PART ONE

The Immortality Promise

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The Aging Cure

Is aging a disease or a natural process that has existed forever? You may be surprised to learn that aging has not existed forever. Approximately four and a half billion years ago, a single cell came into existence that was the progenitor of every living organism that has existed on our planet ever since. This single cell did not age; it had the capacity to divide indefinitely. It could produce an infinite number of copies of itself, and it would not die until some outside environmental event, such as an erupting volcano, killed it.

The ancestry of every living cell in your body can be traced back to this very first cell. This lineage is called the cell's *germ line*.

Three billion years after the first cell appeared, some of the cells from this germ line began to form multicellular organisms, such as worms, insects, fish, and finally humans. The germ line was passed from one generation to the next, and it remained immortal. Even with the inclusion of multicellular organisms, the germ line itself showed no signs of aging.

However, the cells that form the body of an organism, called *somatic cells*, began to age. Their ability to reproduce themselves indefinitely came to an end. Until recently, scientists were only able to speculate why somatic cells die.

We now know why. Unlike germ cells, somatic cells contain a gene that controls the production of telomerase, and this gene is turned off. Without the ability to produce telomerase (except in trace amounts), the telomeres of somatic cells become shorter and shorter with each replication, until the cell finally goes into senescence and dies.

The speed at which our telomeres shorten is determined by the outcome of the endless war our organism wages on the damaging forces that actively attempt to destroy our molecules, our cells, and our entire bodies. At every moment we are engaged in an internal struggle against negative forces, including oxidation, glycation (described later), inflammation, DNA gene mutation, and abnormal methylation (described later). Simultaneously, we are also dealing with external threats: environmental toxins, natural catastrophes, war, and other forms of violence. When we lose any of these battles at any level—biochemical, cellular, systemic, or in the whole organism—death can and does occur.

At every level, life is a balance between entropy and defense, degradation and restoration. Our bodies are miraculously designed to defend us from any attack. At every level, we have specific ways of minimizing, avoiding, replacing, and repairing damage.

As you mature into an adult human being, at some point, usually around age forty, your body is no longer able to build new proteins as quickly as it loses them. You can synthesize them as accurately as before, but there are also more damaged proteins, because they don't recycle as fast as they did when you were younger. As a result, the damaged proteins linger. It's not that there are fewer proteins to go around; it's just that the turnover slows down. Protein synthesis declines by more than half, and so does protein breakdown. Our cells don't recycle as well as they once did, and as a result, the number of damaged proteins in our

bodies at any given time increases. As the balance shifts toward the forces of decay, we age faster. Age-related defects in metabolism add to pathology. The pace of telomere shortening picks up.

The aging process we are describing here is strikingly similar to what happens when our bodies develop specific diseases, including Alzheimer's disease, diabetes, cardiovascular disease, and even cancer. The core cause of type 2 diabetes, for example, is a gradual decline in the number of beta cells in the pancreas. These beta cells make and release insulin. Alzheimer's disease is

How We've Extended Life Expectancy

Since 1900, the average life expectancy in the United States has risen nearly 60 percent, from 47.3 years to 78 years. The following is a list of factors that account for much, if not most, of this improvement:

Antibiotics
Antioxidants
Better diets
Better teeth and gum hygiene
Blood pressure medicine
Cleaner water
Coronary artery bypass surgery
Hormone replacement
Improved management of hazardous chemicals
Improved public awareness of nutrition
Improved sewage systems
Medications that improve vascular health
More effective cancer treatments
More exercise
Reduced smoking
Refrigeration
Some vaccines

associated with an accumulation of amyloid plaques (an abnormal protein breakdown product that interferes with normal cell function, among other processes) and tangles in the brain. Heart disease is associated with the buildup of fatty plaques and the gradual hardening of the arteries. And cancer, of course, is associated with the growth of malignant cells.

Old age underlies most diseases. We believe that old age actually *is* a disease and it simply has many faces. Each disease is individual and separate from all others, yet the erosion of the telomere plays a role in all diseases of aging. One disease can hasten another. If the telomere did not shorten, most diseases would have a different appearance, and a few might not appear at all. In recent years, overwhelming evidence has emerged that genetic and lifestyle interventions, in parallel, can retard nearly all late-life disease. And guess what: these lifestyle interventions also slow down aging.

