiology, and now nutritional biochemistry), but I also had a burning desire to "build something" that could help people to harness some of these ideas and easily include them in their lives. This led me to a career in product development, starting with "functional foods" at Nabisco Foods and spanning nearly 20 years with many different international companies and academic institutions to my current passion running my own boutique product development company (EQQIL, Inc.) with a range of "balancing" products in circulation with companies around the world.

As a product developer, I need to understand not only the scientific aspects of particular ingredients and formulas, but also the business and market implications, such as cost, profit margins, marketability, and many others. This led me to study business, innovation, and entrepreneurship at the Massachusetts Institute of Technology (MIT), where over several years, I completed both the Entrepreneurial Masters Program and the Advanced Certificate for Executives in Management, Innovation, and Technology ACE in MIT). Studying entrepreneurship after so many years of studying science enabled me to understand one very important fact – that being that "science" can't help anyone unless it reaches the market in a way that people can easily plug into their lives.

Across those years, I've started and sold several different health-focused companies; developed a range of top-selling products (foods, supplements, and cosmetics) and programs (exercise, weight loss, and wellness); written and edited hundreds of articles and books; and given dozens of scientific presentations all over the world. I've been fortunate to help educate a wide range of elite-level coaches and athletes in a variety of sports, including at the US Olympic Training Centers (middle and long-distance runners as part of the US Track & Field Association's Performance Enhancement Team); the US Ski and Snowboard Team (during the 2002 Winter Olympic Games); professional basketball (NBA – Utah Jazz); professional soccer (MLS – Real Salt Lake); and international sports organizations in Canada, England, and Singapore. The scientific conferences are fun and interesting because they contribute new knowledge to the world, but it's the products and programs that I'm most

proud of because they can actually help real people to exert positive change in their lives.

None of this could have been possible without me being exposed over the years to a series of dedicated and inspiring coaches and mentors, as well as a natural curiosity about perfecting the coordination of body, mind, and spirit to help us achieve our best. This is what I hope *Best Future You* can be for you – a virtual coach to guide your curiosity and help you become the best future version of yourself.

Aside from my intellectual and business reasons for doing the kind of work that I do, I have a very personal reason for my work and for writing this book (my twelfth). I want to be always be striving to be the best version of myself. This means that I'm a better student and teacher, that I have a better outlook on life, that I have more stamina and resilience to stress, that I'm a better athlete, a better husband, and a better father. You get the idea – a better (future) version of my current (present) self. The whole idea of this book is to help you become your "best future you" – the best version of yourself. You might be interested in something like that because the best version of yourself might be more energetic or focused or happier than you are now (you'd *feel* better) – or you might have a complexion that is more youthful and radiant or a slim and toned physique (you'd *look* better) – or you might become leaner, stronger, and confident (you'd *perform* better).

The body is a dynamic, ever-changing, always-adapting collection of intricate structures and systems. Sometimes it works perfectly on its own—your lungs fill and empty, your heart beats, and your eyes blink—all without you having to remember to "work" them. But sometimes your body breaks down. In most

circumstances, the damage is only temporary, because your internal repair mechanisms jump into action to fix the damage and get you back to full function. Sometimes, however, the damage persists. You accumulate little bits of damage and dings and creaks over the years, until you find yourself waking up one morning with physical ailments, such an aching knee, a stiff back, or a generalized pain through your entire body. Sometimes the ailments are more "psychological" in nature, such as depression, fatigue, brain fog, lack of motivation, or outright burnout. Sometimes, those little changes in metabolism and cellular function mean that we wake up on the morning of our twentieth high school reunion and somehow we've gained twenty (or more) pounds of belly fat and more wrinkles than we can count.

Whether physical or mental, all these ailments have their roots in problems with the biochemistry of your body. Specifically, I'm referring to the biochemical activity among hormones, enzymes, blood-sugar levels, brain signals, and the other internal interactions that take place below the surface of your skin that you are hardly aware of—until something goes wrong. When the balance between hormones, such as cortisol and testosterone; or between neurotransmitters, such as dopamine and norepinephrine; or between enzymes, such as catalase and glutathione peroxidase, is disrupted, you can be left feeling "blah" and exhausted.

This feeling of exhaustion is caused in large part by internal biochemical imbalances, and I've been invited on numerous national television broadcasts to explain why so many millions of people are more likely to feel tired, stressed, and depressed and less likely to feel energetic, relaxed, and happy. In the type of lifestyle research that I

do, we use natural therapies (nutrition, exercise, sleep, stress management, herbal supplements, and others) to reestablish biochemical balance to improve psychological vigor.

I've written entire books about restoring vigor (*The Secret of Vigor*, 2011), which is defined as a combination of physical energy, mental acuity, and emotional well-being – and the opposite of what we know as "burnout". Our modern scientific concept of vigor is somewhat comparable to the ancient descriptions of vitality and wellness from traditional medicine systems around the world. Nearly every ancient culture has typically held a common belief that true health stems from a strong "life force" in the body. Other names for this life force, or vigor, include:

- Qi (traditional Chinese medicine; pronounced "chee")
- Prana (Ayurvedic/Indian medicine)
- Pneuma (ancient Greek medicine)

Practitioners of traditional medicine might have restored "life force" in their patients by improving their nutrition or administering herbal medicines. These natural therapies often "worked," and patients felt better as a result. What these ancient healers did not fully appreciate was "how" their therapies were working to actually alter biochemical processes in the body. In modern times, millions of people attempt to temporarily reduce fatigue

with unbalanced energy drinks or other stimulants. However, that approach does not restore vigor and is actually more likely to create additional imbalances that further sap vigor in the long term.

Chronic stress—and the underlying biochemical imbalances that it leads to—undoubtedly plays a major role in many of today's modern diseases, particularly depression, chronic fatigue, anxiety, fibromyalgia, and obesity. In fact, according to the Centers for Disease Control & Prevention and the World Health Organization:

- 80 percent of North Americans have enough daily stress to cause health problems.
- Stress contributes to half of all illnesses in North America.
- 70–80 percent of all doctor visits are for stress-related illnesses.
- More than half of all deaths before age sixty-five result from stressful lifestyles.

The good news is that by naturally restoring biochemical balance, you can dramatically reduce feelings of stress, cut fatigue and depression, boost physical and mental energy, and significantly improve vigor.

It may be hard to understand how something as simple as stress can cause so many problems—from depression to heart disease to weight gain. But the fact is, your body's

response to everyday pressures—including deadlines, traffic, money concerns, family conflicts, irritating coworkers, and other worries—is actually a chronic stress response. And that response to chronic stress causes an immediate and profound change in a variety of hormones and related biochemicals in your body. Further, those compounds are distributed throughout the entire body, where they influence the function of every organ and cell.

Initially, the effects of chronic stress are subtle. On the biochemical level, hormone levels change (e.g. increased cortisol and reduced testosterone); blood sugar levels fluctuate more dramatically (because cortisol interferes with insulin, the hormone that controls blood sugar); cellular damage increases (caused by oxidation and inflammation set in motion by blood sugar fluctuations); and brain function is compromised (due to imbalances in neurotransmitters such as dopamine, serotonin, and norepinephrine). Although you are hardly likely to detect such biochemical changes on a daily basis, what you might notice is that you experience a few extra pounds of weight, a slight reduction in energy levels, a modest drop in sex drive, or a bit of trouble with memory or mood. Even then, you probably brush off these health signals as "normal" aspects of aging. However, these common symptoms are actually the earliest signs of depression, chronic fatigue, fibromyalgia, obesity, diabetes, impotence, dementia, heart disease, cancer, and many related conditions—and chronic cellular stress can trigger all of them. Indeed, researchers are discovering that cellular stress may well be the key factor in the very process commonly recognized as "aging."

I've learned through experience with thousands of people who have read my books, attended my lectures,

and enrolled in my programs, that when people become that better version of themselves – that "best future you" – they often feel *so* good that they're motivated to help someone else achieve the same – they pay it forward. I see it in action every day and all over the world – people helping other people to achieve what they've achieved. Many people who witness this phenomenon describe it as "magical" – which it might be in terms of the life-changing benefits that it brings to people, but that "magic" is deeply rooted in the science of maintaining biochemical balance.

If reading this book can give you some ideas and strategies for helping you to feel your best, then that's a win. But, I think our opportunity is much bigger than that. I'm banking on *Best Future You* helping you to feel *so* much better, that you're motivated to help someone you know to feel their best, or look their best, or perform their best – you get the idea.

Chapter 1 - The Battle for Balance

If you think about the modern world in which we live, you'll realize that we're surrounded by almost countless sources of stress. The sources of stress in the modern world are all around us – externally from the environment; internally from our own metabolism; and bombarding us from every corner.

Consider some of the major sources of stress:

- Emotional stress from work deadlines, bills, traffic, relationships
- Physical stress from normal aging, sleep deprivation, lack of exercise (or too much)
- Environmental stress from air/water pollution, sunlight, secondhand smoke, and myriad toxins lurking in our foods, cosmetics, and other products
- Non-Optimal Diet such as too many processed foods and inadequate nutrients from fresh fruits and vegetables

If that news weren't bad enough already, we also have to consider that our bodies naturally produce highly

reactive molecules known as free radicals as a normal part of metabolism (converting food into cellular energy). These free radicals can create a unique type of internal cellular stress that accumulates as we age.

In many ways, we need to accept the fact that our exposure to stressors that can unbalance cellular biochemistry comes from myriad external sources, but also from internal ones – and that they're all around us and unavoidable.

Since this is the world we live in, we need to use as many tools as we can to protect us – and luckily, the natural world has also provided us with numerous tools to both protect and repair our unbalanced cells and realize our best future selves. But, before we can fight that fight, we need to know what we're up against – and knowledge about free radicals and cellular stress is the first step in preparing for the fight.

The Free Radical Theory of Aging & Disease

For more than 50 years, scientists have known the aging process to be linked to the free radicals described above. These highly reactive oxygen molecules, referred to by scientists as "reactive oxygen species" (ROS) are produced during normal metabolism and can react with and cause damage to cellular structures in every tissue and throughout the entire body. Particularly vulnerable to oxidative damage are cell membranes, DNA (genetic material), and mitochondria (where cells generate energy) – and damage in these vital areas often means that cells cannot function properly.

It can be scary to think that our own body is producing these damaging molecules as a normal part of living and breathing – but it's even scarier when you realize that ROS are all around us in the environment in the form of sunlight, car exhaust, air pollution, cigarette smoke, poor diet, and many other sources. Our bodies are constantly being bombarded by free radicals, and constantly under threat of cellular damage and dysfunction – unless we do something to protect ourselves.

Antioxidants are compounds that can react with and quench – or inactivate – a free radical so it cannot cause cellular damage. As such, antioxidants help to protect every cell in our body from damage by free radicals.

Too many free radicals – or too few antioxidants – can wreak havoc on cell membranes and DNA, leading to tissue damage and a wide range of chronic diseases including cancer, arthritis, and heart disease.

The free radical theory of aging (and disease promotion) holds that through a gradual accumulation of microscopic damage to our cell membranes, DNA, tissue structures and enzyme systems, we are predisposed to dysfunction and disease. In response to excessive free radical exposure, the body naturally increases its production of endogenous antioxidant enzymes (glutathione peroxidase, catalase, superoxide dismutase and others), but it has been theorized that our bodies are less able to activate these internal protective systems as we age. Thus, in order to promote optimal health and well-being, many of us probably need to augment our natural defenses by "manually activating" these natural pathways in order to help prevent excessive oxidative damage to muscles, mitochondria and other tissues.

If you've ever noticed an apple turning brown shortly after being cut open or an old car with rust spots all over it, you've actually seen the results of the natural process of oxidation. One simple definition of oxidation is that it describes what happens when oxygen combines with another substance. On a somewhat more technical level, oxidation refers to the "loss of at least one electron when two or more substances interact." How are these electrons lost? They're "stolen" by the highly reactive free radicals described above.

Free radicals are highly reactive and potentially damaging, because they have an "unpaired" electron that wants to "pair" with another electron. Unfortunately, free radicals often try to "take" that needed electron from proteins and lipids (fats) in the cells, creating microscopic damage to cellular structures and leading to tissue dysfunction. Perhaps even worse than the direct damage to DNA and cellular structures is that damage in one part of the cell can set off a chain reaction of damage that can be propagated from one part of the cell to another, just as a campfire spark jumps from tree to tree in a forest and leads to a wildfire.

Free radicals are not necessarily "bad"—a certain amount of cellular "signaling" by free radicals is actually needed for normal physiological functioning, including normal glucose transport, mitochondrial genesis, and muscle hypertrophy (growth). However, unchecked or excessive free-radical activity is what leads to cellular damage—oxidation or oxidative stress—and the cycle of inflammation and tissue dysfunction that follows.

Consuming antioxidant nutrients in the form of brightly colored fruits and vegetables has clearly been shown in research studies to be associated with reduced free radical

damage and improved health. Unfortunately, the practice of “taking antioxidants,” in the form of high-dose vitamin supplements, is being linked by a growing number of scientific studies to more harm than good, which you’ll learn more about in Chapter 3.

Cells are typically able to protect themselves from free-radical damage through the internal (endogenous) antioxidant enzymes described above (superoxide dismutase, glutathione peroxidase, catalase) as well as through antioxidant nutrients found in the diet (vitamins C and E, minerals selenium and zinc, flavonoids, and carotenoids—many of which can directly “quench” free radicals by donating their own electrons).

As you’ll learn in Chapter 4, our bodies possess their own built-in systems of antioxidant and anti-inflammatory defenses that naturally protect us from our stressful environment (collectively known as the cellular defense response, or CDR). However, when these internal systems are overwhelmed by free radicals and other sources of cellular stress, damage may occur to DNA, proteins, and lipids in cell membranes (generally referred to as “lipid peroxidation”). Excessive free-radical production can come from air pollution, cigarette smoke, intense exercise, and even immune-system activity (because immune cells release huge amounts of free radicals such as superoxide, hydrogen peroxide, and nitric oxide as part of their “respiratory burst” to kill pathogens and clear out damaged cell material).

The most common free radicals in the body include superoxide (O2-), hydrogen peroxide (H2O2), hydroxyl radical (OH-), nitric oxide (NO-), and peroxyl radical (NOO-). Superoxide, the most reactive of the free radicals, is formed in the mitochondria of the cell during the normal

passage of molecular oxygen through the electron transport chain during creation of ATP (adenosine triphosphate) for cellular energy. Superoxide is inactivated by the action of the cellular antioxidant enzyme, superoxide dismutase, resulting in hydrogen peroxide (H2O2). At this stage, hydrogen peroxide is still a free radical, but one with a lower potency. Hydrogen peroxide can be further converted into harmless water and oxygen by the activity of other cellular antioxidant enzymes; catalase and glutathione peroxidase.

Chronic Cellular Stress

Conventional wisdom tells us that the way to get healthy is simply to exercise more and eat a better diet. Both these habits are certainly important parts of being healthy and achieving your best, but from my perspective as a nutritional biochemist, I'm going to tell you something you won't hear from anyone else: If you truly want to improve your health and achieve your best future you, it is just as important to get your cellular stress levels under control (that is, restore biochemical balance) as it is to eat a healthy diet and to be physically active.

Quite simply, cellular stress (your degree of biochemical balance - or imbalance) has a bigger impact on your life and well-being than almost anything else you encounter. Most people don't understand this fact, or else they ignore it. Worse, some people think they're "tough" enough to handle all the sources of stress in their lives. But when you consider the myriad sources of environmental, emotional, physical, psychological, and metabolic stress

that we're exposed to in our modern world, nothing could be farther from the truth.

The stressed-out feeling that many people experience on a daily basis may seem "typical," simply because everyone else is experiencing it, too. But that does not mean it is "normal" in a physiological sense, nor is it an indicator of good health or well-being. The body, including the nervous system and endocrine (hormonal) system, was simply not meant for the chronic stress that people face as part of their everyday lives in the twenty-first century. Most people simply endure this "twenty-first-century syndrome," that familiar feeling of always having to be "on," of being rushed, harried, and frantic. That is what chronic stress feels like, and it leads to a state of low vigor or "burnout," with its accompanying fatigue, depression, and mental fog.

As just one indication that chronic stress is taking a toll on all of us, consider this: According to the American Psychological Association, the incidence of depression and anxiety in modern society (around the world) is now ten times higher than it was just a generation ago. Not only are levels of depression and anxiety on the rise, but in the United States alone, close to ninety million cases of diseases with "no known cause" have been diagnosed. These diseases range from chronic fatigue syndrome (CFS), fibromyalgia (FM), vital exhaustion ("burnout"), and irritable bowel syndrome (IBS) to recurrent yeast infections, autoimmune disease, chronic back pain, and other "nonspecific" conditions. The never-ending stress under which people toil on a daily basis plays a role in all these illnesses and conditions, yet Western doctors and researchers are often slow to admit that "mental" conditions, such as stress, can have physical effects upon

the rest of the body. They fail to recognize that stress, which leads to biochemical imbalances, is the underlying cause of cellular stress leading to poor health and low vigor.

What is Cellular Stress?

A simple way to understand the meaning of "stress" is to define it as "the gap between demands and ability to meet those demands." Every individual, of course, has a different capacity to effectively cope with stress and a different level of functioning when faced with stressful situations. The same is true of each of the trillions of cells in the human body. We all know someone who seems to be better "under pressure" than others. But even the rare person who has a high tolerance for stress ultimately has a breaking point. Add enough total stress to anyone – or any cell – and health and performance soon suffers.

To deepen our understanding of cellular stress, it is helpful to recognize the distinctions that many of the top stress researchers in the world use when analyzing this condition. First, is that the type of stress faced by our cousins in the animal kingdom, are typically short-term, temporary, or acute stressors. For example, if you were a zebra, you could consider a lion chasing you to be an acute stress. The lion charges at you from the bushes, you mount a "fight or flight" stress response to respond to the stress – and (assuming you get away) the stress response is over and done within a few minutes. That sort of short-term acute stress is distinct from the type of stressors that modern humans routinely face, because our stressors are longer-term, repeated, and chronic.

However, unlike animals, humans undergo not only physical stress but also psychological and social stress. Certainly, some sources of psychological stress are grounded in reality, such as the pressure you feel to make your monthly rent or mortgage payments. Other psychological stressors emanate from our imagination—for instance, the stressful encounters that you can imagine having with your boss, coworkers, kids, spouse, or others. So not only do you have to cope with real-life stressors, but your large, complex, and supposedly "advanced" brain has also developed the capacity to actually create stressful situations where none previously existed.

Earlier I described how the body can protect itself from cellular stress (oxidative stress) with "antioxidants" – which we can define as "substances that decrease the severity of oxidative stress caused by reactive oxygen species (ROS)." There are two main types of antioxidants:

- Exogenous (meaning "outside" the body) – which includes dietary antioxidants such as vitamins A, C, & E, minerals such as selenium and zinc, and phytonutrients such as flavonoids (e.g. from blueberries, cranberries, grapes, etc) and carotenoids (including beta-carotene, lycopene, and lutein from carrots, tomatoes, peppers, sweet potatoes, etc).

- Endogenous (meaning "inside" the body) antioxidants are enzymes that are naturally

manufactured within each of our cells, such as superoxide dismutase (SOD), catalase, glutathione peroxidase and a variety of others.

Our internal protective antioxidant enzymes tend to be much more potent and effective in counteracting the damaging effects of free radicals compared to exogenous dietary antioxidants. This is because dietary antioxidants can only scavenge free radicals in a "one-to-one" relationship – for example, one molecule of vitamin C (antioxidant) quenching one molecule of hydrogen peroxide (free radical). This 1:1 relationship is referred to as "stoichiometric" scavenging – and while important and essential to normal biochemical function in the body, it pales in comparison to the potency of the "catalytic" scavenging of free radicals that is possible with endogenous antioxidant enzymes. The antioxidant enzymes produced by each and every one of our own cells is approximately 1 million times more effective than exogenous antioxidants because the catalytic process allows each antioxidant enzymes to react with and deactivate millions of free radicals every second.

Antioxidants – right where you need them most

Even if we understand that overexposure to free radicals and underexposure to antioxidants can lead to damage and dysfunction in the body, we often fail to stop and ask ourselves which of our body's systems might benefit the most from increased antioxidant protection and

reduced cellular stress. The correct answer, of course, is "all of them" – but just to make sure, take a minute to think about which parts of your body are exposed to the highest levels of free radical exposure.

- For athletes, the lungs, muscles, and cardiovascular system are subjected to high free radical loads as a result of the increased oxygen and blood flow demands of exercise.
- For those of us exposed to polluted air – or secondhand cigarette smoke – or car exhaust, the free radicals that you're breathing in that "bad air" is certainly harming your lungs, but those free radicals are also transmitted to every tissue in the entire body by our blood supply.
- For sunbathers, the skin can benefit from the increased protection that antioxidants provide against the oxidizing ultraviolet radiation of the sun. Likewise, anybody that spends time outdoors exposed to the sun should be concerned with the potential for ultraviolet radiation to damage eye health.
- For anyone who hits the drive thru for a fast food meal deal (even occasionally), consider that the fat and sugar in that burger, fries, and soft drink will unleash a storm of free radicals, inflammatory

compounds, and other cellular stressors. Combine that with the fact that most people simply don't consume enough brightly colored fruits and vegetables, and we clearly have a cellular stress "gap" between our free radical exposure and our antioxidant shield.

"Stressed Out"—The Downside of Chronic Stress

When people reach a breaking point in the face of too many pressures and worries, it is common to hear them say they are "stressed out" – and the very same process is at work at the cellular level. There is a difference between being "stressed" (that you can adequately respond to) and being "stressed out" (which exceeds our capacity to cope). When you are "stressed," your body undergoes an adaptive response. Being "stressed out" suggests that your body is unable to mount an effective stress response - leading to biochemical imbalance - aka cellular stress.

The bad news is that modern society makes chronic stress largely inescapable. In numerous research studies, scientists have shown that overall cellular stress is significantly related to the degree of "daily hassles" (more hassles = higher cellular stress) as well as to age (higher age = more accumulated cellular damage) and to hours slept (less sleep = more cellular damage). Worse than that, scientists at Rockefeller University in New York have suggested that being "stressed out" may be the primary cause of many common "modern" diseases, such as

chronic fatigue, fibromyalgia, post-traumatic stress disorder (PTSD), depression, and burnout. In addition, researchers in Boston have suggested that chronic psychological stress is a primary cause not just of generalized cellular damage, but also of a variety of inflammatory diseases, including insulin resistance, diabetes, obesity, and heart disease.

When it comes to managing your weight or combatting obesity, you also have to seriously consider the impact of the cellular stress that accompanies chronic psychological stress. To begin with, the level of oxidation/inflammation in your body and the accumulation of abdominal fat (belly fat) are inextricably linked. That link takes place because cortisol, free radicals, and cytokines promote fat storage in a "chicken-and-egg" scenario in which it's often hard to tell which came first (cytokines are a class of hormone-like signaling proteins that play a central role in the immune response and in the level of inflammation found throughout the body). So, when we gain belly fat, we often don't know which came first; the stress (which causes an overexposure to cortisol); or the oxidation (caused by free radical overload); or the inflammation (altered by cytokine imbalance).

On the cellular level, oxidation/inflammation leads to obesity, which leads to more stress and oxidation/inflammation, which leads to more obesity. On the other side of the coin, reducing obesity has the opposite effect: Weight loss leads to a substantial improvement in biochemical balance and a drop in all forms of cellular stress, with drops in oxidation (free radicals), inflammation (cytokines), glycation (blood glucose), and stress hormones (cortisol). So the "chicken-and-egg" scenario that plays out across different types of cellular stress can run two ways, positively as well as negatively.

When these sources of cellular stress are locked in a downward spiral (moving toward “imbalance”), more inflammation and more obesity result; and when that cycle is reversed (moving toward “biochemical balance”), people experience weight loss and feel better. As you can see here and as you will learn throughout this book, it is the ability to manage chronic cellular stress that determines whether these biochemical cycles turn in the right direction.

Sleep Loss and Cellular Stress

Have you ever had the experience of being exhausted during the day and all you can think about is getting some sleep? And then, when your head finally hits the pillow, you’re wide awake! Logically this “dynamic duo” of fatigue plus insomnia (or what we call “nighttime restlessness”) would seem to be opposites: If you’re so tired, why can’t you fall asleep? But they are commonly found together in the two-thirds of the North American population who report experiencing chronic stress and who also gets inadequate sleep (we often refer to these folks as the “tired and wired” - and they number in the millions). The common element? You guessed it: disruptions in the body’s biochemical balance. That imbalance is characterized by too much cortisol, too little testosterone, and the cascade of metabolic disruptions including oxidation/inflammation that lead cellular stress.

In the previous section, I discussed what happens when stress-induced imbalances in free radicals, cortisol, and cytokines precipitate a downward spiral that leads to cellular stress states such as obesity. By the same token, the combination of daytime fatigue/exhaustion and

nighttime insomnia/restlessness also sets off a vicious cycle in which stress makes it hard to relax and fall asleep —which then leads to more fatigue. And being more fatigued after a sleepless night makes it harder to deal with stressors, which then causes even more difficulty falling asleep the next night…and the next night and the next after that in a repetitive cycle that ultimately ends in burnout.

In the long run, when you sleep fewer hours than the recommended eight hours per night, you can experience annoying side effects, such as headaches, irritability, frequent infections, depression, anxiety, confusion, and generalized mental and physical fatigue. Not only can the lack of sleep leave you feeling lousy and low on vigor, but research shows that even mild sleep deprivation can actually destroy a person's long-term health and increase the risk of burnout, diabetes, obesity, and breast cancer. In many ways, sleeping fewer than eight hours each night is as bad for overall wellness as gorging on junk food or becoming a couch potato!

On the biochemical level, one of the major problems with the modern "late to bed, early to rise" lifestyle is that your cellular stress levels never have enough time to fully dissipate as they are supposed to overnight – they become chronic stressors rather than acute (temporary) stressors. As a result, your body never has a chance to fully recover and repair itself from the detrimental effects of chronic stress – and thus, is always out of balance. And when your biochemical balance is out of whack, it puts your overall metabolism into a downward spiral, accelerating the "breakdown" of tissues and sending your energy, mood, and mental focus into a tailspin, leaving you with low vigor.

