BOUNDLESS

UPGRADE YOUR BRAIN, OPTIMIZE YOUR BODY & DEFY AGING

BEN GREENFIELD

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LONGEVITY DECODED

ANCESTRAL WISDOM AND MODERN SCIENCE TO MAXIMIZE HEALTH AND LIFE SPAN

Demographers, epidemiologists, gerontologists, and other researchers on aging have long puzzled over the theoretical question of the maximum human life span, along with the host of proposed practices that could help us achieve that potential. In the past decade alone, we have seen a veritable laundry list of tactics we can use to make ourselves more age-resistant, from nutrients, vitamins, and pills—including vitamin D, aspirin, metformin, magnesium, pterostilbene, resveratrol, blueberry extract, nicotinamide riboside, and rhodiola—to lifestyle practices such as shivering our asses off; self-imposed starvation; fecal transplants; strict veganism; injections of growth hormones, testosterone, stem cells, exosomes, and the blood of younger healthy humans; and, speaking of younger humans, simply having more children.

The fact is, compared to the biblical Methuselah, who purportedly lived to the ripe old age of 969, we do not seem to be moving the antiaging dial much. Researchers estimate that in the US today, the average adult life expectancy is still only about seventy-seven—and, disturbingly, that's now plummeting due to high rates of chronic diseases (many of which are preventable with simple lifestyle changes you'll learn about in this chapter). Despite the Chinese lore of the recently perished, allegedly 256-year-old Li Ching-Yuen, the longest-lived person on record is Jeanne Calment of France, who died in 1997 at 122 years and 164 days old.

Then there's a Jamaican woman named Violet Brown, who died in 2017 at 117. (She claimed her secrets to longevity included church, no pork, no chicken, and no rum!) At the time of this writing, the oldest person alive is Kane Tanaka of Japan, aged 115 years and 336 days.

But when we observe nature, some amount of immortality, or at least a significantly longer life span, appears to be achievable. Take the naked mole rat, for example. The naked mole rat's cells themselves seem to make proteins—the molecular machines that make bodies work—more accurately than human cells do, preventing it from developing age-related illnesses like cancer

The 256-Year-Old Man

Imperial Chinese government documents from 1827 congratulate Li Ching-Yuen on his 150th birthday, and documents from 1877 congratulate him on his 200th birthday. This Chinese herbalist and martial artist died in 1933 and claimed to have been born in 1736, although other records suggest he was actually born in 1677.

Is this possible? The longest confirmed life span on record is that of Jeanne Calment, who lived to be 122, and Li Ching-Yuen is reported to have lived to be 256, more than twice as long as Madame Calment! It strains credulity, but let's take a look at his life, shall we?

Li Ching-Yuen began his career as an herbalist at ten years old. He spent the majority of his life in the mountains of China eating a diet of herbs and rice wine and gathering plants and herbs, including wild ginseng, goji berries, lingzhi mushrooms, gotu kola, and he shou wu. These herbs are known to have potent longevity benefits, but are they enough to lend someone 256 years of life?

Surprisingly, Li Ching-Yuen did not ascribe his incredibly long life to his diet or even to his practice of qigong. While on his deathbed, Li said, "I have done all that I have to do in this world." In the West, aging is seen as an enemy to be conquered and overcome with technology and supplements. In fact, there's an entire philosophy, transhumanism, that holds that the human race can, through science and technology, evolve beyond its current physical and mental limitations. Li's last words suggest a very different outlook on life. He recognized that he had certain tasks to complete in this life, and when he had performed them, he willingly lay down to rest, knowing that he fulfilled the entirety of his life's purpose.

Li also gave longevity advice that flies in the face of the modern, hard-charging, go-hard-or-go-home outlook that many people subscribe to. When asked by the warlord Wu Pei-fu what the secret to long life is, Li is said to have replied, "Keep a quiet heart, sit like a tortoise, walk sprightly like a pigeon, and sleep like a dog." Li believed that the calmness and peace of mind with which he approached daily life contributed the most to his longevity.

Perhaps there is something to be learned from such a calm, long-lived man. Setting aside whether he was really 256 years old at his death, it seems pretty obvious that he did live a very long time and proved that there is much more to longevity than injecting yourself with all sorts of bizarre concoctions and engaging in the latest biohacks.

and Alzheimer's. And unlike in humans, the way these ugly little creatures handle glucose doesn't seem to change with age, reducing their susceptibility to diseases like diabetes. The naked mole rat also possesses genes that allow it to process oxygen more effectively than other rodent species, which may contribute to its impressive twenty-to-thirty-year life span.

The naked mole rat is not the only animal scientists are now probing to pick the lock of long life. With a rampant metabolism and a heart rate of one thousand beats per minute, the hummingbird should, on paper, be riddled with rogue, DNA-destroying free radicals, but the tiny birds seem relatively bulletproof against heart disease. Then there are lobsters, which seem to have evolved a protein that repairs the telomere tips of their chromosomes, allowing for a decreased rate of telomere shortening that most animals are incapable of achieving. (Recall from chapter 9 that telomeres become shorter each time the cell divides; once they're short enough, the cell can no longer repair and undergoes accelerated aging or, worse, becomes cancerous).

Consider Adwaita, the giant tortoise from India who died of liver disease in 2006. At the time he died, he looked just as young as a spry teenage tortoise—but carbon dating of his shell showed that he was over 250 years old. Some clams and oysters also don't seem to experience an increased risk of mortality as they age. For example, measuring the growth rings of one ocean quahog revealed that it had lived 507 years, and annual growth rings of other bivalves reveal an average life span of over 400 years. Even certain trees enjoy extreme longevity: a bristlecone pine named Methuselah in California is 4,851 years old!

Finally, as if rats, hummingbirds, lobsters, tortoises, clams, and trees were not enough to make us longevity-seeking humans a bit jealous, we mustn't forget one animal on earth that may hold the master key to immortality: *Turritopsis dohrnii,* also known as the immortal jellyfish. Most jellyfish, when they reach the end of their lives, die and melt into the sea, but not the immortal jellyfish. Instead, it sinks to the bottom of the ocean floor and its body folds in on itself—assuming the jellyfish equivalent of the fetal position—and regenerates back into a baby jellyfish in a rare biological process called transdifferentiation, in which its old cells somehow transform into young cells. The stem cells that allow for this continuous self-renewal express high levels of FOXO genes, which also play a key part in human longevity.

So is there a human equivalent to the immortality powers these animals seem to have tapped into? Many in popular antiaging and longevity circles have suggested that, in the next several decades, we could indeed unlock the secrets to living to approximately 120 to 140 years old. Indeed, many biohackers and antiaging enthusiasts such as Peter Diamandis, Elon Musk, Dave Asprey, Tony Robbins, and even li'l ol' me are striving to live longer than 160 years.

This chapter will not only teach you many of the advanced longevity secrets of the fringe biohackers but also reveal everything you need to know about why the world's more traditional longevity all-stars not only live longer but also tend to live better. They have strong connections with their family and friends. They are active. They wake up in the morning knowing that they have a purpose, and the world, in turn, reacts to them in a way that propels them along. An overwhelming majority of them enjoy life even in old age. They share common behavioral and lifestyle characteristics—such as close family relationships, avoidance of smoking, a plant-based diet, moderate and daily physical activity, social engagement, and participation in a community that includes people of all ages—even though they are all from different areas of the world and of different races, nationalities, and religions.

After spending nearly two decades immersed deeply in the health, fitness, nutrition, and longevity industries, I have come to the realization that embracing both modern science and ancestral wisdom can allow one to live a long and healthy life whose span rivals and even exceeds that of our ancestors. That is why my children and I forage for wild plants (a longevity tactic you'll learn more about in this chapter) but do so using a plant identification smartphone app that allows us to identify everything from mushrooms to plants with incredible accuracy—we can tap into a bit of better living through science so that we don't get poisoned or make fatal mistakes that our ancestors might have made while foraging. It's also why I own a quaint and simple, off-the-grid, barn-style home in the forest where we grow most of our own food, yet I fill that barn with tens of thousands of dollars' worth of modern antiaging biohacking equipment. And it's why, the last time I disappeared into a seven-day high-country elk bow-hunt in the mountains of Colorado, I had a neurofeedback brain-training device neatly tucked away in my camouflage backpack.

In this chapter, you will discover exactly how to live a happy, long, and fulfilled life with one foot planted in the realm of ancestral living and the other foot planted in the realm of modern science and biohacking. Granted, there are entire books and fantastic websites—most of which I have read word for word—that could fill thousands of pages of antiaging advice. My favorites are linked to on BoundlessBook.com/19. But for the purposes of this book, I have decided to give you the best of the best: the techniques I have personally tried, the tactics that are steeped in research, and the strategies that have thousands of years of practice behind them. So you can think of this chapter as a cookbook for longevity that gives you all the low-hanging fruit and teaches you all the basics of living a long and happy life while also exposing you to the more advanced practices that have emerged in the past several years.

But first, before I get into life-extending strategies, it is important to understand exactly how we age in the first place.

HOW WE AGE

There does not appear to be one single cause of aging. When I interviewed antiaging pioneer and impressively bearded Aubrey de Grey on my podcast, he outlined seven separate aging mechanisms his SENS Research Foundation (the acronym stands for "Strategies for Engineered Negligible Senescence") has identified and researched: mutations in chromosomes, mutations in mitochondria, junk inside cells, junk outside cells, cell death, protein cross-linking, and cell senescence (a phenomenon in which a cell can no longer divide but does not die, which would let other cells divide). Many longevity scientists would argue that plenty more than seven aging mechanisms exist, including my friend Dr. Harry Adelson, who theorizes that aging is due to a loss of available stem cells, and Dr. Michael Rose, who argues that aging is related to our loss of reproductive usefulness as we age.

These mechanisms are important to understand because, in order to truly enhance longevity, we should ideally address each and every element that might be causing us to grow old too soon. As you'll see, most are related to a simple accumulation of damage: breakages in the molecular machinery of cells, an accumulation of metabolic waste products that your body cannot break down, and the failure of biological systems that are increasingly unable to cope with the damage. Over time, this damage can affect every cell in every organ, structure, and tissue. Let's take a closer look at how this damage process affects the biological systems in your body.

Bones and Skeletal System

In men, bone density starts to diminish at age thirty-five. In women, this process occurs even earlier, with peak bone density occurring at around age thirty, and postmenopausal women experience an accelerated rate of bone loss. The foot arches become less pronounced, contributing to reduced height. The discs that separate your vertebrae lose fluid, which aggravates this effect even more. The long bones of the arms and legs become brittle due to mineral loss. Joints become stiffer and less flexible and can lose some of their fluid, causing the cartilage to rub together and wear out. Calcification, the depositing of minerals in and around some joints, also occurs.

After thirty, skeletal muscle mass declines more than 20 percent in both men and women in the absence of triggers such as regular exercise, muscle loading, adequate protein, and, based on recent research, heat stress. With this gradual muscle loss, known as sarcopenia, strength and flexibility decreases, along with coordination, balance, and height. The deterioration of the central nervous system can also lead to a reduced ability to recruit muscle fibers. Posture deteriorates, and the overall risk of bone breakage increases. The gradual breakdown of the joints can lead to inflammation, pain, stiffness, and even physical deformities such as a hunched back or bowlegs.

Physical activity—particularly stressing the muscles and long bones of the skeletal systems—can help to slow many of these aging mechanisms, as can regular sauna exposure, healthy protein intake, and pulsed electromagnetic field therapy (discussed in chapters 6 and 12).

Digestive System

As digestive activity gradually slows with aging, you are more likely to get constipated frequently, which can often be exacerbated by medications, such as proton pump inhibitors and antibiotics, and by medical conditions, such as diabetes and irritable bowel syndrome. The muscle contractions that push food along your digestive tract can slow down with aging, causing waste to move more slowly through the colon, and the longer it takes to move through the colon, the more water it loses, which exacerbates constipation. Lower physical activity levels in older people can also contribute to the effects of constipation.

A condition known as diverticulosis can develop, which occurs when small pouches in the lining of the colon bulge through weak spots in the intestinal wall. This can lead to gas, bloating, cramps, and even more constipation. A more severe form of this condition, diverticulitis, occurs when the pouches become inflamed, leading to abdominal pain, cramping, fever, chills, nausea, and vomiting. Cancerous or noncancerous polyps can also form in the colon. Gastroesophageal reflux disease (GERD) is the most common age-related gastrointestinal disorder and occurs when stomach acid rises into the esophagus, causing heartburn and other symptoms.

Natural digestive enzyme production decreases with age, leading to a loss of protein absorption, which can further aggravate sarcopenia. Enzyme depletion even outside the digestive system can also be an issue, since enzymes are responsible for constructing, integrating, transporting, providing, and eliminating a host of nutrients and toxins. Research has shown that people who have a chronic disease or poor energy levels tend to have fewer enzymes in their blood, urine, and tissues.

Chewing food more thoroughly, eating adequate fiber and fermented foods, supplementing with digestive enzymes, and consuming amino acids—along with implementing the strategies in the gut and immune-system chapters of this book (chapters 13 and 15)—can all help to slow the aging of the digestive system and depletion of enzymes.

Respiratory System

Maximum lung capacity and maximum oxygen utilization (VO_2 max) decrease gradually after about age twenty-five, especially if you're not frequently exercising. You also experience decreases in measures of lung function such as vital capacity (the maximum amount of air that can be breathed out following a maximum inhalation), a weakening of the respiratory muscles, and a decline in the effectiveness of lung defense mechanisms, including reduced numbers of white blood cells on the surface of the lung alveoli.

As the muscles and tissues around your lungs, particularly the diaphragm, weaken, you experience a decreased ability to breathe enough air in and out, as well as a decreased ability to keep airways sufficiently open. The alveoli can lose their shape and become looser and more dysfunctional. Even the skeletal changes in the spine and ribs can impact the effectiveness of your respiratory system, and the part of the brain that controls breathing may also lose some of its function as you age.

All of these changes in the lung tissue can cause air to become trapped in the lungs, making it harder to breathe. Decreased lung capacity negatively impacts overall health in several ways. For example, one study that followed 5,200 individuals for three decades demonstrated that lung volume was the greatest predictor of health and longevity!

Regular cardiovascular exercise and the adoption of the type of breathwork practices and protocols described in chapter 3 can help to support the aging respiratory system.

Urinary System

After about age thirty to forty, two-thirds of us undergo a gradual decline in the rate at which our kidneys filter blood. The kidneys begin to lose tissue, and the number of filtering units known as nephrons decreases. The blood vessels that supply the kidneys can harden, further impairing the kidneys' filtration rate.

The bladder wall loses its elasticity, meaning it cannot hold as much urine as before, and the muscles controlling the bladder begin to weaken. The urethra can become blocked by an enlarged prostate gland in men or by a prolapsed (fallen) bladder or vagina in women. A loss of bladder control is quite common for women, especially around menopause, and medical conditions such as diabetes or a history of voluminous endurance sports can also contribute to this incontinence.

Simple strategies to control these issues include deep pelvic core training, adequate hydration and mineral intake, limited consumption of dehydrating foods such as alcohol and caffeine, and avoidance of excess protein.

Reproductive System

For women, menstrual cycles stop at around age fifty-one and the ovaries halt production of estrogen and progesterone. The ovaries also stop producing eggs, and after menopause, you can no longer become pregnant. Vaginal walls become thinner, drier, less elastic, and possibly irritated, which can often cause sex to become painful. The risk of vaginal yeast infections increases, and the external genital tissue and breast tissue thins. The pubic muscles can lose tone, resulting in a prolapsed vagina, uterus, or bladder.

Men do not experience a major change in fertility with age, but testicular tissue mass decreases and testosterone gradually declines, along with blood flow to the reproductive organs. Sperm production falls, though it doesn't stop. The volume of ejaculated fluid often remains constant, but there are fewer living sperm in it. The prostate gland enlarges as some of the prostate tissue is replaced with scar-like tissue. Men can also experience problems getting an erection. Based on the theory that reproductive uselessness can accelerate aging because we are no longer able to propagate the population, it is important to maintain regular sexual activity with age and even utilize many of the sexual enhancement biohacks from chapter 18, such as acoustic sound wave therapy, infrared therapy, or stem cell injections.

Endocrine System

The hypothalamus, located in the brain, produces hormones that control the other structures in the endocrine system. Although the levels of these regulating hormones stay the same as you age, the responses of the other endocrine organs to those hormones can diminish.

At thirty years old, human growth hormone begins its regression in both men and women and declines at a rate of around 14 percent per decade. When women transition into menopause, progesterone, testosterone, and estrogen levels begin to fall. At fifty, thyroid activity begins to decrease, and hyper- or hypothyroidism may develop.

Also at fifty, men may begin to experience andropause (the male version of menopause, most notably accompanied by a decrease in testosterone). In both men and women, a decline in DHEA (a potent hormonal precursor) can cause increased vulnerability to a variety of cancers. At sixty, as insulin production decreases and insulin cell receptor sensitivity lowers, the ability to metabolize sugar declines, and insulin resistance or diabetes becomes more prevalent. At seventy, hormones that protect against the loss of calcium in bones decline, making osteoporosis more prevalent.

One reason that the natural hormone replacement industry is now booming is that it can be effective for mitigating many of the endocrine issues that occur with age. However, more ancestral practices, such as organ meat consumption, regular sex, care for the gut, and the avoidance of modern plastics and endocrine-disrupting chemicals, can be equally effective strategies.

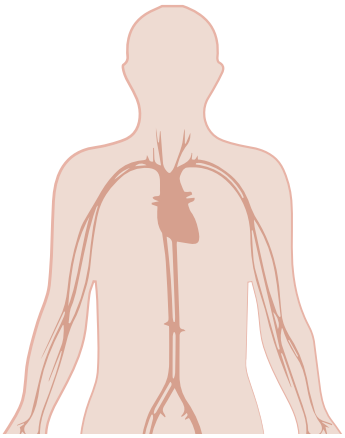
Circulatory System

At around forty years old, your heart muscles thicken and blood vessels stiffen, which can cause the heart to fill with blood more slowly (this can often occur earlier if you're a hard-charging athlete). This forces the heart to work harder to pump blood through the vessels and can lead to high blood pressure and other cardiovascular problems, such as cardiac arrhythmias. The receptors that monitor blood pressure when you change positions can also deteriorate, which can cause dizziness when you stand up from sitting or lying down. This process can be further exacerbated by calcification, or excess calcium deposits, in the body, which manifests as the stiffening of joints, plaque buildup on the teeth, a hardening of the arteries, impaired brain function, and general aches and pains. Many individuals over sixty have enlarged deposits of calcium mineral in their major arteries, often caused by a lack of minerals in the diet, dehydration, limescale in tap water, and even synthetic calcium supplements.

Abnormal heart rhythms can develop, leading to arrhythmias like atrial fibrillation. The heart's natural pacemaker, which controls the rate of the heartbeat, can develop fibrous tissue and fat deposits in some of its pathways and lose some of its cells, resulting in a slower heart rate. The walls of blood vessels, especially the smaller capillaries, can thicken, resulting in a slower rate of exchange of nutrients and waste products. The blood itself can change: the total water content of blood falls, and your ability to produce new red blood cells and certain white blood cells deteriorates.

The circulatory system also includes the lymphatic fluid that circulates through the body, and if the lymphatic circulation stagnates, toxins can accumulate and immune cells are not delivered to the areas of the body where they are needed most, resulting in the deterioration of immunity and a weakened ability to fight infection and disease.

Regular cardiovascular exercise, hydration, regular exposure to heat and cold, and the lymph-fluid-circulating strategies from chapter 15 can all help to stave off these issues.



Nervous System

The nervous system doesn't decline with age as dramatically as some of the other systems, but during normal aging, some nerve cell structure and function is indeed lost, which causes messages to be sent more slowly. Waste products can collect in brain tissue, causing plaques and tangles. The most severe decline in mental function is a result of diseases such as Alzheimer's and other forms of dementia, which some doctors attribute to these plaques and tangles. (Plaques are actually a part of the immune system and release antimicrobial agents to deal with bacterial, viral, or fungal infections in the brain, but over the course of a lifetime they can accumulate in neural tissue, which causes cognitive decline.) Even diabetes can affect thinking and behavior in older individuals.

By age forty, the lenses in the eyes begin to stiffen, resulting in vision impairment, particularly when focusing on near objects. Hearing loss might develop, which occurs sooner in men than in women, and memory also tends to worsen.

By paying close attention to and implementing the strategies found in chapters 1 through 7, you can significantly support your nervous system and keep these issues at bay.

Skin

Stem cell production and stem cell availability both decline with age, and one result of this is that the skin's epidermal cells slow in their reproduction. Melanocytes, which produce pigmentation, decrease in number while the remaining cells increase in size. This can cause thinner, more translucent skin, as well as large pigmented spots like liver spots. Skin injuries, tearing, and infections become more frequent as skin integrity deteriorates.

Loss of fat and collagen in the underlying tissues can cause skin to sag and wrinkle, and the connective tissue loses its strength and elasticity, a process known as elastosis. The blood vessels in the skin become more fragile, and bruising, bleeding under the skin, cherry angiomas, and other conditions become more common. The skin becomes dry and itchy as the glands that produce oil reduce their production levels. The fat layer beneath the cutaneous layer of skin thins, leading to an increased risk of skin injury and a reduced ability to maintain consistent body temperature. Sweat glands produce less sweat, making it harder to cool off and increasing the risk of overheating or developing heat stroke.

Stem cell–supporting strategies, along with the beauty tactics from chapter 17, can help to keep all this from occurring or minimize these effects.

Underlying Causes

So what are the underlying causes of this type of full-body, systemic damage that occurs with age? There are a variety of factors that can aggravate or accelerate age-related deterioration, but the following processes are the major culprits.

CHRONIC INFLAMMATION

Inflammation can often go on for years without your noticing until accelerated aging and disease suddenly set in. As a matter of fact, of the ten leading causes of mortality in the US, chronic inflammation contributes to at least seven:

- Alzheimer's disease
- Stroke
- Chronic lower respiratory disease (asthma)
- Cancer
- Diabetes
- Heart disease
- Influenza and pneumonia

GLYCATION

Glycation occurs when sugars in the bloodstream attach to proteins to form harmful molecules called advanced glycation end products (AGEs). The more sugar in your diet or the more chronically elevated your blood sugar levels, the more likely it is that AGEs will develop, which can cause inflammation and cell membrane damage that can result in the development of degenerative diseases such as diabetes, atherosclerosis, chronic kidney disease, and Alzheimer's disease.

METHYLATION DEFICITS

Methylation—the process of transferring a methyl group from one molecule to another—is a crucial biological process that's involved in removing toxins, growing and repairing cells, and metabolic functioning. Methylation deficits are linked to a number of health conditions, including diabetes and cancer, and are caused by a variety of factors, including stress, nutrient deficiencies, and genetics.

DEGRADING MITOCHONDRIA

A growing number of cell biologists have proposed that the number and functionality of mitochondria can determine your potential for longevity, and one major theory of aging—the free-radical theory—posits that the oxidation of cells by reactive oxygen species (ROS) plays a leading role in the weakening of vital functions in aging organisms. The mitochondrial interior has been researched and found to be particularly susceptible to this oxidation. In addition, since mitochondria exhibit less damage in women than in men, scientists have speculated that the health of mitochondrial DNA might be a factor in why women live longer than men.

Poor lifestyle factors, such as bad air, unclean water, artificial light, electrical pollution, inflammation, a nutrient-poor diet low in antioxidants, lack of exercise, and many, many others, can contribute to poor mitochondrial status.

The Most Important Data to Track

Because of the dangers of chronic inflammation and glycation, I am convinced that the two most important markers you can track for overall health and longevity are your levels of inflammation and your glycemic variability. For inflammation, hs-CRP is a simple value to track (see chapter 16 for more details), but an advanced inflammatory panel from a company such as Quest Diagnostics can also test markers such as myeloperoxidase, Lp-PLA2, dimethylarginine, oxidized LDL, prostaglandins, and fibrinogen. For glycemic variability, blood glucose and hbA1c are the best markers, although a continuous glucose monitor, such as the Dexcom G6, can give even better data. Chapter 16 has more details on tracking your biomarkers, including sections on hs-CRP and continuous glucose monitors.

Overmethylation and Undermethylation

For the carnivores out there those who just have to have their meat, the meat eaters who say, "I like my steak. I like my steak with eggs," there is a problem. Most meat, particularly muscle tissue, contains high amounts of methionine, which is a potent methyl donor. Over the next few paragraphs, you will learn what exactly a methyl group is, why it may be bad for you to overconsume strong methyl donors, and how to eliminate the side effects of overmethylation or undermethylation.

A methyl group is a carbon atom attached to three hydrogen atoms. It is an abundant organic compound that is derived from methane. Normally, methyl groups are attached to larger molecules, but on their own, they can be a methyl anion, methyl cation, or methyl radical. Methylation occurs when a methyl group is taken from one compound or molecule and is transferred to another—for example, a methyl group can be added to your DNA from a methyl donor like methionine. The process is largely responsible for switching genes on and off and silencing viruses. When your body experiences normal methylation, less desirable genes, such as those that code for cancers and autoimmune diseases, are switched off while helpful genes are switched on. Methylation is also required for cell division, neurotransmitter synthesis and metabolism, detoxification, cellular energy metabolism, the formation of protective myelin sheaths around neurons, and early central nervous system development.

The critical functions of methylation mean that when the process malfunctions, your body can go haywire quickly. Undermethylation is a state of low methylation, either because your body is unable to adequately transfer methyl groups or because you're not consuming enough methyl-donating compounds or foods. Overmethylation is a state of high methylation. Neither of these states is necessarily bad (undermethylation, for example, is often associated with attention to detail, slight perfectionism, and high levels of personal accomplishments), but they both have the capacity to cause different kinds of mental and physical stress.

Because it can keep serotonin levels low, undermethylation can cause you to be a dopamine-seeking, hard-charging high achiever. It can lead you to pursue perfection and achievement and has been associated with obsessive-compulsive tendencies, a low tolerance for pain, and ritualistic behaviors. A state of undermethylation can also make people more susceptible to depression.

Overmethylation is associated with creativity and sensitivity. If you are prone to overmethylation, you probably exhibit high levels of empathy for others but also experience sleep issues, food and chemical sensitivities, hyperactivity, panic attacks, and a tendency to gain unwanted weight. Overmethylation has also been highly correlated with schizophrenia.

If you are prone to undermethylation, you will do well with a high intake of muscular meats. Because you do not have enough methyl groups being transferred to places that need them—like your DNA—you might need to consume a higher amount of meat to compensate, especially if you consume high quantities of plant matter and folate, as these do not supply sufficient amounts of methyl groups necessary for good health in undermethylators. In addition, folate acts as a serotonin reuptake promoter. Drugs like antidepressants and selective serotonin reuptake inhibitors are received very well by undermethylators, so any compound like folate that exerts the opposite effect could be devastating to undermethylators.

If you are prone to overmethylation, the last thing you need is a higher intake of methyl donors like muscle meat (such as daily servings of steak and chicken). This would be an instance where vegetarianism or a largely plant-based diet could be beneficial. If you are an overmethylator, you need to consume adequate amounts of protein, but don't become an extreme carnivore and load up most of your plate with cuts of animals and the rest of the plate with one-tenth of an inch of vegetables (that ratio should actually be reversed!).

As a word of caution, the only way to know for sure whether you are prone to undermethylation or overmethylation is to undergo DNA testing via a testing service such as 23andMe or, for even more targeted data, a company like StrateGene, Youtrients, or TreeOfLife.

FATTY ACID IMBALANCES

Fat is a vital nutrient, and the human body needs an optimal ratio of omega-6 to omega-3 fatty acids to support normal cell membrane function in aging cells. As you have already learned, a diet high in omega-6 (often because of a high intake of vegetable oils) and low in omega-3, DHA, and monounsaturated fats can create deficits or imbalances in fatty acids.

IMMUNE DYSFUNCTION

Autoimmune diseases develop when your immune system turns on itself, resulting in inflammation and organ and cell damage. Autoimmune diseases—which include rheumatoid arthritis, lupus, multiple sclerosis, thyroid disease, and inflammatory bowel disease—are becoming increasingly common, especially in an era of chemical exposure, antibiotic overuse, and unhealthy guts.

TELOMERE SHORTENING

Telomeres are the segments of DNA at the end of our chromosomes, often compared to the plastic tips of shoelaces that keep the laces from fraying. Telomeres prevent chromosomes from becoming damaged or tangling with one another. When chromosomes do become damaged, this can cause the destruction of genetic information, leading to cellular malfunction, which increases your risk of disease and overall mortality.

Telomerase is an enzyme that lengthens telomeres and keeps them from wearing out too fast or too early and can be deleteriously affected by lack of exercise, chronic stress, low plant consumption, and a lack of mindfulness practices such as meditation and yoga.

DNA EXPRESSION

Geneticists and oncologists have long recognized that overexposure to environmental assailants such as chemicals and radiation can cause DNA damage and affect the way genes are expressed. Nutrient depletion and other environmental factors, such as electrical pollution and poor air, light, and water, can also alter gene expression. Researchers have also demonstrated that our genes can respond to our conscious thoughts and emotions and even our unconscious beliefs.

If you feel that you are constantly fighting an uphill battle against the aging processes of damage and degradation, you are right. Fortunately, basic and natural habits to enhance longevity have long been studied, and many directly affect the exact biological mechanisms involved in aging. Consider this chapter to be your guidebook to managing and mitigating the issues you have just read about, beginning with the longevity basics, then progressing to the more advanced tactics and biohacks.