The belief that aging is an immutable process, programmed by evolution, is simply wrong. Aging is a disease, and just as we do with other diseases, we should create drugs and other technologies to cure it. The mere fact that aging has existed in the genetic code for roughly one billion years doesn't change this. Thousands of other diseases, from hemophilia to cystic fibrosis, have lurked in our genes for far longer than recorded history.

Immortality Is Just around the Corner

Do we currently have the knowledge and the technologies to live forever? At this precise moment in time, the answer would have to be no. We can dramatically slow down diseases and the aging process far more than most people realize, but we do not yet have the "magic bullet" to indefinitely extend human life.

We now know, however, what the solution most likely will be, and there is every reason to believe that it will be available sometime in the next twenty years. It will be a drug therapy that turns on the telomerase gene in healthy somatic cells.

At least one biotechnology company we are familiar with, Sierra Sciences in Reno, Nevada, is completely devoted to discovering chemical compounds that, as the company describes it, induce telomerase gene activity in normal human cells without killing them. Sierra Sciences found its first telomerase inducer on November 6, 2007, and as of this writing, the company has screened more than 250,000 compounds and found 38 different chemicals that induce telomerase expression. The most potent of these, however, is only 12 percent of what they believe they need to make a human cell immortal. Sierra Sciences is currently screening 4,000 compounds a week.

Another company, T. A. Sciences, Inc., in New York City, has a supplement in pill form that it claims has been lab tested and shown to turn on telomerase and lengthen the shortest telomeres. This is critically important because it only takes one short telomere to send a cell into crisis. This product, TA-65, contains a single molecule of the astragalus plant, which has been used in Chinese medicine for thousands of years, often in combination with other herbs, to strengthen the body's immune system. The company purifies the rare (expensive!) substance through an extensive process, which also factors into its high price, from $2,400 to $8,000 per year.

The efficacy of TA-65 is incremental. It does seem to stop telomere shortening and minutely lengthen telomeres, but not in the profound way that future drugs will. One natural compound that may prove more powerful and more affordable may be available by the time this book is published. You can find updates on it at www.maxlife.org/telomeres. Still, TA-65 is currently being used by the authors of this book, and Dr. Woynarowski is one of the physicians who is licensed to distribute it.

Living Long Enough to Live Forever

The telomere theory of aging, though it is gaining traction, is not the only theory of what causes aging. Because aging is not

a simple process and may indeed have multiple causes, there are quite a few feasible ideas floating about. Here's a short list.

Other Theories on the Cause of Aging

- *Disposable soma*. We are just a temporary house for our genes. At some point, our genes get tired of us and move out.
- *Free radicals*. Free radicals cause mutations in our proteins and our DNA. When enough free-radical damage accumulates, we die.
- *Vital substance*. We have a limited amount of some undiscovered vital substance.
- *Gene mutation*. The accumulation of mutations causes aging. This ties into the free-radical theory above.
- *Reproductive exhaustion*. After a burst of reproductive activity, a switch is flipped. We die rapidly.
- *Aging by design*. We are simply programmed to die.
- *Wear and tear*. Aubrey de Grey, an Oxford biogerontologist, likens the aging process to an old car, where our body parts simply wear out over time.
- *Waste-product accumulation*. Like a clogged water filter with too much debris, our cells and bodies no longer function as they should.
- *Cross-linkage*. A process called *glycation* causes sugar molecules to bind with protein molecules, creating globs of gunk called *advanced glycation end products* (AGEs). These build up, causing diseases that age us and eventually kill us.
- *Immune system*. The decreased efficiency of the immune system causes aging.
- *Errors of repairs*. The inaccurate repair of cellular damage causes aging.
- *Order to disorder*. A decrease occurs in the efficiency of the systems *that maintain order. Thing*s get messed up, we age, they get more messed up, and we die.

One thing all of these theories have in common is that they are all related to accelerated telomere loss and damage.