Balancing Biochemistry

When measuring the state of their health through lab tests, people often want to get their "numbers" down. For instance, they may strive to lower their cholesterol or to lower high blood-pressure readings. But when it comes to the subject of cellular stress, the goal is not simply to "lower" oxidizing free radicals or inflammatory cytokines or even stress hormones like cortisol – but instead to maintain proper balance. In fact, many stress physiologists believe that the problem is not so much the absolute level of cellular stress that people are exposed to, but their degrees of variability in that exposure that lead to imbalances that further lead to tissue dysfunction and systemic disease. In other words, people should aim to have neither high levels of cellular stress – nor low levels – but rather, a "just right" level that fluctuates normally in response to stress and adaptation. In coming chapters, we'll look more at how chronically high cellular stress is bad, but also how chronically low cellular stress can also be bad—and especially how "flat" levels of cellular stress/adaptation that show little to no fluctuation seem to be just as bad as either extreme, because they lead to problems with biochemical balance and to adverse changes in other aspects of biochemistry farther "downstream" in the metabolic cascade.

You've just learned a great deal about biochemistry, and at this point you have a better understanding of how exposure to our external and internal environments affects your biochemical balance. You may also have come to realize that chronic cellular stress is not only a major stumbling block to developing daily vigor but a drastic threat to your long-term health as well. As you continue

reading, you will recognize that the importance of balancing cellular stress is at the very heart of, and sets the foundation for, everything that we might do to improve how we feel, look, and perform.

Chapter 2 - Managing Cellular Stress – the Basis for Feeling, Looking, and Performing Your Best

You've been introduced to the concept that numerous factors can "stress" cells and wreak havoc on cell membranes, mitochondria, and DNA, leading to tissue damage and a wide range of chronic diseases, including cancer, chronic fatigue, diabetes, arthritis, and heart disease. Certainly, it's logical to conclude that having cells with "less damage" (and better balance) is better than having cells with "more damage" (and less balance) – better for your health, better for how your mind and body function – and better for your long-term risk of chronic diseases. Of course, the challenge is knowing the most effective way to protect cells from damage, because, as you also learned in the preceding sections, the sources of damaging cellular stressors is external, internal, and unavoidable in our modern world.

Consuming antioxidants and phytonutrients in the form of brightly colored fruits and vegetables has clearly been shown in hundreds of research studies to be associated with reduced cellular damage and improved health. This research has led to many in the nutrition and health arenas to push the idea that if antioxidants in natural foods are beneficial, then we should take even more of them in pill form. Unfortunately, the practice of "taking antioxidants" in the form of isolated high-dose vitamin supplements is being linked in a growing number of research studies to more harm than good.

At the same time, exciting new research is also demonstrating how we can actually encourage the human body to protect itself from cellular stressors by turning on its own built-in and ultra-powerful cellular defense systems. This internal network of protective proteins, the Cellular Defense Response (CDR), is already inside every one of our 100 trillion cells—and its protective properties are more than one million times more powerful than typical antioxidant supplements.

Modern Science Meets Ancient Wisdom

Ancient medicine systems from around the world, particularly traditional Chinese medicine (TCM) and traditional Indian medicine (Ayurveda), have used blends of herbs and spices to protect the body, alleviate the symptoms of aging, and promote longevity. Theses herbal/spice blends, including many of the herbs listed above, don't "give" the body antioxidants like vitamin E or beta-carotene. Instead, these proven and invigorating botanicals amplify the body's cellular production of its own internal and super-potent protective enzymes (superoxide dismutase, catalase, glutathione, and many others) for vastly superior cellular protection benefits.

Biochemical and genetic research studies are showing us how these ancient herbal blends work—by activating a family of cellular "switches" (the CDR) to induce a series of cellular anti-stress genes and increase production of internal antioxidant enzymes and related protective proteins.

One way to think about the coordinated cellular defense response (CDR) and the multiple cellular defense

pathways that can be activated by certain herbs and nutraceuticals, is to think about the protection to our national defense provided by multiple armed forces. In many different ways, our nation, cities, and communities are protected from various threats by the local police or fire departments; the CIA/FBI; the National Guard, and all the way up to the "big guns" of the Army, Navy, Air Force, and Marines. The "level" of response and protection will depend on the route and the type of threat (stressor) encountered. When we activate the local and national defenses to protect the country, it's very similar to activating the wide range of cellular defense responses (CDRs) through multiple internal biochemical pathways that go by abbreviated names such as NfkB, SIRT1, Nrf2, mTOR, HSP70, and myriad others.

You might think of the CDR pathways as an internal "thermostat" for cellular stress. Whenever a cell is under stress—whether from oxidative stress, inflammatory stress, or any type of other stress that our modern world might throw at us, the CDR pathways sense the stress and induce numerous protective responses. Some of these responses help to reduce free radical damage, or oxidative stress (antioxidant enzymes), while others help to clean up damage (housekeeping proteins), and still others prepare our cells for exposure to future stressors (heat shock proteins).

This natural induction of CDRs is very much a "master regulator" of the body's antioxidant and protective response—and the same mechanism at the heart of numerous new biotechnology and pharmaceutical research projects. In many ways, the natural induction of CDRs is the future of holistically maintaining proper internal balance, protecting our bodies from destructive

environmental factors, and encouraging the repair mechanisms to help us thrive in the face of a world filled with biochemical imbalancers and cellular stressors.

Don't Take Antioxidants— Make Antioxidants!

Interestingly, while we know that there are numerous CDR-inducers in the natural world, we also know that specific combinations of ingredients can maximize gene expression in hundreds of genes associated with superior health of tissues and organs throughout the body. This suggests that our cells possess all the genetic resources required to maintain proper oxidative balance, promote health, and slow the aging process at the genetic level by naturally activating our CDR pathways.

Think about that for a moment. Every cell in our body has the ability to protect itself from the stressful, damaging, dangerous environment around us. Without that ability for self-protection and self-preservation, our cells would succumb to a buildup of damage and cellular dysfunction – and they would die. I wouldn't be here writing this, nor would you be there reading this. At first glance, you might think that referring to the CDR pathways as a "fountain of youth" is a bit of an overstatement. However, we also have to keep in mind the words of Nobel-prize winning author, Albert Camus, "All great thoughts have a ridiculous beginning," and realize that the CDR pathways have only been known to scientists for a little over twenty years. This makes the entire concept of "cells protecting themselves from stress" so novel as to sound somewhat ridiculous –

except for the fact that we already have thousands of scientific studies showing exactly that to be true. For example, we know that lacking an adequately functional CDR pathway means that cells age faster and die sooner, because they lack the ability to protect themselves from cellular stress, but also because they lack the ability to repair damage and adapt to future stressors. With age, both the level of total CDR proteins and the efficiency of their activation decline – leading to reductions in levels of internal protective enzymes and increases in markers of cellular stress.

From my perspective, as a scientist who has been educating about wellness and performance for close to three decades, harnessing the CDR pathways is in many ways the Holy Grail of health and longevity. Three important methods have been scientifically proven to increase both CDR protein levels and activity to reduce cellular stress:

1. Regular exercise
2. Diet high in brightly-colored fruits/vegetables
3. CDR-activating phytonutrients (plant-derived bioactives)

Scientific studies have demonstrated the CDR-activating benefits of a wide range of phytonutrients, such as catechins (from tea), curcumin (from turmeric spice), quercetin (from apples and onions), flavonoids (from dark chocolate), carotenoids (such as lycopene form tomatoes),

xanthohumols (from hops in beer), resveratrol (from red wine), anthocyanidins (from pine bark), and many others.

So, if our bodies have the ability to produce their own protection from cellular stress, and we can stimulate that protection with herbs, spices, and plant compounds, you might be asking yourself why everyone isn't following this approach already. Why isn't everyone inducing this natural "fountain of youth" to improve their health and possibly extend their lifespan? One reason is because we've only known about the CDR pathways for about 20 years – since their discovery by several research groups in the early-to-mid-1990s. In nutrition research and biochemical circles, 20 years is practically yesterday, so while the idea of CDR activation for reducing cellular stress and promoting health is well-accepted among scientists, it has not had time to "cross-over" into the mainstream public knowledge (even among health professionals, most of whom have never heard of CDRs).

This idea of "making antioxidants" (naturally within our cells) compared to the standard approach of "taking antioxidants" (in the form of isolated high-dose vitamin supplements) is a fundamentally different approach to protecting the body from cellular stress—and might just be the future of how we protect ourselves to enhance our overall well-being and improve how we feel, look, and perform at all levels.

British science-fiction writer Arthur C. Clarke famously said that, "Any sufficiently advanced technology is indistinguishable from magic" – which is exactly where natural CDR pathway activation stands today. The "technology" is actually very old, ancient in fact, because it relies on the phytonutrients in herbs, spices, and plants used in traditional medicine to combat cellular stress and

restore balance. But the "magical" aspect is due to the relatively newly discovered CDR pathways through which these phytonutrients exert their healthful benefits. For those individuals open-minded enough to see the possibilities, the future is indeed bright, especially because that magical future is actually right here for them to take advantage of today.

The Goldilocks Approach: Getting a "Just Right" Balance

For many years, I've been a huge fan of the TED Talks series of lectures—"Ideas Worth Spreading"—and have always wondered if someday I'd get to deliver one of my own.

Twice in 2014, I was invited to the TED stage to present my ideas about cellular stress and biochemical balance - first in April at TEDxSandy (Utah) and again in September at The 431 Project (Vermont). Both of these events were locally organized TED events focused on stress and health, and can be viewed on YouTube or linked to from my blog site at www.ShawnTalbott.com.

Since my main area of research and education concerns the concept that "biochemistry drives behavior," I discussed in these talks how being in balance—or being "just right"—can help us to become the best version of ourselves (Best Future You). By "best future you," I mean that the reason we feel, or look, or perform at our best level, is because of biochemical changes in our individual cells. It's this internal cellular balance that leads us to feel energetic (or fatigued), or to look vibrant (or worn out), or

to perform at our peak mental and physical potential (or feel like we're burned out).

Relationship of Cellular Stress to Health Outcomes

Recall from above that every cell in our body contains an exquisitely designed system of protective enzymes and repair proteins. This built-in surveillance system, called the CDR-pathways, is very much like an internal cellular thermostat for stressors that can damage our cells and ruin our health. The CDR-pathways sense – and respond to – a variety of damaging cellular stressors such as reactive oxygen molecules from sunlight or air pollution. Left unchecked, these cellular stressors cause damage to delicate cell membranes, genetic material (DNA), and mitochondria (our cellular energy factories) – leading to disease, dysfunction, and what we observe as the "aging" process. As cellular damage accumulates, each of the trillion cells in our body works less and less efficiently – and we're less likely to feel energetic, or focused, or motivated, or even as happy as we could be. However, by naturally triggering CDRs, and protecting our cells right down to the genetic level, we have a built-in "switch" that can help us to feel fantastic, look younger, and achieve peak performance. This scenario of being able to feel our best, look our best, and perform our best, is what I refer to as your "best future you" – and it's achievable by triggering CDRs.

In January 2015, I delivered a scientific poster presentation at a research conference held at Cambridge

University in England. The focus of the 3-day conference was solely on CDR metabolism and the potential health benefits of CDR activation. Some of the most interesting presentations showed how the CDR pathways is involved in protecting cells from a variety of stressors that can lead to cancer, arthritis, heart disease, and neurological problems such as Parkinson's and Alzheimer's. Improving CDR metabolism, especially when we do it naturally with balanced phytonutrients, has the potential to deliver an amazing collection of wellness benefits, including:

1. Slower Aging (less oxidation)
2. Reduced Pain (less inflammation)
3. Reduced Cancer Risk (oxidation/inflammation)
4. Higher Energy (lower fatigue)
5. Better Mood (reduced depression)
6. Younger Looking Skin (fewer wrinkles)
7. Improved Mental Focus (reduced brain fog)
8. Less Body Fat and Easier Weight Loss (improved metabolism)
9. Enhanced Physical Performance (endurance/stamina/power/muscle)
10. Improved Stress Resilience (less tension/stress)

Manage Cellular Stress to Feel, Look, and Perform at Your Best

Now that you have been introduced to the concept of oxidation and related cellular stressors and learned a little about how they can contribute to cellular damage and dysfunction, it is time to consider what you can do to manage this process to improve how you feel, look and perform. Remember, as long as the body is not overrun by free radicals and other damaging toxins, it can generally prevent or repair normal, day-to-day cellular damage via induction of the CDR pathways. The trick to fighting those cellular stressors, as with so many other aspects of health, is to find the right balance.

When it comes to antioxidant nutrition, your best approach is to eat five to ten servings of brightly colored fruits and vegetables throughout the day. In general, brighter is better, with each color group representing a major class of antioxidants: Think red tomatoes (lycopene), orange carrots (beta-carotene), blueberries (flavonoids), green spinach (chlorophyll), yellow squash (lutein), purple grapes (resveratrol), red onions (quercetin), and blackberries (anthocyanins). Try to get a few servings of each color group every day, because, even though a particular "color" indicates a predominant family of antioxidant nutrients, each fruit or vegetable choice also contains hundreds of other nutrients that work together to deliver balanced protection against cellular stressors.

If you have trouble consuming all the fruits and vegetables that you need, and you choose to supplement your diet to boost your antioxidant levels and overall cellular protection, then keep this in mind: It is the overall collection of several complementary antioxidants that's

important, not any single “super” antioxidant. Often, you’ll see advertisements touting the “best” or “most powerful” antioxidant nutrient. But recent scientific research clearly shows that supplementing with too many isolated or unbalanced antioxidants may be even worse for long-term health than getting too few antioxidants.

Excessive levels of antioxidant supplementation (for example, too much isolated vitamin E or beta-carotene), can actually lead to more oxidation, cellular stress, and tissue damage rather than protection. That happens because, under certain circumstances, excessive doses of unbalanced dietary antioxidants can become pro-oxidants and can interfere with the body’s own protective mechanisms, particularly the CDR pathways. In other words, instead of fighting oxidation and reducing oxidative stress, the excess intake of these nutrients can actually promote oxidative damage in cells throughout the entire body.

The Antioxidant Network

If you’re overexposed to free radicals or other cellular stressors on a regular basis (i.e. polluted air, cigarette smoke, exhaust fumes, sun exposure, heavy metals, chronic stress, etc) or your diet is less than optimal (low in fruits/veggies or high in processed carbs and sugars), then it is almost certain that you could benefit from some bolstering of your cellular defenses.

The concept of an “antioxidant network” in the body emphasizes the idea that our best defense against free radicals is a collective protection of several antioxidants that is most important, rather than any single “super”

antioxidant. This is a large part of the reason for recommending that we all strive to eat 10-12 servings of brightly colored fruits and veggies throughout the day—just like those described in earlier paragraphs. Ideally, you want to try to get a few servings of each color group everyday so you get an ample supply of different types of complementary cellular protectors.

But what if you have difficulty consuming all the fruits and veggies that you need? If you're like most people, you've probably considered supplementing your diet to improve your antioxidant intake. If so, keep in mind two critically important factors. The first is the growing list of large-scale research studies, some of them mentioned earlier, that have revealed health problems associated with high-dose antioxidant supplements. The second is to understand that the body is actually able to increase production of its own internal antioxidant enzymes (glutathione peroxidase, catalase, superoxide dismutase). Remember—these internal antioxidant enzymes are as much as one million times more effective in fighting free radicals than standard antioxidants supplements, meaning that "making" your internal antioxidants may be much safer and more effective than "taking" external antioxidant products.

As stated above—and it is worth stating again, because it is a crucial point—when it comes to antioxidant supplementation, "more" is not "better," because it is the overall collection of and balance between several antioxidants that is important, rather than any single "super" antioxidant. This concept of balancing supplemental antioxidants is referred to as the "antioxidant network." This network generally comprises five major classes of dietary antioxidants, as shown below:

- Vitamin C "complex" (ascorbic acid plus flavonoids)
- Vitamin E "complex" (4 tocopherols & 4 tocotrienols)
- Thiols (sulfur-containing compounds, such as lipoic acid and cysteine)
- Carotenoids (including beta-carotene, lycopene, and lutein)
- Flavonoids (including polyphenols from citrus, anthocyanins from berries, and catechins from tea)

Small, combined doses of these antioxidant nutrients consumed in one's diet will help combat free radicals directly. Further, they can also regenerate one another following free radical quenching, thus delivering a more effective and safer antioxidant regimen than one with higher doses of single isolated antioxidant nutrients. This combined approach to antioxidant supplementation is also logical because certain antioxidants will work primarily against certain free radicals and in specific parts of the body (for example, vitamin E against hydroxyl radicals and within cell membranes or vitamin C against hydrogen peroxide and within aqueous spaces).

Thousands of studies have clearly documented the beneficial effects of dozens of antioxidant nutrients when consumed as part of a diet rich in fruits and vegetables, and thousands of nutrients and phytochemicals possess significant antioxidant activity. Increased dietary intake of antioxidant nutrients—such as vitamins C and E, minerals

such as selenium, and various phytonutrients that include extracts from grape seed, pine bark, and green tea—have all been linked to reduced rates of oxidative damage. This intake of antioxidants may also help reduce the incidence of chronic diseases like heart disease and cancer.

But mega-dose supplementation with isolated synthetic antioxidants can easily become a case of "too much of a good thing" and actually begin to interfere with normal cellular metabolism. This concept of antioxidant network balance—not too few, but also not too many—requires remembering that cells need representatives from each and every one of these categories to mount the strongest antioxidant defense. Think of it in sports terms: Even if you were the best swimmer in the world (say, Olympic gold medalist Michael Phelps), you're not going to win the Ironman triathlon (swim/bike/run) without also being a strong cyclist and runner. The analogy of baseball works as well. If your team included the best home run hitter, but had only poor pitching and fielding, then your baseball team would probably not win the World Series. The same thing holds true with your antioxidant defenses—green tea, vitamin E, or beta-carotene may all be wonderful antioxidants on their own. But combining them to create a network that performs together in different parts of the body and against different types of free radicals is by far the most effective.

Just as with other aspects of your health and lifestyle, if you keep the concept of "balance" in mind when it comes to your antioxidant nutrition, then your body will be healthier, stronger, and more able to respond to the demands of living, working, and "playing" at the highest level possible.

Chapter 3 - Antioxidants are Killing You – by Making Cellular Stress Worse

In the last two chapters, we discussed how excessive exposure to a variety of stressors, such as free radicals, can lead to cellular stress, damage to cell membranes and DNA, and a host of potential health problems. We also learned about the potential for bioactive nutrients to restore biochemical balance and protect us from the damaging effects of cellular stress. So far – so good.

How then, is it possible that certain antioxidant supplements might actually be "bad" for us? How could the vitamin pills that we think are protecting us are actually causing us harm by accelerating the aging process and even increasing disease risk?

Let me make one point very clear. I am a staunch advocate of the regular use of properly balanced dietary supplements. I've written two popular and award-winning textbooks about dietary supplements, taught graduate-level university courses about the science behind dietary supplements, and designed and researched several dozen dietary supplement products for many different companies in the nutrition industry. I'm also a frequent and enthusiastic consumer of dietary supplements—both for myself and for my family.

I very much view supplements as one of the most powerful tools— along with proper diet, regular exercise, adequate sleep, balanced stress, and social connection—for maintaining health and improving quality of life.

However, when it comes to certain supplements, especially antioxidants, it can be too easy to get too much of a good thing. As alluded to briefly in the preceding sections, a growing number of research studies are showing that high-dose antioxidant supplements, including vitamin E, selenium, and beta-carotene, may have a dark side, upsetting and interfering with our body's natural protective defenses.

When we consider cellular stress, we need to keep in mind the "Goldilock's Principle" of biochemical balance – meaning that we want our exposure to cellular stressors to be "just right" – not too high or too low. This also means that while we certainly don't want to have "a lot" of stress exposure, we also don't want to have "none" – because optimal health and peak cellular performance is typically found when we have "some" stress as well as ample capacity to adapt to that stress.

It has been estimated that approximately 2 to 4 percent of all oxygen consumed by our body is converted to reactive oxygen species (ROS) with the potential to damage cell membranes, DNA, mitochondria, and other cellular structures. This amount of ROS would be roughly equivalent to an annual creation of nine pounds of free radicals created by the human body. Nine pounds per year is what we might consider to be our "baseline" or "normal" exposure to cellular stress from free radical exposure – but that does not account for the "extra" cellular stress that comes from exposure to free radicals from sunlight, air pollution, secondhand smoke, or stress. If our only source of cellular stress was our normal baseline metabolic production of free radicals, then we could likely adapt just fine on a diet of brightly colored fruits and vegetables. But, if we're not eating those daily 5-10 servings of fruits/

veggies, or if we have "extra" exposure to additional cellular stressors, then we might need the added support and protection from dietary supplements. But, which supplements to choose and which supplements to avoid?

How Can Antioxidants Be Dangerous?

There is no denying that a range of national nutrition surveys show clearly and convincingly that nutrient inadequacies are widespread in the United States – and that multivitamin supplements can help to "close the nutrient gap" that so many people are failing to attain through diet alone. There are also several large long-term controlled research trials where relatively low doses of balanced/mixed blends of vitamins/minerals/antioxidants have shown certain potential health benefits.

Scientists have known for many years that high doses of isolated nutrients can actually cause more problems than they prevent. Recent examples are beta-carotene in smokers (leading to more lung cancer) and vitamin C in cancer patients (which protects cancer cells more effectively than it does healthy cells). The "take-away" message from such studies is not that antioxidant vitamins are always "bad" – but rather that synthetic, isolated, high-dose antioxidant supplements are bad.

Consider several recent examples in prominent scientific and medical journals, showing that high-dose antioxidant supplements can lead to higher rates of lung cancer with beta-carotene and vitamin A (New England Journal of Medicine, 1996), higher rates of skin cancer with vitamins C & E and the mineral selenium (Journal of

Nutrition, 2007), and higher overall mortality (death) rates from a variety of antioxidant vitamins and minerals.

In 1994 the Alpha-Tocopherol, Beta-Carotene (ATBC) Lung Cancer Prevention Study was published in the Annals of Epidemiology – and the results shocked the nutrition and medical communities. ATBC was a very large clinical study of more than 29,000 male smokers aged 50-69 years old designed to investigate the protective effects of vitamin E and beta-carotene on preventing lung cancer and other cancers. Subjects took 50mg/day of vitamin E (alpha-tocopherol), or 20mg/day of beta-carotene, or a combination of both, or a placebo, for an average of 6 years. Results showed no benefit of vitamin E and a significant 16% increase in lung cancer risk with beta-carotene.

In 1996, results of the Beta-Carotene and Retinal Efficacy Trial (named "CARET") were published in the New England Journal of Medicine (NEJM). CARET involved more than 18,000 smokers, former smokers, and workers exposed to asbestos to investigate the effects of 30mg/day of beta-carotene plus 25,000IU/day of retinol (vitamin A) on the incidence of lung cancer. After an average of 4 years of supplementation, the risk of developing lung cancer was increased 28% with increased death rates from lung cancer (+46%), cardiovascular disease (+26%), or from any other cause (+17%). The results were so dramatic that the researchers (from some of the top universities and cancer research centers in the country) decided to stop the study almost 2 years earlier than planned.

Since those initial studies in the mid-1990s, there have been thousands of research studies on the positive and negative effects of antioxidant supplements – with most of the largest and longest trials coming to the same

conclusion that high-doses of isolated unbalanced synthetic antioxidants are increasing risk for cancer, heart disease, and overall mortality (death rates). For example…

- The "SU.VI.MAX" study (Journal of Nutrition 2007) followed more than 13,000 subjects taking supplements of vitamin C (120mg), vitamin E (30mg), beta-carotene (6mg), selenium (100mcg), and zinc (20mg) for 8 years – finding a 68% increased risk of all types of skin cancer and a risk of melanoma skin cancer that was more than 4-times higher in the antioxidant users.

- The Iowa Women's Health Study (Archives of Internal Medicine, 2011), found increased death rates (mortality) in nearly 39,000 women (average age of 62 years old) among users of antioxidants supplements, including multivitamins (+6%), zinc (+8%), and copper (+45%).

- The SELECT trial (SELenium and vitamin E Cancer prevention Trial) published in 2011 in the Journal of the American Medical Association (JAMA) followed more than 35,000 men from 427 study sites in the USA, Canada, and Puerto Rico over a period of almost 4 years. Subjects took

200mg/day of selenium, or 400IU/day of vitamin E, or both, or a placebo. Subjects supplemented with selenium alone and the combination of vitamin E plus selenium had an increased prostate cancer risk (9% and 5% higher, respectively), which did not reach statistical significance, but vitamin E users had a significant 17% increase in their development of prostate cancer.

- More than two-dozen recent studies over the last 4-5 years have additionally shown that high-dose antioxidant supplements can actually block many of the healthy adaptations associated with exercise. Regular physical activity is well-known to improve cardiovascular function, enhance insulin signaling (reducing risk for diabetes), accelerate weight loss, reduce blood pressure and cholesterol levels, and increase maximal oxygen uptake – but high levels of antioxidants such as resveratrol (250mgday for 8 weeks), vitamin C (1,000mg/day for 11 weeks), and vitamin E (235mg for 11 weeks) have been shown to blunt these positive effects.

Again and again, we are finding that unbalanced, synthetic, isolated, high-dose supplements fail to keep us healthy and fail to prevent disease (and may actually

cause cellular damage that accelerates the disease process in certain cases). This is especially important because more than half of Americans report taking at least one supplement on a regular basis - that's a lot of vitamin users.

CDR Activation is the Future of Cellular Protection

So if the so-called antioxidant supplements that we take in huge doses are actually harmful, is there anything we can do to enjoy an optimal level of protection from free radicals and the damage they cause?

Luckily, a growing body of scientific findings is revealing how we can support the body's own protective measures, primarily by turning on its own internal antioxidant defense systems. This internal network of antioxidant enzymes is approximately one million times more protective compared to typical antioxidant supplements.

This idea of "making antioxidants" (naturally within our cells) compared to the standard approach of "taking antioxidants" (in the form of high-dose vitamin supplements) is a fundamentally different approach to protecting the body from oxidative stress.