12 ESSENTIAL HABITS TO ENHANCE LONGEVITY

Dan Buettner wrote the book *The Blue Zones* with the goals of discovering which populations in the world had the highest number of centenarians (people who live to be over one hundred) and teaching the world how to use the lessons from these populations. The five Blue Zones where Buettner and his team of researchers discovered the longest-living people on earth were Okinawa, Japan; Sardinia, Italy; Nicoya, Costa Rica; Ikaria, Greece; and the Seventh-Day Adventists

in Loma Linda, California. Buettner discovered several characteristics that the people in these zones shared, such as these:

- A lack of smoking
- A high intake of wild plants
- A regular intake of legumes, usually prepared using ancestral methods such as soaking, sprouting, or fermentation
- Constant moderate physical activity, not as isolated exercise sessions or gym workouts but as a natural part of life (e.g., gardening, yard work, walking, and bicycling)
- Healthy family relationships and social engagement (despite less use of social media, people are extremely socially active and integrated into their communities)

Other key characteristics Buettner identified were low-to-moderate alcohol intake (especially wine and other fermented beverages), caloric moderation and fasting, a strong life purpose, low amounts of stress, and engagement in a spiritual discipline, religion, or belief in a higher power.

So how can you practically implement these habits into your own life? Here are a few potent and highly effective strategies, and some of the more common roadblocks I have seen people run into during my own consulting and coaching.

1. Don't Smoke

Your telomere length is measured in base pairs, which are the building block units that make up the ladderlike rungs of DNA. In childhood, telomeres are about fifteen thousand base pairs long, but by the time we reach old age, they have shortened to about three thousand base pairs, which equates to a loss of about two dozen base pairs per year. The oxidative damage inflicted by smoking a pack of cigarettes every day destroys an additional five pairs each year. So if you smoke for forty years, it can rob you of more than seven years of life (obesity has a similar effect: the telomeres of obese women can be as much as 240 base pairs shorter later in life than those of lean women, which is roughly equivalent to about a loss of about nine years of life).

Granted, there are some cases in which smoking can be beneficial. Think back to chapter 5's discussion of smoking or vaping loose leaf tea, organic tobacco, essential oils, and marijuana. In moderation, the stress-reducing and energy-enhancing benefits of this practice likely outweigh any cons derived from exposure to heated, potentially carcinogenic compounds, especially when vaping. In addition, as you learned in chapter 5, it really isn't the nicotine in cigarettes or cigars that is harmful.

But unless you have been living under a rock, you are no doubt aware of the dangers of chronic smoking. Cigarette smoking causes almost *half a million deaths each year*, nearly one in five of all deaths in the United States. Secondhand smoke isn't much better, causing frequent and severe asthma attacks, respiratory infections, ear infections, sudden death in children and infants, cancers like coronary cancer in adults, and, highly relevant to what you'll discover about longevity later in this chapter, extreme hampering of effective stem cell mobilization (the movement of stem cells to other areas of the body from their storage in bone marrow). In other words, don't smoke—period. As much as possible, limit your exposure to secondhand smoke. Not only that, but because air pollution has been directly linked to a decrease in telomere length, act proactively: if you live in an apartment complex, work in an office, or frequent areas that expose you to airborne pollutants, then use HEPA air filtration, houseplants that filter the air, and other air cleanup tactics you will find in chapter 20. In addition, increase your intake of whole-food, plant-based antioxidants or full-spectrum antioxidants from supplements.

Undoing the Damage of Smoking

The negative effects of smoking are well known, and it is therefore not surprising that one feature of Blue Zones is a lack of smoking. Downsides to smoking include:

- Habit formation from the effects of nicotine on the central nervous system
- Withdrawal symptoms like anxiety, irritability, depression, headaches, and sleep problems when you try to quit
- Emphysema, the irreversible destruction of the air sacs in your lungs
- Chronic bronchitis, the permanent inflammation in the lining of the breathing tubes of the lungs
- Lung cancer
- The constriction and damage of blood vessels, which can lead to peripheral artery disease
- Hypertension, a condition of chronically elevated blood pressure
- Increased risk of stroke

If you have been smoking, the good news is that much of the damage can be reversed. The first thing to do is to stock up on supportive nutrients and supplements for the moment you quit. When you quit smoking, your adrenal glands, which secrete antistress hormones, must adapt to the lack of nicotine and other addictive chemicals. You can support your adrenals with adaptogenic herbs or supplements such as St. John's wort or ginseng. Research has shown you can minimize the damage to your arteries by taking a taurine supplement once a day for two months. Since smoking also damages skin collagen and elastin, eat a diet rich in proanthocyanidins, a phytochemical found in red wine, grapes, apples, blueberries, black currants, hazelnuts, pecans, and pistachios. The polyphenols found in kale and sprouts can also repair your lungs' alveoli and bronchioles, so a former smoker's diet should contain high amounts of these foods too.

When it comes to risk of smoking-related diseases such as esophageal and lung cancer or cardiovascular disease, Dr. William Li's excellent book *Eat to Beat Disease* points out specific antioxidant-rich compounds that can lower the risk of these diseases, such as black raspberries, extra-virgin olive oil, and fermented forms of soy such as miso, natto, and tempeh. In addition, one study examined the effects of drinking four cups of green tea per day on the stem cells and blood vessels of smokers, and noted a 43 percent increase in endothelial stem cells over two weeks, along with a 29 percent increase in vascular function.

Once you give up smoking, your body will begin to respond immediately. Six hours after quitting, circulating levels of the poisonous gas carbon monoxide will decline, and your heart won't have to work so hard to pump oxygen. Within twelve weeks, your lung function will significantly improve and coughing, sinus congestion, shortness of breath, and fatigue levels will all decline. During this time frame, your lungs' hairlike cleaning structures called cilia will regrow, similar to the way that the intestinal cilia can become restored and renewed after you stop eating an inflammatory diet. After three months, your sexual performance will improve as testosterone levels normalize. After nine months, your risk of heart and cardiovascular complications will fall. After one year, it will be like you never smoked, especially if you use the strategies above.

Other dietary strategies that can help to reverse the effects of smoking include these:

- Foods high in vitamin E, like eggs, nuts, and dark leafy greens
- Foods high in CoQ10, like salmon, beef, broccoli, and avocado
- Vitamin-C-rich foods that contain high amounts of bioflavonoids, like grapefruit, spinach, and citrus fruits (especially kiwi)
- Foods rich in vitamin B complex, like dark leafy greens, eggs, fish, and liver
- A full-spectrum multivitamin rich in antioxidants

2. Eat Plants

Aside from the Seventh-Day Adventist population of Loma Linda, California, most centenarians are not vegans or vegetarians. But most do follow a predominantly plant-based diet, usually because they depend on their own homegrown or locally grown foods. Long-lived Sardinians, Nicoyans, and Okinawans tend to consume nutrient-dense produce they grow in their own gardens and supplement them with smaller amounts of animal protein, along with traditional staples like legumes, ancient grains (such as quinoa, amaranth, and millet), sweet potatoes, and corn tortillas.

Plants deliver plenty of fiber, including insoluble fiber, a natural anticancer agent, antioxidants, oxidized cholesterol reducers, blood-clotting factors, and essential minerals. Perhaps most notably, plants—especially wild plants, as I'll explain later in this chapter—possess natural built-in defense mechanisms that subject the body and gut to mild amounts of stress, causing a hormetic response that can allow the body to better mount its own antioxidant defenses. Thus, trace amounts of saponins in quinoa; lectins in soy and potatoes; gluten in wheat, rye, and barley; anthocyanins in berries; resveratrol in grape skins and red wine; EGCG in green tea; sulforaphane in broccoli and other cruciferous vegetables; catechins in cacao; and other controversial compounds are actually good for you. Even plants' phytochemicals, which contribute so many of the benefits of a plant-heavy diet, induce a mild, hormetic cellular stress that precondition your body to respond better to other, more severe stressors. One excellent book that explores this topic is *Eating on the Wild Side* by Jo Robinson, which even advises cutting up or tearing apart plants such as kale several hours before eating them. This action causes the plant to believe it is being attacked by a wild animal and to amp up its natural defense mechanisms, which then mildly stress your body upon consumption.

In many of the Blue Zones, red meat is typically eaten only a few times a month—notably during holidays and festivals—although sheep's or goat's milk, eggs, and fish are eaten often, usually two or three times per week. The animal products that are consumed tend to be raised locally, grass-fed, pasture-raised (or wild-caught, in the case of fish), and free from many of the harmful substances commonly used in conventionally raised meat and dairy, like antibiotics and growth hormones. Author Michael Pollan's recommendation to "eat food, not too much, mostly plants" is sage advice, especially for those genetically predisposed to thrive on a higher vegetable intake and lower meat intake.

When you do consume meat, rather than simply consuming the muscle, which inevitably contains high levels of methionine and low levels of glycine, which can be a mortality risk factor, consume the glycine-rich offal, such as the organ meats, marrow, and bone broth. If, for gut health or immune reasons, you plan to follow a plant-restricted diet such as the carnivore diet, consider tapping into the cellular resilience benefits that plant intake can bestow by engaging in other forms of mild stress, such as frequent sauna visits, cold thermogenesis, fasting, smart amounts of exercise, and exposure to sunlight radiation, and eat plants low in natural defense mechanisms or plants treated to deactivate their defense mechanisms (read Dr. Steven Gundry's book *The Plant Paradox* to learn more about this strategy).

Finally, if you have existing gut issues such as IBD, diverticulosis, or diverticulitis, you may want to be careful with excessive fiber intake from plant matter and should instead choose herbs and spices over "big-ass salads" and giant kale smoothies.

3. Avoid Processed and Packaged Foods

Refined carbohydrates, artificial flavors, processed vegetable oils, and natural sweeteners are very rare in longevity hot spots. It's not that those living in the Blue Zones never let themselves enjoy guilty pleasures; it's just that their guilty pleasures are typically antioxidant-rich treats such as local red wine (one to two glasses per day), sake, coffee, herbal tea, or simple desserts such as nuts, cheese, and berries or grapes. Soda, sports drinks, candy bars, and packaged baked goods—including giant bags of sweet potato chips or bottles of sugary so-called superfood kombuchas—simply are not prevalent in these diets. You also won't find these populations consuming high amounts of popular so-called health foods that you find in the healthy-foods section of many supermarkets, convenience stores, and airport newsstands, such as packaged dried fruits, trail mix, energy bars, and other items that notoriously include blood-sugar-spiking or inflammation-producing compounds such as vegetable oils and simple carbohydrates, often deceptively labeled as "organic sunflower oil," "cane sugar," or "agave syrup."

What Did Your Ancestors Eat?

Ancestral dieting seems to have become quite sexy of late. As we learn more about genetics and how diet is controlled by and impacts genetic expression, it seems to make sense that you should eat what your ancestors ate. After all, you have inherited a set of genes that developed and adapted to specific environments and diets, so it seems worth maximizing that genetic potential.

For example, in my case, as someone from predominantly Northern European ancestry, I eat plenty of fermented foods, meats, fish, eggs, berries, and raw dairy, without a large intake of citrus fruits or other foods my ancestors would not have encountered in their local habitat. If you are of Scandinavian origins, your ancestors had good access to fish rich in omega-3s and vitamin D, so you likely need a diet higher in fish and vitamin D for optimal longevity.

Certain genes can also influence these decisions. For example, MTHFR mutations that create a poor ability to methylate tend to cluster in regions and populations where a group's traditional diet was rich in folate. In a study of people in sixteen different regions of the world, Mexicans, Hispanics, Italians, and Chinese were more likely than others to carry MTHFR mutations that increased the need for dietary folate. So if you have Chinese heritage, or your grandparents migrated from Italy, or your dad was Hispanic, you should probably eat more folate-rich foods, such as leafy greens, organ meats, and pastured egg yolks.

Or take the AMY1 gene, which codes for salivary amylase production. Salivary amylase digests starch and carbohydrates, and the more AMY1 copies you have, the more salivary amylase you produce when you eat carbohydrates—and the more likely it is that your ancestors ate relatively high amounts of starch, and the more likely it is that you can handle a slightly higher carbohydrate intake. Populations that are traditionally more agricultural, such as Japanese and continental Europeans, or populations that are high-starch foragers, such as the Hadza tribe in Tanzania, have all been shown to possess more AMY1 copies than populations that consume less starch, such as those in areas of Turkey and the Congo. If your ancestors came from a region that ate more carbohydrates, you can likely thrive on natural starches such as sweet potato, yam, plantain, other roots and tubers, fruit, and rice.

One final example is the lactase persistence gene. Lactase is an enzyme that enables an adult to digest lactose without getting gut distress, diarrhea, and all the other mayhem that can happen with lactose intolerance. As you can imagine, cultures that have not traditionally raised dairy livestock, including those in Asia, Africa, and most of India, rarely carry the lactase persistence gene. In contrast, if you are of European descent, you are probably lactose tolerant.

Eating according to your ancestry is fascinating, isn't it? For an even deeper dive, I recommend reading *Returning to an Ancestral Diet* by Dr. Michael Smith and *The Jungle Effect* by Dr. Daphne Miller.

Instead, nutritional evaluations of diets in the Blue Zones have revealed a high consumption of whole, real foods that your great-grandparents would have recognized and a nutritional profile very similar to the Mediterranean diet. The diets include plenty of herbs such as thyme and rosemary, foods low on the glycemic index and free from added sugar, healthier starches such as purple potatoes, yams, taro, or lentils, and foods high in natural fats such as extra-virgin olive oil and fish.

The way I like to think about this is to look into what your ancestors would have eaten, including investigating your genetic history using a service such as 23andMe to see where your ancestors lived, and then to eat a genetically appropriate diet based on what your ancestors would have consumed.

4. Eat Legumes

A legume is a dry fruit contained within the shell or pod of a plant; the most well-known are beans, peas, peanuts, and alfalfa. Beans, in particular, seem to reign supreme in many Blue Zones. In Nicoya, black beans are eaten in large quantities. In the Mediterranean, lentils, garbanzo beans, and white beans are popular. In Okinawa, soybeans are eaten frequently. This raises an eyebrow among many nutritionally savvy folks, especially in an era of the popular Paleo diet, which frowns upon beans and legumes because they contain high amounts of gastric irritants and natural plant defense mechanisms such as phytates and lectins. But the fact is, legumes are rich in plant protein, vitamins, minerals, appetite-satiating and gut-supporting fiber, and, just as significantly, slow-burning carbohydrates that do not cause a large amount of glycemic variability.

It is unclear whether the longevity gained from legume consumption is conferred by the inclusion of slow-release carbohydrates with the exclusion of blood-sugar-spiking refined carbohydrates such as white flour, or whether the nutrient density of legumes is what makes them so special. I suspect it is both. If you want to include a daily dose of legumes in your diet, I recommend you use the same ancestral preparation techniques used in longevity hot spots, including sprouting, fermenting, and soaking. You'll find instructions for preparing a wide range of legumes on Boundlessbook.com/19.

5. Incorporate Low-Level Physical Activity Throughout the Day

You won't find many longevity hot spots engaged in soul-crushing CrossFit workouts or long, teeth-gritting forays on an elliptical trainer or stairmill. Centenarians in the Blue Zones tend to lead very active lives, yet they rarely set foot in a gym or complete a formal exercise program. Instead, being active is simply built into their life: they walk on average five to six miles a day, farm, garden, spend time in nature, do many chores with their hands instead of machines, and tend to engage in spurts of high-intensity movement or structured movement through enjoyable exercise that rarely involves pounding away on a treadmill or inching under a barbell for a squat. These spurts involve activities such as yoga, tai chi or qigong, hiking, and games or social sports, such as soccer.

Take Dr. Shigeaki Hinohara, a Japanese longevity expert and physician who died at the ripe old age of 105. In a *New York Times* story on Dr. Hinohara, he described daily habits such as always taking the stairs (two steps at a time) and carrying his own packages and luggage (my own rule: I carry my bags through every airport and up hotel stairs as high as the fourth floor). Incidentally, in case you are interested in what this fellow ate, 130-pound Hinohara's diet was relatively

spartan: coffee, milk, and orange juice with a tablespoon of olive oil for breakfast; milk and a few biscuits for lunch; vegetables with a small portion of fish and rice for dinner; and exactly 3.5 ounces of lean meat twice per week.

In chapters 9 and 16, you can learn plenty about how I hack my environment using everything from a standing desk to kettlebell swings to replicate the kinds of movements involved in gathering, gardening, and hunting throughout the day, despite being relegated to a traditional post-industrial office setting. In stark contrast, my wife Jessa spends her days hauling alfalfa for the goats, feeding the chickens, pushing around wheelbarrows full of compost and rocks, chopping wood, fixing fences, planting trees, raking, shoveling, pulling weeds, and gardening. Admittedly, I am a bit jealous of her routine because she spends most of the day in the sunshine and fresh air working with her hands in an ancestral way, but at the end of the day, we have both achieved a similar amount of low-level physical activity.

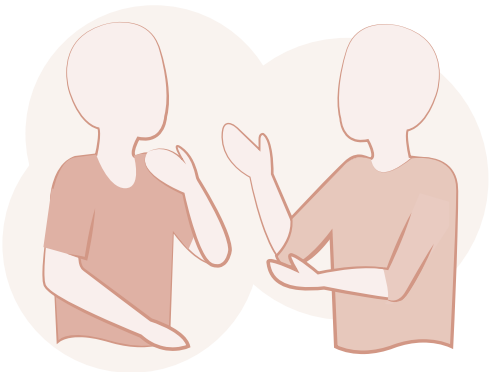
Think about it like this: unless you are a professional athlete or one of your primary goals in life is to train for and complete a triathlon, obstacle course race, CrossFit qualification, or some other modern-day equivalent of a battle that requires you to train like a warrior, visiting the gym at some point during the day should be an option, not a necessity. Research backs this up, showing that it doesn't matter how hard you exercise at the beginning or the end of the day if you have your butt planted in a chair for eight continuous hours during the rest of the day.

6. Prioritize Social Engagement

In most of the Blue Zones, strong relationships come naturally because social connectedness is ingrained in the culture. Compared to most hyperconnected Western societies, they tend to be much more engaged with, conscientious toward, and helpful to each other and more willing to empathize, express feelings, and wear their emotions on their sleeves.

For example, Okinawans have *moais,* which are groups of friends and families who live together their entire lives, spending time talking, cooking together, and supporting each other. Sardinians often finish their days in a local bar, where they meet their friends for a glass of red wine. Seventh-Day Adventists in California mingle with one another weekly or even daily during religious services and the observation of the Sabbath.

Family is also very important for people living in the Blue Zones. For example, during their daylong Sabbath celebration each week, the Seventh-Day Adventists focus on family, God, socializing, and spending time in nature. Nursing homes and hospice care are rare in the Blue Zones because people are expected to honor, value, and take care of the elderly, especially older family members. As a result of their pivotal role in society, elders are far more likely to have a social network, frequent visitors, and trusted caregivers, resulting in less stress, more purposeful lives, and, ultimately, a longer life span. As a matter of fact, I feel that the pros of prioritizing social relationships and family dinners, even if it means occasionally staying out past your bedtime or eating late at night, outweigh the cons of the possible disruptions to your circadian rhythm (especially because you can limit nighttime artificial light exposure by donning a pair of blue-light-blocking glasses or consuming a family dinner by candlelight).



7. Drink Low-to-Moderate Amounts of Alcohol, Especially Wine

In four of the five Blue Zones, people engage in moderate and regular alcohol consumption. Take the Sardinians, for example. They are famous for their regular consumption of a regional red wine called cannonau, a dry wine that contains two to three times the flavonoid content of other wines. Not familiar with cannonau? It is known elsewhere and more popularly as grenache. Consuming wine with or before a meal can improve the absorption of the artery-scrubbing flavonoid antioxidants in the wine, and studies have shown that the consumption of wine as part of a Mediterranean diet can reduce the risk of cardiovascular disease and cancers. Regular low-level physical activity boosts these benefits even more. According to a study performed by the European Society of Cardiology, moderate wine drinking and regular physical activity is a potent combination for cardiovascular disease prevention. Indeed, Sardinian shepherds often walk up to five miles a day to tend to their flocks—and carry along a lunch of unleavened bread, fava beans, pecorino cheese, and a local cannonau wine.

You are no doubt familiar with resveratrol, a polyphenol found in the skin of grapes that may protect the body against the oxidative damage that increases the risk of cancer, heart disease, and dementia. Resveratrol can also combat the formation of the plaque found in the brains of dementia patients. This may be why the weekly consumption of alcohol is associated with better cognitive function in old age. Plenty of additional research backs up the link between wine intake, reduced stress, and longevity (and as I'll explain later in this chapter, certain compounds very similar to resveratrol can be used in a more concentrated supplement form).

This type of frequent, moderate alcohol consumption is one of my own nightly habits—most often accomplished via a digestif and bitters-rich Moscow mule, a shot of a clean-burning alcohol such as gin or vodka on the rocks with a splash of lemon and hefty dose of bitters (a drink I affectionately call a "Ben and Jitters"), or a glass of organic, biodynamic red wine. As a matter of fact, I have one drink just about every night and very rarely have two or more drinks, and since I began this practice six years ago, I have never once been drunk or experienced a hangover (aside from my very brief holiday stint investigating hangover pills for a *Men's Health* magazine article).

Don't care for alcohol or have a history that makes it something you need to be careful with? The good news is that tannin-filled, antioxidant-rich beverages such as coffee and tea may confer similar benefits. Sardinians, Ikarians, and Nicoyans all drink copious amounts of coffee, and people in every Blue Zone drink tea, including Okinawans, who nurse green tea for much of the day, and Ikarians, who thrive on the frequent consumption of a tea made with rosemary, wild sage, and dandelion. On BoundlessBook.com/19, you'll find links to some blog posts that provide more information on the benefits of coffee and tea consumption, but in a nutshell, these types of tannin-rich compounds seem to directly decrease the rate at which telomeres shorten, even after adjusting for confounding variables.

8. Restrict Calories and Fast

Caloric restriction (CR) is a reduction in caloric intake that is not associated with malnutrition or starvation. Long-term CR has been associated in multiple studies with better weight management and slowed aging, as well as a reduced risk of diseases related to metabolic health, such as type 2 diabetes, heart disease, and cancer. But for active athletes, exercise enthusiasts, or people who already have a healthy body-fat percentage, long-term CR can have some downsides, particularly making one cold and hungry because of a drop in metabolism and lean muscle mass. Who wants

to live a long time if you have low libido and look like a poster child for an antistarvation campaign? Sure, if your goal is rapid weight loss or you are morbidly obese with lots of stored fat to burn, CR is a good strategy to accelerate fat loss, but even that strategy should be combined with periods of time during which you provide your body with ample calories and nutrients, such as a weekly refeed.

Intermittent fasting (IF) is probably the most popular way to get the benefits of caloric restriction without starving yourself. At its most basic, IF simply involves alternating cycles of eating and fasting, but the term encompasses many kinds of fasting, including these:

- **Time-restricted feeding:** consuming all food within a three-to-twelve-hour window each day, so you fast for at least twelve hours daily
- **Alternate-day fasting:** fasting for twenty-four hours, then eating normally for twenty-fours, then fasting for twenty-four hours again, and so on
- **Eat-stop-eat:** fasting for twenty-four hours once or twice a week
- **Fasting-mimicking diet:** consuming small amounts of food, about 40 percent of your usual calories, for three to five consecutive days
- **Feast-famine cycling:** eating according to the seasonal availability of foods
- **Warrior diet:** fasting during the day and eating a huge meal at night

I'll talk in more detail about a fasting-mimicking diet and feast-famine cycling later in this chapter.

Research suggests that in mice, IF can prevent and reverse obesity and metabolic problems, even when the mice eat an unhealthy diet. Researchers at the Salk Institute for Biological Studies performed an experiment that appeared in the journal *Cell Metabolism*. During the thirty-eight-week study, the scientists fed groups of adult male mice one of the following diets:

- High-fat
- High-fructose
- High-fat and high-fructose
- Regular mouse kibble

The caloric intake for each group was the same, but in each group, some of the mice could eat whenever they wanted while others were restricted to feeding periods of nine, twelve, or fifteen hours. On weekends, some of the time-restricted mice were allowed to cheat and eat whenever they chose. Halfway through the study, a few of the unrestricted mice were moved to the time-restricted groups.

By the end of the study, the unrestricted mice of each diet group were obese and metabolically ill. On the other hand, each diet group's mice that were restricted to nine or twelve hours of feeding per day were lean and healthy, even if they had been allowed to cheat on weekends. In addition, the unrestricted mice that were moved to the time-restricted groups had lost some of the weight they had gained! In other words, it doesn't matter whether a diet is high-fat, high-sugar, or both, or whether the diet is high-calorie. The most effective factor in maintaining a lean body is eating all of a day's meals within a short period, preferably somewhere in the range of eight to twelve hours each day.

Research also suggests that IF is effective in people, promoting fat loss and improving insulin sensitivity. Fasting also allows your gut to heal if you have been consuming gluten, gliadin, or other gut irritants, although these benefits, and the many longevity-related benefits of fasting, reach peak effectiveness after sixteen hours of fasting.

Centenarians in locations like Nicoya, Sardinia, and Okinawa are unlikely to use fasting-related terms like *time-restricted feeding*, but they do tend to eat relatively small portions of whole foods, consuming a low-to-moderate-calorie diet by being mindful of their hunger and avoiding calorie-dense, fat- and sugar-laden processed and packaged foods. Okinawans practice the traditional cultural rule of *hara hachi bu,* which means eating until they are about 80 percent full. Most meals are consumed within an eight- to twelve-hour window, referred to by researchers as a "compressed feeding window"—which perfectly matches the "new" 16-8 diet.

So why do all these different forms of fasting seem to work so well? The most recent research on fasting suggests that it all comes down to mitochondria, the tiny cellular power plants. Inside our cells, mitochondrial networks generally alternate between "fused" and "fragmented" states. Calorie-restricted diets and fasting promote homeostasis and induce a healthy fluctuation between fused and fragmented states, allowing mitochondria to live longer by cycling between a natural growth and repair process. They also increase fatty acid oxidation, which leads to fewer free radicals and less damage to your cells and the mitochondria contained within them.

In chapter 12, I detailed my own daily and weekly fasting practices—which are designed to make sure I get adequate nutrients for my active lifestyle—and explained who should be particularly careful in their approach to fasting. Later in this chapter, I'll talk about my two favorite longer-term fasting practices.

My podcast with Dr. Jason Fung (linked to on BoundlessBook.com/19) is an excellent resource that takes a deep dive into fasting, as is Dr. Fung's comprehensive book *The Complete Guide to Fasting.* Later in this chapter, I outline in detail two of my favorite forms of longer-term fasting.

9. Possess a Strong Life Purpose

An eleven-year NIH-funded study that investigated the correlation between having a sense of purpose and longevity showed that those who expressed a clear purpose for their life lived longer than those who did not, and those with purpose also stayed immersed in activities and communities involved in fulfilling that purpose. This idea of purpose is even expressed in idiomatic terms in Blue Zones: Okinawans refer to purpose as *ikigai* (translated as "reason for being"), and Nicoyans call it *plan de vida* ("reason to live").

I recommend that you know your purpose and be able to express it in one succinct sentence. My purpose in life is to empower people to live an adventurous, joyful, and fulfilling life. Need help identifying your purpose? A manual to identifying your life's purpose, such as Mastin Kipp's *Claim Your Power*, can help. If you want to begin as simply as possible, start with my friend Mark Manson's advice and simply choose to "do stuff that makes you forget to eat and poop."

10. Have Low Amounts of Stress

It is a well-known and heavily researched fact that chronic stress leads to inflammation and serves as the foundation for nearly every age-related disease. Centenarians in most of the world's longevity hot spots do not avoid all stress but do have built-in systems that allow them to manage stress on a daily basis. For Sardinians, this might mean having a glass of wine and a social dinner with family or friends at the end of the day. For Seventh-Day Adventists, it could involve a quiet nature walk on the Sabbath. For Okinawans, it is the concept of *taygay* (translated as "easygoing personality"), which is based on the idea that life simply unfolds at its own pace. In Okinawa, if an event is scheduled to begin at noon, *taygay* may mean that people on Okinawan time begin showing up thirty minutes to an hour later, which isn't necessarily something I recommend if you

don't want to get fired from your job. But you get the idea: ruthlessly eliminate haste and hurry from your life. For the best stress-reducing tips, including breathwork strategies, my most potent tactic for stress, which relies on zero supplements or fancy hacks, revisit chapter 3.

One breathing concept that was not explored in chapter 3 is quite fascinating and directly tied to longevity. My friend and former podcast guest Anders Olsson has studied animals' life spans in relation to their energy expenditure, metabolism, and oxygen utilization. In his fantastic blog post "Breathe Less, Live Longer," he notes that a common denominator for long-lived species such as the naked mole rat, the bat, the short-beaked echidna, the bowhead whale and the Greenland shark is that they have slow respiration and a high tolerance for carbon dioxide (CO_2). A fast and shallow breathing pattern corresponds to low CO_2 tolerance, while deep relaxation and breathing low and slow corresponds to a high tolerance for carbon dioxide.

Anders teaches two ways to increase the levels of carbon dioxide in your body: (1) reduce your outflow of CO_2, and (2) increase your production of CO_2. When you slow down your breathing, less CO_2 is lost via exhalation, and when you perform rigorous physical activity, more CO_2 is produced. A great method to train yourself for CO_2 tolerance is to combine the two by performing low-intensity physical activity (e.g., a brisk walk or bodyweight strength training) while breathing only through your nose. Over time this CO_2 tolerance training resets the breathing center in your brain stem and allows you to tolerate higher and higher levels of CO_2, which in turn may help you to live a longer life. (To learn more about Anders's research, check out the link on BoundlessBook.com/19.)