But just as the telomere theory of aging isn't the only theory, telomerase activation isn't the only proposed method for obtaining an infinite life span. One intriguing idea comes from nanomedicine, a branch of nanotechnology. The idea is to create microscopic machines to be sent on missions inside our bodies to inspect, repair, and reconstruct cells.

Nanomedicine theorist Robert Freitas, who is the senior research fellow at the Institute of Molecular Manufacturing in Palo Alto, California, points out that if "the idea of placing millions of autonomous nanobots inside one's body might seem odd, even alarming, the fact is that the body already teems with a vast number of mobile nanodevices." In other words, biology itself provides the proof that nanomedicine is feasible.

We are quite positive that the cause of and the solution to aging lies in telomere biology. If we are wrong, and it lies elsewhere, what difference will it make, as long as you are still around to benefit from another solution? The more important question is "What will it take to keep you alive long enough?"

Aubrey de Grey, the Oxford biogerontologist we quoted earlier about hundred-year-old cars, says, "The people who are working on [these cars] aren't doing any more sophisticated work on them now than they were doing fifty years ago, when the cars were only three or four times as old as they were designed to be. When you decide to do sufficiently comprehensive maintenance, that's it. You can keep the machine at a manageable level of damage, a level that is not prejudicial to the functioning of the machine."

De Grey has a point. Mechanical maintenance of your body will help to keep it running. There is an important difference, however, between cars and humans. Unlike cars, our bodies contain hidden destructive forces. If these forces are not counteracted, they can cause you to age even faster than normal. Identifying and controlling them is central to your battle to keep your telomeres as long as possible for as long as possible.

If we could remove the genetic factor from aging and disease, we would still be left with about 70 percent of the real causes. According to the Human Genome Project, 30 percent of what

happens to us is determined by our genes and inheritance; the other 70 percent is determined by our environment and how well we maintain ourselves (like the vintage automobiles). That's good news; it means that maintenance gives us two-to-one odds that we can influence our future health in a very positive way.

To understand aging and illness as well as more subtle problems like sexual dysfunction, brain fog, fatigue, and weakness, you need to penetrate to the level of the individual cell. You also have to keep a kind of biological flowchart in mind: cells form tissues, tissues form organs, organs form organ systems, and organ systems form organisms (you and us!) when they operate in synchronized fashion. You are only as good as your weakest link (which might just be your shortest telomeres!), so even a small population of dysfunctional cells can put a big load on the rest of your body, ultimately leading to sickness and death.

The Major Aging Factors

At the cellular level as well as at higher levels, three major aging factors—oxidation, inflammation, and glycation—can wreak havoc in our bodies. They work in concert, feed upon one another, and make one another stronger and far more deadly. Abnormal methylation is also a factor in aging.

Showing you how to minimize the impact of these aging factors is a major purpose of this book. We want you to defeat oxidation, inflammation, glycation, and abnormal methylation so that you can extend both your health span and your life span. We want you to be available for the even more potent anti-aging telomere therapy that is bound to come along in the near future.

Oxidation

The first aging factor, oxidation, is represented by free radicals, high-energy molecules that are unstable because each has a single,

unpaired electron in its outermost shell. This electron is essentially homeless; it keeps trying to find a partner, even when that means stealing an electron from, and damaging, other molecules. Free radicals roam about our bodies with haphazard abandon, interfering with normal cell function. Like molecular sharks, they are constantly hungry, latching on to almost any nearby molecule, damaging it by changing its shape and making it useless or even dangerous. The damaged molecule becomes a misshapen, crippled player on the molecular team. Not only does it no longer function by itself, it interferes with the functioning of its surrounding teammates.

In this way, free radicals are infectious, passing on their unpaired electrons to other victims, which then pass on electrons that become the source of further damage. The chain of damage extends indefinitely and terminates only when the single electron finds a suitable mate and at last settles down and is once again at peace.

Ironically, the most common free radical in your body is oxygen, an element you cannot live without. Although molecular oxygen is relatively stable, it takes only a very small energy fluctuation to form single oxygen atoms, which are remarkably reactive with other molecules. The damage that single oxygen atoms do is specific, depending on exactly which free radical gets loose—the solubility, acidity, and proximity to specific sites all determine what is damaged.