As we've discussed previously, at the very center of this cellular protective response is a family of coordinated pathways collectively known as the Cellular Defense Response (CDR) that serves as a "master regulator" of the body's antioxidant response. You might think of the CDR as a "thermostat" within our cells that senses the level of

oxidative stress and other stressors and turns on internal protective mechanisms.

Soon after CDR was identified (about 20 years ago), a flurry of scientific discoveries began to show how CDRs also regulate genes involved in the production of not only a wide range of antioxidant enzymes (including SOD, glutathione, and catalase), but also important anti-inflammatory proteins and detoxification or ‘‘stress-response’’ genes. These protective pathways are involved in seemingly unrelated areas of health from immune function to tissue repair to cognitive function—but they all share in common the CDR “switch” that enables cells to protect themselves from both internal and external environmental challenges. In effect, CDR induction enables our cells to makes their own “medicines” to help us survive—and thrive—in stressful situations.

Many CDR inducers are naturally occurring and plant-derived, such as sulforaphane from broccoli and curcumin from turmeric, but some others are synthetic compounds being developed as pharmaceutical treatments. Several CDR inducers have progressed from laboratory experiments to human clinical trials and eventual development into pharmaceutical treatments.

The next section outlines some of the natural options for inducing CDR, which has even been shown to modulate gene expression in hundreds of genes associated with superior health of the heart, colon, brain, and literally every tissue and organ system in the body. These scientific findings suggest that our cells possess all the genetic resources required to maintain proper oxidative balance, promote health, and slow the aging process at the genetic level (provided that those cells can adequately activate the CDR pathways as needed).

What Should You Do To Protect Yourself?

Considering the latest studies (and the thousands of studies that have come before them), I still recommend the following when it comes to daily supplementation:

1. **Eat Plenty of Veggies and Fruits:** Focus your efforts on consuming at least 5-10 servings of brightly colored fruits and vegetables every day. The brighter the better, because brightness indicates a higher (and still safe) concentration of protective phytonutrients.

2. **Make, Don't Take, Your Antioxidants:** Forget about "taking" antioxidants (from high-dose "multi" supplements) and start "making" your own antioxidants (by naturally activating the CDR pathways). Effective ways to naturally activate the CDR pathways include:

- Exercise, which "turns on" certain antioxidant systems
- Intermittent fasting also turns on CDR and survival genes
- Many foods have a general activation effect on CDR (blueberries, tea, coffee, broccoli, cabbage, wasabi, Brussels sprouts, onions)

- Focus on spices and herbals as supplements to specifically induce CDR (green tea, turmeric, quercetin, pine bark)

3. **Use Other Supplements:** Keep taking certain other (non-antioxidant) daily supplements depending on your specific needs, for example:

- Vitamin D (up to 5,000IU/day of vitamin D3)
- Omega-3 fatty acids (1,000mg of EPA & DHA from properly purified and concentrated fish oil)
- Calcium (up to 500mg from supplements)
- Magnesium (up to 250mg from supplements)
- Probiotics (beneficial bacteria to maintain gastrointestinal and immune function)
- Consider further supplementation based on individual lifestyle goals. For example, if you're an athlete, you may want a supplement to help you recover better/faster from your workouts or if you're a busy mom, you might want a supplement to help with energy or stress levels - or if you're trying to lose weight, you might want a supplement to help control appetite and burn fat.

4. **No More "Mega":** It bears repeating because it's so important: stay away from mega-doses of ANY supplement, but especially avoid mega-doses of any

antioxidant vitamin or mineral because we already have very good scientific evidence that pharmacological levels of such nutrients can cause more harm than help in the human body.

Final Thoughts

Many scientists, including myself, believe that CDR activation is the "future" of cellular protection and health promotion. This foundation of naturally activating CDRs to "solve" the problem of oxidative stress and other forms of cellular stress is a fundamentally different approach to restoring balance in the body—and one that establishes a solid foundation for healthy living and helping us all to feel, look, and perform at our best.

Much of my research and writing over the past several years has been focused on the general concept of psychological "vigor," defined as a sustained 3-tiered mood state characterized by physical energy, mental acuity, and emotional well-being. In short, a state of high vigor is how people want to feel on a daily basis—and the maintenance of biochemical balance and management of cellular stress are vitally important cornerstones of improving vigor and helping us to reach our peak potential.

The next chapter explores how cellular stress can be effectively managed throughout the body by natural CDR induction, which ultimately helps lead to enhanced vigor and improvements in our mental, physical, and emotional function – helping us feel, look, and perform at our best.

Chapter 4 - Don't Take Antioxidants— Make Antioxidants

The question has been asked for generations—what can I do to improve my state of health? From the perspective of maintaining health and wellness, the proper management of biochemical balance and cellular stress is thought by many scientists to be among the most important (if not the most important) aspects of human metabolism.

We've known for more than 50 years that the cellular basis of "aging" is directly linked to highly reactive molecules called "free radicals" or "reactive oxygen species" (ROS). These ROS can react with and cause damage to cellular structures throughout the body, especially to cell membranes, DNA (genetic material), and mitochondria (where cells generate energy). As this cellular damage accumulates, our cells cannot function properly, and we recognize the common symptoms of "aging," such as reduced energy levels, creaky joints, wrinkled skin, and many others that make us feel and look older and worn out. Too many people think that theses age-related changes are "inevitable," but the scientific evidence shows us quite clearly that by managing oxidative stress within healthy ranges, we can help people not only reduce the signs of aging, but to feel, look, and perform at their best.

As a scientist who has studied biochemical balance and cellular stress for the majority of my career, I can say with conviction that the proper management and balance of cellular stress is often the fundamental difference between a healthy life filled with abundant vigor, and an unhealthy life or feeling burned out and exhausted. Dozens

of peer reviewed scientific studies at universities around the world and published in some of the most prestigious scientific journals show how a range of natural ingredients help to activate the body's own protective mechanisms. The right blends and combinations of phytonutrients have been shown to reduce cellular damage by as much as 40 percent within thirty days (an astonishing amount of protection in such a small period of time).

As mentioned, at the heart of this cellular protective pathway is the Cellular Defense Response (CDR) that serves as a "master regulator" of the body's antioxidant response. Again, the best way to think of CDR is as a "thermostat" within our cells that senses the level of cellular stress and turns on internal protective and repair mechanisms. Interestingly, while we know that there are numerous CDR-inducers in the natural world, we also know that specific combinations of ingredients can maximize gene expression in hundreds of genes associated with superior health of tissues and organs throughout the body. This suggests that our cells possess all the genetic resources required to maintain proper oxidative balance, promote health, and slow the aging process at the genetic level by naturally activating the CDR pathways.

CDR: The Past

It can be scary to think that our own body is producing the damaging ROS molecules described above as a normal part of living and breathing, but it's even scarier when you realize that ROS and other cellular toxins are all around us in the environment in the form of sunlight, car

exhaust, air pollution, cigarette smoke, poor diet, and many other sources. Our bodies are constantly being bombarded by free radicals and related stressors, and constantly under threat of cellular damage and dysfunction—unless we do something to protect ourselves.

In the late 1960s, researchers at Duke University, discovered that the body produces its own protective enzyme called superoxide dismutase (SOD) that is able to counteract the cellular damage caused by free radicals. For more than twenty years, scientists knew that SOD and other protective proteins, such as catalase and glutathione, could help reduce cellular stress, but nobody knew how to naturally increase levels of these proteins in the body. Attempts to develop oral versions of SOD and glutathione were met largely with failure, because as large proteins, they were quickly inactivated by digestive enzymes in the gastrointestinal system – so none of their protective activity reached the cells of the body. In the mid-1990s, researchers in Japan and around the world discovered the molecular "switch" that turns on the production of SOD and related cytoprotective enzymes. Further research, including thousands of studies published within the last few years, shows us quite clearly that our individual cells possess an entire system of interconnected protective mechanisms that counteract cellular stress, enhance cleanup of cellular damage, and slow the aging process.

CDR: The Present

Today, we have a good understanding that CDR is the basic foundation for the body's cellular protective response. We know that myriad CDR pathways act in

concert as a “master regulator” of the body’s antioxidant, anti-inflammatory, stress resilience, internal repair, immune surveillance, and detoxification responses. Soon after scientists identified CDR, a flood of scientific findings began to further reveal how CDR also governs genes responsible for the production of not only a wide range of antioxidant enzymes (SOD, glutathione, and catalase, etc.), but also important anti-inflammatory proteins and detoxification or ‘‘stress-response’’ genes. It’s important to emphasize that these protective pathways governed by CDR are involved in extremely critical areas of health from immune function to tissue repair to cognitive function – so it’s a much bigger and more important discovery than “just” being a more effective approach to reducing oxidative damage. In essence, the activation of CDR allows our bodies’ cells to create the necessary “medicines” that help us survive and thrive in the face of the numerous health threats populating today’s modern world.

CDR: The Future

The future of CDR is an exciting one for sure. As I’ve mentioned, many in the scientific and health arenas strongly believe that CDR activation is a key player in how we safeguard our cells, tissues, and organs towards the ultimate end of improving overall wellness in all aspects of mind and body. This foundational idea of naturally activating CDR to “solve” the problem of a variety of cellular stressors is a fundamentally different way of restoring balance in the body. In fact, it’s one that enables people to effectively address the root causes of the health

problems that are preventing them from feeling, looking, and performing at their best.

Natural Induction of CDR

A number of natural dietary compounds have been shown to modulate gene expression in hundreds of genes associated with superior health of the heart, colon, and brain—suggesting that our cells possess all the genetic resources required to maintain proper oxidative balance, promote health, and slow the aging process at the genetic level by triggering the CDR pathways.

Interestingly, many "healthy" foods may actually owe many of their health-promoting benefits to the induction of CDR pathways by naturally occurring bioactive compounds. As a nutritionist, I certainly want to encourage everyone to eat as many servings of brightly colored fruits and vegetables on a daily basis (ideally 10-12 servings based on the latest anti-cancer and heart- health recommendations). But as a "realist" I also understand that getting enough fruits and veggies is difficult for many of us. Whether due to cost, convenience, or personal preference, the average person consumes only a little more that two servings of fruits and vegetables (and often, that means a slice of lettuce on your hamburger with a side of French fries).

When we can't consume those 10-12 servings of vegetables and fruits, the next-best approach is to use targeted dietary supplements to naturally induce CDR—and here we have a wealth of scientific evidence for combinations of herbs that reduce cellular damage by inducing CDR. Many of these herbs have been used for

thousands of years in traditional Chinese medicine (TCM) and traditional Indian medicine (Ayurveda). Very often, TCM and Ayurvedic blends are synergistic blends of herbs in small doses that, because of their synergy, have a profound effect in the body.

Hundreds of natural bioactive plant compounds are known to trigger the CDR pathways – and dozens more are being discovered every year. In many cases, the main reason that a particular fruit, vegetable, spice, or herb is "good for us" is because of its ability to trigger CDR and set in motion the production of the cell's own protective proteins. We've known for decades that foods like tea, berries, and citrus fruits contain antioxidants (flavonoids) that reduce risk of diseases such as cancer, heart disease, diabetes, and dementia. Just in the last few years, we've learned that these flavonoid-rich foods are "good for us" because they naturally trigger CDRs – thus setting in motion our internal protective mechanisms. Recent scientific evidence is uncovering that the anti-inflammatory effect of healthy spices such as turmeric (curcumin) and ginger (gingerols) is due to CDR triggering; that the mental-focus benefits of herbs such as ashwagandha (withaferin) and bacopa (bacopasides) are due to CDR triggering; that the anti-cancer effects of green tea (catechin), pine bark (proanthocyanidins), garlic (allicin), and broccoli (sulforaphane), are due to CDR triggering. Unfortunately, even as modern scientific evidence is rapidly accumulating about the health benefits of triggering CDR, we're eating fewer fruits and vegetables than ever, using lower amounts of spices, and almost completely ignoring the natural herbal medicine chest that is right at our fingertips.

CDR Synergy

Above, I discussed some of the powerful individual herbals that have been shown to enhance the activation of CDR. In a recent presentation that I delivered at the first-ever scientific symposium dedicated to understanding the coordination of CDR pathways (January 2015 it Cambridge University in England), I outlined the ability of certain combinations of phytonutrients to display "synergy" in the ability to activate CDR pathways. Synergy refers to the ability of a combination of ingredients to produce a combined effect greater than the sum of their separate effects. It's like finding that instead of one plus one equaling two (what we call an "additive" effect), we find that one plus one equals five or ten (a "synergistic" effect).

At the Cambridge University conference, I presented a range of scientific data on blends herbs with demonstrated effects in reducing oxidative and inflammatory stress. The findings of these studies, which show a definite array of benefits for inducing CDR and significantly reducing cellular stress, have been published in several prestigious, peer-reviewed scientific journals (many of which you can locate on research databases such as www.PubMed.gov).

The sections that follow will outline examples of CDR activation, reduction of cellular stress, and health benefits in several important areas: cancer, cardiovascular disease, brain & neurological conditions, skin, and other tissues and functions.

CDR and…Cancer

More than one thousand scientific publications describe the relationship between CDR activation and various types of cancer. As described earlier, natural activation of CDRs is perhaps the most important approach to cell defense and survival, because of the simultaneous protection of cells and tissues from a variety of toxicants and carcinogens.

Because CDR activation increases dozens of cellular protective functions, several pharmaceutical activators of CDR are under study in clinical trials. For instance, researchers from the National Cancer Institute state in their review of several studies, that CDR pathways are, "a promising molecular target for cancer prevention" (Cancer Prevention Research, 2008). Researchers from China found that CDR pathway activation, "plays a critical role in the protective mechanism of cells" (Food Science and Human Wellness, 2013). Other findings from a study published in the July 2004 issue of Molecular Cancer Therapeutics suggest that CDR can positively influence the expression of genes linked to cancer inhibition. And recently, results from a Rutgers University-based study found that the defense enzymes mediated by CDR-signaling pathways can contribute to cellular protection against . . . carcinogens (Pharmacology & Therapeutics, 2013). While more research is still needed, these studies and others comprise a growing body of evidence demonstrating that CDR activation is indeed a potentially powerful weapon against cancer.

Skin Cancer

Researchers from the Department of Pharmacology, Toxicology & Neuroscience at Louisiana State University found that CDR-activating herbs could suppress both the development and spread of skin cancer. Elevated levels of protective antioxidant enzymes, including MnSOD (+21%) and SOD (+35%) led to a 57% reduction in number of skin tumors (PLoS One, 2009). In a follow-up study, the same research group found that CDR-activating herbs significantly reduced the development of skin cancer following exposure to carcinogenic (cancer-causing) chemicals (PLoS One, 2010) – suggesting that the multiple modes of action in CDR-activating herbs could potentially be used as novel chemopreventive agents due to their ability to modulate underlying mechanisms involved in carcinogenesis (Enzyme Res. 2011).

Colon Cancer

Due to the multiple modes of action of CDR-activating herbs, researchers from the Department of Medicine at the University of Colorado at Denver investigated effects on activation of CDR and dozens of cellular protection genes (Mol Aspects Med. 2011). CDR-activating herbs significantly modulated 25 of 28 (89%) colon carcinoma gene targets, leading the authors to conclude that CDR activators "may well spawn a new class of drugs to target the so-called 'diseases of aging,' including cancer, cardiovascular diseases, inflammatory and autoimmune diseases, and neurodegenerative diseases."

Breast Cancer

CDR-activating herbs were shown to suppress the growth and spread of breast cancer by researchers from the Feist-Weiller Cancer Center at Louisiana State University (The FASEB Journal. 2012). The study compared the potential of CDR-activating herbs and Tamoxifen (an existing drug used to treat breast cancer) to reduce the growth/spread of human breast cancer cells. Results showed that CDR-activating herbs and Tamoxifen were effective in reducing breast cancer cell growth by many of the same biochemical signals (PGDF, IL-5, MCP-1, Angiogenin, GM-CSF, and IL-6).

Ovarian Cancer & Myeloma (Bone Marrow Cancer)

Researchers from the Mayo Clinic College of Medicine (Prasongsook, Biomedical Sciences Thesis, 2014.) showed that several CDR-activating herbs produced a range of significant anti-cancer effects against ovarian cancer and myeloma (bone marrow cancer). In a series of studies funded by the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health (NIH), CDR-activating herbs were shown to have anti-cancer effects in ovarian cancer cells and myeloma (bone marrow cancer) cells, while sparing normal healthy cells. CDR-activating herbs showed anti-tumor and anti-proliferative effects (reduced tumor formation and growth) across 8 different ovarian cancer cell lines, including both chemotherapy-sensitive and chemotherapy-resistant cells (Cisplatin/cisplatinum and

Taxol/paclitaxel). CDR-activating herbs showed selective cytotoxicity (cell-killing) effects in ovarian cancer cells and myeloma cells – while sparing normal (non-cancerous) cells.

The Importance of CDR Balance for Cancer

In addition to the wide range of "anti-cancer" studies suggesting a chemo-preventive role of CDR-activation, there are a handful of recent studies pertaining to the role of one specific CDR pathway (Nrf2) in both cancer prevention and cancer development/progression. Some of the recent publications include effects on cellular metabolism due to mutations in certain genes that may increase the risk of some types of cancer (such as the human BRCA1 gene associated with risk for breast cancer).

What some of these mutation studies suggest, is that some forms of cancer can "hijack" different aspects of CDR metabolism, such as the Nrf2 pathway, to help those cells escape detecting and elimination. The way that this happens in certain types of cancer is by continuously activating the Nrf2 pathway (an abnormal process called "constitutive" activation). In this mutated scenario, the protective Nrf2 pathway is "always on" – which is an abnormal situation that is completely different from the temporary induction (transient or pulsatile), whereby the Nrf2 pathway and other CDRs protect cells. It is through the pulsatile nature of CDR-induction that many scientists feel that cells are optimally protected by natural dietary ingredients such as sulforaphane from broccoli, flavonoids

from berries, and herbal constituents including pine bark, green tea, turmeric, and others.

It might help to think of the difference between abnormal constitutive (always "on") activation compared to natural pulsatile (fluctuating "on/off") activation of the CDR pathways as you might think of the light from a desk lamp. When you need more light, you flip the switch and the light bulb brightens the desktop until you flip the switch back off. This is all good—you get light when you need it and dark when you don't. But, it can all go wrong when you flip the switch on and forget to switch it off—because the light comes on and stays on—and you end up burning the house down because the bulb got too hot and caught the drapes on fire!

In this light bulb example, the light is neither good nor bad—but it's the balance of when we have it switched on or off that determines the ultimate outcome. CDR induction is something that has the potential to help virtually anyone to effectively manage and balance their biochemical balance and cellular stress, by transiently activating cellular protective mechanisms against damage caused by various stressors. But, like every biological system, it comes down to a matter of proper balance, which is where natural pulsatile induction of the CDR pathways really shines.

When it comes to people undergoing active treatment for cancer (i.e. chemo- or radiation therapy), it is typical for oncologists (cancer doctors) to want no dietary or herbal supplements in the mix. This is because every type of cancer, every regimen of treatment, and every patient is a unique collection of variables. As such, it's prudent to remove the potential variable of any supplements and the potential for cancer cells to be "protected" by those

supplements from the oxidizing effects of their chemo/radiation therapy. Another reason for discontinuing all dietary supplements during cancer therapy is that optimal chemotherapy and radio-therapy doses have been determined in groups of people who were not taking supplements, making it prudent for the patient to be in a similar condition to the clinical trial groups. Yet an additional reason for stopping supplementation during cancer therapy is that some chemotherapy agents require processing by liver enzymes, the levels of which might be changed by CDR induction in the liver, the body's primary detoxification organ.

In many situations, the cancer doctors will want patients to stop any supplements during active therapy, but then allow the supplements to be added back into the mix after the therapy is completed to support the CDR induction benefits for immune system function, normal cellular defenses, etc. (but that is always a discussion for the patient/doctor to have and a decision for them to make together).

CDR and… The Cardiovascular System

Cardiovascular diseases are the leading cause of death and disability in the developed world. A critical component to the development – or prevention – of cardiovascular disease is proper balance of internal cellular defense systems, including antioxidant enzymes, detoxification proteins, and housekeeping proteins.

Several cardiovascular diseases are associated with suboptimal cellular defenses, (and thus with elevated cellular stress), including atherosclerosis (blockage of

blood vessels), hypertension (elevated blood pressure), and heart failure (loss of contraction ability). Atherosclerosis is an inflammatory disease characterized by dysfunction of the blood vessel lining (endothelial tissue), leading to cholesterol blockages, narrowing of the blood vessels, and poor blood flow.

In a study from the Department of Medicine at the University of Colorado at Denver (Free Radic Biol Med. 2009), researchers found a significant and synergistic increase in HO-1 (3-9 times) and glutathione (2-4 times) with CDR-activating herbs compared to any of the individual ingredients.

Researchers from Virginia Commonwealth University published a study in Circulation, the scientific journal of the American Heart Association (Circulation. 2009), showing how CDR-activating herbs protect heart muscle cells. The study looked at the damaging effects of high blood pressure, finding that CDR activation increased HO-1 levels to reduce heart muscle damage, protect blood vessels, and improve heart function (despite continued hypertension).

Biomedical engineers from The Ohio State University (Free Radic Biol Med. 2011) have shown that CDR activation via CDR-activating herbs is effective in elevating protective enzymes including SOD (3-fold), HO-1 (7-fold), and catalase (12-fold) – leading to improved blood vessel health. Phytonutrient activation of the CDR pathways was able to keep blood vessels open by reducing overgrowth of the interior linings of specific blood vessels used in coronary bypass grafts (human saphenous veins). Prior to this study, only daily aspirin and anti-cholesterol drugs (statins) have been shown to keep these types of grafts open and unclogged.

Exercise scientists at Colorado State University have shown in two different studies that CDR activation protects coronary arteries (Oxid Med Cell Longev. 2012) and heart muscle cells (Free Radic Biol Med. 2013). In these studies, there was a significant increase in CDR pathway proteins as well as protective antioxidant enzymes, including HO-1 (+778%), SOD (125%), and GPx (120%) – leading to a significantly lower rate of heart cell damage and death.

CDR activation is important to maintaining the health and function of the endothelial tissue, and thus of the entire cardiovascular system. For example, CDR activation is know to directly protect blood vessel linings from cellular stress, but also to improve production of nitric oxide (which increases blood flow) and boost cellular energy levels (through mitochondrial support) – leading to an overall improvement if cardiovascular efficiency and function. In addition, CDR activation leads to increased production of specific anti-atherogenic (heart protecting) enzymes such as heme-oxygenase-1 (HO-1), superoxide dismutase (SOD), and glutathione peroxidase (GPx), which can protect blood vessels from inflammation, reduce high blood pressure, and improve the efficiency of heart muscle contraction.

It is interesting to note that individuals with insufficient CDR activation are likely to be at higher risk for not just cardiovascular problems, but also problems related to cellular damage throughout the entire body, especially those tissues with the highest energy needs (heart, muscle, and brain).

CDR and…Brain and Nervous System

Aging is characterized by a progressive decline in the efficiency of cellular function and the increased risk for disease and death – not a happy future! At the very heart of the aging process is the balance between cellular stressors and our ability to maintain biochemical balance and avoid cellular damage in the face of those stressors. The "free radical theory of aging" suggests that reactive oxygen molecules (free radicals) produced during cellular energy metabolism have damaging effects on all cells and across all tissue in the body – causing cumulative damage over time that ultimately results in aging, dysfunction, and death.

Each of our cells has a built-in system of defense to protect from damage by cellular stressors – the CDR pathways. In the aging (healthy) brain, as well as in the cases of several neurodegenerative diseases, there is a dramatic decline in the body's ability to mount a robust defense against cellular stressors – which increases the vulnerability of the brain and the entire nervous system to damage. For example, oxidative damage to the DNA and cell membranes has been detected at levels more than 10 times higher in the brains of Alzheimer's disease patients and 17 times higher in the brains of Parkinson's disease patients compared to healthy subjects.

Brain neurons and nerve cells in general are high in lipids (fats) that are highly susceptible to attack by free radicals. High levels of damaged fatty acids, as well as damaged proteins, have been identified in aging brains and associated with cognitive deficits. In the brain, such damage to fatty acids and proteins is known to set off an immune/inflammatory response that often leads to further cellular damage when prolonged. Elevated levels of inflammatory cytokines leads to a vicious cycle of further

cellular damage that propagates through a chain reaction across tissues.

Natural plant-derived bioactive compounds (phytonutrients) have been shown to exert both antioxidant and anti-inflammatory effects in brain tissue. For example, known CDR-activating phytonutrients such as EGCG from green tea, curcumin from turmeric, and quercetin from onions have been shown to reduce amyloid plaque accumulation (Alzheimer's) and increase regeneration of dopamine fibers (Parkinson's), suggesting a general neuro-protective benefit of natural CDR activators. Indeed, population studies have shown a dramatic protective effect of diets high in fruits/vegetables and healthy oils (Mediterranean and Okinawan diets) on risk for dementia, Alzheimer's, and other neurodegenerative diseases.

Although the range of brain and nervous system diseases is varied with distinct pathologic features, there is considerable scientific evidence to support oxidative stress as a common pathogenic mechanism in many neurological conditions. Oxidative damage occurs early in virtually all nervous system disorders, including chronic conditions such as Alzheimer's, Parkinson's, Multiple Sclerosis, and ALS (amyotrophic lateral sclerosis), as well as acute brain injury such as stoke and traumatic brain injury (TBI, including concussions), suggesting that oxidative stress plays a prominent role in disease progression. CDR activation is known to be disrupted in many nervous system disorders and brain levels of protective antioxidant enzymes (superoxide dismutase, catalase, glutathione, etc) are typically reduced in neurodegenerative disorders as well as during normal aging. For example, neurons with low CDR activity are more susceptible to oxidative and inflammatory stress, but cellular damage can be reduced

through CDR activation. In both Alzheimer's disease and Parkinson's disease, researchers from the University of Pennsylvania and University of Pittsburgh (J Neuropathol Exp Neurol. 2007) have described an insufficient and disrupted activation of the CDR pathways in neurons located in the areas of the brain affected by the disease process.