11. Engage in a Spiritual Discipline or Religion, or Believe in a Higher Power

In chapter 15, I described how much more meaningful and hopeful life can be when we believe that our story has a great Author, rather than believing that everything we see and experience is meaningless and without purpose, or that we are simply a bunch of chunks of spiritless flesh and blood floating through space on a giant rock before eventually dying and passing away into nothingness.

While many would scoff at the belief that there are gods and demons, spirits and angels, and even one single almighty creator of the planet, research has shown a connection between longevity and faith. One study analyzed the relationship between religious practice, stress, and death in middle age, and controlled for socioeconomic factors, health insurance status, and healthy behaviors. The researchers found that churchgoers have a significantly lower risk of dying, and after adjusting for age, sex, race, and chronic medical conditions, churchgoers were 46 percent less likely to die in the follow-up period after the study compared to non-churchgoers. Non-churchgoers had significantly higher rates of blood pressure and a higher ratio of total cholesterol to HDL cholesterol, along with a significantly higher mortality rate.

It turns out that data from the Blue Zones backs this up. All but 5 of the 263 centenarians Dan Buettner interviewed for his book belonged to some faith-based community. Research also shows that attending faith-based services at least four times per month can add four to fourteen years to life expectancy. In all Blue Zones, centenarians were part of a religious community. I can't sum it up any better than Buettner, who concluded that "people who pay attention to their spiritual side have lower rates of cardiovascular disease, depression, stress, and suicide, and their immune systems seem to work better.... To a certain extent, adherence to a religion allows them to relinquish the stresses of everyday life to a higher power."

In the Bible, 1 Peter 5:7 recommends that we "cast all our cares upon Him," and in multiple other verses of the Bible, we are told not to be so stressed about the common things the rest of the world tends to fret about, like food, water, and shelter. Being able to trust in and talk to a higher power is certainly something that has given me a great deal of hope, confidence, clarity, peace, and direction in life. Frankly, I believe that a religious practice that includes spiritual disciplines such as fasting, meditation, prayer, silence, solitude, worship, and study contributes even more significantly to longevity than a salad of wild plants, a glass of red wine, or a dose of sunshine. If I had to choose just one section of the Bible that best explains to how to optimize your health and longevity through simple religious practices and commonsense morality, it would be Proverbs 3. I keep a four-minute audio recording of this chapter on my mp3 player and listen to it at least once per week.

12. Remain Reproductively Useful

This last natural strategy for optimizing longevity simply makes logical sense: don't become reproductively useless. In other words, the more consistently you can send your body and brain the message that you are still a valuable, contributing member of society, particularly when it comes to the propagation of your species, the longer nature will want to keep you around. Don't retire. Don't quit learning new things. Don't surround yourself with older, sedentary people in a nursing home or hospice setting. Instead, continue to have sex, have children, or both.

Take, for example, the tiny town of Acciaroli, Italy, where one in eight citizens is over one hundred years old. The elders in this particular Blue Zone are not your average centenarians—they are healthy, consistently happy, and, you guessed it, horny. In the findings of a recent study on why these residents live so long is the observation that sex is rampant among them. Incidentally, the study also noted that the high consumption of parsley, sage, and rosemary, all of which are aphrodisiacs, is prevalent in this region.

Let's take a closer look at what research has to say about this. In a fascinating paper on proposed models of aging, one form of aging—referred to as the Kirkwood and Holliday model—describes mortality as increasing in direct correlation to decreasing fertility (a drop in hormones, childbearing, and frequency of sex). According to this model, the more an organism invests in the maintenance of their own biology (such as feeding and physical activity) compared to propagation of their species (such as mating rituals and reproduction), then the faster aging may actually occur. Basically this model posits that the majority of an organism's expendable energy should be focused on reproduction and that when it comes to prioritizing your antiaging efforts, having sex or making babies trumps taking care of your body in other ways! A form of this model is also known as the reproductive potential hypothesis, which maintains that life-span regulation has evolved in such a way as to maximize individual reproductive success, and research has indeed shown that women who bear children later or simply bear more children experience enhanced longevity.

The benefits of regular sex and childbearing seem to be backed up by laboratory research from Dr. Michael Rose, who explained his theories on the evolution of aging to me at a cocktail party at the Ancestral Health Symposium (you'll find a link to his website on BoundlessBook.com/19). Dr. Rose proposed that aging is not a positively selected, programmed death process and has not evolved for the good of the species, as many would think. Rather, aging exists because natural selection is weak and ineffective at maintaining survival, reproduction, and cellular repair as we enter old age. In a paper published in *Philosophical Transactions of the Royal Society B*, he described how senescence (age-related deterioration) is detrimental to reproductive success. The damage

that occurs during aging clearly shortens our life span, but longevity can also be shaped by selection for an increased number of what are called lifetime reproductive events, or the number of times you reproduce or attempt to reproduce.

In his book *Does Aging Stop?* Rose suggested that aging can indeed stop or plateau in the later stages of life, pointing to the demographic data in his large-scale fruit fly experiments as well as data on humans, both of which support the hypothesis that acceleration in death rates can halt in later life. While Rose had plenty of tips for enhancing this plateau, including the controversial idea that grain and agriculture consumption could accelerate age-related damage, one of his more potent suggestions was to have plenty of children and plenty of sex early in life, then continue to have children as late as possible, or at least to engage in frequent sexual intercourse to as ripe an age as possible. For multiple reasons, I am a fan of this idea, although I don't see any issues with using contraception so you don't have dozens of children running around your house, which I suspect might trigger a stress-related law of diminishing returns when it comes to longevity.

The quite possibly fabled but intriguing Li Ching-Yuen, who purportedly lived to the ripe old age of 256, was said to be a much-loved figure in his community, marrying twenty-three times and fathering over two hundred children. If it turns out that the story of Yuen is true, he may be the best example of the fact that maintaining reproductive usefulness with age could be an excellent idea indeed.

ADVANCED ANTIAGING BIOHACKS AND STRATEGIES

While the daily practices above are incredibly important for a long life, the fact is that we live in an era in which those basic antiaging tactics can now be combined with the more advanced tactics and biohacks used by the longevity and antiaging community. In this section, I will offer more advanced tactics that you can implement for longevity, including some practical recommendations.

Because many of the health, antiaging, and longevity strategies I am about to explore may seem—and often are—fringe, out of the ordinary, or even mildly excessive, allow me to clarify my take on the concept of implementing as many techniques as possible to enhance the quantity and quality of your years: *I am not a transhumanist.*

I do not believe that immortality for its own sake is a noble pursuit, nor do I believe that we as humans are capable of attaining a perfect body or brain. I do not believe that grasping at straws to hang on to every last shred of life, especially when driven by a fear of death, is a healthy way to live. I have witnessed many colleagues, friends, and antiaging-industry leaders spend too much of their precious time biohacking their bodies to live longer while simultaneously sacrificing time with their family and friends, a robust spiritual practice, and simple enjoyments, such as learning to play the harmonica or creating a beautiful watercolor painting or gardening with their children.

I am a Christian, and therefore I believe in a natural cycle of birth and death, followed by the ultimate resurrection of our bodies into a state of heavenly glory, unlike anything we would ever be able to accomplish here on earth. But importantly, I also believe that each and every person, including you, was born with a unique purpose, set of skills, and calling, and that to achieve that purpose to the very best of your ability, you must equip yourself with a sound body and mind and take steps to ensure you don't come down with cancer when you are fifty or have a heart attack when you are sixty or lose your memory when you are seventy because you made poor decisions about your health earlier in life.

In other words, the longer you are on this planet, the better able you are to fulfill your purpose in life, whether that's inspiring others to greatness, discovering the cure for cancer, making beautiful art, or writing books that delight children around the world.

Furthermore, I believe that God has surrounded us human beings with wonders and mysteries in both the natural world and the scientific domains that allow us to engage in better living via a marriage of ancestral wisdom and modern science, and that to ignore our ability to garden, forage, and create new tinctures, capsules, oils, devices, machines, and techniques that allow us to live healthier and longer is to neglect a big part of what it means to be an intelligent human being who is far different from the rest of the animal kingdom. It is to neglect our unique ability to explore, to invent, and, ultimately, to create.

So now that I'm off my soapbox, let's dive into some of those very discoveries, strategies, and inventions.

1. Longer-Term Fasting

I've talked already about time-restricted feeding and the other kinds of fasting protocols that fall in the "intermittent fasting" category and all the reasons you may want to make fasting a daily practice. But for the purposes of overall wellness and longevity, I am also a big fan of the following two longer-term fasting approaches.

FEAST-FAMINE CYCLING

My friend Dr. Dan Pompa calls the ancient healing strategy of seasonal diet variation based on food availability a feast-famine cycle. Many ancient cultures and modern Blue Zones follow this kind of pattern of fasting and feasting.

Humans have not always had grocery stores and Uber Eats services that provide food of all kinds 24-7. Instead, we have traditionally been forced to eat seasonally according to what plants are in season, what animal protein is available, and what nutrients are needed most at different times of year. For example, in the winter, many Native American tribes would give their dogs the muscle meat and subsist themselves primarily on fats, especially the organ fat from the kidneys, liver, and gut, because what they cherished most was the caloric density and nutrients from the organs. In the summer, these same tribes would eat more roots and berries, prickly pears, beans, pods, mustard seeds, cholla blossoms, acorn squash, pumpkins, and a variety of gourds—a much higher percentage of carbohydrates than in the winter, when consumption of saturated fats reigned.

In his book *Nutrition and Physical Degeneration*, Weston A. Price described this Native American practice this way:

> [Native Americans] cycled between the summer cultivation of starches and fruits and far greater reliance on fats from animals (particularly organ meats and marrow) during winter. . . . The successful nutrition for nine months of the year was largely limited to wild game, chiefly moose and caribou. During the summer months the Indians were able to use growing plants. During the winter some use was made of bark and buds of trees. I found the Indians putting great emphasis upon the eating of the organs of the animals, including the wall of parts of the digestive tract. . . . These Indians obtain their fat-soluble vitamins and also most of their minerals from the organs of the animals. An important part of the nutrition of the children consisted in various preparations of bone marrow, both as a substitute for milk and as a special dietary ration.

How it works: Science has shown that periods of caloric restriction and seasonal feast-famine dietary variations promoted health in indigenous cultures by forcing the body to use fat instead of glucose as a primary fuel during the winter months. This also gave the digestive system a rest and gave cells a chance to engage in the natural cell turnover known as autophagy.

How to do it: Dr. Pompa's 5-1-1 strategy, which combines seasonal eating with cyclic ketosis, is a great place to start. For five days of the week, follow a lower-carb, ketogenic diet (outlined in chapter 13) or, especially if you are attempting to lose weight, a calorie-restricted diet, primarily consisting of foods that are available locally and seasonally. One day of the week, fast for twenty-four hours (from dinnertime to dinnertime). The remaining day of the week, have a feast day, eating any of your favorite healthy food—especially carbohydrates—ad libitum, until you're full.

The 5-1-1 rule can be modified based on body fat, schedule, and physical activity levels. For some, a 4-2-1 or 2-2-3 approach works even better. Bonus points if you eat seasonally as you implement this approach, such as by eating more carbohydrates in the warmer months and more proteins and fats in the colder months: fresh fruits and berries in the spring, tubers and squash in the fall, heavier cuts of meat and fermented foods in the winter, and so on.

FASTING-MIMICKING DIET

Fasting usually involves abstaining from everything but water and perhaps black coffee and tea—no calories are consumed for the length of the fast. However, another effective approach to fasting was developed by Valter Longo and is outlined in detail in his book *The Longevity Diet:* the fasting-mimicking diet.

The fasting-mimicking diet (FMD) allows you to fast while consuming a minimal number of calories, so you can supply your body with nutrients while getting the benefits of fasting.

There are two ways you can implement an FMD:

- Alternate-day modified fasting, which is eating minimal calories every other day for a twenty-four-hour period
- An extended FMD, which is the program Longo advocates in his book and which involves consuming minimal calories for five consecutive days

As a word of caution, like other forms of IF, an FMD may be harmful for people who already have little body fat, the elderly, and children.

How it works: A typical alternate-day fast requires you to completely fast for a full twenty-four hours, then eat to satiety for the following twenty-four hours. It seems to be more effective than daily caloric restriction for maintaining long-term weight loss and allows your body to enter a powerful state of autophagy during the fasting stages. Fasting for longer periods, from three to five days, can stimulate adaptive responses such as autophagy, weight loss, and a long-term reduction of IGF-1, glucose, and markers of inflammation and aging.

An FMD produces many of the same physiological effects as these kinds of fasts but still provides your body with optimal nourishment, without activating the pro-aging pathways, including the growth hormone, insulin, and insulin-like growth factor 1 (IGF-1) pathways, which are activated by normal diets. When you follow an FMD, your body does not recognize that it is being fed and so believes that it is in a period of fasting. This can strengthen the immune system by triggering it to replace old T cells to combat particular invasive microbes; it can also improve insulin sensitivity.

How to do it: An FMD is low in calories and particularly low in protein. Longo's formula is based on meals of about 360 calories each: 9 percent from protein, 44 percent from fat, and 47 percent from carbohydrates. The diet is followed for five consecutive days; there are three meals on the first day that amount to a total of 1,090 calories, and two meals on each of the next four days, amounting to a total of 725 calories each day. However, you don't have to follow this protocol for five consecutive days—you can also alternate between normal eating days and low-calorie FMD days.

Longo owns a company called L-Nutra that premeasures and prepackages these meals as Prolon meal kits, which consist of vegan foods from natural sources. Should you choose to follow Longo's FMD diet, you can use these kits for a five-day protocol once per quarter for impressive longevity results.

However, I am not convinced that the minimalist meal kits Longo's company sells are necessary, and although they're convenient and done-for-you, they are also relatively low on the nutrient-density scale compared to fresh, whole foods. But with wild plant intake and small doses of superfoods such as spirulina, chlorella, bone broth, berries, seeds, or nuts—along with a few biohacks such as essential amino acids and ketone esters—you can easily put together your own minimal-calorie alternative to the packaged version.

One excellent example of a DIY approach can be found for free at FMDrecipes.org, which contains a full list of recipes for an FMD diet, based on Longo's research. For example, the Eggplant Pâté with Vegetables simply involves blending tahini, eggplant, oil, and lemon juice in a food processor, then adding salt, cumin, and fresh garlic to taste, and serving with a pile of vegetables. The Hearty Red Cabbage Slaw requires chopping cabbage, carrots, cilantro, and an apple in a food processor, then tossing the mixture with chopped nuts, pureed avocado, salt, pepper, lemon, lime, and garlic. While these recipes are not affiliated with Dr. Longo or his lab, they follow the macronutrient proportions laid out by his research and can help you achieve your FMD goals.

Dr. John Douillard also just released a five-day Ayurvedic cleansing approach to an FMD, which is, in my opinion and based on my own trial with his products, the best of both worlds: it combines a done-for-you diet that is shipped to your house with a real-foods approach. This protocol, called a "Kaya Kalpha" cleanse, includes daily consumption of the Ayurvedic cleansing stew Kitchari, which Dr. Douillard ships in dried packets to your home, along with a selection of ghee, herbs, and spices to maximize lymphatic drainage during your fast. I've tried both the Prolon kit and the Kaya Kalpha cleanse and have felt more clean energy and fewer appetite cravings with the latter approach to an FMD.

Finally, as a word of warning, it is usually not recommended to follow an FMD—or any form of fasting—for more than a few days at a time.

2. Hormetic Stress

While chronic exposure or overexposure to stress can result in inflammation and even life-threatening conditions, hormetic stressors are acute stressors that stimulate a favorable and beneficial adaptive response following brief exposure. These types of stressors range from the fasting protocols outlined above to exposure to cold, heat, or pathogens, to brief, intense bouts of exercise.

Many scientists believe that if you do not expose yourself to different hormetic stressors, your body may never develop an adequate adaptive response to high levels of oxidative stress (remember that the free-radical theory of aging posits that aging is the result of oxidative damage to our cells). Here's how it works: when you experience a hormetic stress, it signals your body to enter

a stress-resistant mode that tells your cells that it is probably not a good time to grow old and die. For examples, rats forced to swim in freezing-cold water every day tend to live longer. Giving worms electric shocks, restricting their calories, keeping them cold, and briefly exposing them to heat makes them live longer—with these techniques, researchers have made roundworms live up to ten times longer! On the other hand, mice raised in a sterile environment free of pathogens do not live nearly as long as mice that are exposed to bacteria and viruses in a dirtier environment.

Some practical ways to experience hormetic stress each day include lifting heavy stuff (refer back to chapter 9), not stuffing yourself with antibiotics (this can even mean not using antimicrobial or antiviral essential oils every day), engaging in hot-cold contrast therapy (such as alternating between hot and cold water when taking a shower—refer back to chapter 12), eating plants with a high polyphenol content (many of the beneficial compounds found in plants are actually noxious and stimulate a hormetic response), drinking wine for its polyphenols and similar compounds, such as tannins and anthocyanins, and even consuming alcohol for its own sake (small doses of ethanol may initiate a stress response). Below are a few of my favorite forms of hormesis.

HYPERBARIC OXYGEN THERAPY (HBOT)

HBOT delivers high-pressure air that is 100 percent oxygen, typically via a full-body chamber or a face mask. These higher pressures enhance oxygen delivery to every tissue in your body. HBOT is often used to treat decompression sickness, infections, air bubbles in your blood, and wounds that are not healing as well as they should due to diabetes or radiation injuries.

How it works: Oxygen binds to the protein hemoglobin in your red blood cells. HBOT results in a ten-to-twenty-fold increase in blood plasma oxygen levels, including a significant increase in red blood cells. It also promotes tissue repair, the formation of new blood vessels (angiogenesis), wound healing, and the controlled release of reactive oxygen species in damaged and infected tissues, which can stimulate a beneficial hormetic response. HBOT may also have antifungal effects, caused by the reversal of fungal growth and the restoration of a normal immune response. Finally, the slight increase in free radicals and ROS from HBOT induces a hormetic response that can build cellular resilience, and the treatment may also induce mitochondrial biogenesis and DNA repair.

How to do it: After suffering a concussion, I spent sixty to ninety minutes a day for multiple days immersed in over two atmospheres of high pressure inside a hyperbaric chamber (you can often find one near you by googling the name of your city plus the term *hyperbaric oxygen*.) I can now simulate a full twenty-four hours in a hyperbaric oxygen chamber by doing a thirty-minute cycling workout twice per week while using a hyperoxia (or hypoxia) device called a LiveO2, which I talked about in chapter 11.

WILD PLANTS

Humankind has foraged for food, medicine, and health-enhancing compounds for thousands of years. In fact, it is entirely possible that there are plants growing right in your own backyard that can be used to enhance digestion, increase cognitive performance, and improve endurance. You just have to know how to use them.

A wild plant is any noncultivated plant or herb that, when consumed, lends some kind of benefit to your immune system, digestive system, cardiovascular system, or nervous system, or even several of these systems at once. Plants that grow wild are exposed to more environmental stressors than much of the domesticated produce you find in the aisles of the grocery store, and they can pass on their built-in stress-resilience factors to your body when you consume them. Take mint, for example. The dainty, mild taste of the small mint leaves I can buy in a small plastic

container from the grocery store absolutely pales in comparison to the intense flavor and potency of the beat-up wild mint that grows in the forest behind my house—and the latter confers far more benefits.

How it works: Fruits and vegetables contain potent compounds that improve your health in a variety of ways, including phenols, polyphenols, phytochemicals, chlorophylls, and cytokines. The scientific term for this is *xenohormesis*, which simply means that environmentally stressed plants can produce compounds that can confer stress resistance and survival benefits to animals that consume them. These xenohormetic plant compounds can, when ingested, improve longevity and fitness by activating your stress response.

There are thousands of such plants that you can forage and consume. Clover, cattail, chicory, greater burdock, amaranth, field pennycress, plantain, kelp, fireweed, and even the lowly dandelion in your backyard are just a few examples.

How to do it: A local wild-plant-foraging class or meetup is a good way to get up to speed on what is growing wild in your area, and a trip to your local farmers market for ugly, dirty, bitter, sour, and misshapen produce can also leave you with a whole canvas bag or burlap sack chock-full of xenohormetic goodies. The trick is to eat as wide a variety of wild plants and herbs as you can by mixing them into teas, smoothies, stir-fries, salads, and other dishes throughout the week. If you are on the go or don't have time to forage, one of my favorite resources for organic, heirloom wild plant extracts and powders is Dr. Thomas Cowan's Vegetable Powders (you'll find a link on BoundlessBook.com/19).

As a general rule, if you cannot clearly identify a plant or herb and are not sure if it is poisonous, do not consume it. Stay away from plants that have milky or discolored sap; spines, fine hairs, or thorns; beans, bulbs, or seeds inside pods; a bitter or soapy taste; foliage that looks like dill, carrots, parsnips, or parsley if you aren't 100 percent certain of the identification; almond scents in the woody parts and leaves; grain heads with pink, purplish, or black spurs; and three-leaved growth patterns. Two apps that I've found to be particularly helpful for identifying wild plants are FlowerChecker, which gives you access to a team of live botanists, and PlantSnap, which uses artificial intelligence for plant identification.

HYDROGEN-RICH WATER

Hydrogen-rich water is essentially purified water infused with molecular hydrogen (H_2 gas dissolved in the water). In chapter 12, I explained that I use this form of hydrogen to improve my recovery and performance. I drink hydrogen-rich water from an H_2-water generator and travel with hydrogen tablets (Quicksilver Scientific and Water & Wellness are two good sources). Other good ways to get hydrogen-rich water include the H2Bev molecular hydrogen drink, although this is less travel-friendly because it's a canned beverage, and the hydrogen tablets from Drink HRW. Molecular hydrogen medicine capitalizes on the therapeutic benefits of hydrogen, which has both antioxidant and cytoprotective effects. It is nontoxic, even at high concentrations, and diffuses rapidly among your cells.

How it works: Molecular hydrogen has been shown to produce a profound improvement on stem cell availability, decrease the rate at which telomeres shorten (which are one of the major biomarkers for aging), and activate the same SIRT1 pathways targeted by sirtuin-rich foods such as blueberries and green tea, which results in improved mitochondrial function. It also increases the expression of antioxidative enzymes in the Nrf2 pathway, indicating that the mild hormetic stress caused by H2 increases resilience in cells stressed with excess oxidation from sources such as airline travel or heavy exercise. I'm personally convinced that very few modern nutritional interventions rival the anti-inflammatory and antioxidant benefits of hydrogen-rich water.

How to do it: Molecular hydrogen is usually consumed via tablets, canned hydrogen-rich water, or machines that generate hydrogen-rich water, such as a Trusii generator. There is no current upper limit of toxicity for hydrogen-rich water; I personally consume about 40 ounces of the water per day from the machine in my home and drink two or three 6-to-8-ounce glasses (two hydrogen tablets per glass) per day when traveling. Because molecular hydrogen also inhibits NADPH oxidase (NOX), an enzyme that can lower your levels of NAD (a molecule explained in detail later in this chapter), you can compound the beneficial effect by pairing hydrogen-rich water with other natural NOX inhibitors you'll find in this chapter, particularly foods such as pomegranates, blueberries, grapes, green tea, and berberine.

For a potent combination of NOX inhibition and hydrogen, there is even a liquid fermented beet product infused with hydrogen-rich water, available in a small, BPA-free can, that you can purchase from my friend Dr. Mercola (there's a link on BoundlessBook.com/19). Interestingly, in most cases, you'd benefit from the performance-enhancing benefits of beets by swishing them in your mouth so that your mouth bacteria enhance the conversion to nitric oxide, but hydrogen water actually does this for you, so no swishing is required. Fermented beets and hydrogen-rich water are a match made in heaven.

BHB SALTS

A BHB salt is a compound that consists of sodium (Na^+), potassium (K^+), and the ketone body beta-hydroxybutyrate (BHB). These salts are involved in the transcription and upregulation of the enzymes in your body's natural antioxidant pathways. They are also believed to induce ketosis and provide the same longevity benefits as caloric restriction. They can serve as a primary source of fuel for the liver, heart, diaphragm, and other tissues, and even act as an alternative fuel supply for our bodies when blood glucose levels are low.

How it works: Impaired mitochondrial function often results in excessive production of reactive oxygen species (ROS), which is involved in the development of many chronic diseases, including cardiovascular disease, diabetes, neurodegenerative disorders, and cancer. Moderate levels of mitochondrial ROS, however, have been shown to protect against chronic disease by upregulating mitochondrial capacity and endogenous antioxidant defenses. This phenomenon is called mitohormesis, and it's induced through exercise or dietary modifications such as a ketogenic diet—anything that increases reliance on mitochondrial respiration.

The consumption of BHB salts elevates BHB in a way that expands the benefits of nutritional ketosis beyond what could normally be achieved with carbohydrate restriction because it increases levels of available ketones higher than what you may be able to naturally achieve by simply restricting carbohydrates. BHB salts enhance antioxidant activity by inhibiting class I and IIA histone deacetylases, regulators that repress the transcription of the FOXO3a gene, a key gene involved in cell autophagy and inflammation. The metabolism of BHB salts also causes a negative redox potential (a greater tendency to accept electrons) of the NADP antioxidant system, which can scavenge free radicals. Adding BHB to cultures of *C. elegans* worms has been shown to extend their life span, and higher doses of ketone bodies may also extend human life spans.

How to do it: Add one to two servings of a BHB salt powder to a morning smoothie, blend it into a coffee or tea concoction, or consume it preworkout or during a workout, preferably combined with essential amino acids and electrolytes. There are a variety of companies now producing BHB salts, and you'll find links and discounts on BoundlessBook.com/19 to several, including Ancient Nutrition, Perfect Keto, KetoBlitz, and KetoForce. For a more efficient and effective way to deliver ketones into the body, you can also use ketone esters (see page 511), although they are far more expensive—$15 to $30 per serving compared to $2 to $4 per serving for ketone salts.

COLD THERMOGENESIS

Cold thermogenesis (CT) is the practice of intentionally exposing parts of the body to cold to induce an adaptive, beneficial hormetic response. CT practices include cold baths, cold showers, ice soaks, going outside on a cold day, keeping your house cold, or spending time in a cryotherapy chamber. Years of research have shown that cold exposure can cause significant increases in metabolism and calorie-burning, increase insulin sensitivity, reduce systemic inflammation, improve sleep and recovery, and potentially fight certain types of cancer. In summary, cold thermogenesis is a potent method to promote overall longevity and health.

How it works: As I talked about in chapter 8, CT is most often championed as a weight-loss strategy because it helps burn fat. Cold exposure also shuts down inflammation caused by exercise and wounds and activates the sympathetic, fight-or-flight nervous system, which regulates the mobilization and metabolism of stored fat.

But CT also enhances longevity, as does any exposure to hot or cold that mildly stresses the body. We can see this in many animal studies. For example, in 1986, a researcher at Washington University immersed lab rats in cold water for four hours each day. The rats burned so many extra calories that they ate twice as much as control rats, but they weighed less and lived 10 percent longer. Two decades later, researchers at the Buck Institute for Aging Research exposed lab worms to repeated heat shocks, and these worms lived 10 to 20 percent longer, largely by generating a surge of a protective compounds called heat shock proteins.

Many other animal studies have also shown that animals live longer when exposed to hormetic stresses such as starvation, toxins, radiation, infections, heat, and cold. It seems to be a universal adaptation—for instance, in general, when cold-blooded animals are exposed to cold, their metabolisms slow and they live longer, but when warm-blooded animals are exposed to cold, their metabolisms speed up to maintain body temperature, and they also live longer. It appears that both responses are part of an ancient genetic mechanism that senses temperature and slows aging as a survival mechanism. The theory goes that when something in the environment, such as a famine or cold snap or epidemic, is killing off part of the population, the rest of the population responds by getting tougher and living longer.

How to do it: Rather than spending the time and expense to hunt down a cryotherapy chamber, I take a cold shower or jump into a cold pool, lake, river, sea, or my home cold pool setup for at least two to five minutes twice a day. This type of cold-water immersion has repeatedly been shown to be superior to cryotherapy for tapping into the many benefits of cold. Many of my clients who are too busy to get wet wear a Cool Fat Burner vest or a Cool Gut Buster belt for thirty to sixty minutes per day while they are working.

Finally, one to two times per week, I recommend a longer ten-to-twenty-minute cold soak or ice bath that brings you to a state of shivering, or a series of two to three rounds of two-to-three-minute cold baths interspersed with two-to-three-minute sessions of Wim Hof or box breathing (see chapter 3). These longer, more intensive, and colder soaks can significantly enhance the conversion of white fat to brown fat (a key part of how CT helps burn fat—see chapter 8 for details) and can also be used as a quick hangover cure, cognitive boost, or what I consider to be a "cup of coffee for your entire body." But this kind of extended exposure can be overly stressful if done too often, so I recommend limiting it to one or two sessions per week. Interestingly, the genes responsible for enhancing life span in response to cold also seem to be activated by eating Japanese horseradish (wasabi). So perhaps a post-CT visit to your local sushi joint may also be in order.

HYPERTHERMIA THERAPY

As the name implies, hyperthermia therapy involves exposure to high temperatures and can include dry sauna, infrared sauna, heating mats, hot tubs, hot springs, sauna suits, or exercise on a hot day. Traditionally, hyperthermia therapy has principally been used to treat cancer, but the heart health and cellular resilience processes that it triggers make it a strategy for increased life span as well. While overheating and entering a state of extreme hyperthermia, in which your body temperature rises too high, is incredibly dangerous, controlled heat exposure is a powerful way to improve your longevity and well-being.