As you age, free-radical damage to your DNA increases. Certain areas of your DNA are especially vulnerable to free-radical damage. This is important because there are only limited amounts of DNA available, the repair mechanisms are not perfect, and DNA is the blueprint for all other molecules in your body.

Countering the effects of these free radicals are "reduction molecules" that function like free radical "sponges" soaking up excess energy without being damaged themselves or causing damage to other cells. This balance is a critical part of cellular biochemistry. Only when the situation becomes unbalanced do

problems occur and you have what is called *oxidative stress*. This happens when there are too many free radicals or relatively not enough reduction molecules, or when the regenerative and repair machinery of the cell is too sick or old to keep up with free-radical generation and is unable to neutralize it.

As you'll see in the chapters on supplements and nutrition (chapters 2 and 6, respectively) there are many ways to decrease the production of free radicals and thereby minimize the damage to your telomere segments as well as the rest of the cell. In general, these supplement and food choices will also benefit the health of your mitochondria, the engine inside cells where energy is burned and where free radicals originate. In chapter 2 you will learn a great deal about mitochondria.

Inflammation

The second aging factor is inflammation. Only a decade ago, inflammatory diseases were believed to be confined to conditions with obvious, or acute, inflammation, such as the inflamed joints of arthritis, the inflamed airways of asthma, or even the inflamed skin of acne. Since then, however, a chronic, or silent, inflammation has been discovered to play a main role in diseases that had not been considered inflammatory at all, including heart disease and other vascular diseases, Alzheimer's disease, diabetes, and certain types of cancer. The symptoms of chronic inflammation are altogether different from the symptoms of acute inflammation. Chronic inflammation is hardly noticeable until catastrophe strikes.

Chronic low-grade inflammation can smolder silently within your body for twenty or thirty years and even longer without causing any obvious or outward problems. But all that time it is eroding your health and taking years from your life.

Cardiologists once thought that heart disease was caused simply by the buildup of cholesterol deposits inside the walls of the coronary arteries. Now we know that chronic inflammation is a

fundamental reason for cholesterol being deposited in the arteries in the first place.

We know that chronic inflammation is also at the root of Alzheimer's disease. In the brain, it increases the production of soluble amyloid protein and increases its conversion into insoluble amyloid fibrils, which are toxic waste products that interfere with normal brain functioning and kill brain cells.

In type 2 diabetes, chronic inflammation is behind the formation of a different type of amyloid that forms in the pancreas. The chronic elevation of blood sugar and insulin levels increases inflammation in the bloodstream, triggering a cascade of events in the pancreas of type 2 diabetes patients similar to what is seen in the brain of an Alzheimer's patient.

Although it is premature to come out and flatly say that inflammation is the primary cause of all nongenetic diseases and of aging, it certainly plays a major role.

Chronic inflammation affects the telomeres as well, causing them to shorten at a faster than normal rate. Recent research seems to indicate that there may be tissue-specific telomere shortening in many diseases. People with heart disease, for instance, may have shorter telomeres in their heart tissues than in other places. People with Alzheimer's disease appear to have a disproportionate shortening of their brain telomeres.

Like many things, the amount of inflammation in your body is largely under your own control. You can reduce inflammation by eating more vegetables and, in particular, medium- and low-glycemic fruits for their antioxidant value, increasing your fish or fish oil consumption, getting a decent amount of the right kind of exercise, improving your stress response, and sleeping better. Importantly, as you will learn in our chapter on nutrition, there is an eating plan based on the age-old trends of hunter-gatherers that we, along with some top evolutionary scientists and researchers, believe can naturally reduce inflammation by matching your nutritional genetics with what you eat. This plan is called the Paleolithic Diet.

The nutrition, exercise, and stress reduction sections of this book are all keyed toward helping you to lower your inflammation levels.

Glycation

Glycation is the third aging factor. You may not realize it, but there's a double-edged sword hiding in seemingly harmless foods such as bread, salad dressing, fruit juice, ketchup, mustard, and some brands of tomato sauce, to name a few. All of these everyday consumables could be contributing to the slow and steady destruction of your cellular health, thanks to one dangerous ingredient: sugar. The odds are that sugar is sabotaging your health and making you age faster right now, at this very moment.