Other studies (Free Radic Biol Med. 2009) have shown that CDR-activating herbs often work synergistically. This means that when several CDR-activating herbs are used together on cells, their antioxidant effect is more than the sum of the effects from the individual ingredients. In a recent study funded by DARPA (Defense Advanced Research Projects Agency of the United States Department of Defense), CDR-activating herbs were found to induce CDR and protect brain cells subjected to the stress of high altitude. Results showed that CDR activation was effective in supporting a healthy response to "leaky" blood vessels in the lungs and the brain caused by being at high altitude. CDR-activating herbs were found to induce CDR at a higher degree than a range of prescription drugs for treating altitude sickness and reduce cerebral vascular leak by 62%, suggesting a promising approach to supporting brain health during various forms of cerebral stress.

These and other recent scientific findings have linked CDR activation not only to an elevated antioxidant capacity, but also to increases in other types of protective proteins such as brain-derived neurotrophic factor (BDNF – a brain protein associated with stimulation of neuron growth and with anti-depressive effects). Interestingly, several established natural CDR activators such as curcumin, sulforaphane, spirulina, cannabidiol, and

melatonin, have been shown to exert neuroprotective effects in brain and nerve tissue. While the brain-protective benefits of isolated phytonutrient bioactives is extremely interesting, even more interesting is the emerging approach of scientifically examining the synergistic combinations of nutrients to determine improved potency and efficacy for maintaining optimal brain health and preventing neurodegenerative diseases.

CDR and…Skin (and Aging)

Who among us, whether we're young or mature, wants to look old and worn out? Nobody! Undoubtedly, women are the primary target market for cosmetic marketers because every woman wants to have beautiful, radiant, youthful, and healthy-looking skin. But so do men!

You've heard the old saying, "Beauty is more than skin deep" – and it's true – especially when you realize that our body has a built-in "beauty protection" network inside of every cell, including our skin cells. You'll often hear that the skin has "two layers" (the dermis and epidermis), but the epidermis (uppermost layer) is actually comprised of five distinct layers and the dermis (deeper layer) has two different layers – so our skin actually has seven different layers that protect our delicate (internal) tissues from the damaging (external) environment.

Emerging science is discovering a new approach to caring for your skin, one that addresses what goes on inside you and at the deeper layers of skin (not just the surface) in order to bring forth the most glowing, clear, healthy skin on your outside. Achieving healthy beautiful skin is truly an inside-out process. Looking better, feeling

better, having more confidence, and causing your exterior to reflect your beautiful interior (and vice versa) is what the latest skin science in all about.

Nobody wants to look like they're aging. Americans spend hundreds of millions of dollars every year on lotions, creams, and coatings to be applied to the surface of the skin (the dead part, called the stratum corneum). Many of these concoctions do a wonderful job of smoothing out wrinkles and giving the appearance of younger, healthier skin. The illusion of healthier skin, however, rapidly fades when the beauty cream wears off.

What we perceive as "aging" is actually a complicated and multifaceted phenomenon related to skin breakdown and repair—a cyclical process that we scientists refer to as "tissue turnover." In the case of skin, we call it "collagen turnover." The most effective solution to a multifaceted problem is a multifaceted solution, and that's exactly what topical CDR activation is all about.

Today, the scientific community accepts the fact that chronic cellular stress leads to rapid breakdown in a variety of tissues, including brain neurons, blood vessels, muscles, immune cells, and many more – including skin. Cellular stress in skin cells inevitably leads to skin problems, such as wrinkles, acne, and uneven skin tone.

CDR regulates our body's response to cellular stress and numerous studies have shown that both topical and internal/systemic activation of the CDR pathway can have a wide range of beneficial effects on skin, including reduced rates of skin cancers, protection from ultraviolet radiation, reduced inflammation, enhanced barrier function, and improved wound healing.

In a series of clinical and laboratory studies, various CDR activators (extracts of turmeric, green tea, brassica,

pine bark, and plantain) have been shown to improve skin tone, reduce wrinkles, and generally enhance youthful appearance. These studies show how topical application of CDR-activating herbs results in dramatic improvements in key beauty benefits, including an extremely high percentage of women who felt that their skin was improved in the following ways: looking smoother, younger, firmer, more even tone, and with fewer wrinkles. In another series of laboratory studies to investigate the biochemical and genetic mechanisms underlying such rapid and dramatic clinical benefits, researchers treated isolated skin samples daily with CDR-activating herbs. Findings showed clear evidence of the CDR-activating herbs to:

- Increase CDR-pathway protein levels in skin (thus improving *biochemical* resistance to oxidative stress)
- Boost skin protection from ultraviolet (UV) light exposure (by reducing *genetic* DNA damage)
- Fight the signs of aging though *all* layers of the skin (resulting in the previously observed clinical benefits of superior protection, appearance, and healthy youthfulness)

The future of science and medicine is targeting the CDR pathways to not only protect our health, but also to actively improve how we feel/look/perform. CDR activation, especially when optimally-synergistic in nature, represents a huge and exciting advance in the pursuit of anti-aging benefits. These benefits extend from *feeling* your best (abundant energy, good mood, sharp mental focus), to *performing* your best (high motivation, balanced metabolism, strong body and mind), to *looking* your best

(healthy youthful skin). Now is the time for you to take advantage of your body's natural CDR capabilities to enjoy a new level of wellness and vitality!

CDR And… Anyone Who Breathes Oxygen?

Oxygen is indispensible to the lives of all mammals on earth, with energy-production and metabolism linked to oxygen-generated ATP production in the mitochondria. Mitochondria are the "energy factories" in each of our cells – every body has trillions of mitochondria – and more than 90% of the oxygen taken up by the body is used by our mitochondria to generate cellular energy from our food. It has been estimated that 1-4% of consumed oxygen is converted to damaging free radicals (super oxide, hydrogen peroxide, hydroxyl radical) and that the rate of free radical generation is proportional to the amount of mitochondria and our rate of energy production (so the more energy we generate, the more damaging free radicals).

All cellular membranes and cellular components (as well as our genetic material, and the mitochondria themselves) are susceptible to attack by free radicals, but the cells of all mammals have a built-in protective pathway that senses cellular stress, minimizes cellular damage, performs a "housekeeping" cleanup/repair function, and reduces cellular stress (CDR pathways). Nutritional antioxidants, from our diets, are referred to as "non-enzymatic" antioxidants (factors such as vitamins C & E, beta-carotene, etc) because they function in a "one-to-one" relationship to quench or counteract free radicals and interrupt the chain-reaction spread of free radical damage. The type of antioxidants that our cells can manufacture

themselves are “enzymatic” proteins such as super oxide dismutase (that fights the super-oxide radical), catalase (that fights hydrogen peroxide), and the family of glutathione enzymes such as glutathione peroxidase/ transferase/reductase (that fight a range of peroxide/ hydroxyl radicals and perform a wide range of detoxification functions).

Among all mammals, management of oxidative stress is important for long-term health. When oxidative stress is low, the body’s own internal protective mechanisms (CDR-mediated enzymes), coupled with dietary antioxidants (non-enzymatic) from a balanced diet high in brightly colored fruits and vegetables, nuts, and whole grains, is likely to provide enough protection. However, when mammals are exposed to elevated levels of oxidative stress, our body may not be able to mount an effective level of protection. Consider some of the common factors that increase our oxidative stress:

- Low fruit/vegetable intake (reduced intake of dietary antioxidants)
- High processed food intake (increased intake of oxidizing factors such as simple sugars and refined carbohydrates)
- Being overweight (even by a few pounds, and especially if the fat is located in the abdominal area, can lead to higher levels of oxidative stress)
- Sunlight exposure (ultraviolet radiation)
- Air pollution (cigarette smoked, car exhaust, particulate matter)

- Exposure to pesticides, herbicides, and other toxins (including mold, phthalates in plastics, PCBs in farmed fish, asbestos, heavy metals, chloroform, chlorine, and even many pharmaceutical drugs)
- Exercise (increased demand for oxygen consumption and energy production)
- Stress (increased stress hormones such as cortisol, which can lead to higher free radical production)
- Aging (increases free radical production and reduces CDR activation)

When you look at the list above and think about which mammals are exposed to high levels of oxidative stress due to their high metabolism, high activity levels, pesticide/herbicide exposure, and,relatively long life – I hope you think about yourself as an example of a mammal who needs efficient CDR activation. How about man's best friend - your dog? Numerous research studies have documented the range of age-related diseases, including arthritis, mental/memory deficits, and cancer – all of which are related to cellular stress, and all of which occur in both humans and canines. For example, the brains of aged dogs accumulate oxidative damage to proteins and lipids (fats), in the same way that occurs in humans – often leading to dysfunction of neurons (brain cells) and a wide range of behavioral and cognitive defects. Considering that the brain of both humans and dogs consumes approximately 20% of the body's total oxygen, and has

both a high content of polyunsaturated fatty acids (very high susceptibility to damage by free radicals) and a low endogenous antioxidant activity relative to other tissues (low ability to protect itself), it is quite logical for us to observe such high rates of age-related brain dysfunction in aged humans and aged dogs. With more than 50 million senior and geriatric dogs in North America (over the age of 7 years), there is a huge potential to help reduce oxidative stress and improve health by improving social interaction, restoring activity levels, and reducing senility associated with advanced age. Indeed, numerous studies have shown that reducing oxidative damage in the brain can lead to significant improvements in cognitive function in aged dogs.

For example, in a recent placebo-controlled study of 80 dogs (Experimental Biology Scientific Conference, April 2015), researchers found some important benefits of CDR-activating herbs for improving health and performance in older dogs. These dogs were 8 years old on average, and were supplemented with the herbal blend or a placebo for 60 days. The group taking the CDR-activating herbs had a dramatic 36% increase in catalase levels (one of our body's most powerful protective enzymes), while the placebo group showed an 11% reduction in catalase levels. This tells us that in a similar manner to how CDR-activation works in humans, the herbal blend is increasing cellular production of our natural internal protective antioxidant enzymes. It's also noteworthy that with this heightened level of cellular protection in the CDR-herb group, the dog owners noticed a significant 23% improvement in their dog's cognitive function and overall physical function. These results demonstrate an important wellness benefit of reducing oxidative stress in dogs.

How to Enhance CDR to Reduce Cellular Stress: A Summary

When it comes to optimally protecting your body—and actively improving how we feel/look/perform—we can all take a range of proactive steps to induce our body's own protective mechanisms:

1. **Stop Taking High-Dose Synthetic Antioxidant Supplements:** The research shows that taking high doses of isolated, synthetic antioxidants (like vitamins A, C, E, beta-carotene, etc.) actually causes harm to the body.

2. **Get Active:** It's clear that exercise "turns on" the CDR pathway and its family of internal antioxidant, anti-inflammatory, cellular repair, and detoxification systems.

3. **Practice Intermittent Fasting (IF):** At least once per month consume nothing except water for 24 hours. Research shows that this type of intermittent fasting can turn on CDR pathways and increase the production of cellular survival genes.

4. **Eat the Right Foods:** Many foods have a general induction effect on CDR, meaning they help spur the production and activity of cellular protection and repair. These foods include blueberries, tea, coffee, red wine, apples, onions, broccoli, Brussels sprouts, cabbage, wasabi, and many others.

5. **Boost CDR with Properly Balanced Herbals:** As mentioned, there are several proven and powerful botanical ingredients that act specifically to induce and activate CDR for the production of antioxidant enzymes and protective proteins in the body. These herbals include pine bark, green tea, turmeric, quercetin, CoQ10, cannabidiol, and many others. The antioxidant enzymes and other protective agents activated by the CDR pathways provide far-greater safeguarding properties than "standard" antioxidants, which means you'll enjoy a significantly wider spectrum of health benefits.

Final Thoughts

When you consider the studies outlined above (as well as the hundreds of similar studies being conducted, published, and presented every month), a very clear picture emerges whereby:

1. Free radical imbalances and related sources of environmental and other stressors lead to cellular stress and cellular damage within cells throughout the body and in every tissue measured.

2. Induction of the CDR pathways effectively reduce cellular stress, prevent tissue damage, enhance internal cellular protective mechanisms, and restore cellular balance (homeostasis).

3. The spectrum of health benefits created by CDR-activating herbs is extremely impressive, bestowing aid in the areas of skin, heart, brain, antioxidant activity, genetic expression, and general anti-aging benefits—the list goes on and on.

While it's very logical to assume that cells that are "less damaged" and "more balanced" would also be associated with "superior function" as well as with feeling, looking, and performing at our best, such studies are currently underway and have yet to be reported in the scientific literature. It just makes sense that healthier cells equate to more efficient bodies and minds— but at this point, we simply don't have specific research data to point to. These types of longer-term lifestyle studies are currently underway in research laboratories and universities around the world. We expect these studies to show a clear link between the prevention of cellular stress and the enhancement of myriad lifestyle factors including increased energy and mood, enhanced weight loss and beauty, and superior mental and physical performance.

I don't know about you, but I'm not inclined (even as a scientist) to wait for the specific study that "proves" to me that it's better to have cells with less cellular stress and lower levels of damage—I think there's more than ample evidence for a health benefit of naturally inducing CDR pathways. I think you'll agree with me that naturally "making" antioxidants is a healthier and more effective approach than "taking" antioxidants.

Chapter 5 – Pillars of Health

In some of my earlier books, I've written about different aspects of metabolism and biochemistry that can become unbalanced and lead to ill health, weight gain, and poor performance. In many ways, harnessing the CDR pathway and its role as a "master switch" in directing the body's response to cellular stress, brings many different aspects of biochemistry together under a concerted and coordinated approach to helping us feel, look, and perform at our best. I refer to each of these four major aspects of biochemical balance as "pillars" of health, including oxidation, inflammation, glycation, and allostation – with imbalances in any of them leading to elevated cellular stress and tissue dysfunction.

For example, scientists and doctors agree that excessive inflammation (due to an imbalance in signaling molecules called cytokines) can lead to accelerated tissue damage and breakdown, so it makes a lot of sense to control inflammation to reduce cellular stress and promote overall health.

But, if you look deeper to find the causes of inflammation, you quickly see other factors that you can control. Because oxidation (caused by free radicals) leads to inflammation at the cellular level, why not also control oxidation as another "trigger" of cellular stress?

Great idea—but why not look even farther up the metabolic chain of events to see if you can control or modulate the causes of oxidation? Doing this shows that glycation (cellular damage caused by overexposure to certain sugars) can lead to oxidation (which can, in turn, lead to inflammation).

Should you stop there? Of course not, because when you look even higher up the metabolic stream, you see that an imbalance in stress hormones such as cortisol and the resulting allostation (inability to adapt to and recover from stress) can lead to glycation, which can lead to oxidation, which in turn leads to inflammation.

Unfortunately, existing scientific or medical research doesn't go any farther "upstream" with regard to the biochemistry of cellular aging and health promotion. Balancing stress hormones is about as far "upstream" as you can go at this time—but that's still pretty good. In addition, we know from both laboratory research and clinical experience that such a coordinated approach to restoring biochemical balance can be very effective in reducing cellular stress through CDR activation. In fact, at the recent Cambridge University scientific conference on CDR metabolism, there were research reports linking CDR pathway activation to improvements in each of the four pillars of health.

Obviously, each of these four aspects of your body's biochemistry is intimately intertwined and interdependent on the others, so saying that any one of these "pillars" is "first" is somewhat arbitrary and situation-dependent. That said, the important take-away message is that having an imbalance in any of the individual aspects (inflammation, for example) can set off a biochemical cascade leading to imbalances in another (such as oxidation) and ultimately increasing cellular stress. They're all intertwined and interdependent. The different aspects of biochemistry act almost like a set of dominoes—when you touch one, you set off movement and changes in all the others. The good news is that when you restore balance in any one area, you can also get the benefit of restored balance in other

areas, with the end result being reductions in cellular stress and optimal levels of health and well-being.

Free Radicals, Antioxidants and Health: A Summary

Before getting into the details of balancing each pillar of health, let's recap the process of oxidation and cellular stress discussed in previous sections. For our discussions, we'll consider oxidation as the "first pillar" of metabolism that can interfere with and disrupt other metabolic or biochemical pillars (inflammation, glycation, and allostation) leading to cellular stress. As such, managing this process is one way to both directly strengthen this key pillar of health, as well as to indirectly support and strengthen other important aspects of cellular metabolism.

Overexposure to free radicals—and the cellular "oxidative" damage they can cause—leads to tissue dysfunction, DNA damage, reduced mitochondrial-energy production, and the ill health that you generally recognize as aging, illness and burnout. Too much oxidation and the resulting cellular stress is bad.

Free radical damage can be reduced by the balanced activity of internal antioxidant enzymes and dietary antioxidant nutrients—remember, not too few or too many, but "just right." The sum of the antioxidant network is more effective than its individual components. In practical terms, this means you want to consume a variety of antioxidant nutrients every day.

Finally, and perhaps most importantly, we especially want to focus on naturally inducing our body's own

protective pathways—particularly the CDR pathway. Consuming more brightly colored vegetables and fruits help do this by virtue of their high content of flavonoids, carotenoids, and other phytonutrients. But triggering CDR pathways is perhaps best done by consuming concentrated herbal extracts such as pine bark, quercetin, green tea, turmeric, and ginger (among others) to increase levels of protective antioxidant enzymes as well as induce a range of housekeeping "cleanup" proteins to facilitate cellular repair. The CDR pathway, which triggers the release of these ultra-powerful antioxidant enzymes, also helps switch on DNA-repair enzymes and regulates chronic inflammation and immune function—all key areas of human health.

For those of us striving to be our "best selves" in terms of how we feel, look and perform, we need to understand that proper management of cellular stress is perhaps the most fundamental aspect of our biochemistry to get under control. Without cellular balance, we're more likely to experience a wide array of detrimental effects, including excessive inflammation, problems with cell-to-cell communication, higher risk for DNA damage, disproportionate levels of fatigue, depression, and brain fog, and trouble maintaining both body weight and skin tone. The list of problems associated with unchecked cellular stress goes on and on, but the bottom line is that by restoring biochemical balance and properly managing cellular stress, we can put our bodies on a very strong foundation of cellular balance that can lead to us achieving that "best self" that so many of us have been striving for.

Inflammation – The World on Fire

The word "inflammation" is derived from the Latin "inflammare"—meaning to "set on fire"—because an injury or infection is typically red, warm, and painful. Think of pain and inflammation as different sides of the same coin – they are driven by different—but related—biochemical factors. Pain and inflammation are normal body processes. Without them, you would literally not be able to survive for very long. Pain is a signal to your body that damage is occurring, and you need to stop doing whatever is causing that damage. Inflammation is a process controlled by the immune system that protects your body from invading bacteria and viruses, but this process also helps regulate heart function, blood flow, and many vital functions. Maintaining a normal balance of pain signals and inflammation is critical to good health and balancing cellular stress.

When this balance becomes disrupted, you experience more inflammation and increased pain along with less flexibility and reduced mobility. When you have too much inflammation, this process—which is supposed to be protecting you—actually causes more and more damage. For example, an overactive inflammatory response is known to stimulate bone breakdown (leading to osteoporosis), interfere with cartilage repair (leading to a worsening of arthritis), and accelerate muscle breakdown (leading to flare-ups in fibromyalgia). Inflammation is also involved in emotional balance and brain function (depression and anxiety). So when your body experiences too much inflammation, you simply don't feel happy. Instead you feel mentally exhausted and burned out—obviously, the opposite of vigor.

Your doctor may also give your unbalanced inflammation another kind of label—one that ends in "-itis." In medical terminology, "-itis" is used to denote inflammation. Therefore, you may have arthritis (inflammation of the joint—"arthros" is Latin for joint), tendonitis (inflammation of the tendon), or fasciitis (inflammation of the fascia—the tough layer of connective tissue over muscles, tendons, and ligaments that can become inflamed following excessive exercise or with lower-back pain and fibromyalgia).

Normal Versus Chronic Inflammation

The normal process of inflammation helps dismantle and recycle older tissues that have become damaged or worn out or that simply need repair. This process of normal healthy inflammation is called "turnover," and it occurs when older tissue is replaced with newer tissue. Before the age of thirty or so, this normal turnover process tends to be perfectly balanced—for every bit of tissue that is damaged and removed, another similar (or greater) bit is put in its place. This means that, under ordinary circumstances, you're always making your tissue stronger and more resilient. After about age thirty, however, the turnover process becomes somewhat less efficient year after year – partly due to a progressive age-related reduction in our body's ability to activate CDR pathways. This causes a very slight loss of healthy tissue—you continue to break down and to remove some tissue, but the amount of healthy tissue added back is just a little bit less than it should be. As you age, the turnover process becomes less and less efficient, and your body's ability to heal itself from

injury is reduced. This imbalance in tissue turnover and the "normal inflammation" process is the primary cause of the loss of flexibility, vigor, and the various "-itis" diseases that people tend to encounter as they get older.

Let's keep in mind that not all inflammation is bad. As you've just learned, inflammation is part of the normal healing and turnover process for any tissue. But when you experience too much inflammation, things go awry – and this state of "too much" inflammation is referred to as "chronic inflammation." With chronic inflammation, healing is suppressed, and tissue destruction is accelerated. Your body simply cannot heal itself or stop the damage when inflammation gets out of control. To illustrate this point, think about the ocean crashing against a protective seawall. The seawall represents your tissues, and the ocean is your inflammatory process. Over time, that wall will become broken and weakened by the crashing waves and will need to be repaired to return to optimal functioning. If the pace of repair fails to keep up with the pace of destruction, then the seawall fails, and the ocean comes rushing in (leading to tissue destruction and dysfunction). You need to maintain the integrity of the seawall (your tissue) by keeping up with repair and maintenance—but you can't do that if the ocean is continually crashing down on you.

Another way to think of chronic inflammation as you would a fire in an apartment building. Let's say you live in a twenty-story apartment building, which represents your body. Then, a fire (inflammation) breaks out on the fifteenth floor, causing destruction (tissue damage) to the entire floor. But your penthouse apartment on the twentieth floor is fine. To put out the fire, you call in the firefighters (immune cells), which may cause a bit more damage by

tearing down some walls and spraying water (cytokines, hormone-like signaling molecules secreted by immune system cells), all in an effort to solve the bigger problem of putting out the fire. Let's now say that the fifteenth floor is a complete loss, while other floors suffer some repairable damage (water damage on the fourteenth floor and smoke damage on the sixteenth floor). The repair process begins on all three floors, with carpenters, painters, and other "builders" brought in to repair the damage. On floors fourteen and sixteen, where the damage is less severe, the repair process might be complete within a few weeks, but on the fifteenth floor, where the fire was concentrated and the damage was most severe, the repair process may take a year.

Your body also has an entire team of "builder" cells in each and every tissue. In cartilage these "builders" are called chondrocytes, in bone they are called osteoblasts, in muscles they are myocytes, in skin they are keratinocytes, and in some other tissues they are fibroblasts—the list goes on and on – and they all respond to cellular stress through the CDR pathway. In your own tissues, you can have the equivalent of a raging fire and firefighting (tissue damage and inflammation). But if you're not able to shut off this process—that is, if your level of inflammation is thrown off by something—then your body is in a continual state of destruction and pain. You'll never be able to get to the rebuilding and repair stages unless you can shut off this process of chronic inflammation. A number of mechanisms are in place to shut down the process of inflammation, including the naturally short half-life of cytokines and other inflammatory molecules and the production of anti-inflammatory cytokines (with such names as TGF-beta and IL-10). Unfortunately, immune-system cells can remain in a

state of chronic inflammation if the “cell-damage” signals keep coming from free-radical damage (leading to oxidation) and from cortisol-induced tissue breakdown (leading to allocation – covered later in this chapter); or if signals to “shut down” the inflammatory process are not “heard” by target cells (as in the case of cells damaged by glycation, a subject covered in next section).

Unfortunately, chronic inflammation is not confined to the tissue in which it starts. Cytokines—such as those labeled IL-6, IL-8, and TNF-alpha—are able to leave the original site of inflammation. They can then travel in the blood to spread inflammatory signals through the blood vessels and into every tissue in the body (leading to metabolic diseases, such as obesity, diabetes, and depression, and structural/damage diseases, such as Alzheimer’s, Parkinson’s, and arthritis). Because most of the cytokine molecules are produced by immune-system cells (specifically by macrophages, neutrophils, and NK cells of the innate immune system), numerous drug companies attempt to control chronic inflammation by suppressing immune function. The problem, of course, is that wholesale suppression of immune function also limits your body’s ability to protect you from actual pathogens—so you’re “protected” from chronic inflammation but become more susceptible to infections and certain cancers. Not a great trade-off!

Keep in mind that the biochemical processes of oxidation and inflammation are inextricably linked—they go hand-in-hand through common immune system pathways. The immune system responds to and creates oxidative “free radicals” and responds to and creates inflammatory cytokines. “Normal” inflammation exists to protect us from invading pathogens (viruses, bacteria, and even

uncontrolled cell growth that could lead to cancerous tumors). Sometimes, however, the walling-off and destroying process of the immune system's inflammatory response doesn't shut off the way it is supposed to. Immune-system cells, such as macrophages (which fight bacteria), neutrophils (which fight viruses), and natural killer cells (which fight tumors), respond to free radicals as if they were toxins. A small amount of free radical signaling is a "good thing" for immune cells, keeping them vigilant to defend us against "real" pathogens. But when free radical exposure becomes excessive, immune cells release a wide array of pro-inflammatory cytokines, such as interleukins (IL-1, IL-6, TNF-alpha), to "wall off" tissues from further free radical damage. Unfortunately, the typical Western lifestyle is a perfect recipe for increasing chronic inflammation, with its high intake of sugar, refined carbohydrates, and saturated fats. That diet, combined with low levels of fiber, infrequent exercise, and sleep deprivation, make it more likely that inflammation becomes too high—and stays that way.

To sum up: The walling-off aspect of the inflammatory process is an ideal response to keep viruses or bacteria from moving into other parts of your body, but free radical–generated inflammation encourages immune cells to fight "yourself" in a vicious cycle of oxidation/inflammation, which ends up creating more problems and eventually leading to a higher state of cellular stress.