How it works: A recent study on hyperthermia published in *JAMA Internal Medicine* describes typical sauna use by Finnish adults—more specifically, the Finnish practice of frequent sessions in a dry, hot sauna heated to between 170 and 176 degrees Fahrenheit.

In this groundbreaking study, over 2,300 middle-aged men from Finland were divided into different groups based on how often they used a sauna: once a week, two or three times a week, or four to seven times a week. They were also sorted according to the duration of their typical sauna session: fewer than eleven minutes, eleven to nineteen minutes, or longer than nineteen minutes. After two decades, the researchers found that the higher the frequency of sauna use, the lower the risk of sudden cardiac death, fatal cardiovascular disease, and all-cause mortality. Compared with short sauna sessions (less than eleven minutes), men who spent between eleven and nineteen minutes in the sauna had a 7 percent lower risk of sudden cardiac death. For those with even longer sessions—nineteen minutes or more—the risk of sudden cardiac death was much lower (52 percent lower risk).

Why does a sauna provide such powerful medical benefits? The researchers pointed to previous studies that suggested the heart rate increase triggered by heat exposure may mimic the cardiovascular stress of exercise, and they also suggested that frequent sauna use could improve lung capacity. But there's also another factor involved.

Hyperthermic treatment of up to 120 degrees Fahrenheit for a wet sauna and between 158 and 212 degrees Fahrenheit for a dry sauna has been shown to cause a significant expression of heat shock proteins (HSP) in muscle. HSP have been implicated in longevity and aging in many species because they chaperone misfolded or newly synthesized proteins, protect cells from protein misfolding, and strengthen the immune system. The induction of HSP could potentially maintain protein homeostasis and improve longevity by refolding damaged proteins, which accumulate during aging and are toxic to cells. A decrease in HSP in aging is associated with the disruption of cellular homeostasis, which causes cancer, cell senescence, and neurodegeneration. The triggering of HSP is also correlated with 30 percent more muscle regrowth after a week of physical immobilization. That means that if you can't weight train, you have a recovery day, or you are injured, you can still maintain muscle using heat therapy. Sauna therapy can also increase oxygen consumption and red blood cell production following exercise, improve stress resistance, and aid in the detoxification of chemicals and heavy metals.

How to do it: At least twice per week (though you can do this every day), try to get into a dry sauna (at 170 to 180 degrees Fahrenheit), wet sauna (at 110 to 120 degrees Fahrenheit, and make sure the water is filtered), or infrared sauna (at about 130 to 160 degrees Fahrenheit) for fifteen to forty minutes, or until you achieve a noticeable rise in heart rate, sweat production, or both.

If you don't have access to a sauna, consider saving harder workouts for the afternoon heat of the day, perform your normal workout wearing multiple layers of clothing, or even drive home from the gym with the heater on full blast or the a/c turned off in your car. For a more relaxed and passive form of hyperthermia, I take my daily nap on a Biomat, which I increase to its maximum

temperature for a combination of hyperthermia and infrared exposure, and I often lounge on the mat while reading or stretching. Performing some of your hyperthermia in a state of parasympathetic nervous system activation—instead of simply exercising while hot—may enhance the detoxification effects.

Hyperthermia can also be a very useful strategy for decreasing cold and flu duration, and one trick I use if I feel as though I may be coming down with something is lying on my back on the floor of an infrared sauna for a longer, forty-five-to-sixty-minute session, or I'll wrap my body in blankets (the silver Mylar space-age-looking blankets work quite well), lie on my Biomat, and sweat in a parasympathetic, nearly comatose state of meditation for forty-five to sixty minutes. If you opt for a wet sauna or steam room, ensure that any water piped into that room is filtered for elements such as chlorine or fluoride.

Finally, keep in mind that the sauna culture in Finland is far different from that in many other countries. For example, when I make my annual foray to Finland and visit the Finnish Sauna Society (an experience I highly recommend), they aren't tapping on their phones, chatting, watching a built-in sauna TV, or doing anything else. They're simply sitting silently, breathing and meditating, and then socializing in the cold air outside the sauna. I suspect that these regular moments of relaxation and fellowship are significant contributors to the longevity-enhancing effects of the sauna that have been demonstrated in Finnish men.

UVA AND UVB RADIATION

UVA and UVB radiation, along with UVC radiation, comprise the UV radiation that is given off by the sun. As you no doubt know, sunblock is designed to minimize exposure to these rays because they can cause cellular damage and even lead to cancer. But when you expose yourself to low, controlled levels of UVA and UVB radiation, you can actually trigger a hormetic stress response. As with cold and heat exposure, it is about finding and using the right amount of exposure.

How it works: One of the primary ways that UVB exposure enhances health is by elevating levels of 25-hydroxyvitamin D, the major circulating form of vitamin D, in people with low baseline levels. Vitamin D is essential for protein, bone, and calcium homeostasis, and a deficiency in 25-hydroxyvitamin D is associated with an increased risk of age-related chronic diseases, including Alzheimer's, Parkinson's, cognitive impairment, and cancer, so UVB exposure has a wide range of health benefits. UVA exposure, on the other hand, generates nitric oxide, which reduces blood pressure and can act as an antimicrobial.

The benefits of UV radiation don't stop with UVA and UVB. It is well known that inducing low or intermittent levels of repairable damage in cells and tissues—such as occurs with UV exposure—is a good thing because it triggers short-term bursts of more aggressive cellular maintenance, and the end result is a net gain in the quality of the cellular environment—meaning fewer damaged proteins. In one fascinating study from the 1980s, researchers assessed the effects of radiation hormesis on both young and old dogs. They reported a gain of remaining life expectancy of 15 percent in older dogs and 50 percent in younger dogs. Some of the short-lived bird species in Chernobyl have developed enhanced anticancer mechanisms by producing higher levels of antioxidants to protect their DNA, and one Taiwanese study even noted a hormetic response in humans exposed to cobalt-60 radiation! While I don't think this means you need to go pitch a tent at the base of Chernobyl, these studies, along with several others, do indicate that low-intensity ionizing radiation is a hormetic stressor.

How to do it: They're often vilified as cancer chambers, so you may be surprised to learn that tanning beds, especially those outfitted with UVB bulbs, can be a good way to get UV exposure. A lot of people sell used tanning beds online, mostly because they consider tanning to be unhealthy;

a used tanning bed, including the bulbs, will usually cost you between $1,500 and $2,000. Higher-end tanning beds are a lot more expensive but not necessarily better—most contain plenty of useless options, such as Bluetooth and aromatherapy.

Once you have a tanning bed, I recommend outfitting it with a type of lamp called a Wolff Dark Tan II Plus, which combines the highest UVB rating with the lowest UVA rating (UVA rays may be more carcinogenic than UVB rays), or another good lamp called a Collatan Maxi Twist. Some high-end tanning beds emit UVA, UVB, and red light, such as the Ergoline 1600 from Europe, but these cost well over $30,000. There are online resources for more healthy done-for-you UVB tanning bed options, and on BoundlessBook.com/19, you'll find links to these as well as to links for good lamp and bulb options.

Should you decide to forgo the tanning bed, the most natural way to get low-level doses of UVA and UVB radiation is with multiple ten-to-thirty-minute sessions of exposure to sunlight, particularly between the hours of 10:00 a.m. and 4:00 p.m. This can be as simple as saving your daily phone calls or podcasts or audiobooks for a walk in the sunshine or having lunch outside with as much skin exposed as possible. If your skin burns, it is a telltale sign you have gone far past the level of healthy hormesis.

Incidentally, there is some research on the benefits of exposing your body to red and near-infrared light before and after UV ray exposure, particularly with respect to skin protection and vitamin D production, so getting evening sunlight (which has more red and near-infrared rays) and using light-producing devices such as infrared panels in conjunction with sun exposure can be a good biohack for limiting any potential sun damage. A similar effect can be obtained by taking the supplement astaxanthin.

Finally, for heaven's sake, please moderate your use of sunscreen, which *Outside* magazine has called the "new margarine" because, although it was once considered convenient and safe, it is now associated with a growing number of issues, such as vitamin D and nitric oxide deficiencies, increased risk of blood clots, and high blood pressure. Please also pay close attention to the discussion of lighting in chapter 20, which has plenty more about how light can help or hurt your health, depending on how you use it.

3. Caloric-Restriction Mimetics

Earlier in this chapter I talked about the health benefits of limiting the number of calories you eat each day. Caloric-restriction mimetics (CRMs) are simply drugs or other natural compounds that mimic the benefits of true caloric restriction.

RAPAMYCIN

Rapamycin, also known as sirolimus, is a medication traditionally used to coat coronary stents, prevent organ transplant rejection, and treat a rare and difficult-to-pronounce lung disease called lymphangioleiomyomatosis. Rapamycin also inhibits excess activation of immune T cells and B cells by reducing their sensitivity to interleukin-2, specifically by inhibiting the mTOR signaling pathway, which is a master regulator of cell growth and metabolism—this inhibiting effect is similar to the effects of caloric restriction. Since mTOR inhibition is synonymous with longevity, rapamycin is now being studied and utilized by many longevity enthusiasts as an antiaging compound.

Rapamycin is produced by the bacterium *Streptomyces hygroscopicus* and was isolated for the first time in 1972 by Canadian researchers from samples of *S. hygroscopicus* found on Easter Island. It was given the name rapamycin after the native name of the island: Rapa Nui.

How it works: Rapamycin is known as an antibiotic and immunosuppressant. But in mammals, rapamycin also targets the mTOR signaling pathway. As DNA or cells become damaged, stimulation of growth pathways in those cells leads to aging and eventually cell death. MTOR pathways, among others, drive this type of aging. By inhibiting these pathways, rapamycin slows the aging process.

Downregulation of the mTOR pathway has been implicated in various human diseases like cancer, diabetes, obesity, neurological diseases, and genetic disorders, and because it inhibits mTOR, which also increases the cleanup process of cellular autophagy, rapamycin has been shown to help treat certain diseases.

How to do it: Rapamycin can be taken orally, either as a tablet or in a solution. Although the ideal dosage ranges from 0.5 to 2 mg, the proper dosage can vary because absorption varies from person to person, so blood levels are measured to make sure that each person has the right dose for their condition. It's best to have a medical professional keep track of blood levels following ingestion.

Rapamycin is one of the more recent and more powerful of the compounds that extend life span in rats, but because it can suppress the immune system, it also appears likely to increase the risk of infectious diseases and even diabetes. It also has side effects that limit its usefulness for longevity. Additionally, mice fed rapamycin often suffer testicular atrophy, and some of the other possible adverse effects include impaired wound healing, lung toxicity, reduced immune function, and an increased risk of cancer—so I am still on the fence about it. However, some smart practitioners, such as my friend Dr. Peter Attia, use rapamycin successfully in their practices by closely monitoring dosing schedules and selectively targeting specific anabolic and catabolic pathways with cycling dosage. So under the care of a good functional medical practitioner, you can likely use it with less risk.

But there is also a natural substance called spermidine that has been shown to induce similar cellular autophagy effects as rapamycin with no known side effects. Researchers have given animals oral supplements of spermidine and found that they lived longer and were less likely to have liver fibrosis and cancerous liver tumors, even when genetically predisposed to those conditions.

Spermidine is found in high concentrations in wheat germ, dark leafy greens, pears, whole grains, mushrooms, and smelly, fermented cheeses, and it can be purchased as a supplement. You can read plenty more about spermidine's role in autophagy in the book *Glow 15* by my friend Naomi Whittel.

METFORMIN

Metformin (Glucophage, Glumetza, Riomet, and Fortamet are some of its brand names) is a modern pharmaceutical that is often advertised as being able to extend life "for a nickel a pop." It belongs to the biguanide compound family, a chemical group that has been used to treat diabetes since the 1950s. Metformin is synthesized from the guanidine, which is found in French lilac and was used in medicine as early as the Middle Ages. The synthetic versions belong to a family of drugs known as biguanides, and the star member is metformin. It was first approved as a drug in Europe in 1957, and 37,000 tons of metformin are now produced annually, mostly in India.

Because it is an activator of the AMPk pathway and is particularly effective at improving glycemic control with a low risk of inducing hypoglycemia, metformin may seem like an ideal CRM to enhance your chances of living a long life in good health. When I first learned about metformin, I thought it might be a bit too good to be true, but it turns out that unless you overdose with metformin, or have liver or kidney issues, or you are an athlete for whom maximum oxygen utilization is important, it may be one of the safer and more effective antiaging pharmaceuticals.

How it works: Metformin improves glycemic control primarily by inhibiting hepatic gluconeogenesis, which is the liver-based production of glucose from noncarbohydrate sources like lactate, glycerol, and certain amino acids. It also acts by opposing the action of glucagon. Glucagon is secreted by the pancreas when blood levels of insulin and glucose fall too low and stimulates the liver to convert glycogen stores into glucose, which is then released into the bloodstream. By inhibiting this process, metformin can improve insulin sensitivity and prevent hyperglycemia-induced aging brought on by the inflammation and AGE damage caused by elevated blood glucose.

Metformin can also reduce inflammation and cell death related to nonalcoholic fatty liver disease, and fibrosis, which is the thickening or scarring of tissue, particularly connective tissue, because of disease or physical stress. Finally, metformin inhibits oxygen consumption in the mitochondria, which can lower metabolism—another potentially life-extending mechanism, but one that I consider to be unfavorable for active individuals and athletes.

How to do it: Metformin is a prescription drug. Like any prescription drug, it can be ordered from online pharmacies, but this is risky, and my advice is that if you want to find out more about using it, you should speak to your doctor or health-care provider.

An effective dose of metformin for reducing the effects of hyperglycemia and acting as a caloric-restriction mimetic is 1,500 to 2,000 mg per day. Should you decide for forgo the pill, you may be interested in a slightly less concentrated version in a goat's rue supplement or French lilac tea, both of which are full of many of the same active ingredients as metformin.

KETONE ESTERS

Ketones have been studied for faster weight loss and reduced hunger, enhanced cognitive performance, blood glucose regulation, better mental focus, lower risk for disease, and lower inflammation, and now there is a growing body of research on their longevity benefits too.

Ketone supplements are often referred to as "exogenous ketones." Endogenous ketones are ones your own body creates as you restrict carbohydrates or calories and burn fat, but exogenous ketones are consumed just like any other supplement—yet they have the same benefits as endogenous ketones. The body produces three kinds of ketones—acetoacetate, beta-hydroxybutyrate (BHB), and acetone—but the ketone found in ketone esters is BHB, primarily because research has shown that it is the ketone the body can use most efficiently.

Unlike BHB salts, which I talked about earlier in this chapter, ketone esters consist of the BHB ketone itself without any salts or other compounds bound to it. This allows the body to use the ketones more quickly, which raises blood ketone levels more significantly than MCT oil or BHB salts.

Most of the use of ketone esters has been limited to laboratory research, but they are moving into the commercial spotlight, and the world's first two ketone ester drinks, HVMN Ketone and KetoneAid KE4, are now on the market.

How it works: You get the same life-extending properties of caloric restriction and fasting by being in a state of ketosis, so ketones—whether exogenous or endogenous—qualify as a caloric-restriction mimetic. The drop in insulin and insulin-like growth factor receptor signaling that happens when you're in ketosis increases the transcription of genes that encode antioxidant enzymes, such as catalase, glutathione peroxidase, and superoxide dismutase, as well as hundreds of other genes—which makes ketosis an effective method for combating free-radical damage.

Earlier in this chapter, in the section on BHB salts, I explained why the ketone body BHB improves autophagy, reduces inflammation, and eliminates free radicals. It's particularly effective when delivered in the ester form. Ketone esters also have the ability to power mitochondria in aging individuals who have a more limited ability to use glucose for energy, making them a powerful, multimodal choice as a longevity-enhancing compound.

Is There a Dark Side to Metformin?

As Tim Ferriss reported in his book *Tools of the Titans*, metformin is widely used among CEOs, Silicon Valley executives, billionaires, and world-class performers for its antiaging properties. Among metformin's fans are Robert Hariri, CEO of cellular therapy company Celularity; Craig Venter, genetic sequencing pioneer and cofounder of Human Longevity; Ray Kurzweil, futurist and inventor; and Ned David, molecular biologist and cofounder of Unity Biotechnology.

But many people are concerned about potential problems with this supposed wonder drug. In recent years, evidence has accumulated that metformin may not be all it's cracked up to be.

For example, metformin falls into a category of biguanide molecules that can increase the generation of lactate, which then enters the circulation and produces lactic acidosis. Phenformin, another member of the biguanide family, was a popular medication for diabetes but was withdrawn from clinical use in the 1970s because it caused severe lactic acidosis. Although phenformin is associated with a ten-to-twenty-fold greater incidence of lactic acidosis than metformin, metformin's effects are still significant.

Problem is, the 1940s study that linked metformin to lactic acidosis looked at patients who were already in end-stage renal failure and also were obese and diabetic. Several other studies have shown that lactic acidosis rarely happens in normal patient population groups. While metformin is contraindicated in those with renal impairment, the reported incidence of lactic acidosis in clinical practice is very low (fewer than ten cases per hundred thousand patients).

Although metformin has been the most commonly prescribed drug for the treatment of type 2 diabetes for more than five decades, its bioenergetic mechanisms remain largely unknown. This ignorance has triggered many endeavors to uncover how exactly it works—but the results are often contradictory. One study found that while metformin may play a big role in managing cardiovascular risks, it doesn't necessarily improve hyperglycemia and, on average, has little effect on insulin requirements for diabetics. And while there were two deaths in the placebo group, there were five among the patients taking metformin.

Metformin may be beneficial for cardiovascular health when used on its own. But one study found that combining metformin with sulphonylurea (another common diabetes medication) may result in an increased risk of mitochondrial dysfunction, cardiovascular complications, and all-cause mortality. However, this study looked at morbidly obese diabetics who were using anywhere from 6 to 9 g of metformin per day—three to five times the usual dose. Other studies show it's actually the opposite: that metformin may reverse mitochondrial dysfunction.

Many people are also concerned that metformin can cause vitamin B_{12} deficiency—at least one study has found that it stimulated vitamin B_{12} malabsorption. Decreased B_{12} concentrations can cause increased homocysteine concentrations, which is (surprise!) an independent risk factor for cardiovascular disease, particularly in individuals with type 2 diabetes. During the fifty-two months of the study, B_{12} concentrations in the metformin group got progressively lower over time, and this can result in macrocytic anemia, neuropathy, and mental changes. The same can be said for metformin's effect on folate levels, especially in women. But, of course, both B_{12} and folate are incredibly simple compounds to supplement with, and they can easily be stacked with a metformin protocol to avoid deficiencies.

Another study looked at the relationship between metformin, exercise, and blood glucose levels and found that an earlier study had showed that combining metformin and exercise had the same benefits for diabetes as metformin alone and exercise alone. In fact, exercise and metformin may have contradictory effects on diabetes. First, metformin reduces blood glucose levels, but exercise tends to increase levels of glucagon, the hormone that deals with low blood sugar by mobilizing the body's stored carbohydrates. When the two are combined, glucagon concentrations rise as the body tries to compensate for the effect of metformin. Second, by increasing the heart rate, metformin has the potential to elevate rating of perceived exertion even at lower exercise intensities, which means it could lead to the prescription of lower exercise workloads than are commonly recommended. There is also a study out of Taiwan showing that in diabetics, taking metformin for long periods of time (twelve years or more) can nearly double the risk of Alzheimer's and Parkinson's—but, like the studies on lactic acidosis, this study involved the heavy use of metformin for extended periods of time.

And then there's a concern about liver toxicity. In one person with nonalcoholic fatty liver disease, metformin was pegged as the cause of jaundice, nausea, fatigue, and unintentional weight loss—the drug had caused

abnormalities in liver enzymes. Another case involved a seventy-three-year-old Japanese woman who experienced fatigue, jaundice, nausea, vomiting, anorexia, and abdominal pain due to severe hepatotoxicity that resulted from metformin. But once again, like the person with nonalcoholic fatty liver disease, the patient already had a compromised liver.

Next comes metformin's potential impact on exercise performance. One study showed that metformin can decrease VO_2 max (–2.7 percent), peak heart rate (–2.0 percent), peak ventilation (–6.2 percent), peak resting energy expenditure (–3.0 percent), and actual exercise duration (–4.1 percent). While these reductions are certainly slight and potentially nonsignificant for the average exercise enthusiast, they do suggest that for a professional athlete (especially a professional endurance athlete), the use of metformin may spell the difference between a first-place finish and not even making the podium. A more recent study highlighted that metformin has also been shown to hamper endurance and limit mitochondrial proliferation in response to an exercise protocol.

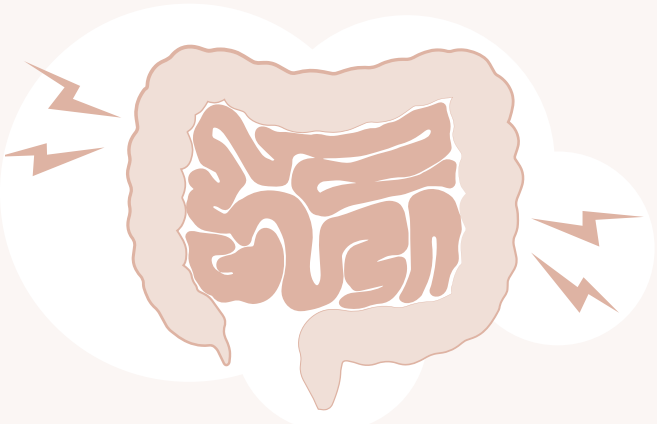
Finally, there's the concern that metformin causes GI upset. But this seems to happen only in people with bacterial imbalances in the gut (as discussed in chapter 13) and may occur because metformin is working directly to alter the microbiota. Research is now showing that metformin can actually alter the gut composition in a favorable manner by increasing levels of several different short-chain fatty acid bacteria. It may also decrease inflammation in the gut in a manner that increases insulin sensitivity and lowers blood glucose.

With all of this back-and-forth on metformin, I decided to get the opinion of my friend Dallas Clouatre, a well-established author and consultant in alternative and complementary medicine, and my guest on the podcast episode "How Low-Fat Diets Make You Fat" (he also, incidentally, introduced me to a very effective alternative to metformin: bitter melon extract). Here's what he had to say:

My thoughts on metformin are that it is interesting but overhyped. Keep in mind that it works primarily on the liver (which contributes to 30 percent of glucose clearance from meals) and not on the peripheral tissues (70 percent of glucose clearance). It likely does promote a longer "health span" given that lowering insulin and IGF-1 along with mTOR, typical of caloric restriction and of those who naturally live to extreme old age, is usually a good thing. Of course, any item that keeps insulin levels low along with keeping blood glucose in the low-normal range will lower mTOR. Downsides of metformin include reduced efficacy with advancing age, reduced efficacy with prolonged use, and GI tract issues in some individuals. Given that rehabilitation of the mitochondrial electron transport complex [which is deleteriously affected by metformin] is a normal function of a good night's sleep, for me, it is difficult to suggest the chronic intake of a drug that works by gumming up a natural process of the body.

I'll sum it up here: don't use metformin if you have liver or kidney issues, and definitely don't overdose on metformin. If you get gut discomfort while using metformin, consider waiting it out to see if your gut flora becomes balanced and your symptoms subside, which typically takes eight to twelve weeks. If you use metformin, supplement with vitamin B_{12}, and if you're a woman, monitor your folate levels and consider supplementation with a good multivitamin that contains a natural form of folate like methyltetrahydrofolate (MTHF). Finally, if you're a professional athlete or aerobic performance is very high on the totem pole for you, I'd avoid metformin.

For myself, my current habit of taking bitter melon extract is working just fine to control my blood glucose levels, but because metformin appears to have several beneficial side effects beyond blood glucose control, I may begin supplementing with it in the future. However, I encourage you to look into natural alternatives that can have similar blood-sugar-stabilizing and longevity-enhancing effects. You'll discover many such compounds in this chapter.



Additionally, in the presence of high glucose concentrations, ketone esters significantly increase the rate of muscle glycogen synthesis following exercise. One study pointed out that consuming ketone body esters leads to a state of pure ketosis unaccompanied by the elevation of free fatty acids, which could prove to be beneficial in treating certain neurodegenerative diseases such as Alzheimer's and Parkinson's.

Ketone esters can also inhibit NF-kB, a proinflammatory transcription factor that regulates the expression of over five hundred genes involved in cellular transformation, survival, proliferation, angiogenesis, inflammation, and more. Inhibiting the NF-kB signaling pathway has been shown to reverse several aspects of aging, most notably cardiac hypertrophy, a condition in which the heart muscle thickens due to genetics, excess exercise, or chronically elevated blood pressure. NF-kB can block the production of stem cells in older individuals, and since NF-kB increases significantly with age, particularly in the hypothalamus, it is regarded as a pro-aging compound. Downregulation of NF-kB has been shown to significantly extend life span, memory, strength, skin quality, and more.

Because they are in a D-BHB configuration that does not require them to be bound to a salt, ketone esters are known to raise blood levels of BHB more than BHB salts or MCT oils. When consumed in a drink, the ester bonds in a ketone ester are broken by gut enzymes, releasing butanediol and D-BHB into the blood. Butanediol is an alcohol that is structurally similar to BHB and is metabolized by the liver to form D-BHB. All the D-BHB resulting from this breakdown travels straight into the bloodstream because the liver is unable to use ketones.

How to do it: Once per day, preferably in a fasted state, drink a serving of ketone esters. You can also combine ketone esters with a carbohydrate source such as dextrose or ribose for a potent physical and cognitive performance aid, or with an essential amino acid source for long-term stable energy, even in a fasted state. I have used this strategy during triathlons and obstacle course races with great success, but try it during training first to ensure the esters don't result in any annoying GI distress for you.

As a word of warning, no matter what you mix them with, ketone esters taste pretty horrible, so be prepared to pop some mint gum in your mouth afterward or chase them with a very small portion of fresh juice or your favorite stevia-sweetened beverage. I have successfully experimented with and use HVMN Ketone and KetoneAid KE4 drinks.

BLOOD-SUGAR-STABILIZING HERBS AND SPICES

Chapter 8 explained the importance of controlling glycemic variability and why, especially if you want to enhance longevity, you should place a high priority on lowering blood glucose levels and inflammation. In many respects, low, stable blood glucose can act very similarly to caloric restriction, which is why I consider most insulin- and blood-glucose-stabilizing compounds—including bitter melon extract, Ceylon cinnamon, apple cider vinegar, berberine, rosemary, curcumin, fenugreek, Gymnema sylvestre, and capsaicin—to be caloric-restriction mimetics. Many of these compounds also work in on anti-inflammatory compounds, giving you a double-whammy effect when you include these regularly in your diet, as is a common practice in many of the Blue Zones.

How it works: The mechanisms vary depending on the herb or spice:

- Bitter melon contains a lectin that lowers blood glucose by acting on surrounding tissues. It also suppresses appetite.
- Ceylon cinnamon lowers blood glucose and reduces inflammation, which contributes to weight gain.
- Apple cider vinegar has been shown to reduce blood glucose levels in diabetic rats, possibly because its acetic acid restricts the digestion of starch.

- Berberine exerts a hypoglycemic effect, particularly in people with type 2 diabetes, and also regulates lipid metabolism.
- Rosemary has been shown to lower blood glucose, possibly by increasing liver glycolysis.
- Curcumin, the active ingredient of turmeric, and ginger have both been shown to reduce blood sugar levels in diabetic rats.
- Fenugreek seeds, which are common in South and Central Asia, reduce fasting blood glucose levels and improve glucose tolerance.
- *Gymnema sylvestre* helps control blood sugar levels by blocking the absorption of sugar molecules in the intestines.
- Capsaicin, the active ingredient in cayenne, reduces blood glucose by increasing insulin.
- Finally, vanadium and chromium are minerals that, taken together, appear to have a blood-sugar-lowering and insulin-stabilizing effect like metformin's.

How to do it: It's not rocket science: simply fill your pantry and cupboards with a wide variety of the herbs and spices listed above. You can also use blood-glucose-controlling and insulin-sensitizing supplements such as Kion Lean, Gymnema sylvestre, or berberine before high-carbohydrate or high-protein meals. I also recommend a shot of apple cider vinegar in a couple beverages throughout the day (a splash or two of cocktail bitters can also be highly effective), ample use of Ceylon cinnamon in smoothies or shakes, and liberal use of rosemary, fenugreek seeds, ginger, and cayenne when cooking.

4. Sirtuin-Activating Compounds (STACs)

STACs are chemical compounds that affect sirtuins, which are a group of enzymes that use NAD+ to remove acetyl groups from proteins via a process that can allow for proper genetic expression, less protein damage, and extension of life span. Some of the better-researched foods and supplements rich in STACs are blueberry extract, cacao flavonoids, green tea extract, resveratrol, curcumin, black currants, and fish oil.

How it works: Sirtuins influence a wide range of cellular processes, including circadian rhythms, mitochondrial biogenesis, aging, transcription, apoptosis (cell self-destruction), inflammation, and stress resistance, as well as energy efficiency and alertness during low-calorie situations. STACs are also considered to be caloric-restriction mimetics, and in studies, they have been shown to help prevent aging-related diseases such as Alzheimer's, type 2 diabetes, and obesity.