When your body is exposed to too much sugar, including too many carbohydrates that convert to sugar when you eat them, the process of glycation is triggered: the sugar molecules attach themselves to the molecules of proteins and fats (lipids). The result is

Basic Sugars and Sweeteners

Are you confused by all of the different sugars and sweeteners? It's no wonder, because there are so many of them. This list should help you to sort it out:

- *Dextrose, fructose, and glucose*. All are monosaccharides, or simple sugars; the difference lies in how your body metabolizes them. Dextrose and glucose are essentially the same; however, food manufacturers usually use *dextrose* on their nutrition labels.
- *Table sugar*. Half glucose and half fructose, disaccharide, or table sugar, is a complex sugar formed from two simple sugars.

- *High fructose corn syrup (HFCS)*. HFCS, which is 55 percent fructose and 45 percent glucose, may well be the most damaging of all sugars. You can trace the rise of diabetes in the United States with the increased use of this corn-based product. It is everywhere, including in most sodas and even in some breads.
- *Ethanol*. The form of alcohol that is in alcoholic drinks, ethanol is not a sugar, although beer and wine contain residual sugars and starches.
- *Sugar alcohols*. Examples are xylitol, glycerol, sorbitol, maltitol, mannitol, and erythritol. These are neither sugars nor alcohols but are becoming increasingly popular as sweeteners. They are incompletely absorbed in your small intestine, so they provide fewer calories than sugar but often cause bloating, diarrhea, and flatulence.
- *Sucralose (Splenda)*. This is not a sugar, despite its sugar-like name and the deceptive marketing slogan "made from sugar." Splenda is a chlorinated artificial sweetener in line with aspartame and saccharin, with detrimental health effects to match.
- *Agave syrup*. Falsely advertised as "natural," agave syrup is highly processed and is usually 80 percent fructose. It does not even remotely resemble the original agave plant.
- *Honey*. Honey is about 53 percent fructose, but in its raw form it is completely natural and has health benefits, including antioxidants, when used in moderation.
- *Stevia*. This is a very sweet herb derived from the leaf of the South American stevia plant, which is completely safe. This does not raise your blood sugar, and many people like its taste.

called *cross linkages*. The molecules involved become damaged, the cell membranes become less elastic, and some cells die.

The result of glycation, as noted earlier, is the formation of clumps called AGEs. Over time, AGEs accumulate throughout your body, triggering chronic inflammation and damaging just about every tissue. Think of it this way: if you took a sugared soda, poured it on the floor, and let it dry without wiping it up, you'd have a sticky mess. The same thing happens inside your cells when AGEs are formed.

AGEs trigger the abnormal clumping of blood platelets, which causes the blood vessels to narrow and thereby contributes to high blood pressure, vascular disease, and heart attacks. AGEs are also linked to insulin resistance, poor blood sugar control, and the accumulation of damaging amyloid substances in the brain. The more we learn about AGEs, the more we realize that they are implicated in a whole range of diseases, including rheumatoid arthritis, kidney disease, inflammatory bowel disorders such as colitis, and inflammatory skin conditions such as eczema. They can even damage your eyes.

You can reduce the number of AGEs in your system by cutting back on sugars, avoiding simple (as opposed to complex) carbohydrates, learning how to detect hidden sugars in processed foods, and avoiding food that has been browned by high-temperature overcooking. Most of our food has some sugar in it, and overcooking (including microwaving) a food causes the sugar to caramelize, which results when foods form AGEs.

In a study published by the *Journal of Clinical Endocrinology and Metabolism* while we were writing this book, researchers from the National Institute on Aging and the Mount Sinai School of Medicine divided forty healthy participants and nine participants with kidney disease into two groups. One group ate a normal, high-AGE diet, and the other group reduced AGE intake by half by avoiding high-temperature cooking. The groups' caloric and nutrient intake were identical. After four months, the low-AGE group—including those with kidney disease—showed dramatic

improvements in markers of inflammation and in blood-vessel health. To cut down on AGEs, the researchers advised "keeping the heat down and the water content up in food and avoiding pre-packaged and fast foods." Meat eaters may wish to avoid well-done meat.