Glycation – Sugar Coated Cellular Dysfunction

Glycation is a process by which a sugar molecule (typically glucose or fructose) becomes bonded to a protein or lipid (fat). Most often, glycation occurs in the body when glucose or fructose in the blood remains too high for too long and becomes bonded to cell-surface proteins. A glycated protein—referred to as an "AGE" (advanced glycation end-product)—can be highly reactive and set off a chain reaction of oxidative and inflammatory damage in whatever tissues they occur. AGEs also tend to be "cleared" from the body very slowly, so once they're formed, they have the potential to stimulate these damaging chain reactions for prolonged periods of time.

Some of the main dietary offenders that lead to AGE accumulation and upset biochemical balance are high-sugar foods (such as soda, ice cream, donuts, cookies, or sweetened breakfast cereals) and other foods that quickly convert to sugar or glucose in the bloodstream (including highly processed grains, such as white bread, rolls, or instant rice). Sugar can be toxic to many tissues by permanently attaching to proteins through the glycation process. Wherever sugar attaches, it triggers cellular microdamage that creates inflammation. The inflammation, in turn, accelerates protein breakdown, thus resulting in damage to surrounding tissues. To make matters worse, glycation also leads to cross-linking of proteins, changing healthy tissues from soft, supple, and flexible to stiff, brittle, and painful. These stiffened sugar-protein bonds form in every type of tissue, including joint cartilage, muscle tendons, brain neurons, blood vessels, skin, and even immune-system cells, which is why scientists are finding links between glycation and chronic diseases of "aging," such as cardiovascular disease, Alzheimer's disease, and arthritis.

There are many reasons to keep a tight control of glucose levels. Glucose, which you may often hear called "blood sugar," is the preferred source of energy for the brain, and glucose helps you fully metabolize calories from fat. Blood sugar levels that drop too low may stimulate hunger and cravings, while glucose levels that rise too high will slow your ability to burn fat.

A key intermediary in the interrelationships between blood glucose (glycation), free radicals (oxidation), cytokines (inflammation), and stress hormones (allostation) is the hormone insulin. Most people associate insulin problems with diabetes because of its primary role in regulating blood-sugar levels, but insulin has many additional functions in the body. Not only does insulin regulate blood-sugar levels within an extremely narrow range, but it is also responsible for getting fat stored in the fat cells (adipose tissue), getting sugar stored in the liver and muscle cells (as glycogen), and getting amino acids directed toward protein synthesis (to build muscle). Due to these varied actions, insulin is sometimes thought of as a "storage hormone," because it helps the body put all these sources of energy away in their respective "storage depots" for use later.

The abnormal insulin metabolism described above—known as insulin resistance—leads to a reduction in the body's cellular response to insulin. That reaction, in turn, interferes with regulation of blood sugar, increases appetite, and blocks the body's ability to burn fat due primarily to direct "blocking" of insulin function by cortisol as well as indirect interference with insulin activity by oxidative free radicals and inflammatory cytokines. When insulin resistance is combined with a poor diet (high in fat and/or refined carbohydrates), the result is the metabolic

condition known as Syndrome X, a disorder that can have an impact on virtually every disease process in the body.

We know that inflammation in any tissue can be caused by excessive exposure to free radicals and lead to accelerated "aging" and generalized tissue breakdown. AGEs demonstrate a "direct" problem with cell-to-cell signaling that is compromised by sugar-coated proteins. "Indirect" damage is also caused by an AGE-stimulated increase in oxidation and inflammation. Stress hormones, which we'll discuss in the next section, stimulate the creation of AGEs through an increase in blood-sugar levels.

People with diabetes are obviously at high risk for developing AGEs in a wide range of tissues because of their problems regulating blood-sugar levels. The extreme development of AGEs in diabetics is a key reason for their high rates of oxidative and inflammatory diseases, including nephropathy (kidney damage) and circulatory problems (due to blood-vessel damage).

There are numerous ways to stabilize glucose and reduce your development of AGEs—some of which might seem quite obvious, as you'll see in the short list below, but are also quite effective.

Tips for Stabilizing Glucose

* Consume fewer high-sugar foods (soda, baked goods, refined carbs).

* Consume more low-sugar foods (vegetables, lean meats, healthy fats).

* Consume fewer fried foods (high-temperature cooking creates AGEs in the foods).

* Maintain healthy blood-sugar levels (80–100mg/dL) by:

  - getting regular (intense) exercise
  - getting eight hours of sleep each night
  - incorporating stress-reduction practices into your daily life
  - supplementing with specific glucose-controlling and CDR-activating dietary supplements

The next section, about "allostation" and stress hormones such as cortisol, describes how cortisol exposure stimulates a rapid increase in blood-glucose levels via several mechanisms, including stimulating the release of glucose stored in the liver, interfering with insulin's action to stimulate cells to absorb glucose from the blood, and stimulating overall appetite with specific cravings for sweets. Adding to the connection between cortisol and insulin resistance are an interesting series of studies showing that inadequate sleep causes insulin resistance. This is particularly important because of the well-known link between sleep deprivation as a unique type of cellular stress and elevated cortisol levels. Sleep researchers from the University of Chicago and several other universities have shown that inadequate sleep leads

to a cascade of biochemical events, starting with increased cortisol levels, which induces insulin resistance, leading to higher blood-sugar (glucose) levels, causing increased measures of oxidative and inflammatory damage, stimulating appetite, and eventually leading to abdominal fat (belly fat) gain. The research team compared "normal" sleepers (averaging eight hours of sleep per night) to "short" sleepers (averaging six hours or less of sleep per night). They found that the "short" sleepers secreted 50 percent more cortisol and insulin and were 40 percent less sensitive to the effects of insulin than the "normal" sleepers. Missing a couple hours of sleep can basically put you into a pre-diabetic state with all the associated cellular stress and eventual health problems.

Allostation

Human beings were simply not meant to "carry around" constant disturbances in their stress response to the point that this response reaches the state called "chronic stress." Humans were built to respond to stress quickly and then to have stress hormones dissipate immediately. That is the "acute-stress" response or "temporary" stress, and our bodies do perfectly well when stress comes in periodic bursts, but also goes away or subsides periodically giving us time to recover and adapt. When the body is exposed to wave after wave of chronic stress from the modern lifestyle, it begins to break down.

Animals don't normally harbor chronic stress the way humans do, but when they do (during stress experiments, starvation, injury, etc.), they get sick just like humans do. In study after study, it quickly becomes obvious that the

stress response, although helpful in certain situations, turns negative when the body begins to perceive everyday events as "stressful" events. Over time, stress-related diseases result from either an over-exaggerated stress response (too much response to what should have been a small stressor) or an under-exaggerated ability to shut down the stress response (which causes levels of the stress hormone cortisol to remain elevated and biochemical balance to fall apart).

Because the modern world rarely requires the evolutionary fight-or-flight response to stress, people deny their bodies their natural physical reaction to stress. Unfortunately, the brain still registers stress in the same way as it always has. But because people no longer react to that stress with vigorous physical activity (fighting or running away), the body "stores" the stress response and continues to churn out high levels of stress hormones. Before you know it, you find yourself suffering from "burnout" or simply "tired/stressed/depressed" and feeling as if you have no control over the many stressors in your life. In one of the more ironic twists visited upon humans as "higher" animals, the brain is so "well developed" that the body has learned to respond to psychological stress with the same hormonal cascade that occurs with exposure to a physical stressor. This means that just by thinking about a stressful event, even if that event is highly unlikely to actually occur, you cause your endocrine system to get into an uproar that interferes with your biochemical balance—leading you toward elevated levels of cellular stress and tissue dysfunction.

Cortisol is the body's primary stress hormones – produced by the adrenal glands. Its main "acute" functions are to increase blood-sugar levels (via insulin antagonism),

reduce inflammation, and stimulate immune function. Its main “chronic” effects are to increase blood-sugar levels (via appetite stimulation, so you eat more), increase inflammation, and suppress immune function. When you encounter anything that causes you to feel stress, your cortisol levels go up. If you experience stressful events on a regular basis and are unable to effectively rid yourself of the stressor, then your cortisol levels stay constantly elevated above normal levels. The elevation of cortisol leads to further problems with biochemical balance, such as reduced testosterone and interference with other hormones (such as insulin and thyroid hormones).

This process can be compared to what happens with a line of dominoes, where tipping one hormone off balance (cortisol) leads to a disruption in the next (testosterone) and the next (insulin) and the next (serotonin) and the next (thyroid) and so on, until eventually the balance of your entire system is upset and you feel terrible. Also lined up like dominoes are the other four pillars of health, where cortisol excess increases levels of inflammatory cytokines, oxidative free radicals, and glycating sugars. This increase in stress-induced oxidation/inflammation is due, in part, to the fact that excess cortisol stimulates a chronic immune response that is accompanied by a “respiratory burst” of free radicals from macrophages and related immune cells. And this response is also partly due to the increased creation of AGEs (advanced glycation end-products) that is triggered by the cortisol-induced elevations in blood sugar.

Elevated cortisol levels are also associated with reduced levels of testosterone and IGF-1 in subjects exposed to high stress (IGF-1, or insulin-like growth factor 1, is related to growth hormone). Because testosterone and IGF-1 are anabolic or muscle-building hormones, the

subjects exposed to high stress also tend to have reduced muscle mass and higher body-fat levels. And they also tend to have a higher body mass index (BMI), a higher waist-to-hip ratio (WHR), and abdominal obesity (an "apple" shape). Researchers at the Neurological Institute at the University of California at San Francisco (UCSF) have linked excessive cortisol levels to depression, anxiety, and Alzheimer's disease as well as to direct changes in brain structure (atrophy) leading to cognitive defects—meaning that cortisol can shrink and kill brain cells. All this research points to a consistent reproducible finding—that chronic stress leads to a cascade of biochemical, hormonal, and metabolic disruptions that result in a heightened state of cellular stress and an accelerated "breakdown" in tissues throughout the body, including the brain, heart, blood vessels, muscles, bones, skin, immune-system cells, etc. At the same time, these disruptions also suppress the "buildup" of healthy tissues, because chronic stress retards tissue growth and adaptation—except for one tissue – abdominal fat (which accumulates in response to disruption in any of the four pillars of health). The major problem with abdominal fat, aside from the fact that nobody wants a pot belly, is that this type of fat is also highly associated with increased cellular damage from glycating sugars, oxidative free radicals, and inflammatory cytokines, all of which increase the risk of developing heart disease, diabetes, and cancer.

Stress researchers, including myself, frequently study competitive athletes. For obvious reasons, athletes are extremely interested in balancing the "dose" of stress they deliver to their bodies with the amount of recovery necessary for optimal performance. Keep in mind that we need to consider all sources of stress that an athlete is

exposed to including emotional stress such as relationships and finances; environmental stress such as the sunlight they're exposed to and the air they're breathing; cellular stress from exposure to free radicals, cytokines, glucose, and cortisol; and of course the physical stress of their training regimen. Counteracting the muscle-wasting and fat-gaining effects of prolonged cellular stress becomes a large part of maximizing performance gains while minimizing the risk for illness and injury. For many athletes, the delicate balance between training stress and recovery poses a significant dilemma: To become faster and more competitive, they have to train hard, but training too hard without adequate recovery will just make them slow, because they'll be tired or get sick or hurt.

Athletes who excel at the highest levels are those who are most adept at balancing the three primary components of their programs: training, diet, and recovery. A phenomenon known as "overtraining syndrome" has been linked to chronic cortisol exposure and heightened cellular stress, exactly the same situation that the average non-athletic person faces in their battle with daily stressors and the struggle to maintain biochemical balance. Although chronic overtraining is easy to recognize by its common symptoms of constant fatigue, mood fluctuations, and reduced mental and physical performance (sounds a lot like the burnout and lack of vigor suffered by many non-athletes), it may be difficult to detect in its earlier stages, just like the early stages of stress. Therefore, competitive athletes, like everyone, need to become adept at balancing exposure to cellular stressors with protection and recovery to approach the optimal physical and mental performance they are looking for.

Numerous studies convincingly show that reducing cellular stress—including restoring balance between various measures, such as cortisol, testosterone, glucose, cytokines, CRP, free radicals, and many others—also reduces the risk of dying and increases lifespan. Positive changes in psychological measures of stress, such as a greater sense of "meaningfulness in life," have also been associated with improvements in cellular stress markers. But this "psycho-biochemical" effect appears to cut both ways, because individuals with "downward" financial mobility (such as job loss) tend to have higher indices of cortisol/cytokines, and those individuals with the highest financial stress (poverty) have been shown to have a striking six-year-shorter life expectancy attributable to increased disease risk from excessive cellular stress. In similar fashion, the risk of developing burnout, chronic fatigue syndrome (CFS), or post-traumatic stress disorder (PTSD) has recently been shown to be approximately three times higher in subjects with elevated psychological stress and dysregulations across the four pillars of health.

I hope that this chapter has given you an appreciation of the importance of restoring biochemical balance within each—and between each—of the four pillars of health. In some ways, it may seem that balancing stress hormones is the most important task in reducing cellular stress, because these hormones are so intimately linked with our biochemistry.

But, as stated throughout this section, the pillars are interdependent and intertwined with each other, so it makes sense to strengthen all of them simultaneously to create a truly comprehensive approach to optimal health. This is precisely what efficient activation of the CDR pathways offers us – a "master regulator" of the cellular

response to stress, no matter the source of the stress. As with the example of the dominoes, if you make a positive change regarding one of the pillars, you will set off positive reactions in all the rest. This is what we will discuss in the chapters to come.

Chapter 6 – Feel Your Best

Biochemistry Drives Behaviors

In seeking to build our "best future you" with the energetic feel, youthful look, and peak performance that we all desire, it's important to remember that this state of health is characterized not only by physical aspects of cellular stress, but that state of balance is also transmitted to emotional and mental aspects of health.

When speaking before thousands of people around the country, one of the most important concepts that I try to convey to my audiences is that "biochemistry drives behaviors" and vice-versa. The reason that you "feel" a certain way is because of your underlying biochemistry. The degree to which you're exposed to free radicals, cytokines, cortisol, dopamine, serotonin, insulin, or hundreds of other cellular stress "signals" in the body will influence your feelings of energy, happiness, mental clarity, creativity, appetite, and motivation—in short, your vigor.

Think about how you feel when you're under stress: You often eat more (and eat more junk) and exercise less. You tend to be constantly tired during the day and yet can't relax enough to get a good night's sleep. Stressed-out people also have more heart attacks, more depression, more colds, and less sex. And stress-induced disruptions in their internal cellular biochemistry are at the root of it all. I cannot think of a more dismal picture – and it all links back to the ability of our trillions of individual cells to protect themselves from stress and to repair the damage caused by stress.

Brains, Biochemistry, and Behavior

As I have continued my research in this area over the past several years, I have discovered that the influence of cellular biochemistry goes far deeper than ever imagined. In fact, cellular biochemistry not only drives emotions but motivates actions as well.

Breakthroughs in brain research are giving amazing new insights about these connections between biochemistry, the brain, and behavior. And frankly, it is a complex issue that may be hard to understand. It can be mind-boggling—literally—to realize that your thinking can change not only your moods but also the actual shape and function of your brain. Those changes affect your biochemistry, your level of cellular stress, and, of course, how you feel, look, and perform.

As you read this chapter, these complex concepts will become clearer. For now, let me give you a brief explanation and illustration to show you how these connections between mind-body-biochemistry actually work. First, you have to conceptualize the biochemical processes of your body as a circular loop, not a straight, linear progression. What happens internally is that your cellular biochemistry affects your brain circuitry, which affects your behavior, with each influencing and feeding back on each other. This loop has no "start" and no "end," and each process constantly modifies the others.

What all this means is that the reason that we "feel" a particular way, or the reason that we "behave" a certain way, or the reason our brain "perceives" a certain thing,

comes back to how effective and efficient our cells are at managing cellular stress.

The good news is that if you positively change one aspect of this picture, you'll inevitably exert a positive change the others as well. For example, if you change your behavior—say you begin to take short walks every day or go to sleep fifteen minutes earlier each night—you will, in turn, change your cellular biochemistry and your brain function and performance. Those brain alterations will put you into a mental and emotional state where you will want to continue the behaviors that are creating the positive mood and mental clarity—and the changes in your cellular biochemistry will, in turn, reinforce this "virtuous circle."

Unfortunately, the "circle" can spin in the opposite direction as well. Suppose that instead of walking every day, you act like a "couch potato," sitting on the sofa watching TV for long stretches and eating greasy, sugary foods? That behavior will lead toward fatigue, mental sluggishness, and negative emotions. As your behavior begins having detrimental effects on your brain function and biochemistry, a downward spiral toward burnout is set in motion. If you feel caught in that downward spiral, you are not the only one. Keep reading.

Low Vigor and High Cellular Stress? You're Not Alone

Do you ever feel that you're working harder and harder but still getting further and further behind? If so, you have a lot of company. The average American workweek, research shows, has mushroomed from forty hours to fifty

hours in the past twenty-five years. That level is higher than in any European country and equal to that of Japan. Those extra ten hours of work, however, have not gained workers much. In fact, U.S. workers today are behind in their ability to maintain the same overall standard of living enjoyed a generation ago. At the same time, our expectations have not changed. Even during tough economic times, people still feel pressure to be—or have—the best, whether they strive to own the best car or house or to be the best worker or parent. Talk about stress! And all those expectations are driving many to an early burnout. It is even becoming evident in kids, who run from school or day care to the babysitter to soccer to homework at the same frantic pace. Is it any wonder that the use of Ritalin and Prozac among North American children has increased, as has the diagnosis of ADHD (attention-deficit hyperactivity disorder)?

Consider this too: When the American Psychological Association (APA) released its annual 2010 survey, Stress in America, it showed that the picture of an "overstressed nation" is as bad as it has ever been. One of the most striking conclusions from the APA survey was that "stress is not only taking a toll on our personal and physical health, but it is also affecting the emotional and physical well-being of children and our families." The survey highlighted the fact that children today are more stressed than in years past and also found that kids easily recognize and identify their parents' stress levels as a key source of their own stress.

As you might imagine, the most common sources of stress identified in the APA survey were money (76 percent), work (70 percent), and the economy (65 percent).

But “family responsibilities” also emerged as a significant source of stress (73 percent).

Health experts identify a “healthy stress level” at about a 3 to 4 on a 10-point scale, with 1 representing low stress and 10 indicating extreme stress. Healthy intermittent exposure to stress can actually be a good thing. Some stress researchers, including myself, refer to this intermittent or “temporary” stress as “eustress”—that is, the type of stress that helps motivate you to meet a deadline or to achieve a goal. But chronic stress (or “distress”) leads to problems with biochemical balance, cellular stress, tissue breakdown, and a wide range of physical and psychological health problems that clearly keep us from feeling, looking, or performing at our best.

The average stress level reported in the APA survey was 5.5, with 24 percent reporting stress levels at 8 to 10 (on the 10-point scale). Those with “more stress” (average of 6.2) tended to have poor overall health, while those with “lower stress” (average of 4.9) tended to have excellent health. Individuals with even higher stress exposure (in the 8 to 10 range) tended to have significant problems with their weight or even obesity—very likely due to problems with biochemical balance and cellular stress and especially to an overexposure to cortisol and its associated increase in appetite for “comfort foods” and consequent storage of belly fat.

Americans across all age groups and geographic areas generally recognized that their stress levels are “too high” (69 percent) and that stress is not good for their health. But a majority of respondents also reported facing significant challenges in actually practicing healthy behaviors, such as reducing stress, eating better, exercising, getting enough sleep, and losing weight.

Primary obstacles to those healthy behaviors included "being too busy" (22 percent) and a "lack of motivation or willpower" (29 percent). In fact, one of the most interesting aspects of the APA survey was the clear indication that Americans know what they should be doing—but that they are not doing a good job of achieving their health goals. For example, if you look at the "gap" between knowing something is important and actually doing it (achievement), we see the following pattern:

Aspects of Well-Being: Importance vs. Achievement

Behavior	**Important?**	**Achievement?**	**Gap**
Getting enough sleep	67%	29%	38%
Managing stress	64%	32%	32%
Eating healthy foods	58%	31%	27%
Getting enough exercise	54%	27%	27%
Having good relationships	79%	60%	19%

Source: American Psychological Association—Stress in America Report, 2010

How can you close this gap? How can you break out of the negative spiral that pulls you down into cellular stress and psychological burnout and instead turn it around toward building cellular balance and physical and mental vigor? To answer these questions, let's look at the example of reducing cellular stress and building stress resilience in one of our most important tissues, our brain. Consider the brain as the "central computer" that integrates all the environmental, internal, and biochemical cellular signals that, in turn, direct your behavior.

Your Brain on Stress

Chronic stress not only emotionally and functionally affects the brain, but it can also lead to direct physical changes in this most important organ. Research has shown that chronic stress not only increases the incidence of such simple effects as "moodiness," "brain fog," or irritability but can also eventually progress to the development of such physical impairments as full-blown memory loss and dementia. Each of these conditions involves a degree of mental deterioration characterized by damage to and death of nerve cells in the brain. And it has been estimated that as many as 30 to 50 percent of adults in industrialized countries suffer from these degenerative brain conditions. That's a very high percent of the 65 to 90 percent of adults in industrialized countries who suffer from enough chronic stress to result in any detrimental health condition—not just "psychological" or "brain-related" conditions.

The changes in mood that accompany periods of heightened stress also bring reduced energy levels, feelings of fatigue, irritability, inability to concentrate, and feelings of depression—all of which are related to the same class of brain chemicals, the neurotransmitters. Most notable (and scary), perhaps, are the findings that chronic stress can lead to actual physical changes in the arrangement of the neurons (nerve cells) in the brain. In other words, we're talking now about stress being able to exert changes not just in the biochemistry and function or the brain, but directly on the physical structure of your brain.

People suffering from depression are a classic example of elevated cellular stress, with disrupted biochemical balance in hormones, such as cortisol/testosterone, and in brain neurotransmitters, such as dopamine, norepinephrine, and serotonin. The people who are under the highest levels of cellular stress also tend to be the ones who succumb to periods of moderate depression.

So, if cellular stress can change the function and structure of your brain, wouldn't it be cool if brain function could "push" the other way to influence cellular stress? Well, it can. Sports psychologists have known for decades that athletes can use "mental imagery" (basically, thinking about their events) to improve mental and physical performance. Elite-level athletes routinely train their bodies for strength, speed, and agility—and the very best of the best also train their minds and their emotions for optimal performance. The average person has little understanding or appreciation for the fact that it is possible to train and to sculpt mental circuits just as biceps or buttocks can be shaped. The process is a little more complex than the

simplistic “think and grow rich” platitudes that you hear from some self-help gurus, but the general idea is similar. Like sand on a beach or snow on a ski slope, the brain bears the footprints or ski tracks of the decisions that you make, the experiences that you have, and the thoughts that you think. In response to the experiences and actions that you undergo, your brain strengthens the neural connections involved in these experiences and weakens those that are less frequently used. This poses important possibilities for those individuals who are troubled by depression or anxiety, making it possible to “rewire” those areas of the brain (those “pathological” connections) and establish new, better, and healthier connections that lead them away from burnout and toward vigor. Think of “problems”—such as depression, anxiety, fatigue, or burnout—as issues that involve biochemical balance and cellular stress. Rebalancing your internal biochemistry and relieving cellular stress, helps restore mood, energy, and mental focus to help us feel, look, and perform at our best.

What Does “Energy” Mean To You?

Even if you don’t think of yourself as someone who would ever be troubled by anxiety or depression, chances are, if you’re like most other people living in any industrialized country anywhere in the world, your daily routine is hectic and stressful. You may suffer from constant fatigue, have trouble focusing, and you’re at least occasionally tense, irritable, or moody. In fact, you may be experiencing what we often refer to in lifestyle research as a uniquely modern type of fatigue that we call “burnout.”

When we ask people about the source of their fatigue – what makes them feel "tired" – we find a great many factors that lead people to feel a lack of energy. Many of the factors that lead to feelings of low energy are the same factors that lead to poor health, including lack of sleep, inadequate diet, sedentary lifestyle, and excessive stress. As a scientist and lifestyle researcher, I find it interesting that people will often label their lack of mental focus as "tiredness" – and their high stress levels as "fatigue" – and their suppressed mood as "exhaustion" – no wonder we're all so tired!

But what if things were different? What if you could reverse burnout—or avoid it altogether? Suppose, instead of feeling fatigued, you felt physically energized and mentally alert? What if you enjoyed feeling "relaxed alertness" instead of feeling tense, anxious, and irritable? Imagine feeling "in the zone" – compared to the millions of people who constantly feel tired, stressed, and depressed? If you achieved such a level of physical energy and mental acuity, your condition could only be described as being the opposite of "burnout" – and you would have people lined up around the block to get it for themselves.

This state of overall well-being—the opposite of burnout—has also received a name from lifestyle researchers – we refer to it as "vigor" – and I've spent the last decade of my career studying and educating about it.

Outside the research community, however, very few people have heard of the term "vigor" used as a measure of health. And in your own vocabulary, the word may only turn up when you're talking about vigorous exercise or reading cookbook instructions that tell you to shake liquids vigorously.

But “vigor” actually has an official definition in scientific circles: “a three-tiered sustained mood state characterized by physical energy, mental acuity, and emotional well-being.”

This chart may help you see this definition a little more clearly—and it also underscores the differences between vigor and burnout.

Vigor vs. Burnout

Vigor	**Burnout**
Physical Energy (energy)	Physical Fatigue (fatigue)
Mental Acuity (focus)	Mental Exhaustion (brain fog)
Cognitive Liveliness (Happy & Resilient)	Cognitive Weariness (Exhausted & Worn Out)

Vigor is a true measure of wellness, because it encompasses much more than simply feeling “energetic,” being in a “good mood,” or having a “sharp” mind. People with high levels of vigor are those “can-do” individuals who feel like getting things done—whether they are running a marathon or just cleaning out the garage. They’re uniquely

motivated and have the capacity to accomplish what they set out to do, because they're not weighed down by feeling exhausted or unfocused.

Unfortunately, for a lot of people, "vigor" is a state that they have not experienced in many years, but that does not mean they cannot reclaim it.