A new compound on the STAC scene is fisetin, a polyphenol that's found in many tannic drinks, such as tea, wine, and pomegranate juice, and fruits and vegetables, including apples, persimmons, onions, cucumbers, and, in quite high concentrations, strawberries. Fisetin is a potent senolytic, which means it plays a crucial role in reducing the development of senescent cells, restoring tissue homeostasis, reducing a variety of age-related pathologies, and extending both median and maximum life span. Reducing the development of senescent cells has been shown to lead to less inflammation, less molecular dysfunction within cells, and better stem cell function. Quercetin, an antihistamine and anti-inflammatory found in dark leafy vegetables, broccoli, red onions, peppers, apples, grapes, black tea, green tea, red wine, and fruit, can also modulate senescent cell development.

How to do it: Buy blueberry or strawberry powder or fresh, organic blueberries and strawberries and use one serving per day in smoothies, on salads, or in other dishes (look for the smaller, less sugary wild blueberries, bilberries, or wild strawberries). Alternatively, you can use black

currants, although they may be harder to find. Dark cacao powder or cacao nibs, curcumin powder, turmeric root, green tea extract powder, and high-quality, organic green tea leaves are also good sources of STACs, as is a daily glass of organic red wine, a resveratrol-rich supplement such as Thorne ResveraCel, and 1 to 20 g of a high-quality fish oil per day (I take 10 to 12 g of fish oil on any days on which I'm not eating a hefty portion of actual fish—there's much more on fish oil in chapter 12).

Because most of these compounds are also antioxidant-rich foods, which, when overconsumed, may excessively blunt or halt hormesis, I recommend using them like condiments, in smaller amounts, and not as staples. Furthermore, when it comes to managing blood sugar, a handful of blueberries or strawberries is reasonable, but mowing through an entire carton is not.

5. Stem Cells and Stem Cell–Supporting Foods

There's quite a bit about stem cell therapies in chapter 12. As a quick reminder, stem cells can differentiate into more specialized cells and then produce a continuous supply of cells that can heal or build tissue in specific areas of the body. Chapter 12 explained how stem cells are categorized according to how many types of cells they can turn into and how stem cells can help with recovery, but here, I'll explore the nitty-gritty details about the different sources of stem cells, including adipose tissue, bone, placenta, and more, and how they can slow aging. You can consider this section to be your quick reference guidebook on interpreting the emerging and wonderful but oft-confusing world of stem cell therapies.

After all, there is evidence that a loss of endogenous stem cells is linked to aging and that the number of stem cells in your body may act as a biological clock for aging, with fewer stem cells ultimately resulting in overall aging. This makes sense because, as we age, a large number of the stem cells in the bone marrow get mobilized for repair and recovery. This means that everyone—and especially those whose bodies need more repair and recovery, such as professional athletes, those struggling with a chronic disease, and those who have had a large number of injuries or accidents—have fewer stem cells in their bone marrow as they age. The stem cell theory of aging postulates that the aging process is the result of the inability of various types of stem cells to replenish body tissues, so tending to your stem cells is likely one of the more effective steps you can take to enhancing longevity (especially when combined with the other strategies in this chapter). Indeed, after my first intravenous stem cell injection, my biological age based on telomere measurements dropped from thirty-seven down to twenty!

BONE STEM CELLS

The two primary kinds of stem cells found in bone marrow are hematopoietic stem cells (HSCs) and mesenchymal stem cells (MSCs). Both HSCs and MSCs are tissue-specific, meaning they differentiate only into specified, genetically designated tissues. HSCs differentiate into different types of blood cells, while MSCs differentiate into bone, cartilage, fat, and connective tissue located in bone.

How it works: Blood cell turnover, which is extremely high in adult humans, requires highly efficient homeostatic control mechanisms to maintain proper blood quality and volume, and HSCs are the primary agents of this homeostasis. HSCs were the first tissue-specific stem cells to be isolated and have been used in grafts to treat a number of blood cell diseases, such as leukemias and autoimmune disorders.

MSCs have been shown to be able to sustain the growth, viability, and multipotent status of HSCs in cell cultures. They can also heal injured and diseased tissues and organs, reduce apop-

tosis, and modulate immune responses, and the most recent research shows that when MSCs are given to older people in an IV infusion, they increase quality of life and decrease frailty.

Contrary to popular belief, stem cells do not necessarily travel straight to the area they're needed and instantly differentiate into some new form of tissue. It would certainly be convenient if this were the case, but in my podcast with regenerative medicine physician Dr. Matt Cook, he explained that what happens most of the time is that stem cells migrate into tissue and communicate with other cells, such as cytokines and exosomes, to modulate a normal inflammatory or repair response, or to call in other cells to help—such as fibroblast cell to assist with tendon repair. This means that stem cells—whether from fat, bone, umbilical cords, or any other source—primarily work by simply causing your body's built-in repair mechanisms to work more efficiently. If it is indeed the case that stem cells primarily modulate or stimulate an immunomodulatory effect, then the age (or the length of the telomeres) of the stem cells injected is irrelevant because it's other cells that do the healing. This means that harvesting and reinjecting your own stem cells from bone or fat when you are, say, eighty could still be a highly efficacious strategy—especially when they're combined with exosomes.

Exosomes, as you may remember from chapter 12, carry messages from cell to cell and are the "active ingredient" in stem cells, and they can be targeted to a specific cell or cells to enhance particular biological processes. Exosomes are particularly effective with stem cells from bone, which has a slightly lower MSC content than fat, because they effectively upgrade these stem cells closer to the status of fat-derived stem cells.

How to do it: A multitude of stem cell clinics in the United States can harvest stem cells from your bones with a long needle that's placed into the soft center of the bone marrow, often in the hip bones. However, very few medical institutions in the United States currently offer any type of exosome therapy. Dr. Adelson at Docere Clinics in Park City, Utah, employs a large number of exosomes in his stem cell therapy, which can be used in conjunction with any of the stem cell strategies in this section or even by themselves as a potent tissue repair and regeneration aid. Interestingly, recent research has shown that plants also produce exosomes, that, upon ingestion by a human, impart positive changes on the gut microbiome and act as tiny cell-to-cell signaling molecules all on their own. (When you step back, it's quite profound how many of the expensive or complicated methods for health or longevity can be replicated at least in part by natural means: photobiomodulation panels and sunlight, cryotherapy chambers and cold water, NAD supplements and pau d'arco tea, stem cells and fasting, and now, exosome injections and plants rich in exosomes, such as watercress, rosemary, dandelion, nettle, and mint.)

As you learned in chapter 12, Docere Clinics concentrates bone marrow stem cells into a bone marrow aspirate concentrate (BMAC). This BMAC "soup" is then combined with exosomes and reinjected into any joints that need treatment or, in the case of Docere Clinic's full-body stem-cell makeover, into every joint in the body. I underwent this procedure in 2018, and within two months, I began to notice a profound improvement in recovery and overall joint mobility and comfort. I have also had stem cells extracted from the iliac crest bone in my hip and stored with Forever Labs in Berkeley, California.

FAT STEM CELLS

MSCs appear to be very similar whether they are taken from bone marrow, adipose tissue, umbilical cord blood, or any other birth tissue, such as the placenta. The main difference between fat and bone as sources of stem cells is the number of MSCs that each contains. According to Dr. Kristin Comella of the US Stem Cell Clinic, adipose tissue contains about five hundred times

more MSCs than bone marrow. Bone marrow also contains high amounts of white blood cells compared to adipose tissue, so it may be more pro-inflammatory. Adipose tissue–derived stem cells (ASCs) may also have a higher immunomodulatory capacity than their bone marrow–derived counterparts, which could enhance the potential antiaging effect of ASCs.

How it works: ASCs are considered ideal for treatments and regenerative therapies. The main benefit of using ASCs instead of bone marrow–derived stem cells is that ASCs are more readily available (partially due to a worldwide increase in obesity) and can be harvested with minimally invasive, low-risk techniques. ASCs—particularly those derived from brown fat—can be used to support the new growth of bone cells, liver cells, neurons, vascular endothelial cells, heart cells, and, of course, more fat cells.

How to do it: If you are lean, you may have difficulty getting enough stem cells from your fat without a significantly uncomfortable session with a long liposuction needle (which is exactly what happened to me). The US Stem Cell Clinic in Florida is considered one of the go-to clinics for the liposuction extraction of fat stem cells, and both my wife and I have visited the clinic for this procedure. We pay the US Stem Cell Clinic a yearly fee to store our stem cells, and for a nominal fee, they can ship them to any medical clinic for either intravenous or intra-articular (joint) injections by a medical professional.

AMNIOTIC, UMBILICAL, AND PLACENTAL STEM CELLS

Amniotic fluid is the protective fluid that surrounds an unborn baby. During cesarean section deliveries, this fluid can be saved and the stem cells it contains can be harvested, resulting in about a liter of amniotic fluid containing MSCs. As explained in chapter 12, stem cells from umbilical cord blood are not as potent as others, like bone marrow and adipose stem cells, and can develop only into a limited number of cell types. Wharton's jelly is a tissue that surrounds blood vessels in the umbilical cord and contains relatively high concentrations of precursor MSCs that have increased proliferation and differentiation capabilities, especially compared with adult sources of stem cells. Placentas also contain a significant number of MSCs.

How it works: Harvesting these types of stem cells is relatively straightforward. The current procedure for harvesting amniotic fluid adds about ninety seconds to a cesarean operation and is completely safe for both mother and child. The cells can then be used to support the healthy growth of skin, cartilage, cardiac, nervous, muscle, and bone tissues. Umbilical cord blood can easily be harvested following the delivery of a baby. The stem cells it contains have been used therapeutically to treat bone marrow–related stem cell deficits. Placental stem cells are believed to be even more potent than umbilical cord stem cells: research has indicated that they proliferate and expand more easily than umbilical stem cells and have a greater immunosuppressive capacity, resulting in reduced levels of pro-inflammatory T cells. (Indeed, there are several international clinics that offer placental stem cell therapies that contain a high number of stem cells due to expansion, although it is not currently legal in the US to modify stem cells in this manner.)

How to do it: The FDA requires that any birth tissue–based stem cell product in the US, whether amniotic, umbilical, or placental, must be acellular, which means it can't be made of any living cells. If a company in the US claims that such tissue contains living stem cells, they are breaking the law, and using stem cells from these tissues could cause graft versus host disease, a condition in which your body rejects the injected tissue. This risk of tissue rejection that accompanies injecting one person's stem cells into another person's body is why I am a bit gun-shy of using or recommending birth tissue.

I also worry about viruses from these sources. Although tissue bank products are screened for diseases and screening processes are becoming more and more strict, especially in the US, these

tissues are still screened only for diseases we currently know about. But every several years, it seems, we discover a new and scary virus or prion disease, such as mad cow disease, and I don't like to take any chances with foreign tissue injections because of the chance of unknown viruses or protein diseases entering my body—so I'm more likely to recommend stem cells derived from autologous tissues like your own fat or bone. One exception to this rule is Wharton's jelly, which, as mentioned earlier, is harvested from the umbilical cord wall. Because these stem cells must communicate with both the mother's and the baby's tissue, they do not result in an antibody or other immune system response when used in other subjects.

Many US clinics offer amniotic, umbilical, and placental stem cell treatments, but they're likely to be far less effective and contain a lower stem cell count than your own bone- or fat-derived stem cells, especially if they're not combined with exosomes. There are several offshore stem cell centers (Panama is one quite popular location) that use living cells from birth tissue, based on the idea that younger tissue is better. Some centers in Mexico will culture-expand your own stem cells to concentrate their efficacy, a procedure that's banned in the US by the FDA because it's considered excessive manipulation of cells.

APSCS

In the regenerative medicine field there's an increasingly popular cell line called adult pluripotent stem cells (APSCs). This umbrella category includes very small embryonic-like stem cells (VSELs), multilineage-differentiating stress-enduring cells (MUSEs), and marrow-isolated adult multilineage inducible cells (MIAMIs), among others. Since their discovery, APSCs have been widely studied because of their ability to multiply freely and become any kind of cells in the human body. But unlike embryonic stem cells, they do not have known cancer-causing properties or other potential disease risks, and in clinical application, they can be derived autologously—that is, they can be extracted from and reinjected into your own body.

How it works: APSCs are formed in bone marrow, but rather than being stored there like other bone stem cells, they are released into your bloodstream, where they circulate inactive until your body faces extreme stress, such as low oxygen, low body temperature, or significant injuries. Once active, APSCs can home in with surprising accuracy on areas of injury and degeneration to begin the repair and regeneration process. In particular, they have been found to be effective for healing bone injuries and rejuvenating organs, and they have antiaging properties. This is almost like the blood transfusions therapy discussed later in this chapter, but without the need for the blood of a young healthy donor—your own blood goes through a process that makes it young again.

How to do it: I had this procedure performed at the offices of Dr. Halland Chen in New York City (Halland actually combined this procedure with a CoQ10 and NAD IV, as well as adding exosomes to the stem cells). After a physician collects blood (Halland pulled four 60 cc tubes of it from my arm!) or bone marrow samples, ASPCs are separated from other cells via cell-processing technology. Once isolated, the APSCs are exposed to very cold temperatures to simulate hypothermia, which activates them. Finally, the physician combines the APSCs with growth factors harvested from your own platelet cells in the same blood or bone marrow sample. The active APSCs and growth factors can then be returned to your body through an intravenous injection. Once in your bloodstream, the APSCs go to work, seeking out areas of inflammation and injury.

At Dr. Chen's clinic, this process is typically done over three consecutive days. On day 1, a CoQ10 compound, which helps generate energy in the form of ATP, is infused via IV, and you receive an intramuscular injection of vitamins such as NAD to mobilize your body's stem cells into the bloodstream. On day 2, 210 mL of blood is drawn, typically from a vein in your arm, for

cell processing. On day 3, your own APSCs are infused via IV, and a small portion is reserved for injection into a specific musculoskeletal region where inflammation or injury is present.

Currently, Dr. Matthew Cook at BioReset Medical in San Jose, California, and Dr. Halland Chen in New York City are the two doctors I trust to administer an APSC procedure. After I did this protocol, I noted a profound improvement in recovery, sleep, and overall energy levels.

COLOSTRUM

In chapter 15, I explained why colostrum, otherwise known as first milk or nature's first food, is excellent for repairing a leaky gut, reducing inflammation, and building muscle. It's also a powerful antiaging supplement. It serves as a concentrated source of proteins, growth factors, and antibodies that are essential for early development of newborns and beneficial for adults too. Colostrum's properties have been revered for thousands of years across many cultures. In ancient Chinese medicine, it was regarded as a potent health tonic, and for the Maasai people of Kenya and Tanzania, it has long been regarded as a crucial part of a warrior's diet. In Britain, dairy farmers refer to colostrum as "beestings," and they used any surplus colostrum to make an extra-creamy and very healthy pudding.

How it works: Colostrum is far richer in antimicrobial peptides, immune-regulating compounds, and growth factors than normal milk. It contains concentrated, low-volume forms of vital nutrients as well as lymphocytes and antibodies, and it helps to balance the gut microbiota and enhances the growth and repair of several tissue types. It also contains cytokines, which keep communication between immune cells active, and growth factors, which assist with maintenance and growth of certain body tissues, including muscle and the gastrointestinal lining. The lactoferrin in colostrum assists with iron absorption and is a crucial part of your immune defense system, and the growth hormone in colostrum works individually and with the other growth factors in colostrum to aid in the growth and function of gastrointestinal tissues, muscle, and more. The immunoglobulins in colostrum are small proteins that your immune system uses to seek out and destroy foreign antigens.

Finally, colostrum contains proline-rich polypeptides (PRPs—not to be confused with platelet-rich plasma, the other PRP in this chapter), important immune system regulators that encourage the growth of white blood cells and may restore balance in cellular immune functions. PRPs may defend against oxidative stress and support brain health. Studies have now shown that colostrum is a rich source of mesenchymal stem cell–like cells, and one fascinating study showed that, while colostrum alone had a considerable effect on stem cell activity, it was a combination of colostrum, yeast extract, skullcap, zizyphus (also known as jujube), seaweed, and turmeric that had the most profound activity likely to translate into therapeutic benefit.

How to do it: Because it contains few, if any, milk proteins, colostrum is well tolerated even by people who cannot tolerate lactose and dairy. That being said, colostrum from goat's milk is generally better tolerated by those who can't handle cow's milk, because human milk and goat's milk have similar nutritional and hormonal profiles.

You can use a colostrum powder in smoothies or shakes, or take colostrum capsules. Because it can be anabolic in the sense that it increases insulin-like growth factor and growth hormone levels, I don't take colostrum year-round but instead rotate it eight weeks on, four weeks off, throughout the year. In addition, if you have a bacterial overgrowth such as SIBO, colostrum can cause a die-off reaction (known as a Jarisch-Herxheimer reaction), so it's important to start with a lower dose if you have gut bacterial imbalances.

ALGAE

Algae and phytoplankton (more on phytoplankton below) are the foundations of the marine food chain, and in order to hold that position, they must be incredibly nutrient-dense. Pound for pound, algae is the most nutritionally dense food on the face of the planet—a single gram of algae contains the nutritional equivalent of 1,000 g of fruits and vegetables! Spirulina is an extremely nutrient-dense algae that forms tangled masses in warm alkaline lakes, primarily in Africa and Latin America. Chlorella is a single-celled freshwater species of microalgae that contains the highest-density chlorophyll in nature and possesses a nutrient density close to that of spirulina.

How it works: The chemical structure of chlorophyll is very similar to hemoglobin, allowing it to efficiently carry oxygen in the blood and increase your red blood cell count. There is even some recent research that indicates that a combination of chlorophyll in your bloodstream and exposure to sunlight can allow you to produce ATP without consuming any calories! By weight, dried chlorella is about 45 percent protein, 20 percent fat, 20 percent carbohydrates, 5 percent fiber, and 10 percent vitamins and minerals. Algal amino acids are unstructured, which means that your body can absorb them easily and rapidly. This type of nutrient-dense substance can easily be incorporated into a calorie-restriction or fasting protocol without compromising your overall caloric intake.

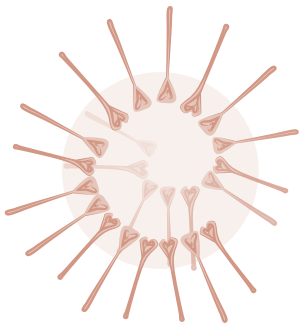
Perhaps most interesting with regard to longevity is chlorella's ability to mobilize stem cells. One study evaluated how an extract from the edible cyanobacterium *Aphanizomenon flos-aquae* (AFA), a form of chlorella, affected human stem cells in vitro and in vivo (in the lab and inside living organisms). A double-blind, randomized crossover study involving twelve healthy subjects found that chlorella helped stem cells travel to the tissues where they were most needed.

Another study demonstrated that spirulina lowered levels of a key neuroinflammatory cytokine in the hippocampus of aged rats, leading to the reversal of age-related cognitive decline and increased neurogenesis. Spirulina protected hippocampal neural progenitor cells from inflammation caused by molecules called lipopolysaccharides—which, interestingly, are often found in a high-fat, high-sugar diet. Spirulina also promoted mitochondrial respiration and the proliferation of stem cells in culture, supporting the hypothesis that a diet enriched with spirulina and similar nutraceuticals may help protect stem cells from damage.

How to do it: Not all chlorella or spirulina is created equal. Since algae is a bioremediant that can detoxify the water it is grown in and retain the toxins, you need to be careful with your sourcing. I eat about twenty to thirty tablets of chlorella and spirulina per day in the form of 100 percent organic, cracked-cell-wall algae from a company called EnergyBits, which is grown in pristine freshwater tanks.

MARINE PHYTOPLANKTON

Marine phytoplankton are photosynthesizing microalgae that grow in oceans all over the world. In addition to comprising the foundation of the entire oceanic food chain, its primary role in the ocean is to turn inorganic raw materials, such as seaweed, minerals, sunlight, and carbon dioxide, into hundreds of different nutrients, including vitamins, bioavailable minerals, all amino acids, essential fatty acids, and carotenoids. In addition, along with algae like chlorella, phytoplankton is responsible for producing up to 90 percent of all oxygen on earth. There are about forty thousand known strains of phytoplankton, and a few of these strains (particularly those mentioned below) are extremely beneficial for humans.



How it works: The phytoplankton strains that possess a nutritional profile compatible with human needs are dense in essential fatty acids (primarily EPA and DHA), which fuel your brain and nervous system; all amino acids, for muscle, brain, and nervous system support; enzymes and pigments that help eliminate oxidative stress and inflammation; and carotenoids, which play a role in regulating gene expression and inducing cell-to-cell communications.

A marine biologist named Luis Lubian, who was involved in an extensive study of more than forty-three thousand types of marine phytoplankton, discovered one strain of phytoplankton that is extremely nutrient-dense and well absorbed. The scientific name of this strain of marine phytoplankton is *Nannochloropsis gaditana*, or "nanno" for short. It contains the right amount and balance of amino acids, enzymes, fatty acids, minerals, and pigments, which are the building blocks our bodies use to repair DNA, produce glutathione, and generate growth hormones and stem cells. In other words, this one unique type of marine phytoplankton gives the body practically all the raw materials it needs to produce healthy new stem cells and neurochemicals.

In addition to nanno, another form of marine phytoplankton, referred to as tetra (its genus name is *Tetraselmis*), has extremely high levels of superoxide dismutase, an extremely powerful antioxidant. It is also very high in vitamin C (a strong electron donor and antioxidant) and has been shown to promote deep sleep.

How to do it: Take one or two drops of marine phytoplankton per day. I prefer Oceans Alive Raw Marine Phytoplankton, which are grown in a photobioreactor with just salt water, carbon dioxide, and sunlight, and then added to a trace mineral solution. The Oceans Alive brand contains both the nanno and tetra forms of the phytoplankton.

ALOE VERA

Aloe plants, also known as burn plant, lily of the desert, and elephant's gall, grow naturally in dry, tropical climates in Africa, Asia, Europe, and the southern and western parts of the United States. Aloe vera is a gelatinous substance derived from the fleshy leaves of the plant and has been recognized for its healing properties for at least six thousand years. A symbol of immortality, it was presented to Egyptian pharaohs as a funeral gift, and over several millennia, humans have used aloe to treat wounds, hair loss, hemorrhoids, and digestive issues.

How it works: Aloe vera contains several bioactive compounds, including vitamins, minerals, amino acids, enzymes, lignins, saponins, and salicylic acid. These, along with the other steroid-like compounds it contains—steroids, carotenoids, terpenes, and phytosterols—allow aloe vera to modulate various biological activities: it helps prevent cancer, scavenges free radicals, and exhibits antimicrobial activity by rupturing bacterial cell walls.

Aloe has been reported in several studies to improve glucose tolerance and overall glucose metabolism. For example, oral intake of aloe significantly reduced blood glucose in diabetic mice within just five days. Consumption of aloe vera juice and glibenclamide, a diabetes medication, significantly reduced fasting blood glucose within two weeks in diabetic human patients, but similar results were reported with the use of aloe vera juice alone. This is likely because the development of diabetes is accompanied by a decline in the number of circulating stem cells, and aloe has been shown to assist with mobilization of stem cells, which can migrate to the pancreas and differentiate into functional insulin-producing cells. Increasing the number of circulating stem cells has been reported to significantly improve the condition of diabetic mice and insulin-dependent human patients. Aloe vera also improves the viability of dental pulp stem cells, so it may have a significant positive effect on oral health.

How to do it: Aloe vera juice is easily consumed as a daily shot or poured into smoothies or shakes. Look for a product that is organic and at least 99 percent aloe. Often referred to on a

product label as aloe vera inner leaf juice, or inner fillet, aloe vera gel is also an option, although many gels use carrageenan, which has been linked to digestive problems—a bit ironic, since aloe gel is often used to aid digestion. But when my friend Shawn Stevenson was recovering from a spinal cord injury using a host of the plant-based stem cell–support tactics in this chapter, he would eat a 3-to-5-inch chunk of aloe vera leaf multiple times per day. If you prefer to use the juice, Lily of the Desert and Nature's Way are two good brands.

COFFEEBERRY FRUIT EXTRACT

I first learned about this little-known nutrient when I interviewed Darin Olien on my podcast. Nicknamed the "Indiana Jones of Superfoods," Olien is a widely recognized exotic superfoods hunter, supplement formulator, and environmental activist who travels the planet discovering new and underutilized medicinal plants. While hiking in Africa, he came across coffeeberry fruit, which has none of the taste associated with brewed coffee beans. It's quite tart and contains three times the amount of antioxidants of powerhouse foods such as green tea and blueberries. Darin reported to me that it is one of the few plants that can increase levels of totipotent stem cells, the ones that have the potential to develop into any kind of cell in the human body (see chapter 12 for more on totipotent stem cells).

How it works: In two clinical studies, coffeeberry fruit extract has been shown to significantly stimulate brain-derived neurotrophic factor, which is responsible for the development, differentiation, and protection of neurons and is also strongly supportive of both cognitive and mental health. In addition, coffeeberry fruit extract significantly upregulates sirtuin enzymes in a manner that can offset the aging process triggered by oxidative stress and support stem cell functions, particularly when the body is under chronic or acute stress. One study observed the effects of four weeks of coffeeberry supplementation in twenty college athletes and found that postworkout antioxidant capacity was significantly higher in the group that took coffeeberry than in the placebo group. The study also found that the coffeeberry group's blood lactate levels were significantly reduced ten minutes after exercise compared to the placebo group's.

How to do it: I buy 100 percent pure Hawaiian coffeeberry extract in a powdered form, which I blend into smoothies or shakes. I typically use it as a part of my shotgun-approach morning smoothie—on BoundlessBook.com/19, you'll find a link to information about what exactly goes into this beverage, but, as you can imagine, it includes several of the supplements listed in this chapter.

MORINGA EXTRACT

Darin also introduced me to moringa, a tree native to parts of Africa and Asia. Its name is derived from *murungaii*, which is the Tamil word for "drumstick." While there are thirty different species of moringa, the most widely cultivated is *Moringa oleifera*, which is native to the foothills of the northwestern Indian Himalayas.

How it works: Moringa contains a number of antioxidants and natural antibiotics, and the phytochemicals in moringa are hepatoprotective, cardioprotective, antinociceptive (pain-reducing), DNA-protective, and antiatherosclerotic.

Different parts of the plant contain different important minerals, as well as protein, vitamins, beta-carotene, and various phenolics. In studies, extracts from the flower of the plant have been shown to cause a significant increase in the proliferation of MSCs, while the root can increase cytotoxicity to cancer cell lines, effectively killing off cancerous cells. Extracts from the leaves are known to combat high blood pressure, reduce insulin resistance, reduce inflammation, and reduce the effects of diabetes. Moringa is also one of the more powerful members of the sulforaphane

family (similar to broccoli sprouts) and can increase activity of the Nrf2 pathway in a manner than significantly increases cell protection and reduces inflammation and oxidation.

How to do it: Like coffeeberry fruit extract, organic moringa leaf powder can easily be purchased online and then added to teas (I've found that it mixes quite well with green tea), smoothies, or shakes. It's one of the compounds that I add to my morning smoothie each day (the full list of ingredients can be found on BoundlessBook.com/19). If you want to get even more creative, simply take half a teaspoon of moringa powder, add a teaspoon of raw honey, squeeze in a little bit of lemon, mix them together, and add water.

The list above contains some of the top stem cell–supporting foods but is by no means comprehensive; nutrition research is constantly unveiling new compounds that enhance stem cell health and mobilization. Other notable dietary additions that may benefit stem cells include dark chocolate and other compounds rich in cacao extract, such as cacao tea; black, green, and oolong teas; foods rich in zeaxanthin, such as mustard greens, watercress, collard greens, Swiss chard, and fiddleheads; black raspberries; and even squid ink (which is used in many popular Mediterranean dishes, such as Spain's black rice and Italy's risotto al nero di seppia and pasta al nero).

6. Injections

In addition to stem cells, other injectable compounds can also have a potent antiaging effect. The following are a few of the more popular injections used commonly by longevity enthusiasts, biohackers, and antiaging medical clinics. Proceed at your own risk if you decide to inject yourself intravenously, intramuscularly, or subcutaneously. Having grown up in a family full of EMTs, I am quite comfortable whipping out needles and administering most of my own injections, especially those that are subcutaneous or intramuscular (just as a diabetic would administer insulin daily), but if you aren't comfortable with this, I recommend making good friends with a nurse practitioner or other medical professional who can assist you.

PEPTIDES

In basic terms, a peptide is simply a small protein consisting of amino acids linked in a chain. To better understand the nature of peptides, it helps to consider that proteins are made up of one or more polypeptide molecules. The proteins that we obtain through food are split by gastric enzymes into small peptides that have many different functions in the bodily systems. When administered via injection (usually subcutaneously, with the equivalent of an insulin syringe), certain peptides are particularly efficacious for joint healing, mitochondrial support, focus, energy, deep sleep, and longevity.

How it works: One of the notable properties of peptides is that they regulate the activity of certain molecules, and because of this, they influence body functions in several ways and can act like both neurotransmitters and hormones. Each organ and body function has its own unique peptide bioregulator. The characteristic of peptides that allows them to slow aging is due to the fact that they've been shown to shortcut the protein synthesis process. This means that when peptide bioregulators are active, organs can build and tissues can develop easier and faster.

In recent years, research has revealed that peptides play a significant role in the regulation of multiple mechanisms of biological aging. This branch of scientific research has led to the peptide theory of aging, which posits that changes in gene expression result in reduced protein synthesis, eventually leading to aging and the development of age-related diseases. By stimulating the body's own peptide production via peptide bioregulators, specific organs, systems or conditions in the body can be targeted by using a specific short-chain peptide to initiate greater protein synthesis.