We agree! Since AGEs have such devastating consequences, anyone would be wise to limit their intake as much as possible.

Abnormal Methylation

Abnormal methylation is another aging factor. Methylation is a simple chemical process in which a methyl group (one carbon atom and three hydrogen atoms) becomes attached to other molecules. It is generally a good thing. Your body uses methylation to help rid itself of a number of dangerous heavy metal toxins. The liver uses methylation to assist in the excretion of external toxins such as pesticides as well as some of its own chemical wastes, such as hormone by-products. Methylation reactions are also critical to normal brain function.

Methylation controls the expression of genes in the body, silencing the bad ones and letting the good ones be "read." It also stabilizes the telomere segments, protecting them from loss due to oxidation, and it may be the reaction that turns on telomerase, the only currently known safe and natural way to lengthen your telomeres.

Unfortunately, depending on age and ethnicity, 10 to 44 percent of people in the United States have abnormal methylation, which can lead to cervical cancer, colon cancer, heart disease, stroke, Alzheimer's disease, and other bad conditions.

No one is sure what causes this, but the good news is that at least one form of abnormal methylation is easy to detect with a simple blood test that measures a chemical in your body called homocysteine. Homocysteine is an inflammatory compound formed by abnormal protein metabolism. Your body can use the methylation process to reduce toxic levels of homocysteine.

In a healthy person, this happens quite easily, but if your methylation is abnormal, homocysteine accumulates to toxic levels. High levels of homocysteine are linked to heart attack, stroke, and atherosclerosis.

If a blood test finds that your homocysteine levels are high, you can reduce them by taking vitamin B supplements, including a larger than normal dose of folic acid, up to 10,000 micrograms per day.

You can help your body to effectively methylate by some of the means we have already discussed and by others we will discuss in subsequent chapters. The choice of foods—mainly vegetables and fruits of a low to moderate glycemic index—gives you a potent dose of antioxidants that aids the methylation process. The proper choice of foods (see chapter 6) also decreases the acid load your body has to deal with and leads to a more favorable methylation environment.

The Lucrative Side of Longevity

If aging is a disease, it must be the mother of all diseases. If we can find a way to intervene against the entropic forces, to slow down or even reverse the accumulation of damaged proteins, we will be on the path to curing not only aging but also all of the diseases associated with aging. We will also realize what enlightened biogerontologists and other scientists who study aging call the *longevity dividend*.

The longevity dividend, first proposed in an article published in the *Scientist* in March 2006, means that in addition to the obvious health benefits, enormous economic good will accrue from the extension of healthy life. Billions will be saved in future health-care expenses, because people who are sick less often and for shorter periods of time will cost the economy much less. Also, by extending the amount of time in the average life span in which higher levels of physical and mental capacity are expressed, many

people will remain in the workforce longer, personal income and savings will increase, and age-entitlement programs will face less pressure from shifting demographics.

Instead of longevity causing us to succumb to bankruptcy, as conventional wisdom would have us believe, national economies will flourish.

The article in the *Scientist* explains, "If we succeed in slowing aging by seven years, the age-specific risk of death, frailty, and disability will be reduced by approximately half at every age. People who reach the age of 50 in the future would have the health profile and disease risk of today's 43-year-old; those age 60 would resemble current 53-year-olds, and so on."

Slowing down aging enough to delay death by seven years, while laudable, is for us an extremely conservative goal. If you are willing to make the lifestyle changes, follow the fitness and nutritional guides, and take up the meditation that we recommend, you should be able to extend your life span and your health span much longer than this—long enough, in fact, to take advantage of therapies that will activate the telomere gene in your somatic cells. This will cause your telomeres to grow and biologically reverse your aging process. Even as you become chronologically older, you will, in fact, become biologically younger.

We suggest that, given the scientific nature of much of what you will be reading, you break this book into manageable sections and take a break as needed, but that you begin the nutritional, exercise, and stress-reduction sections as soon as possible. That way your body will be able to begin turning back the clock as your mind gets up to speed. Once you have fully digested the science behind our program, you will be even more motivated to continue and pleased that you have already begun to do the good work involved in getting more youthful, not older, as time goes on.