Vigor in Ancient Medicine

The term "vigor," as used in today's modern lifestyle research, actually has very old roots in traditional systems of ancient medicine. The modern scientific concept of vigor is somewhat comparable to the ancient descriptions of vitality and wellness from traditional medicine systems around the world. Nearly every ancient culture has typically held a common belief that true health stems from a strong "life force" in the body. I mentioned a few of them earlier, some additional names for this life force, or vigor, include:

* Qi (traditional Chinese medicine; pronounced "chee")
* Prana (Ayurvedic/Indian medicine)
* Ki (Kampo/Japanese medicine)
* Ka (Egyptian medicine)
* Mana (Polynesian medicine)
* Pneuma (ancient Greek medicine)

Practitioners of traditional medicine might have restored “life force” in their patients by improving their nutrition or administering herbal medicines. These natural therapies often “worked,” and patients felt better as a result. What these ancient healers did not fully appreciate was “how” their therapies were working to actually alter biochemical processes in the body and modulate internal biochemistry such as oxidative stress and physiological functions such as neurotransmitter balance and blood flow.

Current Energy Drink Market

In modern times, millions of people attempt to temporarily reduce fatigue with energy drinks or other stimulants. However, that approach does not restore vigor and is actually more likely to sap vigor in the long term. These temporary “fixes” are inadequate solutions, because they do not address the underlying cause of low vigor: biochemical and physiological imbalances.

The “functional energy drink” market is forecasted to surpass $20 billion in annual global sales in 2018. Unfortunately, the entire energy drink market is characterized by an overly simplistic one-dimensional approach to restoring energy levels that is all about “stimulation” with caffeine and sugar.

If we look at what truly drives feelings of fatigue in most people, we see a multi-dimensional combination of low mood, lack of focus, and high stress that leads millions of us to experience what we label as “fatigue” on a daily basis.

When you add up the currently available “solutions” for improving energy, mood, and focus, with those that reduce

stress and tension, you have an annual market that exceeds $100 billion in the United States alone. Clearly people don't feel the way they want to feel – and they're looking for something that helps them feel their best. Given everything that we know about the causes of fatigue, it makes sense to alleviate fatigue (and boost feelings of energy) with a multi-dimensional approach of simultaneously improving mood, sharpening focus, and increasing stress resilience.

The Importance of CDR Activation for Mental and Physical Energy

Biochemical and genetic research studies are showing us how many of the ancient herbal remedies mentioned earlier work by activating the CDR cellular "switch" inside of every cell in our bodies. This CDR switch induces the natural production of internal cellular anti-stress proteins and increases our production of internal antioxidant enzymes.

You might think of the CDR pathway as an internal "thermostat" for cellular stress. Whenever a cell is under stress – whether from oxidative stress, or inflammatory stress, or any type of other stress that our modern world might throw at us, the CDR pathway senses the stress and induces numerous protective responses. Some of these responses help to reduce oxidative stress (antioxidant enzymes), while others help to clean up damage (housekeeping proteins) and prepare our cells for exposure to future stressors (heat shock proteins).

This natural induction of CDR is very much a “master regulator” of the body’s antioxidant and protective response - and the same mechanism at the heart of numerous new biotechnology and pharmaceutical research projects. In many ways, the natural induction of CDR is the future of maintaining proper internal balance and holistically protecting our body from environmental stress.

The CDR pathway is important for protecting every single cell in our body, but nerve cells, especially brain neurons; as well as mitochondria (our internal cellular energy generators) are particularly susceptible to damage from oxidative stress. A recent study funded by the Department of Defense (DARPA – Advanced Research Projects) showed that inducing CDR protects brain cells from oxidative stress induced by high altitude hypoxia (Lisk et al. *Free Radic Biol Med*. 2013 Oct;63:264-73). Another recent study showed that CDR induction may be particularly important for protecting the brain during degenerative conditions such as Alzheimer’s disease (Hybertson et al. *Mol Aspects Med.* 2011 Aug;32(4-6): 234-46). Numerous studies have indicated that mitochondrial dysfunction contributes to neuron degeneration via oxidative stress – and that specific flavonoids such as quercetin, proanthocyanidins, and EGCG can protect neuron growth against mitochondrial-linked pathologies (Dajas et al. *Central Nerv. Syst. Agents in Med. Chem.*, 2013, 13, 30-35). Based on these and numerous other studies, it seems clear that optimal mental energy and performance is supported through variety of mechanisms that hinge on optimal activity of the CDR pathway.

Lifestyle Tips to Pump Up Your Energy

Reduce Stress

1. Mange electronic interruptions: beeps, buzzes and other sounds add an annoying level of stress – be sure to avoid blue-light electronics one hour before bed

2. Recreate to re-create; Allow yourself to decompress Know when to go hard and ease off.

- Take a full day off each week: no work or thought of work
- Get a massage
- Take a bath or yoga class
- Read a "trashy" novel

3. Improve sleep quality; get 7-8 hours a night

- Inadequate sleep is associated with heart disease, diabetes, and obesity, among other chronic diseases.
- Recent investigations have helped prove that eight hours a night is optimum for cellular rejuvenation, and yet, according to one study, 71 percent of Americans get less than that—and are sleep deprived.
- Most Americans get an average of 5-6 hours of sleep per night – enough of a sleep deprivation that

it increases cortisol (by 50%) – interferes with blood sugar – increases appetite for junk food – and accelerates belly fat gain (risk factor for diabetes).

Nutrition: Eat for Energy

1. Eat healthy omega 3s. Omega 3s have been research to increase energy and support your mood, reduce inflammation (fatty fish, nuts and seeds)

2. Eat balanced antioxidants: Brightly colored fruit and veggies reduce oxidation (cellular damage and accelerated aging)

3. Avoid refined carbs, sugar and processed foods (these cause inflammation and glycation and lead to destruction of collagen and elastin)

Exercise: Workout for Body and Brain

1. Duke University researchers have reported 30 minutes of exercise 3-4 days a week is more effective than prescription antidepressants for relieving anxiety and depression

2. Exercise increases production of BDNF (brain-derived neurotrophic factor) which encourages the growth and function of brain cells

3. Exercise induces the CDR pathways inside of all cells to improve "cellular housekeeping" and cellular energy metabolism

Energy improving dietary supplements

1. Avoid sugary and high-caffeine energy drinks (which can reduce energy after the crash)

2. Boost your brain's blood flow with flavonoids (proanthocyanidins from pine bark extract, quercetin from apples/onions, catechins from green tea)

3. Improve brain cell (neurons) communication with smart foods – obtained from foods and supplements (omega 3s from fish, theanine from green tea, B-vitamins from whole grains)

A Multi-Dimensional Approach to Supporting Energy

Caffeine

Caffeine is perhaps the best-known and most-researched enhancer of cognitive function and perceived energy levels. Research on the physiological effects of caffeine in relation to human mental and physical

performance is extensive. Caffeine is quickly absorbed and can appear in the bloodstream within 15-45 minutes of consumption with peak concentrations evident one hour post-ingestion and decreasing by 50-75% within 3-6 hours. Overall, the findings from hundreds of research studies investigating the effects of caffeine supplementation on physical and mental performance indicate a positive combined effect on both the central (brain and nerves) and peripheral (muscle and fat) systems. Caffeine is known to boost the effects of brain neurotransmitters including serotonin (mood), dopamine (concentration), and acetylcholine (focus).

Research also shows that the amount of caffeine we consume matters. Consumption of about 100-200mg (about 1-2 cups of coffee) tends to deliver many of the "energizing" effects of caffeine, without the side effects associated with caffeine over-consumption (tension, irritability, headaches, insomnia). For healthy adults FDA has cited 400mg/day as an amount not generally associated with dangerous, negative effects. FDA has not set a level for children, but the American Academy of Pediatrics discourages the consumption of caffeine and other stimulants by children and adolescents. Finally, caffeine consumption has also been linked to a reduced risk of Alzheimer's disease, Type 2 diabetes and Parkinson's disease, meaning that caffeine can be part of a healthy approach to supporting mental and physical energy levels.

"Energy" Vitamins and Minerals (Niacin, Vitamins B6 & B12, and Magnesium)

Every energy-related reaction that takes place in the body, relies in one way or another on vitamins and minerals as "cofactors" to make the reactions go. For example, B-complex vitamins are needed for metabolism of protein and carbohydrate, while magnesium is needed for proper muscle contraction and nerve function. It is fairly well accepted in the scientific community that subclinical or marginal deficiencies of essential micronutrients, especially the B-complex vitamins and magnesium, can lead to psychological and physiological symptoms that are related to fatigue.

Monterey Pine Bark Extract (New Zealand Pine Bark Extract)

Pine bark extract, particularly from Monterey or New Zealand pine (Pinus radiata), is one of the richest sources of specialized brain-supportive compounds called proanthocyanidins, that have been shown to balance stress hormones and neurotransmitters, including cortisol, epinephrine, and dopamine – leading to improvements in mental focus, concentration, and irritability.

Green Tea Extract

Green tea (Camellia sinensis) has been associated with a wide-range of benefits for health and longevity. In particular, specific polyphenol compounds from green tea

(epigallocatechin-3-gallate; EGCG) may both protect and enhance brain function by blocking the formation of beta-amyloid plaques that have been linked to the onset of Alzheimer's disease and other neurodegenerative conditions. In addition, green tea consumption has been independently associated with significantly better mental function (global cognition), memory (information processing speed), and problem solving (executive function).

DMAE

DMAE, or Di-Methyl-Amino-Ethanol, is a naturally-occuring amino-alcohol that serves as a precursor for production of the brain neurotransmitter, acetylcholine (responsible for nerve transmissions and cognitive function). In the diet, it is found in high concentrations in “brain food” such as anchovies and sardines. DMAE has been used since the 1950s to improve memory, focus, alertness, and mood while stimulating neural (brain) activity. Many researchers believe that DMAE may serve a mental energy function by increasing the brain’s capacity to produce acetylcholine, which commonly declines with aging and memory loss.

Quercetin

Quercetin is a water-soluble flavonoid typically found in red wine, onions, and apples. In the body, quercetin plays a role in both improving blood flow and in elevating

norepinephrine levels, both of which have been linked to increased cellular and whole-body energy levels.

Theanine

Theanine is a unique amino acid found in the leaves of green tea (Camellia sinensis). A unique aspect of theanine is that it acts as a "non-sedating relaxant" to help increase the brain's production of alpha-waves (those associated with "relaxed alertness"). This makes theanine extremely effective for combating tension, stress, and anxiety—without inducing drowsiness. By increasing the brain's output of alpha waves, theanine helps to control anxiety, increase mental focus, improve concentration, and promote creativity.

What Would You Do With More Energy?

I find it interesting that once people understand the actual underlying triggers of their fatigue (low mood, lack of focus, high stress, etc), they are empowered to DO something about restoring their natural levels of mental and physical energy.

I also find it interesting that the type of "energy" (vigor) that people derive from the multi-dimensional approach described above is probably better described as "motivation" because it is a particularly "actionable" type of energy that makes people feel like getting up and doing something. These people tend to use that energy in proactive ways – starting a business, being active with

their family, volunteering in their church or community, even just walking their dog.

However you decide to use your new-found "energy," I hope that you will give some though to "paying it forward" and helping someone that you care about to achieve the same high level of mental and physical energy in their own life.

Chapter 7 - Look Your Best

Our Skin Reflects Our True Health

You've heard the old saying, "Beauty is more than skin deep" – and it's true – especially when you realize that our body has a built-in "beauty protection" network inside of every cell, including our skin cells. You'll often hear that the skin has "two layers" (the dermis and epidermis), but the epidermis (uppermost layer) is actually comprised of five distinct layers and the dermis (deeper layer) has two different layers – so our skin actually has seven different layers that protect our delicate (internal) tissues from the damaging (external) environment.

Emerging science is discovering a new approach to caring for your skin, one that addresses what goes on inside you and at the deeper layers of skin (not just the surface) in order to bring forth the most glowing, clear, healthy skin on your outside. Achieving healthy, beautiful skin is truly an inside-out process. Looking better, feeling better, having more confidence, and causing your exterior to reflect your beautiful interior (and vice versa) is what the latest skin science is all about.

Nobody wants to look like they're aging. Americans spend hundreds of millions of dollars every year on lotions, creams, and coatings to be applied to the surface of the skin (the dead part, called the stratum corneum). Many of these concoctions do a wonderful job of smoothing out wrinkles and giving the appearance of younger, healthier skin. The illusion of healthier skin, however, rapidly fades when the beauty cream wears off.

What is Our Skin Made Of?

Before we get too far into an explanation about how to make our skin look better, let's take a few minutes to understand what our skin is actually made of. Skin is a highly structured group of specialized cells (keratinocytes) and complex proteins (collagen, elastin, keratin, etc). Each of these proteins is a specialized type often referred to as structural protein. It might help you to think of structural proteins as the steel girders and construction rods of the body. If we were to think of the body as a structure such as an office building or skyscraper, then structural proteins would be the steel girders, the iron rivets and the outer surface of the building.

Structural proteins play a vital role in maintaining the basic integrity of various tissues in the body. By integrity, I am referring to the actual "state of repair" of bodily tissues such as your joints, bones, tendons and ligaments. You might visualize healthy collagen as the surface of a brand new highway (smooth, strong, free from damage) whereas an old country road covered with potholes might be a way to visualize unhealthy or damaged collagen. By maintaining proper function and supporting the body's vital cellular renewal processes, we can help to delay or prevent many of the degenerative conditions commonly associated with aging.

Collagen and related structural proteins are constantly in a steady state of turnover - meaning that the collagen matrix is continually being broken down and rebuilt in response to the demands placed on it. Under normal circumstances, turnover is balanced between synthetic

(production) and degenerative (breakdown) processes. This allows periodic removal and repair of damaged tissue and its replacement with healthy new tissue. Under certain conditions, however, the balance between tissue breakdown and repair can become unbalanced - resulting in excess tissue deterioration. Sometimes this is due to extreme cellular destruction, sometimes to inadequate repair and sometimes to a combination of both.

A number of factors are known to influence the body's ability to adapt to conditions which unbalance the cellular turnover process, including:

- Aging causes a number of biochemical and biomechanical changes in skin and other connective tissues. For example, in skin, both the number of cells and their individual activity may decline with age. This means that older skin may be less able to repair damage and less resistant to injury and environmental insults than younger skin.

- Genetic factors are thought to play a role in metabolism of collagen and other structural proteins and may explain some of the variation in risk of collagen-related diseases such as arthritis and osteoporosis, which can be related in certain ways to skin aging (fine lines and wrinkles).

- Physical activity has the potential to significantly influence collagen and structural protein metabolism by enhancing transport of nutrients from the blood into the connective tissues, including skin, where they can be used. Too little activity or

too much mechanical stress may unbalance the collagen repair process and impair connective tissue function.

- Medications, including over the counter pain relievers like aspirin, ibuprofen (Advil) and naproxen (Aleve) can interfere with the normal collagen repair process. Although such medications are widely used for the temporary relief of pain and inflammation of arthritis and other injuries, their overall effect is to address the symptom of pain - not the underlying cause of tissue damage. Chronic use of such pain relievers may actually accelerate connective tissue damage and worsen the very condition from which you are trying to get relief.

Cellular Turnover

As discussed above, collagen and other structural proteins are continually undergoing a process of breakdown and repair. This cycle of tearing down and building back up again is referred to as "turnover" and is a perfectly normal part of keeping the connective tissues such as skin at peak health. The turnover process allows tissues with a high collagen content to adapt to stress and repair themselves after suffering damage. For instance, let's say you "over do it" at the company softball game and wake up with stiff achy muscles and joints the next morning. The pain and discomfort that you are feeling is a

result of damage to your muscles, tendons and ligaments caused by the stress of overexertion. You already know that the pain and stiffness will eventually go away over the next couple of days - that's because your natural turnover process will begin to remove the damaged tissue and replace it with brand new healthy tissue that is just a little bit stronger than it was before. The very same process is at work when we need to repair our damaged skin after too many hours in the sun, or when we're repairing a scratch, cut, or other wound to the skin.

The collagen turnover process can be influenced by a variety of factors including age, physical health and nutrient intake. It doesn't take a rocket scientist to point out the wrinkling of skin, the stiffening of joints and the graying (or loss) of hair as we age. We've known for decades that regular physical activity and proper nutrition can help delay or reverse some of the deterioration of our bodies. In fact, many of the losses in function considered to be "inevitable" consequences of aging are little more than minor inefficiencies and subtle deficits that have built up over many years.

For example, joint stiffness is probably the first consequence of aging that we notice. Why? Because we try to get up from the chair or carry something across the yard and we say, "Whoa, I never felt that before." What you're feeling in this situation is the result of years and years of accumulated stress (and inadequate repair) in your connective tissue. The key to maintaining optimal connective tissue function is to maintain and support the naturally balanced process of collagen turnover.

Virtually each and every situation that we associate with "aging" can be directly attributed to the lifetime balance of degradation and repair within each tissue. In

the innumerable cases that make us feel older (joint pain, weak muscles, stiff tendons and wrinkling skin) a significant underlying connection to collagen health exists. In each case, the balance between breakdown and repair has tilted in favor of collagen loss.

Even if collagen breakdown outpaces repair by just a very slight amount, the combined effect over the years will lead to dysfunction. If you could just give the balance a little bump - and either nudge the synthesis of collagen a little higher or push the breakdown of collagen a little lower - then you'd be back in balance. Even better, if you could stack the deck in your favor, by increasing collagen synthesis above the breakdown rate, then you could actually make gains in those areas that previously gave you grief.

Skin Protein Maintenance - Synthesis, Breakdown and Repair

As mentioned above, skin proteins maintain strength and resiliency by continually undergoing a process of breakdown and rebuilding. This process, known as collagen turnover, is a recycling process that helps get rid of older collagen, elastin, and keratin fibers that may be damaged or weakened, and replaces them with newer, healthier fibers that are stronger and more able to withstand strain. Just as public works crews are sent out to repair potholes in roads, your body has to fight an ongoing struggle to constantly maintain and repair the collagen network.

Without this ongoing renewal and repair process of skin protein turnover, small bits of daily damage would build up and result in a serious deterioration of the tissue. In skin, this leads to the familiar dulling and wrinkling as we age; in joints, this might lead to painful arthritis; in bones it might lead to a stress fracture; and in muscles and tendons the risk for strains and tears might be increased.

I certainly don't need to tell anybody reading this book that skin wrinkles as we age. Wrinkled skin is almost something that we've all come to accept as an inevitable part of the aging process. Have you ever stopped to wonder, though, just why it is that our skin wrinkles as we age? How about the fact that some people have more wrinkles than others? How about whether or not something can be done about it?

Well, there are a number of approaches that can be taken to help combat the appearance of wrinkles in the skin. The basic underlying reason that our skin wrinkles with age is because we "dry out." As we age, our bodies actually lose moisture little by little - and the end result is that we all "shrivel" up a bit. The drying out process can be accelerated by environmental factors such as prolonged exposure to the sun and smoking. Luckily, however, this drying out process can be slowed somewhat by the wide range of topical cosmetics that deliver lubricants and moisturizers back to the surface of the skin. A different approach to preventing the drying and wrinkling effects of aging is to moisturize the skin by providing nourishment from the inside - with balanced nutrition and dietary supplements that help to improve the efficiency of the turnover process.

As we age, the deeper layer of skin, known as the dermis, gets thinner. The progressive breakdown of

collagen and elastin (which can be accelerated by sunlight and cigarette smoke) results in a loss of skin strength and a reduced ability to maintain adequate levels of lubricating fluid. Proper dietary support can help to reduce the destruction of collagen and promote the synthesis of stronger collagen fibers.

Hair and nails are composed of another structural protein called keratin. In many ways, keratin is similar to collagen - both are long strand-like proteins that serve a structural function in the body. The composition of the amino acid building blocks, however, is a bit different between collagen and keratin. In collagen, more than half of the amino acids are accounted for by proline, glycine or hydroxyproline. Keratin also contains fairly high levels of glycine and proline, which account for about 20% of the molecule, but it also contains about 10% of another amino acid called cysteine - something that collagen lacks.

Brittle hair and nails are a common complaint affecting about 30-40% of the population. Although weak brittle hair and nails can be the result of a variety of factors such as environmental exposure, the process of keratin synthesis can be enhanced by the same steps which enhance collagen synthesis.

With age, a number of noticeable changes in collagen structures become apparent. Collagen fibers lose their elasticity - so we may become “droopy” in areas of our body which used to be firm. Collagen in skin begins to lose its ability to hold water, so our skin dries out and begins to wrinkle. The keratinized cells, destined to become strands of hair, become fewer in number and lose their ability to produce pigment - so we either go bald or turn gray. With age, cartilage cells lose their ability to produce new collagen - so we lose cartilage thickness and our joints

begin to ache. Bones become weaker over time as the rate of collagen and mineral breakdown exceeds our ability to replace losses with healthy tissue.

If we could just balance the collagen turnover process, or better yet, tip the scales slightly in our favor - we could balance out the destruction and repair of our vital connective tissues and prevent (or delay) some of the conditions that we normally associate with aging.

Skin Stress

When we're under any type of stress, our body's secrete a higher level of the stress hormone, cortisol. Cortisol isn't "bad" in and of itself. It's a normal part of our physiological makeup. The problem occurs when we're exposed to too much of it on a chronic basis - a scenario that is all too common in today's fast-paced, overbooked way of living.

Because of cortisol's wide-ranging influence on other important aspects of metabolism (especially those metabolic pathways associated most closely with "aging"), it is often called the "death hormone" and is associated with a tipping of the turnover process described above toward the "breakdown" side of the equation. The "death hormone" description is a fairly accurate nickname because cortisol is a hormone that tends to increase with age, and our increased exposure to cortisol as we age has been linked to breakdown and dysfunction in every tissue in the body, especially connective tissues such as skin. This breakdown of our tissue does, in a real sense, bring us closer to death and age us unnecessarily before our time. So whether we're talking about skin, or muscles, or

brain neurons, it makes sense to address cortisol's role in cellular stress and the metabolism of aging.

Since cellular stress is basically the driving force underlying several metabolic pathways, we need to control it in order to slow down the skin's aging process, treat and prevent problem skin, and promote radiant, healthy skin. When we do this, we get unexpected perks: Controlling cellular stress also produces beneficial results in terms of weight loss, improved mood, and enhanced libido!

One major way that cortisol earns its nickname as the "death hormone" is through its destructive effect on collagen, the most abundant protein in the human body (about a third of all the proteins) and the chief structural component of skin tissues (about 90 percent). Collagen serves as the primary framework on which all the major structures in our body, including our skin, are built. It's what wards off lines and wrinkles, and it is about the closest thing we have to a fountain of youth.

The health of our skin is affected by how well we metabolize collagen - that is, how well our systems make collagen available to our bodies for productive use. Collagen metabolism can be influenced by our eating habits, exercise patterns, and lifestyles. When we are under stress, our cortisol levels increase, contributing to a faster breakdown of tissues that contain collagen, such as bone and skin.

Another source of collagen destruction is the drying-out process that comes with aging. However, there are ways to reduce this destruction and promote the synthesis of stronger collagen fibers. Most people try to do this by using topical cosmetics that deliver lubricants and moisturizers back to the surface of the skin in an attempt to slow the aging process. Some of these topical remedies are natural

and work well with the body's own self-healing tendency, but entire premise of this book is that the best, most natural way to care for every one of the trillions of cells in our body (including your skin) is to support the CDR pathways inside of each of those individual cells. This can greatly help bring the collagen-turnover process into balance, and it can even tip the scales slightly in your favor when it comes to repairing vital connective tissues and preventing (or at least delaying) some of the conditions that we normally associate with aging.

If you are still too young to require “anti-aging” advice and your concern is treating and preventing problem skin - for example, if your situation is not dry skin but the opposite: oily, acne-prone skin – then CDR activation (topically and internally) can also be the foundation of inside-out skin care while you are young. Since this is an approach that makes you feel better as well as look better, it can grow with you very comfortably through the years, so that when your skin becomes more mature, it will have the long-term benefit of healthy CDR balance.

The FACE Program

FACE is an acronym that I’ve used for several years when educating people about the value of CDR activation (topically and internally) for reducing cellular stress and improving our ability to protect and repair cellular damage. CDR activation helps to coordinate myriad cellular signals for optimal tissue balance, including Free radicals (“F”), Advanced glycation end-products (“A”), Cortisol (“C”), and Eicosanoids (“E”). Free radicals have to do with oxidation,

AGEs with blood-sugar levels, and eicosanoids (referred to as "cytokines" in other sections) with inflammation.

The premise of “FACE” is that the outward appearance of beautiful skin starts on the inside, and that wrinkled, blemished skin is not an inevitable result of aging. Nor is problem skin something that can only be dealt with by expensive, often abrasive outside-in means. This all-natural approach to beautiful skin and a youthful complexion is based on the latest scientific evidence and years of real-life experience with hundreds of participants.

I never set out to write a book about beauty - or about skin health for that matter. Many years ago, when I was a young Ph.D. student at Rutgers University, my focus was on bone metabolism - specifically, on uncovering the complex interactions between nutrition, lifestyle, and osteoporosis. In our lab, we studied the interplay of diet and exercise on collagen. Through our studies and those of our scientific colleagues, we came to understand that collagen metabolism (and thus the health of our skin and bones and other connective tissues) can be influenced by the stressful world around us. Our lab was among the first in the world to show that the psychological and physical “stress” of dieting for weight loss increased cortisol levels and contributed to a faster breakdown of collagen-containing tissues, such as bone and skin.

Today, the scientific community accepts the fact that chronic cellular stress leads to rapid breakdown in other tissues, including brain neurons, blood vessels, muscles, immune cells, and many more. Because collagen is the chief protein in skin, this cortisol-induced acceleration of collagen breakdown inevitably leads to skin problems, including wrinkles, acne, and uneven skin tone. Collagen breakdown and skin damage can also be hastened by

other factors, including metabolic processes, such as inflammation, oxidation, and glycation. Imbalances in each of these four processes is well documented in the scientific and medical literature as resulting in the rapid and dramatic effects that we view as premature aging – but each of these can be managed within healthful levels via proper activation of the CDR pathways.