I've personally used peptides BPC-157 and TB-500 to enhance healing and recovery. BPC-157 (body protection compound 157), which protects and heals the gut, is found in trace amounts in gastric juices. But it can also be synthesized in a lab. It can be taken in an oral supplement for a systemic effect, or injected subcutaneously or intramuscularly into or near injured or damaged tissues, where it has very powerful biological healing effects. BPC-157 is also known as a stable gastric pentadecapeptide (the name refers to the length of the peptide), primarily because it is stable in human gastric juice; can cause an anabolic healing effect in both the upper and lower GI tract; has an antiulcer effect; and produces a therapeutic effect on inflammatory bowel disease—all surprisingly free of side effects.

As demonstrated in multiple studies, BPC-157 also accelerates wound healing, and, via interaction with the nitric oxide system, protects endothelial tissue and builds blood vessels. This occurs even in severely impaired conditions, such as advanced and poorly controlled irritable bowel disease, in which it stimulates the expression of genes responsible for cytokine and growth factor generation and also collagen formation, along with intestinal anastomosis healing, reversal of short bowel syndrome, and fistula healing—all of which can be extremely frustrating issues in people who have gut pain, constipation, diarrhea, and bowel inflammation. Conveniently, BPC-157 is one of the few peptides that can be taken orally.

TB-500 (also known as thymosin beta-4) is also produced by the human body as well as by various animals. Like BPC-157, it can be synthesized in a lab and used to promote wound repair and healing, particularly because it acts on actin and myosin fibers in tendons, ligaments, and muscles (which is likely why it, along with PEMF, is a very popular healing and recovery strategy used in the horse-racing industry). It also offers many of the same effects as growth hormone, including an increase in muscle growth, improved endurance, reduced pain and inflammation (both acute and chronic), increased flexibility, and increased hair growth. Like BPC-157, TB-500 can be injected in or near any damaged muscle site and sore or injured joint with surprising healing effects, although, as I learned in my fascinating podcast with peptide researcher Jean-François Tremblay, they can act systemically, not just locally, when injected just about anywhere in the body.

Epithalon is another peptide I currently use. It is commonly referred to as the primary antiaging peptide because it is one of the very few synthesized compounds that has been shown to directly activate the telomerase enzyme in humans. Telomerase renews and elongates telomeres, the caps on the ends of chromosomes that protect DNA from damage and cancer-causing errors. A decreased rate of telomere shortening can thus be equated with decelerated aging. By activating telomerase, epithalon directly reduces the effects of time on your telomeres (there's more about herbs and plants that activate telomerase pathways later in this chapter).

Here's one way to understand epithalon's antiaging effects: After fifty to seventy divisions, cells can no longer divide and worn out, damaged, or diseased cells can't be replaced. This is called the Hayflick limit, and reaching the Hayflick limit coincides with the death of a living organism. In sufficient doses, epithalon allows cells to exceed their Hayflick limit, thus extending the life span of the organism.

One study of 266 people over age sixty demonstrated that treatment with epithalamin, the pineal gland extract epithalon is based on, produced a 1.6-to-1.8-fold reduction in mortality during the following six years, a 2.5-fold reduction in mortality when combined with thymulin (very similar to TB-500), and a 4.1-fold reduction in mortality when combined with thymulin and administered annually instead of only once, at the study's onset. Another study examined seventy-nine coronary patients over the course of twelve years and found that the group treated with epithalon enjoyed improved physical endurance, circadian rhythms, and lipid and carbohydrate metabolism compared to the control group after three years of twice-yearly treatments. The treated group

also enjoyed a 50 percent lower rate of cardiovascular mortality, cardiovascular failure, and severe respiratory diseases, as well as a 28 percent lower rate of overall mortality.

In addition to epithalon, I've also injected myself subcutaneously, in my abdomen, with two particularly intriguing antiaging peptides: humanin and MOTS-c. The first, humanin, is naturally produced in small amounts by the human body. Many centenarians produce unusually high levels of this peptide, which is encoded in mitochondria and has been shown to produce strong cytoprotective actions against a variety of stressors and diseases, including oxidative stress, hypoxic damage to the brain, and oxidized LDL cholesterol. It also aids in the repair of mitochondria. The second peptide, MOTS-c, is a potent metabolic regulator that significantly decreases the risk of age-related diseases and acts a bit like "exercise in a bottle." It activates the AMPK pathway and has an exercise-mimicking effect on fat and muscle. It even induces weight loss in mice fed a high-fat diet.

How to do it: When you order peptides, they are typically in a powder form and must be reconstituted by adding sterile or bacteriostatic water, which often comes with the vial of powder. (On BoundlessBook.com/19, you'll find a link to a helpful peptide calculator that will help you do the math to know how much water to add.)

There are a number of ways you can take peptides. The most common method is to inject them subcutaneously with an insulin syringe. Injections are the fastest method and result in high bioavailability of each peptide, and although it's not as deep (and therefore uncomfortable) as an intramuscular injection, it still gets the peptide where it needs to go if you're close to the site of pain or area that needs enhanced recovery. If you're looking for a systemic antiaging effect, a subcutaneous injection near the abdomen typically suffices. Be sure to use an alcohol wipe to clean the injection site. Do not reuse the needles or mix different peptides in the same syringe.

You can also apply peptides topically to several locations on the body, including the inside of the rectum and the vagina. If you choose to apply peptides topically, you may not absorb all of the molecules, but you will still get most of the benefits. For topical application, most people mix the peptides with a cream or gel, or use a ready-made topical peptide.

Taking peptides oral typically means consuming a lozenge called a troche or spraying the inside of your mouth, although supplement companies such as Dr. Seed's are now also selling tablet versions of some peptides, including BPC-157.

Be sure that when you order peptides, you work with a high-quality source such as Peptide Sciences or a physician who is getting peptides from a high-quality source such as Tailor Made Compounding. There are plenty of helpful peptide sources on BoundlessBook.com/19, and I particularly recommend you listen to the peptide podcasts I've done with Matt Cook, Jay Campbell, Jean-François Tremblay, and Dr. William Seeds.

Finally, should you want to replicate or speak with your physician about my current peptides protocol, I've listed it below. (Note: because the world of peptides is rapidly evolving, my protocol changes nearly quarterly, but at the time of this writing, the description below is accurate.) I get most of these peptides through my physician, who orders them from Tailor Made Compounding, and I highly recommend that you visit PeptideSociety.org, the website of the International Peptide Society, to find a physician who can work with you on a peptide protocol.

- **Epithalon:** I use the Khavinson protocol, named after Professor Vladimir Khavinson, perhaps the most distinguished medical gerontology researcher in Russia. Professor Khavinson believes the limit of animal and human life span is approximately 30 to 40 percent longer than the current mean life span, and that the limit of the human life span is 110 to 120 years. The Khavinson protocol is 10 mg epithalon administered three times a week for three weeks, and that exact dosage was studied in a fifteen-year

longevity study in humans that produced impressive results for controlling telomere shortening. The protocol only needs to be done once a year.

- **Delta sleep inducing peptide (DSIP):** This one needs to be used conservatively to avoid tachyphylaxis (diminishing response to successive doses of a drug, rendering it less effective). I inject 150 mcg three times a week, one hour before bed, and deep sleep levels increase by 30 to 40 percent. This can be continued for as long as it's needed, as long as it isn't used every day.
- **TB-500/BPC-157:** I take TB-500 at 1.5 mg (0.5 mL) twice weekly for full-body repair. This can be continued as long as desired. For BPC-157, I use frequent injections of 250 to 500 mcg, and during travel, I rely on the more convenient oral tablets from Dr. Seed's and take four tablets per day.
- **MOTS-c:** For mitochondrial support, I inject 10 mg once weekly. You can time this just prior to endurance exercise for added mitochondrial benefit, and repeat for up to ten weeks in a row every year.
- **FOX04-DRI:** FOX04 can sabotage the survival efforts of lingering senescent cells in old tissues, causing them to self-destruct. It has been studied in aged mice and has been shown to cause destruction of senescent cells without the unpleasant side effects of other drugs that do the same thing, while also producing a wide array of benefits that control age-related decline. I take 3 mg every other day for six days, and repeat this one to three times per year.
- **Semax:** I talked in detail about this peptide in chapter 5. It's used mostly in Russia and Ukraine for a broad range of conditions but predominantly for its studied nootropic, neuroprotective, and neurogenic/neurorestorative properties. It can be administered via nasal spray, at one spray (750 mcg) one to three times daily, or whenever cognitive enhancement is desired. I typically combine this with the transdermal cognitive peptide Dihexa.

THYMUS

The thymus is a small, irregular-shaped, fat-enshrouded gland situated at the front of the chest, between the heart and the sternum. Thymus from veal, lamb, beef, or pork is often breaded, fried, and sold in restaurants as sweetbreads. The thymus gland's primary function is to produce a type of vital white blood cell called T cells. It accomplishes this by producing cells called thymocytes, which are necessary precursors to T cells. T cells, or T lymphocytes, are critical in the maintenance of a healthy immune system.

For example, regulatory T cells maintain immune homeostasis by preventing or limiting T cell activation. Toward the end of an immune reaction, they suppress levels of other types of T cells, including effector T cells, helper T cells, and cytotoxic (killer) T cells, which are all involved in the immune system response. Memory T cells include central memory T cells, effector memory T cells, tissue-resident T cells, and virtual memory T cells. As their names imply, these memory T cells, which are found in lymph nodes and the surrounding tissues, are responsible for remembering previously encountered pathogens and developing long-term immunity and tolerance to pathogens throughout your life.

How it works: Once thymocytes are produced by the thymus, they migrate to peripheral tissues, where they act as the precursors to mature T cells. Since your body cannot properly produce T cells without sufficient precursors, supporting your thymus gland can be crucial for longevity and your ability to combat infection as you experience age-related immune system deterioration.

Indeed, research has indicated that thymus deterioration is closely associated with immunosenescence, the degeneration of the immune system primarily due to alterations in T cell composition. The intriguing fact about the thymus gland is that its size and activity closely parallel the growth and aging processes of the body: it reaches its maximum size and activity during puberty and then slowly atrophies over time, so that after the age of sixty, it is nearly undetectable from the surrounding fatty tissues. As the thymus shrinks, your immune system deteriorates, and your body begins to lose its defenses against age-related diseases.

Interestingly, Vladimir Anisimov, a Russian gerontologist who discovered many of the anti-aging benefits of melatonin and metformin, also discovered the peptide epithalon and found that it was able to suppress cancer and extend the lives of rats and mice in a series of experiments over several decades. Even more notably, when aging humans are given epithalon, their mortality rates drop in half. Its mechanism of action seems to be via both activation of telomerase and the regeneration of the thymus. Since the thymus shrinks gradually over the latter decades of life, any compound that slows the decay of thymic tissue could induce a profound antiaging response.

How to do it: Thymus treatments are usually made from thymic extracts from cows or sheep, and they're taken orally or via intramuscular injections. Should you decide to forgo the relatively expensive intramuscular injections or "glandular" supplements that usually contain a decent dose of thymus and instead take a more ancestral route, you can make it a point to occasionally eat sweetbreads, which can be purchased online from companies such as US Wellness Meats (their beef sweetbread is quite tasty). In addition, the injectable peptide thymosin-alpha can produce similar T-cell-enhancing effects.

For information on how to purchase and use epithalon, see page 526.

PLATELET-RICH PLASMA (PRP)

Your blood consists of several components, but one of the primary components is plasma, a clear, extracellular fluid. Plasma contains a high concentration of platelets, which are small cells generated by bone marrow that play a crucial role in managing vascular integrity and regulating hemostasis (stopping a flow of blood) and can also aid in wound healing.

Platelets can be administered to a site of pain or injury to supply stem cells, protein, and other growth factors that help speed up recovery, injected into any tissue that could benefit from more blood flow (including the genitals, making PRP a popular sexual enhancement procedure), and, like stem cells, they can be used as a preventive protocol or age-reversal strategy. Platelet-rich plasma (PRP) is exactly what is sounds like, plasma that's rich in platelets, usually derived from your own blood (although corporations like the Young Blood Institute in Silicon Valley are now offering plasma from young donors).

Blood platelet levels remain fairly stable throughout middle age (twenty-five to sixty years old), but past the age of sixty, levels fall and continue to decline, and the responsiveness of the platelets themselves also deteriorates. Injections of PRP could, therefore, have antiaging effects such as supporting vascular health in older people, reducing age-related joint pain, and preventing normal age-related degradation of the skin and sexual organs.

How it works: PRP is almost always taken from your own blood. Usually, the amount of blood needed is about the same as what is normally drawn for a standard blood test—one or two small tubes. The blood is placed in a centrifuge to separate the platelets, stem cells, and growth factors from the red and white blood cells. What remains after the red and white blood cells are removed is a concentrate that gets injected into the targeted area.

I have had PRP injected into my penis to give me stronger erections and improve sexual performance (a process known as the P-shot), but the potential benefits go far beyond the bedroom.

The growth factors released after the platelets break down via a process called platelet degranulation can aid in the treatment of tendon, ligament, muscle, and cartilage injuries, as well as early osteoarthritis. Given that tissues like tendons, ligaments, cartilage, and bone heal much slower after injuries than muscle does, PRP injections can be an effective tactic for joint support, especially as the musculoskeletal system deteriorates with age. For example, I've had PRP injected into my knees (in conjunction with stem cells, exosomes, and ozone) for a very powerful joint-repairing protocol).

But PRP is best known for its role in the vampire facial (you may remember a certain Kardashian touting her vampire facial on Instagram a few years back). These PRP treatments on the face are used to treat sagging skin, fine lines, wrinkles, and scarring by promoting collagen growth underneath skin.

In addition, recently a clinic in Athens, Greece, treated 180 women by injecting PRP into the uterus or ovaries to stimulate repair of the female reproductive system. They claim to have treated twenty-seven menopausal women, of whom twelve returned to ovulation!

How to do it: Over ten years ago, my first business partner, sports medicine physician P. Z. Pearce, partnered up with me to invest in a big, fancy PRP centrifuge. Athletes would visit our facility, where we would extract their blood and then spin it in the centrifuge to concentrate the growth factors for reinjection. Just like most PRP research studies, we found that although joint comfort seemed to improve significantly after just one injection, a series of four to six injections seemed to work even better.

Since that time, Dr. Charles Runels has brought PRP to the attention of the antiaging world by developing the vampire procedures, which involve multiple injections of PRP into wrinkled, hairless, or aging areas such as the face, the top of head, or the breasts. These treatments are often combined with PRP injections into the joints. Most antiaging and beauty medical clinics now offer this procedure, and both my wife and I have had our hairlines and faces injected with a soup of BMAC stem cells, PRP, and exosomes, with a noticeable increase in complexion quality and decrease in signs of wrinkling afterward. To stave off facial wrinkling that occurs with age, my wife Jessa has done follow-up treatments of facial PRP combined with stem cells and exosomes from Dr. Amy Killen at the Docere Clinics in Park City, Utah.

As a word of caution, PRP therapy is not for everyone, and the research surrounding it is inconsistent and inconclusive. In older populations, PRP increases the risk of thrombosis and blood clots. Since platelets play a central role in the coagulation of blood, if you have a history or family history of thrombosis or blood clots, it may be better to avoid PRP therapy, unless you are looking into a plasma exchange therapy offered by the Young Blood Institute, which can actually decrease blood clotting risk and "clean out" old blood by filtering the blood and replacing the plasma with that of a healthy donor (however, this protocol is very expensive). Genetic tests will tell you whether you are at increasing risk for clotting, and you should always check with your doctor or health-care professional before getting PRP therapy.

7. Blood Transfusions

This may sound like it is taken straight from a science-fiction novel, but today, older people are injecting the donated blood of younger generations into their own bloodstreams. One company, Ambrosia, based near San Francisco, had a client base of about six hundred people near to or over the age of sixty until they were shut down by the FDA. The company was collecting screened blood from local blood banks and then selling injections to antiaging enthusiasts who were willing to pay the $8,000 fee.

The Young Blood Institute in Silicon Valley has a different approach, which they call therapeutic plasma exchange and advertise as a preventive therapy for age-associated diseases. In this procedure, a patient's plasma, which constitutes about 55 percent of total blood volume, is completely replaced by the plasma of a donor over multiple treatments. During my groundbreaking podcast interview with the founder of the Young Blood Institute, Mark Urdahl, you can hear about the fascinating clinical research currently being done on this form of plasma exchange and discover how this treatment is now being shown to reverse a staggering number of aging-related medical conditions (most notably Alzheimer's)—the podcast is linked to on BoundlessBook.com/19.

How it works: While the whole procedure may seem slightly vampiric, there are animal studies that suggest that injecting the blood of eighteen-year-olds into your own bloodstream could be beneficial. A group of researchers surgically introduced a demyelinating injury in the spinal cord of an old mouse and then exposed the cells in the area to the blood from a young mouse. The result? Some of the immune cells from the young blood helped the old mouse's own stem cells restore the damaged neurons' myelin sheaths. The study concluded that age-related impairment to the nervous system could be reversed by cells in young blood that stimulate greater regeneration signals. Another mouse study found that younger blood, when injected into older mice, introduces growth factors that are believed to have antiaging effects on heart, muscle, and brain tissue.

As for plasma exchange, a host of studies show its potential for removing circulating substances that cause disease or contribute to disease states, removing pro-inflammatory factors (like fibrinogen, IL-6, and TNF-alpha), and even increasing activity in dormant stem cells.

How to do it: Pick up the phone and call the good folks at the Young Blood Institute in Silicon Valley. Admittedly, at the time of this writing, I have not yet spent over $40,000 on young blood transfusions, nor have I committed to having all the plasma in my entire body replaced with that of some healthy college kid in Florida. Nonetheless, I am intrigued by both procedures, and I highly suspect they will become increasingly affordable and popular with time.

In the meantime, it appears that GDF11, one of the antiaging proteins activated with an infusion of young blood, is also increased by the hormone oxytocin, which is activated during childbirth, breastfeeding, and sex. It can even be purchased as a nasal spray. This promises to be an affordable alternative to a blood infusion.

In addition, several medical practitioners, including Dr. Matt Cook in San Jose, California, are now offering ozone dialysis at their practice, which is a quick and relatively inexpensive treatment that may mimic many of the blood-renewal effects of a full plasma transfusion.

8. Bioidentical Hormone Replacement Therapy

Today, many women live one-third of their lives in a state of sex-hormone deficiency. This is especially important because estrogen, which can upregulate telomerase and improve mitochondrial health, is one of the factors in the longevity advantage women have in telomere length and the cellular resilience of female aging biology. And men are not exempt from hormone deficiency: though men are subject to age-related testosterone decline and andropause, these are frequently underdiagnosed and undertreated.

Bioidentical hormone replacement therapy (BHT) is a fast track to restoring levels of hormones that naturally decline with age: the sex hormones estrone, estradiol, progesterone, testosterone, DHEA, and estriol, as well as growth hormone and insulin growth factor-1. Far different from the synthetic hormones that became vilified in the nineties for causing breast cancer in postmenopausal women, BHT involves the use of hormones that are molecularly identical to the hormones that your body naturally produces.

How it works: For women, BHT—especially when combined with peptides—appears to be far safer than synthetic hormone replacement with compounds such as progestin, which is derived from the urine of pregnant horses and has been linked to breast cancer. BHT can be combined with pharmacy compounding, which involves matching injections and pharmaceuticals to each particular patient's needs.

For men who are interested in testosterone optimization, hormone replacement therapy doesn't necessarily need to be "bioidentical" per se, since the synthetic form of testosterone is functionally identical to the natural forms produced by the body.

How to do it: Although in-depth assessments of hormone needs, ongoing hormone testing, and precise follow-up plans should be standard practice, the fact is that many antiaging clinics simply hand over injections, creams, nasal sprays, patches, and other hormone delivery mechanisms with very little systematization. For this reason, it is crucial to work with a practitioner who is willing to take the time to assess your specific needs—and you want to work with someone who uses bioidentical hormones rather than potentially dangerous synthetic chemicals such as progestin.

The best place to start is with a good functional medicine practitioner; you can find a directory at the website for the Institute of Functional Medicine (ifm.org). If your practitioner isn't well versed in hormone replacement therapy, they can direct you to someone who is. Hormones can be administered in a variety of ways, including injections, topical and vaginal creams and gels, oral pills, vaginal rings and tablets, and transdermal patches. In an ideal scenario, these are custom compounded to your specific needs, and your hormone levels are regularly tested and tracked.

One of the more effective treatments for women is the Wiley protocol, a version of compounded BHT that syncs hormones to the natural endocrine cycles of women (there's also a protocol for men). In addition, you'll find a discussion of testosterone optimization in chapter 18.

9. Mitochondrial Support

When mitochondria are stressed by inflammation or free radicals, they can kill the cell they live in via apoptosis (programmed cell death). Mitochondrial damage is a problem seen in many conditions related to aging, including cardiovascular disease, liver disease, Alzheimer's, osteoporosis, and hair loss.

Many of the strategies you have already discovered in this chapter support mitochondrial health. Here I'll explain which nutrients and supplements are known to protect against mitochondrial degradation, mitochondrial aging, and the excessive formation of reactive oxygen species (ROS), which can damage mitochondria.

NICOTINAMIDE ADENINE DINUCLEOTIDE (NAD)

Nicotinamide adenine dinucleotide (NAD) is a coenzyme that is produced by all living cells. NAD's most basic function is to receive and donate electrons during metabolic processes within your mitochondria, making it crucial for normal cellular metabolism.

How it works: NAD is involved in what are known as redox reactions, which are processes vital in all parts of cell metabolism. When glucose and fatty acids are oxidized, they release energy. NAD+, the oxidized form of NAD, picks up this energy and is then reduced to NADH during beta-oxidation, glycolysis, and the citric acid cycle. The NADH is transferred into mitochondria, where it is oxidized by the electron transport chain, which is responsible for shuttling protons across membranes and generates ATP, the energy that drives your body.

NAD+ levels markedly decline with age, creating an energy deficit that decreases the body's ability to maintain normal metabolic activity. Some of the effects of the decline in NAD+ include more chemical stress, inflammation, DNA damage, and failing mitochondria. By age fifty, most people have only half the NAD+ they did in younger years. By age eighty, NAD+ levels drop to only 1 to 10 percent of their original value. This deficiency of NAD+ predisposes the body to accelerated aging and impedes the ability to benefit from other helpful compounds, such as resveratrol and pterostilbene. NAD+ also promotes longevity by providing the same cellular benefits associated with caloric restriction and exercise, so the loss of NAD+ means the loss of these benefits.

How to do it: The gold standard for NAD supplementation is to have a large dose administered via IV in a medical or antiaging clinic (the infusion can take from one to six hours), and then to maintain NAD levels with repeat IVs, an NAD nasal spray or transdermal patch, or daily use of NR (nicotinamide riboside), NMN (nicotinamide mononucleotide), or NAD supplements (see the section below on nicotinamide riboside). The only issue with using oral supplements is lower bioavailability, particularly for neural effects, because oral supplementation does not allow any of these molecules to cross the blood-brain barrier or act on the hypothalamus to induce any positive cognitive effects.

Alternatively, NAD can be administered at home (often with the help of a nurse practitioner) via a drip IV. Masochists or the ultra-daring can even give themselves NAD through their own push IV—for a while, I did this once every two weeks from the comfort of my own home, and it took ten to fifteen minutes per session. Why do I describe this as masochistic? Frankly, mainlining this particular molecule into your bloodstream is incredibly uncomfortable, which is one reason it is usually administered over several hours—so if you opt for the quicker push IV option, prepare to feel as though your entire body is on fire while, at the same time, someone is repeatedly punching you in the gut and chest.

These days, I usually order patches from the NAD Treatment Center in San Diego, which deliver 400 to 500 mg of NAD over a five-to-six-hour period and are very easy to apply and tolerate.

NICOTINAMIDE RIBOSIDE (NR)

Nicotinamide riboside (NR), a form of vitamin B_3, is a precursor to NAD. In fact, your mitochondria prefer NR as an NAD precursor in particular. When taken orally, NR is highly bioavailable and aids in mitochondrial energy production. It exists in high levels in cow's milk.

There is growing evidence that supplementing with NR can promote longevity in life forms ranging from simple worms to mammals like mice. One study showed an average 5 percent increase in the life span of old mice, even though NR supplementation did not begin until the mice were nearing the end of their natural life span (twenty-four months). In people, that would be the equivalent of gaining nearly an additional four years of life, based on today's average life expectancy of about seventy-eight years.

How it works: Nicotinamide riboside has been shown not only to restore NAD+ levels in tissues but also to provide more NAD+ activity than can be obtained from diet alone. NR supplementation is very well tolerated in middle-aged and older adults and can slow cellular aging and improve many age-related metabolic problems, including diabetes and neurodegenerative conditions. In addition, NR has the potential to reduce the declining heart function, high blood pressure, and arterial stiffness that can accompany aging, and it even has beneficial effects on cardiovascular fitness. NR also stimulates a caloric-restriction-mimicking state, which means that it can promote weight loss.

How to do it: Most absorbable, supplemental forms of NR appear under the name Chroma-Dex. Three good NR supplements are Tru Niagen, Elysium Basis, and Thorne ResveraCel, which combines NR with another antiaging compound: resveratrol.

According to the physician who discovered NR, Dr. Charles Brenner, the best way to consume an NR supplement is with one dose in the morning and one in the afternoon, which allows the dosing of the NR to match your body's natural circadian rhythm pulsing of NR. NMN and NAD oral supplements may work similarly, and although research is ongoing regarding the pros and cons of each supplement option, you can think of it this way: at the top of the totem pole in terms of NAD bioavailability and cellular delivery are any mechanisms that bypass digestion or liver metabolism, most notably NAD IVs or patches, or sublingual NMN. The next best option—slightly less potent but more convenient or affordable for many people—is oral NR.

ASTAXANTHIN

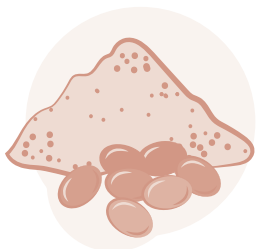
Astaxanthin is a carotenoid that's produced by single-celled freshwater algae. When their environment becomes stressful due to excessively salty water, low nitrogen levels, or high temperatures, the algae produce astaxanthin in lipid droplets, which turn the algal cells bright red and allow them to survive the harsh conditions. In humans, astaxanthin performs similar protective functions by promoting cellular survival.

How it works: Astaxanthin protects your mitochondria by acting as both an antioxidant and a free-radical scavenger. As your mitochondria perform normal respiratory functions, they produce free radicals like superoxide radicals, which interact with proteins, fats, and DNA and cause damage to your cells, ultimately contributing to the aging process. Astaxanthin inserts itself into your cell membranes and mitochondrial membranes, where it inhibits free-radical production and helps eliminate the free radicals that are produced. Astaxanthin's antioxidant activity is fourteen times greater than that of vitamin E, fifty-four times greater than beta-carotene, and sixty-five times greater than vitamin C, making it one of the most potent antioxidants.

Astaxanthin also boosts immune system function by promoting anti-inflammatory activity and increasing the activity of natural killer cells. One study examined the effects of astaxanthin on the production of the inflammatory compounds IL-6 and NF-kB following the introduction of lipopolysaccharides, or LPS (remember from chapter 4 that LPS contribute to age-related chronic diseases). The researchers found that astaxanthin suppressed the production of both IL-6 and NF-kB. In another study, researchers found that astaxanthin increased natural killer cell activity and even increased total levels of T and B cells, which both play a role in fighting infection.

How to do it: You can find different brands of astaxanthin online, and Life Extension offers astaxanthin combined with phospholipids to improve absorption. While an effective dose is 12 mg per day, doses up to 40 mg per day can be taken without any negative side effects. If you want to get your astaxanthin more naturally, you can find it in salmon (in fact, it's the compound responsible for the red color in fish and crustaceans). In a kilogram of salmon, you'll get between 26 and 38 mg of astaxanthin.

Astaxanthin is also a fantastic protective treatment for skin radiation from UVA and UVB sunlight rays (almost like edible sunscreen), and I used to dose with 40 mg prior to and after my Ironman triathlons in Hawaii. After these races, I'd experience minimal burning, even with very small amounts of low SPF sunscreen used during the event.



PAU D'ARCO TEA

Derived from the bark of a tropical evergreen tree in the Amazon rainforest, pau d'arco has long been used by people indigenous to Latin America. Dr. Joe Mercola first alerted me to the fact that pau d'arco tea is a simple, highly affordable but little-known way to treat wounds, aches, pains, malaria and other tropical diseases, and inflammation. It also—you guessed it—boosts NAD.

How it works: Pau d'arco contains a compound called beta-lapachone, which acts as a catalyst for NAD. NAD is also a necessary precursor of the sirtuin enzymes discussed earlier in this chapter, which regulate your body's antiaging switches (such as the genes that promote inflammation and control blood sugar management). So by promoting NAD activity, pau d'arco not only promotes mitochondrial health but also helps regulate genetic antiaging processes.

How to do it: You can order pau d'arco tea in bulk online and keep a giant batch of it in the refrigerator for teas, cold drinks, and smoothie bases. Absorption and delivery of the beta-lapochenes in it can be enhanced by blending the prepared tea with a fat source such as coconut oil, coconut milk, sunflower lecithin, fish oil, or any other source of healthy fats. Pau d'arco supplements in capsule form are also available online, but I personally prefer the tea, which has a pleasant nutty flavor.

CURCUMIN

Curcumin is a compound produced by some plants, most notably turmeric (*Curcuma longa*), a member of the ginger family. Technically, curcumin is considered a diarylheptanoid and belongs to the group of curcuminoids, which are natural phenols responsible for turmeric's yellow color.

How it works: Curcumin is a potent antioxidant and free-radical scavenger that protects cellular function from reactive oxygen species such as superoxide radicals, singlet oxygen, nitric oxide, and hydrogen peroxide. It also enhances your body's natural antioxidant capacity by improving the production of antioxidant enzymes like superoxide dismutase, glutathione, and catalase. As a result, curcumin reduces chronic inflammation throughout your body to protect against age-related chronic diseases.

But the effects of curcumin go further. Chronic inflammation is associated with a condition called epigenetic drift. Within your DNA are compounds collectively known as the epigenome, which is responsible for maintaining your DNA's expression and your cells' identity and function. Over time, your ability to keep your epigenome healthy and functioning declines, so as you age, genes that used to be inactive may be expressed, and genes that used to be expressed may go dormant. This drift may cause stem cell production to decline and increase your risk of cancer and cardiovascular diseases. By reducing the inflammatory pathways involved with this downregulation of DNA expression, curcumin can help to prevent epigenetic drift.

How to do it: Curcumin only constitutes about 3 to 5 percent of the turmeric root, so it's more efficient to supplement with curcumin than to simply eat turmeric. Curcumin also has naturally low bioavailability, but this can be increased by combining turmeric with black pepper or piperine (a black pepper extract), exposing it to low heat (such as cooking fish, vegetables, eggs, or curries with turmeric), or combining it with a high-quality fat source, such as butter, ghee, olive oil, coconut oil, or avocado oil. An effective dose is 1,000 mg, but doses as high as 1,500 mg can be absorbed without any negative side effects.

CARNOSINE

Carnosine is a molecule composed of two peptides: beta-alanine and histidine. It is found in high amounts in skeletal muscle, where it can eliminate excess lactic acid and prevent muscular fatigue during exercise—hence its popularity as a performance supplement. But, as you're about to discover, it's also been shown to have potent antiaging effects.

How it works: Carnosine promotes mitochondrial and cellular function by acting as an antioxidant and free-radical scavenger. Not only does it act on its own to inhibit ROS activity, but it has also been observed in rats to promote the endogenous production of antioxidants like glutathione and superoxide dismutase. One in vitro study also showed that carnosine can reduce the rate at which telomeres shorten, which slows aging. It also inhibits the production of advanced glycation end products (AGEs), which contribute to the development of diabetes and other age-related diseases.

How to do it: A standard effective dose is between 500 to 1,000 mg per day. You can purchase carnosine over the counter or online from companies like Life Extension or Thorne. It's important to note that carnosine's effectiveness is cumulative, meaning that its effects become greater the longer you take it and let it accumulate in your body, so be sure to allow ten to twelve weeks to get the full benefits.

ALPHA LIPOIC ACID (ALA)

Alpha lipoic acid (not to be confused with alpha linolenic acid, the other ALA) is a compound derived from sulfur that's involved in mitochondrial aerobic respiration. While the human body can produce very small amounts of ALA, it is obtained primarily from animal dietary sources—particularly cow's liver, although you can also find it in plant sources like spinach, brussels sprouts, yams, and broccoli.

How it works: ALA acts as an antioxidant within mitochondria, has free-radical scavenging capabilities, and upregulates your own antioxidant-producing abilities by recycling "used-up" antioxidants like vitamin C and glutathione. Because of this, ALA is often called the "universal antioxidant." It's both water- and fat-soluble, so it moves through cell membranes and the blood-brain barrier much more easily than most other antioxidants. ALA also helps maintain DNA integrity as you get older by protecting the epigenome, and it also activates telomerase, the enzyme that lengthens your telomeres.

How to do it: In addition to consuming ALA-dense foods, you can supplement with ALA. The recommended dose ranges from 200 to 600 mg per day, but doses up to 2,400 mg per day have been taken with no observed negative effects. It's important to note that ALA supplements should not be taken with food, which can limit absorption. The best time to take ALA supplements is thirty minutes before or two hours after a meal.

APIGENIN

Apigenin is a flavone found in foods such as parsley, onions, and oregano, but it is best known as the primary active compound in chamomile tea, which has been consumed since the time of the ancient Egyptians and has traditionally been used to treat burns, gastrointestinal disorders, infections, and a myriad of other conditions. It also has antiaging effects.

How it works: Apigenin promotes mitochondrial function by inhibiting the breakdown of NAD, a necessary cofactor in mitochondrial redox reactions, which are crucial in the generation of ATP. So apigenin helps maintain mitochondrial energy production, which can decline with age. In addition, apigenin is another epigenome-protecting molecule that preserves DNA integrity.

How to do it: There's sparse research about the ideal dose of apigenin, but the dose in a few cups of chamomile tea or a few servings of fruits and vegetables per day seems to be effective. Supplemental forms usually come in doses of 20 to 50 mg, and higher doses (3 to 10 mg per kg of body weight) are used to treat anxiety.

SULFORAPHANE

As its name suggests, sulforaphane is a sulfur-based molecule found naturally in cruciferous vegetables like broccoli and brussels sprouts. In the early 1990s, it was discovered that sulforaphane had strong anticancer properties, and since then, it's undergone intensive study to discover other potential health effects.

How it works: While researchers are unsure about sulforaphane's ability to act as a free-radical scavenger, research does suggest that it is more effective at activating your body's antioxidant-producing processes than similar compounds such as curcumin and resveratrol, making sulforaphane a strong protector of mitochondrial and cellular health.

It's also an epigenetic modifier that protects the epigenome and prevents DNA deterioration. In addition, sulforaphane induces autophagy (cell death and recycling) and stimulates the production of more mitochondria to enhance the energy output of each individual cell. Finally, one in vitro study showed that a concentrated oral dose of sulforaphane promoted greater stem cell proliferation and protected stem cells from aging.

How to do it: Broccoli sprouts contain extremely high amounts of sulforaphane (up to one hundred times more than broccoli), and you can also supplement with sulforaphane via compounds such as Thorne MediClear or Life Extension Triple Action Cruciferous Vegetable Extract. An effective dose of sulforaphane is about 10 to 35 mg per day for a 150-pound person, 15 to 45 mg for a 200-pound person, and 20 to 60 mg for a 250-pound person.

QUERCETIN

Quercetin is a plant-pigment flavonoid found naturally in red wine, white wine (white wine actually contains more than red wine), gingko biloba, apples, green tea, St. John's wort, and other plants associated with longevity. It occurs in particularly high concentrations in capers, yellow chili peppers, and onions.

How it works: Quercetin is a very powerful antioxidant, and some research indicates it may be one of the most potent flavonoids for combating free radicals in the body. As a word of warning, though low concentrations in the body are highly beneficial, high concentrations can cause quercetin to become an ROS itself. Currently it's unknown what these concentrations equate to in the human body, but for now, just know that more does not equal better when it comes to quercetin.

Quercetin also enhances your own antioxidant-producing abilities, improving the production of glutathione, superoxide dismutase, catalase, and more. It acts as an anti-inflammatory by inhibiting the release of mast cells and histamines, and it may even inhibit the metabolism of resveratrol, making quercetin and resveratrol a potent one-two combo.

How to do it: The typical Western diet provides about 15 to 40 mg per day of quercetin, but recommended doses range from 250 to 1,500 mg, with the average recommended dose falling around 1 g per day. I use quercetin in powder form in a longevity and autophagy tea introduced to me by my friend Dr. Joseph Mercola—you'll find the ingredients on page 325.

This particular blend upregulates both NAD and autophagy pathways and can easily be added to smoothies or consumed in hot or cold water.

EPIGALLOCATECHIN GALLATE (EGCG)

Green tea has been consumed for thousands of years in Asia to promote longevity and improve health. But the primary active compound in green tea, the ester EGCG, can be delivered in higher doses in supplement form.

How it works: Green tea is a strong antioxidant, and EGCG is the primary molecule responsible for this effect. EGCG also acts as a free-radical scavenger and activates endogenous antioxidant production. In fact, research indicates it is more potent than vitamin E and vitamin C, and it does not blunt the hormetic response to exercise as vitamins E and C do.

EGCG is also an epigenetic modifier that protects the epigenome from deterioration. While the exact mechanism of action is unknown, but we do know that the epigenetic effects of EGCG improve skin cancer outcomes. EGCG also promotes cellular autophagy, particularly in the liver and in macrophage and endothelial cells, although it may reduce autophagy in certain eye cells.

EGCG is also known to improve weight loss by increasing fat oxidation (the caffeine in green tea likely enhances this effect). Finally, EGCG easily crosses the blood-brain barrier and is highly neuroprotective, reducing inflammation in the brain. Thus, they help reduce the likelihood of developing age-related neurodegenerative diseases.

How to do it: The ideal dose ranges from 400 to 500 mg per day, and since the average cup of green tea contains up to 90 mg, it may be more strategic to take an EGCG supplement. Higher doses may cause side effects like nausea and heartburn in many individuals.

FENUGREEK

One of the first, most successful, and longest-lasting human civilizations of all time, ancient Egypt, invented many antiaging tricks. One common antiaging food they consumed was fenugreek, an herb found in the Mediterranean region and parts of China and India. The Egyptians processed fenugreek in a lengthy and complicated ritual that involved drying, threshing, winnowing, and boiling to produce an oil that was then applied to the skin to keep it looking soft, bright, and youthful. The famous Egyptian queen Cleopatra smeared this oil it on her face regularly.

How it works: Fenugreek, a semiarid plant most common in South and Central Asia, helps regulate blood sugar levels and prevents the onset of diabetes, or, if you already have diabetes, helps you manage it. But fenugreek's benefits extend far beyond that and deep into your gut, hormone levels, and mitochondria. A powerful antioxidant, fenugreek can mitigate oxidative damage and abate inflammation. Fenugreek has been shown to possess anti-inflammatory capacities that help ease the symptoms of ulcerative colitis, an inflammatory bowel disease. The water-soluble fiber it contains can help relieve constipation. One study concluded that a fenugreek petroleum ether extract containing naturally occurring linolenic and linoleic acids can shut down systemic inflammation and improve arthritis.

Another study found that, in a group of sixty men aged twenty-five to fifty-two with no history of erectile dysfunction, fenugreek significantly increased sexual arousal, energy, and stamina and helped maintain normal testosterone levels. Given the importance of sex in maintaining biological viability, this could be a potent tool for men. Another study has also shown that the active compound of fenugreek, 4-OH-Ile, promotes the production of new mitochondria in diabetic patients, who often suffer from low mitochondrial numbers and function. Given the mitochondrial theory of aging, this makes fenugreek a good compound to include in any longevity protocol.

How to do it: Rather than a fenugreek supplement, I prefer organic fenugreek seeds, which are quite tasty and have a delicate maple flavor. You can keep them in a pepper grinder or glass mason jar in your kitchen. Sprinkle or grind them into stir-fries, meat dishes, salads, soups, or anything

else for which you desire both the digestion-enhancing and antiaging support of fenugreek seeds. I often combine them with fennel and black pepper for a meat and stir-fry seasoning.

FISH OIL

You'll recall from chapters 4 and 14 that fish oil, whether from supplements or fatty cold-water fish, helps you get the cognitive and physical benefits of the anti-inflammatory omega-3 fatty acids DHA and EPA. It's also important for getting the optimal ratio of omega-6 to omega-3. The anti-inflammatory properties of fish oil make it effective for fighting the signs of aging.

How it works: Both EPA and DHA are precursors of various eicosanoids that are responsible for reducing inflammation. In middle-aged rats, fish oil is known to increase the activities of the antioxidants superoxide dismutase, glutathione peroxidase, and catalase, as well as total antioxidant capacity. It has also been shown to downregulate forty-one genes that are involved in aging and decrease the rate at which telomeres shorten. And because it inhibits inflammatory eicosanoids and cytokines, fish oil has even been shown to be a beneficial replacement for NSAIDs in the treatment of rheumatoid arthritis.

New clinical research studies are now proving fish oil's efficacy for staving off the cardiovascular and metabolic issues, such as diabetes, that can occur with aging, and pharmaceutical companies such as Amarin are now developing drugs based entirely on fish oil. Micronutrients in fish oil such as omega-3 fatty acids and, most notably, vitamin D have also been shown to impact telomere length. Supplemental fish oil at doses of 2.5 g per day has been shown to induce a 32 percent reduction in telomere shortening and also significantly reduce oxidation in blood cells.

How to do it: For my recommended fish oil supplement brands as well as dosages, see chapter 12. You'll also find information on whole-food sources of DHA and EPA in chapter 4.

COENZYME Q10 (COQ10)

Coenzyme Q10 (CoQ10) is a naturally occurring compound found in most aerobic animals, ranging from bacteria to mammals. CoQ10 itself is a powerful tool to have in your antiaging arsenal. Also known as ubiquinone, ubiquinone-Q10, ubidecarenone, vitamin Q10, or coenzyme Q, it is an essential component of the mitochondrial electron transport chain and an antioxidant found in plasma membranes and lipoproteins throughout the body.

Since CoQ10 synthesis can decline as you age, supplementing with it may be extremely beneficial as you get older.

How it works: One study observed the effects of a high CoQ10 intake on old mice with age-related neurodegeneration and found that CoQ10 improves spatial learning and reduced oxidative damage. But these results were not observed in younger mice; they only affected preexisting age-related cognitive decline. It is also known that CoQ10 scavenges free radicals that promote mesenchymal stem cell aging, keeping stem cells younger. Studies have also shown that the antioxidant effect of CoQ10 supplements alleviates cardiovascular disease and inflammation.

How to do it: CoQ10 is found in oily fish like salmon and tuna as well as in organ meats. As a supplement, it's available as capsules, tablets, and oral spray. The ideal dosage ranges from 30 to 90 mg per day divided into several doses, though you can safely take as much as 200 mg per day. As a fat-soluble compound, it is best consumed with a healthy source of fats such as coconut oil or extra-virgin olive oil.

I take CoQ10 in a combination supplement, the Almsbio Glutathione Mito-Therapy+, which contains CoQ10, PQQ, and glutathione (both discussed below), as well as lactoferrin, which is also a good antioxidant. This combination—which you squeeze from a syringe into your mouth, hold for sixty seconds, then swallow—is fantastic for enhancing mitochondrial health. (As a

bonus, it tastes like an orange Creamsicle!) Rather than taking separate CoQ10, PQQ, and glutathione supplements, I recommend simply consuming one serving of Almsbio Glutathione Mito-Therapy+ once per day. You'll find a link and discount code on BoundlessBook.com/19.

PYRROLOQUINOLINE QUINONE (PQQ)

Pyrroloquinoline quinone (PQQ) is an antioxidant that's involved in redox reactions, which change the oxidation states of atoms, in living organisms ranging from bacteria to human beings. More than 175 published studies have shown that it has wide-ranging benefits for memory, general cognition, mood, and mental processing power, making it a popular ingredient in many nootropics. PQQ's benefits also include increased mitochondrial density, defense against oxidative stress, improved learning and memory ability, and reduced inflammation.

How it works: In humans, PQQ interacts with cell signaling pathways and mitochondrial functions. It's an ROS scavenger, which protects mitochondria from the damage of oxidative stress. One study even demonstrated that in mice, the antioxidant and DNA-damage-reducing capacities of PQQ played a role in combating osteoporosis. Another study demonstrated that PQQ contributes to the upregulation of certain compounds involved in repairing the microglia and neurons of the cerebral cortex and parts of the hippocampus following traumatic brain injury.

How to do it: PQQ is found naturally in kiwi, celery, papaya, sweet potatoes, green tea, fermented bean products like natto, parsley, and even human breast milk. I don't necessarily recommend that you ask your friends if you can borrow some breast milk from them, but you can certainly consume the other foods or take PQQ in a supplemental form.

Using PQQ in combination with CoQ10 seems to synergistically increase their potency, so I recommend taking a combination supplement that includes both—I prefer the Almsbio Glutathione Mito-Therapy+, mentioned on the previous page. No matter what PQQ source you use, look for a form called BioPQQ. There are countless forms of PQQ on the market today, but BioPQQ is formulated from natural bacterial fermentation, while other varieties contain mostly synthetic forms of PQQ.

GLUTATHIONE

Glutathione is an antioxidant that occurs naturally in your body and primarily consists of the amino acids glutamine, glycine, and cysteine. Glutathione is a true electron trap, placing it high on the list of antioxidants. In fact, it is one of the few antioxidants that is actually produced by your body, rather than being obtained only through food. It is also known to support whole-body detoxification, including most phases of the liver's detoxification pathways, and help cells grow, multiply, and repair themselves.

Because of its wide range of antioxidant activity, glutathione plays a multifactorial role in aging. Overall, there is a decrease in glutathione levels as we age, and this seems to affect the onset of a large number of diseases.

How it works: The depletion of the reduced form of glutathione (often simply referred to as GSH, it's the stable, nonoxidized form of glutathione) has been implicated in many chronic degenerative diseases, including cystic fibrosis, cataracts, macular degeneration, glaucoma, hypertension, asthma, acute respiratory distress syndrome, Alzheimer's, Parkinson's, Huntington's, myocardial infarction, autoimmune conditions, and even the aging process itself. Indeed, GSH levels have been found to parallel the activity of telomerase, the enzyme responsible for maintaining long, strong telomeres. The depletion of GSH has also been found to induce the loss of mitochondrial function due to the accumulation of damage to mitochondrial DNA. Once transferred into the mitochondrial matrix, GSH plays a key role in the defense against ROS and in

the detoxification of lipid hydroperoxides (damaged lipids in cell membranes) and electrophiles (which are very similar to free radicals). GSH also critically regulates the release of proteins from the intermembrane space of mitochondria; once released, these proteins engage the machinery of cell death, meaning that GSH is a critical nutrient for the support of mitochondrial health as well as overall cellular activity and health.

How to do it: While we do produce glutathione every day, it is also highly available in supplemental forms as well as in whole-food sources. It is true that some ingested glutathione is broken down and oxidized before being absorbed by your cells, but contrary to popular belief, some does, in fact, get taken up into your mitochondria. Research has indicated that glutathione can cross human intestinal cells intact, and you can take glutathione supplements in forms that protect it from being oxidized before it reaches your bloodstream. Sublingual supplements, for example, are better absorbed than oral glutathione. Glutathione can also be bound within tiny fat droplets called liposomes, which protect the glutathione until the liposomes are taken up by your cells, where they are broken down and the glutathione is released.

The Almsbio Glutathione Mito-Therapy+ supplement mentioned on page 538 contains a form of liposomal glutathione. Jarrow Glutathione is also an excellent supplement and is available online. Whichever supplement you choose, oral glutathione doses should range between 250 and 1,000 mg to increase glutathione levels. Over the course of several months, 500 mg per day can be an effective dose. Pork loin, chicken liver, steak, asparagus, broccoli, potatoes, avocados, zucchini, tomatoes, spinach, parsley, and okra are all excellent sources of glutathione, so a diet to support your mitochondrial health should include these foods.

Here are more ways you can increase your glutathione:

- Consume plenty of vitamin C, which helps maintain your body's supply of glutathione.
- Consume selenium-rich foods like beef, chicken, fish, cottage cheese (if you tolerate dairy well), and brown rice, as selenium is a glutathione cofactor.
- If you don't have allergies or sensitivities, supplement your diet with whey protein, which provides a complete amino acid profile. Glutathione synthesis requires the amino acids glutamine, cysteine, and glycine.
- Consume turmeric: the curcumin it contains can help restore glutathione levels and improve the activity of glutathione enzymes.

MITOQUINONE MESYLATE (MITOQ)

MitoQ is an antioxidant that is attracted to the source of most free radicals: mitochondria. Unlike many other antioxidants, it can accumulate in high concentrations in mitochondria. It delivers CoQ10 directly to mitochondria and is believed to increase mitochondria's ability to produce ATP and simultaneously quench free-radical damage.

While there is not a lot of evidence for MitoQ's efficacy, some studies suggest it may have an effect, particularly for neural dysfunction in humans, and for the sake of thoroughness, I have included it as a potential tactic to improve mitochondrial function and reduce the effects of aging.

How it works: Most of the oxidative stress that mitochondria experience occurs on the matrix side of the inner mitochondrial matrix, which is the space within the inner membrane that contains each mitochondria's DNA, ribosomes, soluble enzymes, and other molecules. MitoQ is believed to reduce the effects of this oxidative stress by supporting a catalase enzyme that removes free radicals from mitochondria. In studies, this can increase rodent life span by 10 percent. MitoQ has also been shown to increase life span and reduce telomere shortening in human cells that have undergone oxidative stress and has extended the life span of transgenic worms with Alzheimer's genes (though it did not do so in normal worms).

But, as I mentioned, there is not much evidence to support the idea that MitoQ has a significant effect on oxidative stress, and one study has actually shown that orally administered MitoQ in healthy mice failed to significantly alter mitochondrial function or gene expression and exerted no overall influence on systemic energy metabolism. Another study demonstrated that MitoQ causes mitochondrial swelling in the cells of kidney proximal tubules, which could lead to renal complications. Finally, MitoQ is so potent at lowering ROS that it may actually interfere with the normal cellular signaling mechanisms that rely on adequate levels of ROS.

How to do it: I'm not yet convinced MitoQ is the ultimate wonder drug, especially since CoQ10's effects are well proven, but should you decide to use it, MitoQ is widely available as an antioxidant supplement. As an antiaging tool, a recommended daily dose of MitoQ is 10 mg. As with many of these compounds, you can monitor the efficacy of your supplementation with oxidative stress tests such as the Oxidative Stress Analysis by Genova Diagnostics.

PTEROSTILBENE

Pterostilbene, one of the bioactive components of blueberries, is a derivative of the antioxidant phenol resveratrol and is structurally very similar, but it appears to be better absorbed than resveratrol and may actually be a more potent antioxidant and anticancer molecule. This is especially useful to know when you consider the recent research published in the *Journal of Food Chemistry* that profiled twenty-one commercial grape seed extract resveratrol products and found that nine of them contained peanut skin extract. The combination of antinutrients, lectins, pesticide contamination, and the prevalence of peanut allergies makes peanut skins a very poor source for resveratrol, so proceed with caution when taking resveratrol supplements. Pterostilbene may be a better bet.

How it works: Doses of pterostilbene as low as 10 mg and as high as 500 mg seem to have significant benefit for reducing cholesterol and glucose in animals. But little is known about exactly how pterostilbene works. Some studies report that it has apoptotic and autophagic effects—in other words, it helps eliminate old and damaged cells, which aids in combating various types of cancer. One study has also shown that pterostilbene exhibits strong anti-inflammatory capacities. In plants, pterostilbene plays a cellular defense role, and it may have the same role in humans. Pterostilbene has been noted to inhibit LPS-induced autoimmune responses and may also inhibit the inducible nitric oxide synthase (iNOS) activity that can cause inflammation. As an NADPH oxidase inhibitor, it may also increase levels of NAD.

How to do it: Low doses of up to 10 mg seem to aid in cognition. Higher doses of pterostilbene, ranging from 250 to 500 mg, aid in reducing cholesterol and glucose levels and improve insulin sensitivity in research animals. Generally, the estimated oral dose range for improving your glucose and lipid metabolism is 20 to 40 mg per kilogram of body weight.

C60

C60, also known as buckminsterfullerene or buckyball, belongs to a unique family of molecules called fullerenes. It is a cage-like fused-ring structure that looks roughly like a soccer ball, contains sixty carbon atoms, and was named after the famous author, designer, inventor, architect, and systems theorist Buckminster "Bucky" Fuller.

How it works: C60 and other fullerenes are produced by passing an electric discharge across the gap between two carbon electrodes in a helium atmosphere. The intriguing fact about C60 is that, because it is not found naturally in living organisms, there is no reason to think that would provide any kind of benefit. However, in 2012, a French laboratory announced that feeding C60 dissolved in olive oil to rats nearly doubled their life spans! The addition of olive oil is critical

to the bioactive effects of the buckyballs because pure C60 molecules clump together, clog up cellular metabolism, and appear to be slightly toxic. But when dissolved in olive oil (a process that takes weeks of mixing), the buckyballs provide a host of cellular and mitochondrial benefits.

C60 is a powerful antioxidant that scavenges superoxide, a by-product of mitochondrial energy production that can accumulate and contribute to the development of many age-related chronic diseases. One group of researchers has proposed that C60 has the ability to acquire an overall positive charge by absorbing protons and can thereby penetrate the mitochondria to decrease free-radical production. A carboxyl form of C60 has been proven to prevent nerve cells from dying by dehydration or Alzheimer's-related compounds and allowed mice to live 7 percent longer.

How to do it: C60 is best dissolved in oil—in fact, as noted above, it needs to be dissolved in oil to eliminate toxicity—and this is usually done in a lab with a centrifuge. Most C60 supplements combine C60 with olive oil (although different oils can have different effects—for example, caprylic acid and MCT oil allow C60 to have more activity on brain cells), or you can purchase pure C60 and mix it with extra-virgin olive oil in a blender yourself, although this may be difficult because it can take a lot of blending to get the buckyballs and olive oil to mix. *Always make sure that the buckyballs are dissolved before consuming the concoction*. On BoundlessBook.com/20 you'll find links to several helpful C60 dosing and mixing calculators, DIY oil-dissolving recipes, and other resources. I also highly recommend you go to BenGreenfieldFitness.com/ian to listen to my comprehensive podcast with C60 researcher Ian Mitchell.

MELATONIN

Melatonin is best known as the sleep hormone. It is produced by the pineal gland toward the end of each day to stimulate the sense of being tired so that you will want to go to bed. But melatonin also acts as an antioxidant and mitochondrial protectant.

As you age, melatonin production and deployment can decline, resulting in age-related sleep disorders. Many elderly people—and many health enthusiasts, including myself—take small doses of melatonin to help them sleep. But building evidence suggests that melatonin supplements, especially in larger doses up to 80 mg, can also delay the development of cancers, boost the immune system, and slow the aging process, as well as improve mitochondrial function.

How it works: The interesting thing about mitochondria is that their activity and dynamics exhibit an oscillatory pattern that matches the circadian rhythm–based secretion of melatonin. In fact, melatonin is an antioxidant hormone that is selectively and purposely taken up by mitochondria, where it accumulates in high concentrations. It also acts as a regulator of mitochondrial biogenesis and dynamics, improving the healthy homeostasis of your mitochondria.

In both in vivo and in vitro studies, melatonin has been shown to be effective in preventing the oxidation-induced mitochondrial dysfunction seen in Parkinson's, Alzheimer's, and Huntington's. It is also known to maintain respiratory activity and ATP production in mitochondria.

How to do it: You don't need much melatonin. Many supplement tablets contain 5 mg each, but the truth is that as little as 0.1 to 0.3 mg of melatonin can make a difference, and even that small amount can profoundly increase the quality of your sleep. Many antiaging and cancer physicians prescribe much higher doses, but I'm cautious with high doses because overuse may limit endogenous melatonin production—I only use higher doses if I'm jet-lagged and attempting to reboot my circadian rhythm. I prefer a timed-release version (many brands are available online, but I usually buy Natrol) or the supplement Sleep Remedy, which combines a microdose of melatonin with a few other sleep-supporting compounds, such as vitamin D and omega-3 fatty acids.

SKQS

MitoQ and C60 are SkQs' antiaging cousins. Primarily researched in Russia, SkQs are newly discovered antioxidant compounds that specifically target mitochondria, and they have been studied quite a bit recently to determine if they can slow down the processes associated with aging.

When started late in life, supplementation with SkQ not only prevents age-related decline but also significantly reverses it, acting on pathways for hair loss, low body temperature, body weight loss, and heart, kidney, and liver pathologies, along with stroke, Parkinson's, Alzheimer's, and pancreatic cancer. In doing so, it has been shown to improve mice longevity by about 15 percent. Quite notably, when researchers started giving SkQ to mice in the middle or the end of their lives, it worked to improve quality and quantity of life even at that point, which means it may be an effective antiaging hack for people who spent many decades making poor decisions about their health and lifestyle and then decided to shape up later in life.

In fungi, crustaceans, fruit flies, and mice, SkQ significantly prolongs life span and appears to be especially effective in the early and middle stages of aging. In mammals, SkQs inhibit the development of age-related diseases such as cataracts, retinopathy, glaucoma, balding, osteoporosis, thymus gland degradation, hypothermia, the oxidative damage of lipids and proteins, and a host of other conditions. But that's not all. When eighty-nine animals (dogs, cats, and horses) that had become blind because of retinopathy were given eye drops containing SkQ (now sold under the brand name Visomitin), vision was restored in 75 percent of the animals. The same drops prevented the loss of sight in rabbits and restored vision to animals that had already become blind. So this tiny molecule looks incredibly promising as a therapeutic drug for prolonging youth.

How it works: MitoQ and SkQ both deliver chemical foot soldiers to mitochondria to fight ROS. MitoQ delivers CoQ10, and SkQ delivers plastoquinone. C60 then allows your mitochondria to absorb these compounds via osmosis. So these three molecules—MitoQ, SkQ, and C60—are a mitochondrial stack made in heaven!

SkQ was designed to accumulate inside cells to target free radicals where they do most of their damage: inside mitochondria. Mitochondria pull in SkQ because they are negatively charged and SkQ molecules are positively charged. In research studies, SkQ has been shown to prevent the oxidation of mitochondrial cardiolipin, a crucial component of the inner mitochondrial membrane. Even in very low concentrations, SkQ appears capable of stopping cellular apoptosis that occurs due to DNA damage. At higher concentrations, SkQ prevents the tissue death initiated by ROS.