However, until I conducted a particular weight-loss program, none of this had any direct meaning for me. I am not a dermatologist, but a nutritional biochemist, trained in sports medicine, health management, and exercise physiology. For the last decade or so, my career has been focused on using nutrition and other lifestyle strategies to help people lose weight and improve their health. To this end, I designed and conducted a series of popular and very successful weight-loss programs. They generally run three or four times each year, and we always have a waiting list. They take place near Salt Lake City, Utah, where I now live with my wife and two children.

These programs follow a regimen that I call the SENSE program, because it incorporates Stress/Sleep management, Exercise, Nutrition, Supplementation, and Evaluation. Participants invariably experience fat loss, muscle gain, increased energy, improved mood, reduced stress, elevated libido, and a host of related benefits. Best of all, our participants never feel deprived, hungry, or as though they are following a "diet." In fact, in the early weeks of each session, there are always several participants who declare that the program will never work for them because it's "too easy." Our response is always the same: "Trust us," we say. "Just stick with the program for a few weeks, and you'll see the benefits." They do-and they're amazed.

My discovery of the “CDR/Beauty” connection was something of an accident. During the first few years that we were running the SENSE weight-loss programs, participants would comment that they "felt great" and thought they "looked better." At first, my staff and I always interpreted those positive comments as a reflection of the participants' excitement about finally being able to lose weight and keep it off. Eventually, however, it dawned on us that there might be something more at work here.

We got this "sense" when we recruited a group of participants, who were already fit and lean, to see whether our SENSE program could help them control their perception of stress relative to eating during a traditionally high-stress period of time (the holiday season from Thanksgiving to New Year's Day). These mostly young, good-looking, successful men and women didn't have very much weight to lose; they simply got stressed out during the holidays and gained weight as a result of stress eating.

After they finished the program, they also told us that they felt and looked better, which we found very interesting. We could understand the "feel better" part, because we discovered that their stress and cortisol levels were reduced by about 20 percent after they'd followed the SENSE program. But the "look better" part was a surprise (remember, these folks already looked pretty darn good). Our unexpected discovery was that the same SENSE program that made them feel less stressed out (and that had helped previous overweight participants lose weight) was also delivering some very noticeable beauty benefits. Our participants found that by controlling their overall “psychological” stress levels they were also controlling their underlying “cellular” stress levels. As a result, their wrinkles were reduced, their skin wasn't breaking out, and

their skin (especially facial skin) was clearer, smoother, and more youthful in appearance. Another interesting finding that went hand-in-hand with looking and feeling better was that their sex drive (libido) was improved. Needless to say, this freaked out the parents in the program whose teenagers were participating and grossed out the teens in the program whose parents were participating.

It turns out that all these effects-from weight loss to enhanced mood to healthy skin to improved libido-are the result of controlling cellular stress. However, even when we explained the connections in proper, scientifically sound, and rational terms, our participants insisted on referring to the program as the "fountain-of-youth class."

CDR Offers Multi-Faceted Skin Solutions

Recall from above that we perceive as “aging” is actually a complicated and multifaceted phenomenon related to skin breakdown and repair—a cyclical process that we scientists refer to as “tissue turnover.” In the case of skin, we call it “collagen turnover.” The most effective solution to a multifaceted problem is a multifaceted solution, and that’s exactly what topical CDR activation is all about.

Today, the scientific community accepts the fact that chronic cellular stress leads to a rapid breakdown in a variety of tissues, including skin. Cellular stress in skin cells inevitably leads to skin problems, such as wrinkles, acne, and uneven skin tone. CDR pathways regulate our body’s response to cellular stress and numerous studies have shown that both topical and internal/systemic

activation of the CDR pathway can have a wide range of beneficial effects on skin, including reduced rates of skin cancers, protection from ultraviolet radiation, reduced inflammation, enhanced barrier function, and improved wound healing.

The Science Behind CDR's Skin-Protecting Benefits

In a series of human clinical studies and laboratory studies (isolated skin samples and DNA analysis) CDR-activating herbs such as turmeric, pine bark, quercetin, green tea, brassica, and plantain have been shown to improve skin tone, reduce wrinkles, and generally enhance youthful appearance. In one human clinical study, topical application of CDR-activating herbals showed a dramatic improvement in key beauty benefits, including an extremely high percentage of women who felt that their skin was improved in the following ways: looking smoother, younger, firmer, more even tone, and with fewer wrinkles. These studies indicate a profound ability of CDR-activating herbal blends to treat both intrinsic and extrinsic aging, thus truly delivering on the promise of improving skin on the outside and on the inside. In a series of laboratory studies, isolated skin samples (explants) were investigated to understand the biochemical and genetic mechanisms underlying such rapid and dramatic clinical benefits, American and French researchers treated isolated skin samples daily with CDR-activating herbs and plant extracts. Findings showed clear evidence of the herbs/ extracts to :

- Increase CDR pathway activation in skin (thus improving *biochemical* resistance to oxidative stress)
- Boost skin protection from ultraviolet light exposure (by reducing *genetic* DNA damage)
- Fight the signs of aging through *all* layers of the skin (6-7 cellular layers)

Summary

The future of science and medicine is targeting the CDR pathways to not only protect our health, but also to actively improve how we feel/look/perform. CDR activation, especially when optimally synergistic in nature, allows you to enjoy enhanced anti-aging benefits for a new level of wellness and vitality.

The last chapter covered how CDR activation can help us to Feel Your Best – and the next chapter covers how CDR activation can help us to Perform Your Best. I want to end this "Look Your Best" chapter with a short list of the primary benefits of CDR activation for skin health:

- Minimizes inflammation, irritation and redness
- Reduces wrinkles and improves skin tone
- Safeguards against free radical/oxidative stress
- Protects against UV radiation exposure
- Maintains integrity of key skin structural components

- Minimizes risk of skin cancers and other conditions

Chapter 8 - Perform Your Best

When many people hear the word “performance” they often think about athletes and athletic performance. This connotation is just one of the many ways to properly think about performance. Another definition of performance is simply, “the execution of an action” – while another is “the fulfillment of a promise” – and it is each of these that I think more accurately captures my meaning when I educate people about how reducing cellular stress can improve their performance.

While it’s true that athletes can certainly be among the group of people who want to achieve their highest level of mental and physical performance through optimized cellular stress balance, I also think that everyone should want to achieve their own highest level of performance, no matter what level that may be. For example, you might consider a high level of performance to be one in which you get through a stressful day with enough energy to play with your kids. Another level of performance might be having enough “get up and go” to get up and walk the dog. Yet another level of performance might include starting your own business, or taking up a new hobby, or volunteering in your church or community. These are all examples of how reduced cellular stress can improve performance – and lives – in so many ways that are far outside of the limited thinking around “just” athletic performance (which still might be important for many readers).

I like to think about performance in five stepwise phases that move along a continuum from performance of the mind (mental); to the gut and immune system (which

need to perform well in tandem to keep us healthy); to improved metabolic performance (which enhances fat loss, especially belly fat); to improved general fitness (especially the improvement of muscle mass or lean body mass); and finally to the stereotypical "athletic" performance where you're striving for personal achievement toward a specific goal (competing against yourself or others). The sections that follow will delve into each of these five phases of the performance continuum.

Five-Phase Performance Continuum

- Phase 1 – Mental Performance (brain ergogenics)
- Phase 2 – Gut Health (including immune system function)
- Phase 3 – Body Fat (especially belly fat)
- Phase 4 – Fitness (especially lean body mass)
- Phase 5 – Personal Achievement (Best Future You)

Phase 1 – Mental Performance (brain ergogenics)

In some of the work I've done over the years with elite-level athletes in a variety of sports – including many professional athletes and participants in the Summer and Winter Olympic Games – a common theme is that the athletes standing on the podium not only are the athletes

with the highest states of physical performance but also are the athletes with the highest states of mental performance. Their physical and mental performances can in turn be traced down to the biochemical or cellular level – where we see that the athletes on the podium were effective in reducing cellular stress, while those off the podium typically succumb to one or more problems associated with excessive cellular stress (injury, illness, fatigue, inattention, etc), ultimately leading to poor performance.

The athletes who miss the podium (or even miss qualifying for big events, such as the Olympic Games) are often those whose cellular biochemistry is "unbalanced" and whose cellular stress spiked at the wrong time—leaving them fatigued, unfocused, injured, or sick and allowing a "balanced" athlete to surpass them.

Brain Ergogenics – the Emerging Science of Mental Performance

Exercise makes us tired - that's not exactly a newsflash - but methods to "reduce fatigue" or "prolong endurance" have become the Holy Grail of sports nutrition. Undoubtedly, you've seen numerous "improve endurance" products in the form of energy bars, carb beverages, and related that provide calories to help maintain glucose, reduce lactic acid accumulation, and restore glycogen levels and thus help to delay "peripheral" fatigue (caused when your muscles fatigue).

However, a new category of endurance nutrition products are entering the market intended to improve

“mental energy” and help to delay “central fatigue” (which occurs when the brain basically says, “No more, we’re done”). These new types of products can be broadly grouped into a category that we refer to as “Brain Ergogenics” - to suggest an overall effect of enhancing the brain’s capacity for high-performance work output.

Brain Ergogenics has the potential to be the "next big thing" in endurance performance. We have already gotten pretty close to optimizing the approach to extending endurance through "peripheral" mechanisms, which includes factors occurring outside the brain, in the muscles, blood vessels, etc – such as glycogen levels, oxygen delivery, maintenance of blood glucose, electrolytes for hydration and cramping, etc. However, we have only scratched the surface in terms of extending endurance through "central" mechanisms (brain-centered).

One way to think about obstacles to endurance performance is that you "stop" (or slow down) moving forward due to either peripheral fatigue (you bonk or hit the wall or succumb to the “burn” of lactate accumulation) or due to central fatigue (your brain says "enough") - and both factors can be "pushed back" in various ways to enable us to keep going.

Certainly, dangerous and addictive stimulant drugs such as Adderall (for ADHD) or Provigil (for daytime sleepiness) can stimulate the brain to “wake up” or “keep going” and are effective enough for Americans to spend several billion dollars annually. Although abuse of ADHD drugs like Adderall and Ritalin are a big trend on college campuses (as “study drugs”) and in high-pressure jobs (such as Wall Street), nobody is saying that endurance athletes should turn to pharmacological agents to gain any performance edge in our recreational pursuits, but there is

undoubtedly a market for these types of products as subset of the general endurance/sports nutrition category. People will always be looking for that "extra gear" and targeting the central nervous system is likely to be the next frontier.

Luckily, we have a wide range of non-drug, safe and natural nutrients that can delay central fatigue, such as:

- Caffeine (the most commonly used brain ergogenic)
- Branched-chain amino acids (BCAAs including valine, leucine, isoleucine)
- Other amino acids (like taurine/tyrosine/theanine)
- Flavonoids like quercetin/resveratrol/catechins (which have both peripheral effects on blood flow and also central effects on brain neurotransmitters
- American ephedra, which contains unique neuro-active amino acids that significantly increase positive mood state while reducing negative mood state (meaning that you feel great and have high stress resilience)
- Eurycoma (which balances cortisol/testosterone); Cordyceps (which improves oxygen efficiency); Ginseng (which controls blood glucose) - all may also have central brain effects encouraging an endurance athlete to keep going for awhile longer.

Some of my own research studies for a range of dietary supplement companies, have looked at the

effects of BCAAs, theanine, catechins, cordyceps, eurycoma, etc. on psychological parameters such as "Vigor" (mental/physical energy levels) in endurance athletes. We've been able to show that athletes "feel better" (using mood state surveys) – and often that feeling better translates into a direct advantage for athletic performance outcomes (power output, time to exhaustion, perceived exertion, etc).

Phase 2 – Gut Health (including immune system function)

Gut Health and Immune System Performance

The image of stress-induced ulcers has been with us for decades. You've probably seen, on a TV sitcom or other such venue, the stereotypical portrayal of the stressed-out executive. Deadlines loom, stress builds, and the businessman gulps down antacids to quell the burning ulcer in his stomach. Far from being one of the many Hollywood over-exaggerations, the phenomenon of stress-induced ulcers and other digestive problems has been documented in the medical literature for more than fifty years. From a physiological point of view, we know quite clearly that any stressful event will cause digestion to cease. Blood flow is diverted from the digestive organs to the heart and muscles, secretion of saliva and digestive enzymes is slowed, and intestinal contractions and absorption of nutrients stop. This rapid shutdown of the digestive process makes perfect sense, because from the

standpoint of long-term survival it is more important to get away from the dangerous stressor (the lion) than to fully digest all your food. There will be plenty of time for digestion later; right now you need to save your life. It is interesting to note, however, that even while a variety of cellular stress signals shutting down digestion, these same signals, when kept elevated for more than a few minutes, are telling us to eat—and eat a lot!

Medical evidence shows quite clearly that ulcers of the stomach (gastric ulcers) and intestine (duodenal ulcers) are much more common in people who are anxious, depressed, or under chronic or repeated stress. In these situations, which are all also examples of chronic cellular stress, many of the digestive actions are curtailed, so the body also backs off from its production of other protective measures—such as the mucus that lines the stomach, and the bicarbonate that counteracts the highly acidic gastric juices. Sounds logical, right? And it is. Why should the body take a lot of protective measures against acid that will never be secreted (because you're under stress)? The problems start to occur when a person experiences the repeated cycles of high stress followed by low/normal stress that have become commonplace in our modern society. This sets up the digestive system for total confusion. Most of the time the body won't be able to secrete enough digestive enzymes to properly digest food (producing nausea, constipation, gas, and bloating). During the "lucky" times when a body can secrete enough digestive enzymes to properly break down food, the protective mechanisms are far from fully operational—which puts a person at risk for damage to her gastrointestinal tract (because the enzymes digest the gut's lining in addition to digesting the food). This scenario

says a lot about why several bouts of repeated back-to-back chronic stress are so detrimental to gastrointestinal function – and to the overall function of our immune system, much of which resides in the GI tract.

To compound our “gut” problems, other factors, such as immune-system function and the body's control of inflammation and wound healing, come into play. It is well described in the medical literature that both repeated periods of acute stress and continuous periods of chronic stress are associated with suppressed immune-system activity. This has a direct bearing on ulcer development, because less immune-system activity means more growth and higher activity of a bacterium called Helicobacter pylori, which infects the stomach and causes ulcers in 80 percent of the people infected with it.

Compounding the tissue damage caused by the accelerated growth of H. pylori is a suppression of the body's ability to heal that tissue damage because of an inhibition in prostaglandin synthesis. Prostaglandins are typically produced in response to tissue damage, where they help reduce inflammation and accelerate healing. During times of stress, however, the synthesis of prostaglandins is curtailed, which suggests that stress not only increases the rate at which ulcers may form, but also slows the rate at which they are repaired.

Aside from ulcers, the most common stress-related gut disease may be irritable bowel syndrome (IBS). Most of us will experience some degree of IBS during our lifetime. The name "IBS" is really a catchall for a variety of intestinal disorders, including colitis (inflammation of the lining of the large intestine, also known as the colon), in which abdominal pain is accompanied by diarrhea and/or constipation, bloating, gas, and, occasionally, passing of

mucus or blood. The majority of the gastrointestinal conditions falling under the IBS umbrella are either caused by or exacerbated by periods of heightened stress.

Stress leads to poor digestion, ulcerated stomachs, and inflamed intestines—not a pretty picture. Heightened stress levels have also been linked to adverse effects on the balance of intestinal microflora, which are known to respond to changes in both diet and stress levels. These beneficial bacteria live in our intestinal tract, and while they are intimately involved with optimal gastrointestinal function, they also play a vital role in helping to support immune function. In a study of fighter pilots preparing for simulated battle (a fairly stressful event), distinct reductions were noted in the numbers of "good" bacteria (lactobacilli and bifidobacteria), along with a corresponding increase in the numbers of "bad" bacteria (E. coli, enterobacteria, and clostridia). The outcome for these pilots was, predictably, a sharp increase in their reported incidence of sore throats, headaches, colds, diarrhea, and upset stomachs.

Let's take a moment to think about the most predominant sources of stress that could be at the root of these health problems. In many stress-management clinics, the primary determinants of whether or not a given person will get sick include:

- the number of "major life events" in the past year (divorce, death in the family, change in job or location, etc.)
- a psychological perception that daily demands exceed coping resources and/or your support system

- Financial stress – which we can define simply as "worry about money"

Of this short list of three "sickness determinants," researchers have found that the overall degree of psychological stress is strongly related, in a dose-response fashion, to URTIs (upper-respiratory-tract infections) and other breakdowns in immune-system integrity (such as gastrointestinal health). This means the more stressed out you are, the more likely you are to get sick. Numerous studies in animals and humans have shown that both acute and chronic stress increases susceptibility to infectious diseases. In particular, the risk of URTIs is sharply increased, so that people who are under the greatest stress (or who deal with it poorly) are the ones who most often get these types of sicknesses. Students catch colds during exam week, and accountants get sore throats in April, when they're filing dozens of last-minute tax returns.

So after all this discussion about the suppression of immune-system function due to stress, who do you think gets sick most often? What demographic group, among all others, suffers from the highest incidence of stress-related disease?

Wealthy investment bankers? No.

Stressed-out college students? No.

Single mothers working two jobs and driving beat-up 1985 Ford Escorts? Yes!

The most direct example of the chronically elevated human stress response can be observed every day in the lives of a large part of the American (and worldwide)

population who are battling chronic financial stress. These are the folks who are driving a junker car (and hoping it makes it) to their second job. They are hoping the money from that second paycheck will last until the end of the month when the bills are due. They are not the people whom you see commiserating with each other about their unfulfilling jobs and their “first world problems” such as how they wish they could upgrade their iPhone 5 to a 6. The constant unrelenting stress of making ends meet, job instability, sleep deprivation, poor diet, lack of outlets for stress, and overall lack of control combine to increase the risk of disease by a factor of five to ten.

Many of you reading this book are probably suffering from some degree of financial stress. This is the type of chronic emotional/psychological stress that is always with us. It’s often the first thing that we think of when we wake up in the morning (going to our jobs to make money) – and the last thing that we think of before we go to bed at night (the rent/mortgage, tuition, car payment, groceries, and other bills that we need to pay). It’s the kind of low-grade chronic stress that is with us every time we go to the mailbox (which is filled with credit card bills) or the gas pump. It’s unrelenting for many people.

One interesting study looked at people of varying socioeconomic grades (some were rich and some were poor). Those on the lower end of the socioeconomic ladder (poorer) were significantly more likely to be overweight (with more abdominal obesity – covered in the next section) and to have higher cortisol values in relation to perceived stress. The researchers noted that the "duration of low socioeconomic conditions" (scientific lingo for "being financially-stressed for a long time") seemed to worsen the effects of cellular stress and strengthen the relationship

between cortisol and obesity (meaning that financial stress is bad for health and for your waistline). Overall, the researchers concluded that the stress of a low socioeconomic status is associated with elevated cortisol secretion, cellular stress, and a significant, strong, and consistent relationship with obesity. Closely related to pure socioeconomic studies of stress are the growing arguments that people eat more Big Macs, drink more Coke, and scarf more Oreos not because these companies tell us to eat them (via advertising), but because of stress. Lower socioeconomic populations may eat more junk food because they are more stressed out, not necessarily because Ronald McDonald invites them to "drive thru." Biology trumps advertising.

Phase 3 – Body Fat (especially belly fat)

That last section touched on a vitally important aspect of stress – that it can make you fat. Overexposure to any source of stress sets off a biochemical cascade throughout all parts of the body – right down to the cellular level. Neurological (brain) and endocrine (hormone) pathways are altered in response to stress, with that stress transmitted right down to the cellular and genetic level. Those alterations in nerve/hormone/genes lead to changes in our appetite (we crave more junk food) and in our ability to gain body fat (we burn less and store more, especially in the abdominal/belly region). Many people reading this book have experienced these changes in biochemistry firsthand – as our stress goes up, so does our waistline.

A primary focal point of this book is the close (and increasingly understood and acknowledged) relationship

between cellular stress, the CDR pathways, and our overall metabolism. When we encounter stress and cortisol rises, it interferes with our cells ability to activate the CDR pathway – so we accumulate cellular damage and its associated problems. A key intermediary in the relationship between cellular stress, cortisol and weight gain is another hormone called insulin. Most people associate insulin problems with diabetes because of its primary role in regulating blood-sugar levels (although insulin has many additional functions in the body). Not only does insulin regulate blood-sugar levels within an extremely narrow range; it is also responsible for getting fat stored in our fat cells (adipose tissue), getting sugar stored in our liver and muscle cells (as glycogen), and getting amino acids directed toward protein synthesis (muscle building). Due to these varied actions, insulin is sometimes thought of as a “storage” hormone because it helps the body put all these great sources of energy “away” in their respective places for use later. That's great, but it is exactly the opposite of what the body experiences during the stress response, when the heart and muscles need lots of energy and need it fast.

One of the first signals the body must send out during periods of stress is a message that screams, "No more energy storage!"—and that means shutting off the responsiveness of cells to the storage effects of insulin. When cells stop responding to insulin, they are able to switch from a storage (anabolic/building) mode to a secretion (catabolic/breakdown) mode—so fat cells dump more fat into the system, liver cells crank out more glucose, and muscle cells allow their protein to be broken down to supply amino acids (for conversion into even more sugar by the liver). This is all fine—assuming it occurs

infrequently and for only a short period of time. Telling the body's cells to ignore insulin on a regular basis, as happens with chronic cellular stress, can lead to a condition known as insulin resistance and predispose a person to the development of full-blown diabetes.

Stress makes a person fat primarily because of an excessive secretion of the key stress hormone, cortisol, along with a reduced secretion of key anabolic hormones, such as DHEA, testosterone, and growth hormone. This combination of highly catabolic cortisol and reduced anabolic hormones causes the body to store fat, lose muscle, slow metabolic rate, and increase appetite—all of which have the ultimate effect of making a person fatter. Overall, stress makes you burn fewer calories and consume more food (especially carbohydrates), which increases your stress levels even more! Even the thought of food and the concern about eating can increase stress levels—and therefore cortisol—in people who have restrained their eating habits and are either dieting or are concerned about their weight.

From a vanity standpoint, nobody wants to carry around more body fat than they need to. From a health and longevity standpoint, elevated cortisol levels and related cellular stress also tend to promote fat accumulation in the abdominal area, a condition that is closely associated with heart disease, diabetes, hypertension, and high cholesterol. Researchers are not completely sure why this "stress fat" accumulates specifically around the midsection. Its location here may have something to do with its being available for rapid access when the body needs additional fuel (because fat stored in the abdominal region can be delivered to the bloodstream and tissues faster then fat stored in peripheral

regions such as the thighs and buttocks). But even though the reason for abdominal fat accumulation is still unclear, its consequences are well known. This combination of conditions, known as metabolic syndrome or syndrome X, has been identified by many experts as the most important health danger that we'll face as a worldwide population in the early twenty-first century.

Most of us have grown fatter as we've grown older. It is interesting to note that several recent studies have demonstrated quite clearly that cortisol exposure and cellular damage increase with age, reducing our sensitivity to insulin, and elevating our risk for obesity, diabetes, and metabolic syndrome X. Stressed-out subjects with an altered pattern of cortisol secretion are characterized by a low concentration of cortisol in the morning, the absence of a circadian rhythm, and a huge meal-related surge in cortisol levels—all of which are consistently associated with obesity and related measurements.

People with disrupted cortisol-secretion patterns have higher body fat (particularly in the abdomen), lower muscle mass (particularly in the arms and legs), and reduced basal metabolic rate (BMR, the number of calories burned at rest). On the other hand, lower levels of cellular stress are associated with a more "normal" pattern of cortisol metabolism (high in the morning, with a normal circadian rhythm) and with more favorable measures of body composition (more lean and less fat) as well as a healthier cardiovascular profile (lower blood pressure, reduced cholesterol and blood sugar, and better insulin sensitivity).

All in all, the above scenario makes for very discouraging news: Stress makes us fat. Even worse, however, may be the findings from researchers that have determined that the stress of dieting can make us fat. Why

is this especially bad news? Primarily because at any given moment in our Western society, as much as 50 to 60 percent of the population is actively dieting—and many millions more are at least concerned about what they eat. This makes dieting one of the most common cellular stress triggers, for both men and women—but why are so many people dieting? Aside from the obvious fact that few of us eat right or exercise enough, we also have to contend with mass-media messages equating thinness with beauty, success, and intelligence (and the implication that we can't achieve those things unless we are thin).

Unfortunately, we also have to contend with the very real physiological changes that are occurring within each of us. As we age, cellular damage accumulates, our metabolic rate drops, and most of us begin to pack on the pounds. Adding fat in the abdominal area (in response to cellular stress) changes the body shape from that of an hourglass to more of a shot glass—and repeated diets only compound the problem.

Most of us will experience a drop in metabolism of about 0.5 percent per year after the age of twenty. Now, that may not seem like a large drop, but when you look at it over ten or twenty years, it means that we're burning 5 percent fewer calories at age thirty and 10 percent fewer calories at age forty—and so it goes, with about 5 percent fewer calories burned for every ten years of age. Just imagine: By the time we turn fifty, we're burning 15 percent fewer calories than we did when we were twenty. If you consume two thousand calories per day at age twenty (which is about average), this means you will need only seventeen hundred calories (three hundred fewer calories) at age fifty to maintain your body weight. It also means that if you don't make some serious changes in your diet and

exercise patterns, or at least get your cortisol levels under control, then your fifty-year-old body will be carrying around over thirty extra pounds of fat than when you were twenty!

Exercise and proper nutrition can certainly minimize our age-related drop in metabolism and increased tendency toward weight gain, but they can also help us control our response to cellular stress. The "right" program of diet and exercise will burn calories, shed fat, and relieve stress—but most people have enough experience with these "right" programs to know that diet and exercise have their own limitations. In fact, researchers at the University of Colorado have shown that athletes performing too much exercise (overtrained cross-country skiers) experience the very same adverse effects of elevated cortisol and cellular stress levels, such as mood disturbances, immune-system suppression, and increased levels of body fat. Of particular interest in this study was the finding that the athletes who were working out the most—those putting in the highest mileage and the longest training times—were also the ones with the highest cellular stress levels, the highest body fat levels, and the poorest scores on measures of emotional outlook (more depression). Basically, they were exercising their brains out to get in better shape, but their elevated cortisol levels were hampering, and indeed outright preventing, their progress.

So where does this leave us? In terms of “metabolic performance” for fat loss, we know quite clearly that cellular stress, dieting, and stress hormones such as cortisol are all detrimental to our overall goals of shedding excess body fat. We also know from decades of research that both exercise and good nutrition can be helpful in controlling stress, cortisol, body weight, and a whole host

of related health parameters. Scientists at the University of Goteborg, in Sweden, have shown that high cortisol levels are associated with a high waist-to-hip ratio, excess abdominal fat, elevated insulin levels, and a reduced secretion of growth hormone and testosterone—but they have also shown that a 13–14 percent reduction in cortisol levels is associated with a weight loss of more than twelve pounds. This means that despite the gloom and doom caused by the link between stress, cortisol, and obesity, we have some hope that by controlling cortisol and cellular stress levels, we can make a positive impact on our body weight and level of body fat.

Phase 4 – Fitness (especially lean body mass)

Participating in moderate exercise on a regular basis can reduce body fat, build muscle and bone, improve mental and emotional function, stimulate the immune response, and reduce appetite. Being physically active can also offset some of the destructive effects of chronic cellular stress. No drug can do all that! In terms of improving your general sense of well-being, exercise generates the production of dopamine and serotonin, both of which are "feel-good" anti-anxiety and anti-depression chemicals that are produced in the brain and are responsible for the well-known "runner's high" that can help control the stress response. For example, Duke University researchers have reported that exercise (thirty minutes per day, three to four days a week, for four months) is more effective than prescription antidepressants in relieving symptoms of anxiety and depression.

One of the most important factors when it comes to exercise is your purpose for doing it: The "reason" you should be physically active has less to do with directly burning calories and losing weight (although those may be nice side benefits) and more to do with the fact that exercise can act as a "hedge" against the tendency for stress, sleep deprivation, aging, and poor diet to upset the body's biochemical balance. Many people tend to overestimate the rate at which exercise can burn calories. They fail to realize that you would have to run a half mile to burn off every Oreo you eat and almost 90 minutes to burn off the calories in a Big Mac! So although it is true that exercise does burn calories, its primary value as part of your strategy for reducing cellular stress lies in its profound effects on restoring biochemical balance by modulating levels of cortisol, testosterone, growth hormone, serotonin, and other biochemical compounds in the Four Pillars of Health.

You might be wondering whether a "best" type of exercise will improve biochemical balance. In reality, the best form of exercise is anything—as long as you do it! You simply need to get out there and move your body for at least three to six hours each week (thirty to sixty minutes per day, six days a week). I know that many people claim they are "too busy" to exercise. In fact, being "too busy" is the most common excuse for not exercising. If you buy into that excuse, you need to accept the fact that your biochemical balance will never reach optimal levels and your cellular stress will be higher than it needs to be—simple as that. So I invite you to take a minute to think about all the things on which you regularly spend thirty to sixty minutes each day—television, newspapers, Internet, etc.—and then ask yourself if investing that same amount

of time in your health and in how you feel and look and perform is worthwhile. If you commit to an exercise program, I promise that your investment will produce great rewards.

Because I know how difficult it can be to push back against the stresses you face in the twenty-first century, I have developed a set of exercise recommendations that are designed to deliver the most benefits within the shortest time commitment possible. The most effective way to use exercise to reduce cellular stress is with a three-times-weekly regimen of interval training (either running or walking). I think everyone would agree that walking is a pretty simple exercise that you can easily incorporate into your daily schedule. It doesn't require any fancy or expensive equipment, and you can do it virtually anywhere. To get the most from your walking regimen, you'll want to make sure you have a pair of comfortable and supportive shoes as well as approval from your personal health-care provider that it is okay for you to engage in moderate to vigorous exercise.

Walk outside and enjoy the sights and sounds of your own neighborhood or a local park when the weather is good. Or when it is rainy or snowy, walk around the mall. Many shopping malls have organized walking groups that meet before the stores open and the mall gets crowded with shoppers. When you get comfortable with walking on a regular basis, you can change the route and vary the intensity (walking faster or slower and adding hills or flats). Walking can also be part of developing your "mental" fitness as much as it serves as your "physical" exercise, because it can allow you some time to "get away" and to destress while your mind (and your body) wanders.

The Interval Training Plan described below has been used successfully by many of my clients and readers:

After a six-minute warm-up, the exercise alternates between high- and low-intensity levels as follows:

- one minute high intensity/one minute low intensity*
- two minutes high intensity/two minutes low intensity
- three minutes high intensity/three minutes low intensity
- two minutes high intensity/two minutes low intensity
- one minute high intensity/one minute low intensity

* Note that the intensity levels will be relative to your individual fitness level. A general guideline is that "high" intensity is not an "all-out effort" but rather a level that gets you breathing hard enough that you have difficulty carrying on a conversation with your exercise buddy. The "low" intensity intervals are easy enough to allow full recovery before your next hard interval—and also easy enough for you to talk without getting out of breath.

These eighteen minutes of interval training are followed by six minutes of easy cool-down exercise for a total duration of thirty minutes. Compared to exercising at a steady/moderate "fat-burning" pace for this same thirty minutes, the interval approach will burn more than double the number of calories (less than 200 versus more than 400) and will result in superior reduction of cellular stress via direct control of cortisol, testosterone, glucose, and other aspects of your biochemistry.

Exercise is a vital part of achieving the optimal levels of cellular stress associated with proper tissue repair. Whether we talk about joints, bones, muscles, tendons, or any other tissue, the right amount of the right type of exercise can help stimulate production of new collagen, removal of damaged tissue, and delivery of vital oxygen and nutrients. The body is designed to move. One famous philosopher commented that the human body is the only machine that breaks down from underuse rather than from overuse. (But your body can break down from overuse as well, as evidenced by the numerous overtrained athletes that I have worked with over the years.) In many ways, the motion of exercise or any type of physical activity can be thought of as lotion for your joints and other tissues. The simple act of moving your body helps hydrate joints and stimulate tissue repair throughout the body, while the act of sitting around like a couch potato sends a constant "breakdown" signal (also called "atrophy") to your joint cartilage, bones, muscles, tendons, and ligaments.

Phase 5 – Personal Achievement (Best Future You)

As the reigning "World's Fittest CEO" (2nd place 2013, 1st place 2014) one of the most common questions I get asked is, "How do you stay in shape with all the travel you do?" I travel hundreds of thousands of miles every year all around the world. Whether I'm speaking at a scientific conference in Europe, or educating a group of coaches and athletes in the USA, or even scouting for interesting herbal extracts in Asian markets or the jungles of Brazil or Malaysia, it can be a huge challenge to stay in good physical and mental shape.

In one of my earlier books, The Secret of Vigor, I write about maintaining "vigor" in the face of chronic stress. Vigor is a term from psychology research that means the opposite of "burnout" and is described as a combination of physical energy, mental acuity, and emotional well-being. The book outlines much of the extensive research and complex underlying biochemistry (hormones, enzymes, neurotransmitters) that drives our psychology (how we feel and behave) on a daily basis, but it also breaks down some of the simple "what to do" aspects of improving vigor to boost energy, improve mood, focus attention, and even trim your waistline. I call these "what to do" tips, "VIPs" for vigor improvement practices – and I'll share some of my favorites with you below (5 for Nutrition, 4 for Exercise, and 3 for Mind).

Top 5 Nutrition VIPs

Eat by color – choose bright and avoid white. Brightly colored fruits and veggies are high in protective phytonutrients – so try to include at least one of each "color" in your diet every day. Look for all the colors in the rainbow: Red (lycopene from tomatoes), Orange (beta-carotene from carrots), Yellow (lutein from corn), Green (chlorophyll from spinach), Blue (anthocyanidins from blueberries), Indigo (catechins from blackberries), and Purple (quercetin from grapes). Avoid processed foods based on white flour – such as white bread, rolls, and baked goods.

Is it calorie worthy? Ask yourself whether or not the food you're thinking about eating is really "worth" the calories that you're about to "spend" on eating it. For example, I think it's great to enjoy a nice glass of red wine or a warm chocolate chop cookie, but don't eat a cookie that's only so-so. For example, one of my favorite fitness snacks is low-fat fruit yogurt because it's a rich source of calcium, magnesium, vitamin D, protein, and probiotics – all of which are important for fat metabolism and helping us shed body fat and boost lean tissue.

Practice pairing of macronutrients. Always combine a carbohydrate with a protein and fat. Carbohydrates in and of themselves are not "bad," but both the form of carbohydrate (how much it's processed) will determine your body's biochemical response. For example, the more refined (less "whole") the carb is, the more likely it is to raise blood sugar levels, leading to oxidation, inflammation, and problems with muscle building and recovery. Combining any carb source with some protein and fat will slow it's absorption and lessen it's oxidizing/inflammatory effects in your body.

Eat more healthy (omega-3) fats and fewer unhealthy (omega-6) fats. Fatty fish – like mackerel, bluefish, wild salmon, and tuna are rich omega-3s that improve circulation, reduce inflammation, and reduce the risk of heart disease. Reduce your intake of inflammatory omega-6 fatty acids found in high concentrations in vegetable oils such as corn/soybean/sunflower oil.

Supplement wisely. A big part of my supplement routine to geared toward enhancing my body's own protective and recuperative abilities. This means assuring a high intake of nutrients and herbal extracts that activate natural performance pathways in the body – including turmeric, green tea,New Zealand pine bark, quercetin, theanine, and others. Activating the CDR pathway is a built-in way to turn on your body's own production of antioxidant enzymes and anti-inflammatory proteins. Maintaining mental and physical performance during exercise is my secret weapon to getting into that feel-good "flow" state where energy, mood, and focus are at peak levels.

According to a recent study, elite endurance athletes are more likely have variations in their ability to activate the CDR pathways. The study found that 80% of the elite-level athletes had CDR-related gene variations that may be associated with improved athletic performance, such as increased production of new mitochondria (the cellular components responsible for energy production) and reduced cellular damage from oxidative and inflammatory stress. Another recent study showed that typical antioxidant supplements – such as vitamins C & E, beta-carotene, and resveratrol – may disrupt the cellular adaptations to exercise training, blunting the training-induced increase of mitochondrial proteins, which are

needed to improve muscular endurance. Researchers theorized that the vitamins interfered with cellular signaling and blunted the expression of certain genes, such as those involved in activating the CDR pathway, that are required for muscle adaptations subsequent to exercise training.

Top 4 Exercise VIPs

Practice "MIM" – by making your workout your "Most Important Meeting" of the day. Research shows that exercise is even more effective that prescription antidepressants or ADHD drugs for improving mood and maintaining mental focus – so think of your daily workout as an investment in your career just as much as it is an investment in your physical health and mental well-being.

No "junk" workouts. Similar to the "calorie worthy" diet concept, you want to make sure to avoid "junk workouts" where you're simply going through the motions. When you have limited time and need to squeeze as much value out of each minute, every workout needs to have a focus. This means that you need to decide what type of workout you're doing – such as building speed (hard/fast intervals) or endurance (long/slow distance) or building strength (weights/Crossfit) or balance (yoga, plyometrics, etc). Don't fall into the trap of going at "medium" intensity all the time just to feel like you got a "good" workout – that's the path to mediocre performance.

Get In, Get Out, Recover. I train a maximum of 8-10 hours per week, even when I'm training for an Ironman or an ultramarathon. If you focus on quality workouts with a purpose, you can get a lot of fitness bang for your workout buck – but you also have to recover properly to fully reap

those rewards. Whether we talk about joints, bones, muscles, tendons, or any other tissue, the right amount of the right type of exercise can help stimulate production of new collagen, removal of damaged tissue, and delivery of vital oxygen and nutrients. The body is designed to move – so much so that the human body is the only machine that breaks down from underuse rather than from overuse. That said, it's quite clear that our body (and mind) can break down from overuse as well, as evidenced by the numerous over-trained athletes that I have worked with over the years.

Take a full day off each week. Recovery for both body and mind is so important – and so neglected – I'll emphasize it's importance by giving you another tip about it. A "day off" means no work – or workouts. No thoughts about work or worries about workouts. Take this day to relax, reflect, and recharge, regardless of whether or not a "Sabbath" day of rest has any religious connotations for you. Read a book. Take a walk. Luxuriate in the act of doing nothing. I guarantee that if you give yourself over to a solid month of "do-nothing Sundays" (or Saturdays, or whichever day of the week works best for your schedule), you will feel more physically and mentally refreshed than you could possibly imagine. Doing nothing will give you back a lot.

Top 3 Mind VIPs

Numerous research studies verify the damage to body and mind caused by chronic stress. Being stressed out and sleep-deprived has been shown to increase heart disease and depression, reduce sex drive, suppress immune

function, increase illness/injury rates, and accelerate both muscle loss and weight gain (especially belly fat) by nearly 10 times! Being fat, stressed, tired, sex-deprived, sick, and injured is no way to become the best version of yourself.

Get some sleep. Far and away the most effective stress-management technique you can practice is very simple: Get enough sleep. For example a Yale University study of 1,709 men found that those who regularly got less than six hours of shut-eye doubled their risk of weight gain and diabetes because of elevated cortisol and its interference with insulin metabolism and blood-sugar control. Even one or two nights of good, sound, restful sleep can do more for maintaining your biochemical balance, improving your performance, and reducing your long-term risk for many chronic diseases than a whole lifetime of stress-management classes. It is almost impossible to overstate the crucial role adequate sleep plays in controlling your stress response, helping you lose weight, boosting your energy levels, improving your mood, and, of course, raising your level of vigor.

Manage electronic interruptions. The beeps and buzzes from your computer and iPhone can add an annoying level of stress to your day. Instead of just responding every time you get an electronic interruption, take charge of those devices and set them to only alert you at specific times. Remember that your cell phone is there for your convenience – not the convenience of others. For instance, most e-mail programs are automatically set to check for new messages every five minutes – which means you're interrupted by the "new-message beep" ninety-six times in an eight-hour day! How do you expect to get any "real" work done? Also, consider (as I do) shutting off your e-mail program during certain parts of the day,

enabling you to get your “important” work accomplished whenever you’re most mentally fresh.

Whenever possible, leave the cell phone behind. It may be hard to imagine today, but it wasn’t too many years ago that people got along perfectly fine without cell phones. Try taking a break from your phone when possible by leaving it behind – especially during your workout. I make that recommendation, because if you carry your phone with you —even if you tell yourself that you won’t answer it—a part of your mind still waits for it to ring, or buzz, or play your favorite ringtone. Let that part of your brain relax and forget about the phone every now and then.

Summary

When you consider all of the myriad sources of cellular stress around us, it can be a bit disheartening to think that we can actually fight back effectively. Luckily, however, the discovery of the CDR pathway has given us insight into the precise cellular mechanisms that we can harness to do just that – reduce cellular stress even in the face of what may initially look like overwhelming odds. – and maintain or even enhance our mental and physical performance in the process.

Chapter 9 - Putting It All Together

For more than two decades, I've been doing my best to help people maintain (or restore) "balance" in their bodies and minds. Some people might label my techniques as "nutrition" therapy, while others may refer to them as "anti-aging" approaches, and still others as "anti-stress" programs. From my position as an exercise physiologist and nutritional biochemist, these "labels" are based on the proven efficacy and resounding benefits that people receive from following the advice that I deliver in my seminars, blogs, and books – so no matter what "label" you want to use to describe the focus of my life's work, you can rest assured that there are enough health and well-being benefits to go around.

Let's be honest, very few of the hundreds of thousands of people around the world who attend my seminars or read my blog and books, wake up each morning looking to restore their "biochemical balance" or reduce their "cellular stress" levels. However, the fact that you're reading this book probably means that YOU understand the crucial role that stress in general – and perhaps cellular stress in particular – play in our overall health, well-being, and longevity. At this point in the book, you very likely understand that biochemical imbalances and cellular stress are the root underlying causes of damage, dysfunction, and disease in every tissue in the body. You're undoubtedly aware that thousands of scientists around the world have associated cellular stress with virtually every chronic condition imaginable, as well as with the aging process itself.

All of this means that everybody needs proper daily management of cellular stress if they want to be as healthy as possible. Unfortunately, “optimal health” can often be both a difficult concept to explain, as well as an abstract idea for most people to fully grasp. This is partly due to the fact that the problems associated with excessive cellular stress may take years to manifest – and also may take just as long to resolve when cellular balance is restored. For example, heart disease, cancer, obesity, depression, fibromyalgia, chronic fatigue, arthritis, multiple sclerosis, Alzheimer’s, Parkinson’s and so many other chronic conditions don’t develop overnight – they occur through gradual accumulation of tissue damage that builds up over months and years of our cells being out of balance with elevated levels of cellular stress.

As a scientist who has studied many aspects of biochemical and cellular stress, I often educate my audiences and readers that “biochemistry drives behavior” – which basically means that a key reason that we feel (or look, or perform) a certain way, is because of our underlying biochemistry – right down to the cellular level. In research settings, we can show that disrupted biochemistry often leads us to feel “off” – so we don’t feel our best, or look our best, or perform our best. What scientists often refer to as “cellular stress” – from free radicals (oxidative molecules), cytokines (inflammatory molecules), glucose/fructose (glycating sugars), cortisol (our primary stress hormone), and many others – is what makes each individual cell function poorly. When you have trillions of cells functioning poorly throughout your over-stressed body, then it’s no wonder we don’t feel like we’re at our best.

When we seek to reduce cellular stress, and restore balance within the body, we need to harness the body's own internal protection system by activating the CDR pathway referred to throughout this book. This internal network of antioxidant enzymes, stress proteins, and survival genes has the ability to sense cellular stress – and respond rapidly to reduce damage, accelerate repair, and restore balance. By inducing these mechanisms throughout the body – we can improve the functioning of trillions of cells.

When mitochondria, neurons (brain cells), and blood vessels are kept healthy, we're likely to feel our best. When our skin cells are able to protect themselves from the toxic environment around us (air and water pollution, ultraviolet radiation from sunlight, etc), we tend to look our best. When our muscles, joints, and lungs are functioning at their peak, then we tend to perform our best. Each of these individual benefit categories – feeling your best, looking your best, and performing your best – represents a multi-billion dollar business opportunity that is being aggressively pursued by the nutrition, cosmetic, and pharmaceutical industries. Why? Because these are the benefits that people want – but they're also the benefits that are the most elusive because cellular stress is the underlying factor preventing people from attaining them.

The Fluctuating Nature of Stress

It is important to remind yourself from time to time that neither your stress level nor your response to stress is constant. Instead, there will be periods in your life when you experience more stress or less stress, just as there will

be times when you feel as if you can withstand stress better and times when it is more difficult. Accordingly, you need to alter your exercise patterns, nutrient intake, and supplementation regimen to accommodate your exposure to stress. For example, regular exercise and a balanced diet are always going to be important, but they become even more so during stressful times.

Adhering to your regimen of dietary supplementation is important every day, but even more so when you're under periods of elevated stress. Skipping breakfast during a period of low stress isn't ideal, but it isn't going to kill you. Skipping that balanced breakfast during a high-stress period sets yourself up for poor metabolic control and eventual blood-sugar crashes, surges in appetite, and feelings of fatigue—each of which will be even more pronounced because of your high-stress profile.

In other words, you almost need to do the opposite of what most people are tempted to do during high-stress periods—that is, staying up late to finish work, skipping meals or eating junk food, and neglecting exercise. Obviously, no one is going to maintain a perfectly balanced anti-stress regimen, especially in today's modern "always-on" super stress world. Nevertheless, if you keep some of the suggestions presented throughout this book in mind – and implement them when possible, you'll find it much easier to deal with high-stress periods in your life—and you will feel, look, and perform your best as a result.

Are you experiencing higher-than-normal stress levels in your life? If so, then your cellular stress is likely to be elevated and your biochemical balance is likely to be "off," – and you need to be especially careful about taking steps to activate the CDR pathway to reduce cellular stress and restore that internal balance.

Are you enjoying an interlude that's relatively stress-free and tranquil? Then perhaps you can relax a bit and take pleasure in the welcome fruits of the healthy lifestyle you've created—and commit to maintaining it.

Keep in mind that all of the "pillars of health" that were outlined separately in earlier chapters (oxidation, inflammation, glycation, and allostation), are all interconnected, so any healthy activity you engage in for one of them will affect all the others, leading to a positive spiral in how you feel, look, and perform. For example, using herbal supplements or specific foods to activate the CDR pathway and internal production of protective antioxidant enzymes will complement the anti-inflammatory effects of regular exercise, which will complement the glycation-reducing effects of eating a balanced diet, which will complement the cortisol-lowering effects of getting adequate sleep.

Ancient Wisdom Meets Modern Lab Data

One of the things that I love most about the kind of work that I'm lucky enough to do, is that studying lifestyle interventions (diet and exercise) and traditional remedies (herbal and dietary supplements) provides us with plenty of circumstantial evidence that they "work." In many cases, our Western-style research studies are merely confirming (with objective scientific data) what has already been observed for decades or centuries or even millennia. For example, practitioners of traditional Chinese medicine (TCM) have been using various herbal remedies for more than three thousand years, and practitioners or traditional Indian medicine (Ayurveda) have been using herbs as

medicine for more than five thousand years, but it has only been in the last two or three decades that any of these traditional remedies have been "proven" to work by modern scientific investigations. The TCM and Ayurvedic practitioners "knew" that certain remedies "worked" for certain ailments (such as using eurycoma or ginseng to "strengthen the Qi" – or using turmeric to reduce pain and swelling), but it has taken modern science quite a long time to confirm that these ancient remedies are effective in reducing cellular stress and restoring biochemical balance in the face of many of our own modern stress-related diseases.

As a scientist, I find that theories are nice, but evidence is where the rubber meets the road. In the words of many of my colleagues, I want to "see the data" about a particular approach (including CDR activation) before I will believe it works. Based on the data, scientists and health professionals can understand that a given program has a certain degree of likelihood to actually be of benefit to their clients and patients. Throughout my entire career, I have felt very strongly about continuing to put the traditional herbal therapies "to the test" to see if these ideas would really stand up to the harsh reality of reducing cellular stress and improving how people feel , look, and perform in the modern super-stress world in which we all now find ourselves.

In the wide range of cellular stress studies, it is interesting to note that we can literally trace "systemic" stress (for example, of psychological stress or sleep deprivation) all the way down to the cellular level and even to the genetic level. Likewise, we can trace the phytonutrient activation of a cellular anti-stress pathway (for example, activation of the CDR pathway with turmeric

or pine bark) all the way "up" to a whole-body benefit such as reduce inflammation or to a tissue specific benefit such as improved brain energy and mental focus. It's even more interesting to note that these traditional anti-stress therapies seem to work even better (faster and more effectively) under conditions of higher stress.

For close to a decade, my research associates and I have documented the progress of thousands and thousands of participants who have used the lifestyle interventions described in this book to reduce cellular stress, restore biochemical balance, and improve how they feel, look, and perform. Scientific colleagues around the world have further shown in a variety of research models, that the CDR pathway is the underlying "switch" by which these traditional therapies induce their cellular effects. Many of these peer-reviewed studies are outlined and summarized at my personal blog (ShawnTalbott.com).

Concluding Words

Our grandmothers didn't know about cellular stress or care about CDR pathways, but they knew some of the basic steps underlying our ability to feel, look, and perform at our best: Get enough sleep (which controls cortisol); Eat more fruits and veggies (which controls oxidation) and fewer sweets (which controls glycation); and Exercise (which controls inflammation). Yes, it's a tired old mantra, but these simple steps are probably the most effective tools available for combating stress and raising levels of wellness.

Stress researchers around the world from Yale to Oxford to the University of California have shown over and

over that the best way of "managing" stress, from a physical and a psychological perspective, is to adhere to a handful of basic tenets of good health promotion. Here are my favorite "Magnificent Seven" that I've gleaned from the research:

1. Move it! It doesn't even really need to be "exercise" as long as you're out there moving your body from point A to point B—and often (daily)—and for about an hour per day (though not necessarily all at the same time).

2. Eat right – with fewer of the wrong foods (highly processed grains including soda and baked goods) and more of the right foods (brightly colored fruits and vegetables).

3. Stop eating before you're stuffed. Use the "80 percent rule" so you eat until you're not hungry (80 percent full) – and practice intermittent fasting at least once per month (eat nothing except water from 10pm one night to the following night's dinner at 6pm – around 20 hours).

4. Spice things up – by using spices (turmeric, ginger, rosemary, garlic, etc) and plant extracts (pine bark, green tea, quercetin etc).

5. Find an outlet (for your stress)—everyone has stress that needs to be released. The stress is toxic, and it is stronger than you—get rid of it.

6. Get a life. Cultures with the longest life spans and the highest "happiness quotients" tend to have well-

developed social networks that emphasize making family and friends a priority, living a spiritual life, and encouraging individuals to have a "purpose" in life.

7. **Relax.** Sleep. Be lazy (every once in awhile).

Decades of scientific research show that stress—and failure to adhere to the seven basic tenets listed above—does a lot of "bad things" to people. Most "modern" diseases are stress-related and directly result from the biochemical imbalances that stress creates, but from a simple "quality-of-life" perspective, we know that rampant cellular stress impedes our ability to feel our best, look or best, and perform at our best.

I am continually astounded by the potential for centuries-old natural therapies to cure so many of our modern ailments – by the ability of plant compounds (phytonutrients) to reduce cellular stress and improve how we function physically and mentally. The research breakthroughs over the past few decades have given us the ability to not only survive in the face of a chronically stressful world, but to truly thrive in that world – so that we don't just hope to "get by" but we have a real ability to improve and become that "best future you" version of ourselves.

We are living in a miraculous time in history – where the learning of ancient healers about natural therapies over thousands of years is finally being scientifically proven at the cellular, genetic, and molecular levels. We are the lucky benefactors of this accumulated knowledge and experience, which enables us to bring about meaningful

changes in how our body responds to stress and how we feel every day. I hope that, by this point in the book, you've come to the conclusion that everyone needs to "do something" about their chronic stress exposure and the resulting cellular stress, and I also hope that I've made a compelling-enough case for you to give some of my advice a try. Restoring biochemical balance and reducing cellular stress will truly change your life – and when it does, I hope that you will be motivated to share what you have learned in this book to help others change their lives as well.

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