How to do it: Aside from the relatively inexpensive Visomitin eye drops, SkQ is currently a bit hard to get—and to get the right oral dosage from the eye drops, you'd need to drink nearly an entire bottle at once. As far as dosage is concerned, the approximate midpoint of the range in most mice research, at 5 nm per kg of body weight daily, translates to about 22.4 mcg per kg of body weight in humans, which, for a 70 kg or 154 lb human, would be 1.6 mg per day.

One website selling the raw ingredient used in Visomitin sells 10 mg of SkQ for $225, making this a relatively expensive antiaging supplement for the time being, although several companies are now working on affordable oral solutions. For example, Mitotech SA, a pharmaceutical company founded by Russian researcher Dr. Vladimir Skulachev, is developing SkQ products and drugs that are currently being taken through FDA's regulatory process.

If you want to dive deeper into SkQ science, I encourage you to do some reading of the numerous papers that Dr. Skulachev and his colleagues have published, which are readable and well translated into English. Most of these papers are published in full and are free on the internet, and you'll find links to them on BoundlessBook.com/19.

UROLITHIN A

Urolithin A is produced by the body after you ingest compounds found in particularly high concentration in pomegranates (particularly the bitter components such as the skin and seeds) and can help recycle defective mitochondria. Since it is a metabolite that results from the transformation of the tannins in pomegranate by gut bacteria, it can be classified as a postbiotic.

Some of the earliest research on urolithin A was performed on *C. elegans* worms, which experienced a 45 percent longer life span than worms not given the compound. Rodents given urolithin A experienced markedly improved muscular function and clearance of damaged mitochondria. Compared to a control group, these rodents showed a 57 to 65 percent increase in exercise capacity, 42 percent increase in running endurance, and a 9 percent increase in grip strength—all markers that correlate with longevity.

In addition, researchers have exposed colon cancer stem cells to a mixture containing urolithin A and found it to be effective at inhibiting the number and size of colon cancer stem cells and also in inhibiting the activity of aldehyde dehydrogenase, a marker of resistance to chemotherapy. Urolithin A can also cross the blood-brain barrier to protect against neurotoxicity and amyloid plaque accumulation.

How it works: As you age, ATP production begins to put strain on your mitochondria, and eventually, energy output falls. But when exposed to urolithin A, these failing mitochondria are broken down and eliminated (very similar to taking out the trash!) to make room for new, properly functioning mitochondria to grow.

Ellagitannins and punicalagins are two natural polyphenols found in pomegranates. They have been shown to have anti-inflammatory and anticancer effects, but once metabolized by gut bacteria, they also produce urolithin A in the digestive tract. So supplementation with pomegranate extract, along with specific bacterial species (probiotics) that can help the pomegranate compounds to produce urolithin A, can be an effective approach to maintaining healthy mitochondria.

How to do it: Eating pomegranates, particularly whole pomegranates with skins, seeds, and flesh, can be the first strategy to increase urolithin A. However, concentrated pomegranate extract, particularly when combined with bacterial species called *Gordonibacter urolithinfaciens* and *Gordonibacter pamelaeae*, can allow for significantly higher amounts of urolithin A and the growth of urolithin-producing bacterial strains within the digestive tract.

Very few probiotic formulas actually contain both pomegranate as a prebiotic and the specific bacterial species that have been shown to produce urolithin A, but one company called SEED has produced an impressive formula that contains both. They offer both versions of their probiotic formulas for men and women, and you'll find links to both on BoundlessBook.com/19.

SELECTIVE ANDROGEN RECEPTOR MODULATORS (SARMS)

SARMs are therapeutic compounds that mimic anabolic steroids. The US Anti-Doping Agency points out that the difference between the two is that SARMs have fewer androgenic properties, which permits them to target tissues much more directly and reduces the host of known negative side effects experienced with steroids. Quite simply, SARMs provide the benefit of steroids without many of their dangerous and annoying mental and physical effects. But what many people don't know is that SARMs, in addition to increasing libido, building muscle, and enhancing energy, can stimulate specific pathways that improve mitochondrial health.

How it works: SARMs contain androgen-like compounds that interact with cellular androgen receptors. The androgen receptor then creates a signal that leads to a magnified expression of particular genes, such as those for muscle growth or fat loss. SARMs are a selective receptor

modulator, which means that they can either block or activate hormone receptors depending on conditions, so they have the ability—like adaptogenic herbs—to replicate the effects of hormones in one tissue and at the same time reduce the adverse effects of synthetic steroids or hormones in other tissues.

Several SARMs show a ratio of anabolic to androgenic effects of greater than 3:1 and up to as much as 10:1 (for comparison, testosterone has a ratio of 1:1). This means that SARMs produce anabolic to androgenic effects of up ten times that of testosterone but without the sex drive fluctuations, gastrointestinal disturbances, stroke, blood clots, and other health issues associated with anabolic steroids.

One popular, well-researched, and relatively safe SARM is known as Cardarine, or GW501516 (often called "exercise in a bottle"). Technically, it binds to a PPAR (peroxisome proliferator activator receptor), not an androgen receptor as a SARM normally would, but despite this difference, Cardarine offers impressive results because it activates AMPK, which is responsible for stimulating glucose uptake into skeletal muscle tissue and oxidizing fatty acids. In addition to burning fat by stimulating fatty acid oxidation, Cardarine can increase HDL cholesterol by an average of 79 percent while simultaneously decreasing LDL cholesterol. Molecular analyses have revealed that PPAR is involved in exercise-induced reprogramming of muscle fibers and skeletal muscle metabolism by regulating the expression of genes associated with mitochondrial biogenesis and respiration, and since SARMs upregulate PPAR activity, they can be categorized as mitochondrial support.

Cardarine was developed in the 1990s as a way to prevent and cure breast, prostate, and colon cancer. By the early 2000s, it was discovered that it can also help treat metabolic disorders, including diabetes and obesity. When the fitness community caught wind of these benefits, they quickly discovered that it is also a potent endurance-increasing supplement, and indeed, it has been used by athletes for over twenty years with no reported harmful side effects. Cardarine has also been used in research studies in obese, prediabetic men with metabolic syndrome; these studies showed that it reverses metabolic abnormalities and helps control obesity. In laboratory studies on rats and monkeys, it has been shown to burn fat and build muscle, while also eliminating type 2 diabetes, increasing HDL cholesterol, and lowering VLDL cholesterol.

While some early-1990s studies showed that Cardarine can cause cancer and tumor development with long-term, high-dose use, more-recent studies showed that not only is it harmless under normal use, but it also offers many positive health benefits. As a matter of fact, a study published in 2004 by the American Association of Cancer Research stated that PPAR agonists such as Cardarine have been "shown to have no effect on the proliferation of colorectal cancer cells" and that "under normal culture conditions, PPAR activation has no effect on cell growth." Furthermore, in 2008, Cardarine was studied for treatment of breast cancer and colon cancer. These studies concluded that it can inhibit the growth of cancer cells.

Cardarine has also been shown to cause increased endurance, decreased body fat, and decreased recovery time, and it can also protect the brain, benefit the heart, protect the kidneys, protect against liver damage, strengthen the immune system, and heal skin disorders. Sedentary mice treated with it were able to run on a treadmill for 270 minutes before tiring, compared to untreated active mice, which could only run for 160 minutes! So, like MOTS-c, you can consider this to be very much like exercise in a bottle.

How to do it: SARMs can be taken orally rather than via inconvenient injections. The maximum recommended dose of a SARM like Cardarine is 20 mg per day. If your goal is to increase endurance, you'll want to start with about 10 mg per day. If you're looking for greater gains, particularly for fat loss, go with 20 mg per day and, for best results, take it an hour before exercise.

Cardarine has a half-life of sixteen to twenty-four hours, so you can take 10 mg once per day or, if you are taking 20 mg per day, split your dose into two, taking one dose every ten to twelve hours (most SARMs come in liquid bottles, and one dropperful is typically 10 mg).

Of course, Cardarine is just one example of a SARM. On BoundlessBook.com/19, you'll find links to two articles in which I discuss the SARMs LGD-4033 and SR-9009, both of which stack quite well with Cardarine for even more accelerated fat loss or muscle gain.

10. Photobiomodulation

I've talked about using photobiomodulation—basically, exposing your body and brain to certain light wavelengths—in chapter 6 (for cognitive enhancement) and chapter 12 (for improving physical recovery). Turns out, because photobiomodulation (PBM) works on mitochondria, it's also a good antiaging tool.

How it works: Within your mitochondria is an enzyme called cytochrome c-oxidase (CCO), which catalyzes the reduction of oxygen for energy metabolism and ATP production. PBM can increase activity of CCO and also disassociate nitric oxide from CCO, which restores electron transport ATP production by increasing the electrical potential across the mitochondrial membrane. This increased membrane potential is also believed to produce ROS. ROS can exert a mild hormetic effect (similar to heat exposure, cold exposure, or wild plant intake), leading to increased cellular repair, healing, and gene transcription. The low-level oxidative stress that results from these ROS may also cause stem cells to grow and proliferate, and the ROS themselves serve as signaling mechanisms for cell-to-cell conversation.

In addition, stem cell proliferation can occur when light-based stimulation of the mitochondria leads to a switch from anaerobic sugar-burning glycolysis to highly efficient oxidative phosphorylation. This switch increases the amount of oxygen that mitochondria required by the mitochondria, including those in stem cells, and when these stem cells sense this need for more oxygen, they migrate to tissues with low levels of oxygen that may need enhanced repair.

How to do it: Aside from regular, moderate doses of sun exposure, two of the PBM methods I recommend most often are the Vielight and the Joovv. The Vielight is aimed at PBM for your brain, and you'll find more about it in chapter 6. The Joovv is a larger device that's better for full-body treatments, and you'll find more about it in chapter 12.

But as a word of caution, when it comes to PBM, more is not better: the light frequencies produce ROS, and excessive ROS can cause oxidative damage. The recommended use for the Vielight is one twenty-five-minute session every two days, and for the Joovv, ten to twenty minutes per day, but no more. (You'll learn even more about photobiomodulation in the next chapter.)

11. Sulfur Support

One of the most important antiaging pathways in the body is that of the Nrf2 transcription factor, and one of the best ways to support Nrf2 is to eat foods rich in sulfur. I'll get to why in a moment.

Nrf2 is responsible for unzipping and exposing genes that encode for the expression of antioxidant proteins that protect against oxidative damage. Activating Nrf2 switches on a host of antioxidant pathways, increases glutathione production, and can even trigger the expression of an antiaging phenotype. A phenotype is an observable characteristic that results from the interaction of the surrounding environment (including food) with an organism's genes. So the stimulation of an antiaging phenotype results in an increase in the expression of genetic factors that help to combat the effects of aging, such as enhanced detoxification pathways.

Glutathione acts as a powerful antioxidant within the mitochondrial matrix, and other antioxidants that result from Nrf2-induced transcription also benefit mitochondria in a similar manner.

How it works: If you are familiar with sulfur (hydrogen sulfide, or H_2S), you may know it only as a poisonous gas that smells of rotten eggs and flatulence. But H_2S is also a signaling molecule. Brace yourself: we're about to wade through some thick scientific terminology.

H_2S causes the formation of a disulfide bond between two cysteine residues: cys-226 and cys-613. The resulting compound deactivates what are called keap1 ubiquitin ligase substrate adaptors. When these adaptors are activated, they cause a chain of events that suppresses Nrf2. So by deactivating these adaptors, H_2S creates an environment in which Nrf2 can act freely and promote the transcription of powerful antioxidant genes.

How to do it: One of the best ways to increase the activation of Nrf2 factors is to consume a lot of sulfur. So fill your diet with plenty of sulfur-containing foods from the Brassica family, which includes bok choy, broccoli, cabbage, cauliflower, horseradish, kale, kohlrabi, mustard leaves, radishes, turnips, and watercress. (Added bonus: each of these is also high in isothiocyanates, a potent cancer-fighting agent.) These foods, along with sulfurous and stinky eggs, onions, and garlic, contain sulforaphane, an H_2S-containing compound.

Broccoli sprouts, which can be kept in your freezer and added to smoothies, are a quite potent sulforaphane-containing superfood. According to my friend Dr. Rhonda Patrick, freezing and blending broccoli sprouts appears to be an excellent way to increase sulforaphane's bioavailability by up to three and half times!

Another Nrf2 activator is curcumin, which is found in turmeric, the primary spice in Indian curries—I talked about curcumin as a mitochondria-supporting compound earlier in this chapter. Finally, hydrogen-rich water, also discussed earlier in this chapter, is also a good way to activate NrF2 pathways.

12. The Aspirin, Magnesium, and Vitamin D Stack

Aspirin is a nonsteroidal anti-inflammatory drug (NSAID) most commonly used as a pain reliever, to treat fever, and to reduce inflammation. While I am highly skeptical of using NSAIDs to treat pain or inflammation (in chapter 12, I explained the dangers of using NSAIDs), aspirin is one of the most popular and has even been used to decrease the risk of death following a heart attack, as well as to decrease the risk of certain types of cancer. Magnesium, which you have encountered throughout this book, is a mineral with several important physiological properties. Vitamin D, which should also be familiar to you by now, is one of the primary fat-soluble vitamins that the body requires for many important physiological functions.

How it works: An article on the website of the antiaging guru Josh Mitteldorf, who wrote the excellent book *Cracking the Aging Code*, alerted me to two *Science* magazine articles that featured simple and inexpensive basic measures that reduce risks of all major diseases associated with old age. Two strategies were taking baby aspirin daily and increasing your blood levels of vitamin D.

It turns out that daily baby aspirin is associated with a lower risk of heart disease, stroke, dementia, and several kinds of cancer (although, in my opinion, fish oil can work similarly, with fewer potential side effects). High blood levels of vitamin D are associated with a lower incidence of most cancers, heart disease, and dementia; protection against low bone density and autoimmune disease; and a lower incidence of colds, the flu, asthma, diabetes, stroke, multiple sclerosis, and cognitive decline.

Vitamin D's anti-inflammatory properties likely delay telomere shortening. Two different studies on twins have shown that individuals with the lowest levels of vitamin D had shorter

telomeres that indicated an additional five years of biological aging compared to their twin. Another randomized controlled trial found that vitamin D supplementation at 2,000 IU per day increased telomerase activity by over 19 percent in the blood cells of people who were deficient in vitamin D. In another study, children whose daily milk was fortified with vitamin D caught half as many colds as children without supplementation, so vitamin D likely has a positive impact on the immune system degradation that can occur with age.

Finally, as you have already learned, glycemic variability and insulin sensitivity are two very important longevity parameters to control. A multitude of studies have documented that higher intake of magnesium helps control blood sugar and retain insulin sensitivity with age.

How to do it: In addition to eating a wide variety of foods rich in vitamin D, fish oils, and magnesium (including fatty fish like tuna, herring, sardines, and salmon for fish oil; cheese, beef liver, egg yolks, and mushrooms for vitamin D; and avocados, almonds, and Brazil nuts for magnesium), take a daily dose of baby aspirin or fish oil with a dose of vitamin D with your first meal of the day. Dosages range from 1 to 20 g for fish oil and 2,000 to 6,000 IU for vitamin D, depending on your activity levels and size. Ideally, combine vitamin D with 50 to 150 mcg of vitamin K_2 to increase its absorption. Then, before bed, take 400 to 600 mg of magnesium. Just remember that more magnesium is not better and can cause loose stools.

13. Rhodiola

Because how it works is not fully understood, rhodiola is in a category of its own. This perennial flowering plant has a rich and almost mythical history of use dating back to at least AD 77, when the Greek physician Dioscorides described it in his medical text *De materia medica*. Vikings consumed it to enhance their strength and endurance, and Central Asians used a tea brewed from it to treat colds and flus. Known as the golden root, the root extract of *Rhodiola rosea* has been shown to be particularly effective in preventing age-related decline.

How it works: A group of geneticists from UC Irvine found that feeding rhodiola root to fruit flies allowed the flies to live 20 percent longer. In another experiment, mice were exposed to a lethal dose of gamma radiation, and 90 percent of the mice given rhodiola thirty minutes before radiation survived just fine, in contrast to a 100 percent death rate in mice not treated at all.

Normally, gamma radiation wreaks havoc in cells and randomly breaks apart a host of molecules. Although scientists aren't sure of the exact mechanism of action, it appears that the body has its own built-in chemical machinery for repairing the damage and that rhodiola upregulates this machinery. There is also some speculation that rhodiola may increase stress resilience in a xenohormetic manner, very similar to the extracts from wild plants. (In fact, many of the strategies in this chapter that extend life span also increase stress resilience in some manner as well, making the phrase "harder to kill" an achievable objective for many people if they simply knew what to do.)

One study found that rhodiola consumption is associated with the regulation of the expression of 1,062 different genes, including 72 cardiovascular genes, 63 metabolic genes, 163 gastrointestinal genes, 95 neurological genes, 60 endocrine genes, 50 behavioral genes, and 62 genes associated with psychological disorders, making it a potent supplement for overall longevity and resilience, particularly if you've been exposed to radiation (as most of us living in a postindustrial era of flying on airplanes have!).

How to do it: Rhodiola can be found in many supplemental forms. You can find it available as a capsule or tablet online. Stephen Buhner, a very good herbalist, recommends an extract form from Woodland Essence, and rhodiola is also a key component of TianChi, one of my favorite

Chinese adaptogenic herb blends. Rhodiola doses as low as 50 mg are effective in preventing fatigue, and acute doses of 300 to 650 mg are helpful in combating fatigue and stress (doses higher than that don't appear to give any additional benefit).

14. Deprenyl

Like rhodiola, deprenyl is in an antiaging category all its own. Also known as selegiline, it was developed to treat Parkinson's disease and Alzheimer's, but as early as the 1980s and 1990s, studies in Europe showed impressive increases in the life spans of animals treated with the drug.

Deprenyl helps prevent the breakdown of dopamine, which naturally increases with age. It's most often used with L-dopa to treat Parkinson's disease, but it may also help prevent the onset of neurodegenerative diseases.

How it works: Production rates and levels of the neurotransmitter dopamine remain fairly stable until about age forty-five. After that, brain levels of dopamine decrease by about 13 percent each decade. When the number of dopamine-producing neurons in the brain deteriorate by about 30 percent, Parkinson's can develop.

Monoamine oxidase B (MAO-B) is the enzyme responsible for breaking down dopamine, among other neurotransmitters, and MAO-B levels increase as you age. Deprenyl is a selective inhibitor of MAO-B. Many rat studies have shown that deprenyl can help prevent the onset of degenerative brain diseases and even treat early stages of Parkinson's.

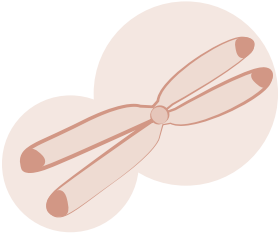
How to do it: Twice-weekly doses of 5 mg can help you maintain dopamine levels and high amounts of what I can best describe as positive energy. Legally, you need a prescription to obtain it, but you may still have trouble getting your hands on it if you do not have a neurodegenerative condition. It is possible to purchase deprenyl through online pharmacies.

For a less powerful but more affordable solution, many of the smart drugs and nootropics in chapter 5 also support dopamine pathways, and the peptide Semax, also discussed in chapter 5, can give you a feeling of cognitive enhancement very similar to that of deprenyl.

15. Telomerase Activators

As you know by now, telomeres—the caps at the ends of chromosomes—are some of the primary, if not *the* primary, biomarkers for biological age. Your body already possesses the necessary machinery to rebuild telomeres in the form of the telomerase enzyme. The problem is that in adults, the gene responsible for the production of telomerase is almost always turned off, so our cells produce very little of it for most of our lives. However, there are supplements and foods you can consume that may switch on this gene.

How it works: Telomerase is an enzyme that possesses its own RNA molecule and appears especially significantly in stem cells and cancer cells. It copies its RNA molecule and tacks it onto the ends of your chromosomes, thereby elongating your telomeres and keeping them from fraying or becoming excessively shortened.



How to do it: Unfortunately, we can't eat telomerase or administer it intravenously. The molecule doesn't survive digestion and won't migrate from the blood into the cell nucleus, where it performs its work. So the best way to maximize the longevity-enhancing effects of telomerase is to switch on the gene responsible for producing telomerase. There are several supplements and foods you can take that may do this, along with a few lifestyle strategies, all covered below.

PHARMACEUTICALS

Many pharmaceutical companies are working on preventing aging via telomerase. While some have attempted to create supplements that will deliver telomerase in a form that will reach the cell nuclei, most focus on signaling the cells themselves to turn on the telomerase gene. That way, telomerase will appear right in the cell nucleus where it is needed.

Sierra Sciences, a private drug company based in Reno, Nevada, has screened over 250,000 small-molecule compounds that it believes could lead to an increase in the expression of telomerase. They claim they have found a compound three times more potent than anything previously discovered at increasing the expression of telomerase in cells, and they market it as telomerase activation molecule 818 (TAM-818). When I interviewed Dr. Bill Andrews, the chief scientist of Sierra Sciences and one of the world's leading experts on telomeres, he told me that he personally uses TAM-818, TA-65 (an astragalus extract), a supplement called IsaGenesis, a vitamin D/K blend, vitamin C, fish oil, and flaxseed oil to maximize telomerase activity. (Warning: Aging Care Capsules, the main supplement that contains TAM-818, and TA-65 are currently several hundred dollars per bottle!)

The peptide epithalon is also an effective telomerase activator—for more on that, see page 528.

ASTRAGALUS

Astragalus is an herb that comes from the root of a perennial plant in the northern and eastern parts of China. It may be able to activate telomerase, but it takes a very large amount of astragalus plant to extract an effective dose.

The pharmaceutical company T.A. Sciences has begun to produce an astragalus extract that has been reported to have telomere-lengthening benefits. Their product—quite popular and hotly debated in antiaging circles—is called TA-65. The primary constituent of TA-65 is cycloastragenol, a purified extract of astragalus root. While initial research indicates that cycloastragenol works to activate telomerase, it is still fairly weak: an effective human dosage would be about 1,500 mg per day, but the capsules that are sold currently contain only about 5 to 20 mg and cost several dollars per dose.

Because TA-65 is so expensive and possibly too weak, it may be simpler to use astragalus itself in high doses or use a product such as the adaptogenic herb complex TianChi, which contains high amounts of astragalus in a pure, concentrated extraction. Astragalus has long been used in traditional Chinese medicine—it's considered one of the greatest chi tonics in Chinese herbology—and is often used as an adaptogenic substitute for ginseng. It is said to build upright chi, meaning that when the lungs are strong and the breath is deep, astragalus promotes good posture and holds the organs in place. Traditionally, it is also said to maintain the protective chi that circulates over your skin to ward off seasonal illness.

Even if you don't believe in concepts like protective chi, there is still a lot of research that supports the use of astragalus to enhance your health and longevity. Some, such as my friends at the supplement research website Examine.com, say that astragalus can provide several health benefits but may not actually extend your life. They say that, like resveratrol, astragalus adds life to your years rather than years to your life. But while there are no studies that show an increase in life span, astragalus has been shown to reduce age-related metabolic and physical decline, and it is known particularly for its cardioprotective and anti-inflammatory effects.

One of astragalus's primary effects is protecting mitochondria. Oxidation can damage the lipids that make up mitochondrial membranes, and astragalus inhibits this oxidation. It also been shown to prevent calcium- and oxidant-induced permeation of mitochondrial membranes. Heart

mitochondria in particular are protected following astragalus supplementation, which also exerts antioxidant and antitoxin effects on cardiac tissue as well as blood vessels, so the herb can also improve and preserve cardiovascular health.

Because astragalus naturally has poor bioavailability, in traditional Chinese medicine, it is often paired with *Angelicae sinensis* (also known as *dong quai* or female ginseng) to increase the absorption of both. The traditional preparation is a 5:1 ratio—30 g of astragalus and 6 g of *Angelicae sinensis*. Online you can also find supplemental forms of astragaloside IV, the active ingredient of astragalus. The standard dose for astragaloside IV is 5 to 10 mg.

If you prefer shotgun approaches for your supplements, the TianChi Chinese Adaptogenic Herb Complex and the Inner Peace Herb Complex made by my friend and Chinese herbalist Roger Drummer both contain astragalus alongside a host of other supportive compounds, including rhodiola, reishi mushrooms, green tea, and acerola cherry. Links to both can be found on BoundlessBook.com/19.

OTHER SUPPORTIVE STRATEGIES

In addition to astragalus, herbs that can increase telomerase production include ashwagandha, bacopa, boswellia, green tea, horny goat weed, and milk thistle. Other supplements that may stimulate the body to express telomerase include the amino acid carnosine, omega-3 fatty acids from fish oil, curcumin, and resveratrol (found in red wine and grape skin extract).

Several varieties of mushrooms have been studied for their ability to increase telomerase activity, particularly in cancerous cells. These include reishi, cordyceps, oyster, shiitake, and wood ear (often listed on mushroom powder and supplement labels as auricularia or auricula). Green tea, oolong tea, coffee, and even being breastfed as a child can all also increase telomere length and telomerase activity!

Stress management and even meditation have also been shown to measurably increase telomerase activity. And, as you may remember from chapter 9, lifting weights is known to profoundly improve telomere length.

16. Fecal Transplants

Fecal transplantation, also known as fecal bacteriotherapy, is the transplantation of a donor's fecal matter into your colon, either through the rectum or through the mouth (cleverly disguised as a poop pill). The idea behind this fairly extreme longevity tactic is to transplant the healthy gut bacteria in a healthy donor's fecal matter. Extreme measures like this may well be worth the gross-out factor: from 1999 to 2007, deaths from gastrointestinal infections grew from seven thousand to seventeen thousand a year, with 83 percent of these deaths occurring among patients over the age of sixty-five, two-thirds of whom died from *Clostridium difficile* infections.

How it works: Think back to chapter 13's explanation of the brain-gut connection. Your brain can often end up downstream of the good and bad events that occur in your gut, and vice versa. That means that if something goes wrong in your intestines and colon, you could suffer major complications in your nervous system, immune system, and endocrine system.

Older people, particularly those in hospitals and nursing homes, often take antibiotics designed to eliminate infections. *C. difficile* tends to plague this population, especially once other gut bacteria, whether good or bad, have been destroyed. Once settled into your gut, *C. difficile* churns out toxins that can damage the lining of the intestines, leading to symptoms that include diarrhea and potentially severe, life-threatening inflammation of the colon. Fecal transplants have

been shown to be effective in shoving *C. difficile* bacteria out of your gut and replacing them with the beneficial bacteria that belong there. Fecal transplants have also been shown to be effective in treating some cases of ulcerative colitis, an autoimmune condition characterized by abdominal pain, bloody diarrhea, ulcers on the colon, and fatigue.

But the effects of a fecal transplant may go beyond simply fixing issues with *C. difficile*. For example, in one study that reminded me quite a bit of the young blood transfusion experiments described earlier in this chapter, transplanting gut bacteria from young fish to old fish extended the mean life span by 41 percent and maximum life span by 30 percent in the old fish. This was due not just to the elimination of *C. difficile* but to a complete overhaul of the entire fish microbiome—or at least that of the colon. This makes sense because one of the primary differences between centenarians and shorter-lived people is that the gut microbiomes of centenarians have specific bacteria that seem to be associated with longevity. So in addition to eating a diet rich in fermented foods, getting dirty by engaging in frequent practices such as being outside, and avoiding antibiotics—all strategies that strengthen the gut microbiome— rebooting our intestinal flora may have a host of benefits.

How to do it: Fecal transplants are best administered by professional medical practitioners in a medical clinic (Dr. Glenn Taylor of the Taymount Clinic is one of the more respected poop-pill practitioners), but they can be performed in your own home using the type of DIY instructions that pop up everywhere from Reddit to Quora. The treatment consists of placing saline-diluted fecal matter into your colon via a nasoduodenal catheter or enema, or consuming encapsulated versions. On BoundlessBook.com/19 you'll find links to websites where you can find clinics that will administer fecal transplants, and you may also want to check out OpenBiome.com, where you can connect with healthy donors for the DIY version.

Should you decide to eschew the fecal transplant, you may be interested in a far more affordable and easy alternative: sunlight exposure. The most recent research seems to indicate that frequent, healthy doses of sun exposure can positively influence the colon's microbiome, if perhaps not as dramatically as a fecal transplant.

Other Strategies

Is what you just read an exhaustive list? By no means! As a matter of fact, I spend plenty of time these days at antiaging conferences, speaking with physicians, poring over studies on PubMed, and reading just about every book I can get my hands on that looks at longevity and life quality. While I tend to slightly favor more natural, ancestral strategies over technological ones, here are just a few of the interesting fields to keep an eye on if you're passionate about antiaging:

- **Cellular reprogramming:** Made popular by longevity researcher Dr. David Sinclair, cellular reprogramming involves, theoretically at a young age such as twenty-five, delivering a genetically engineered virus into your cells. The virus includes Yamanaka factors, which can cause cells to revert to a youthful, stem cell–like state. Then, when aging sets in later in life, an antibiotic is administered that activates the virus, sparking tissue rejuvenation, organ restoration, chronic disease reversal, and even fading of wrinkles and gray hair. Like many new antiaging protocols, the procedure is in research infancy and may carry risks such as cancer and immune system dysfunction, but it's definitely a protocol I plan on paying attention to. Check out Sinclair's book *Lifespan* to learn more.
- **Senolytic medicines:** Senolytics are a class of drugs that selectively induce death of senescent or aging cells, which are thought to be the root cause and driver of many

age-related diseases. The company Unity is one that's developing senolytics. So-called senotherapeutic drugs include a class called genoprotectors, which target causes of aging such as damage to the DNA. One particularly intriguing strategy for slowing senescence is combining the pharmaceutical dasatinib with the nutraceutical quercetin, which in mice equivalent to eighty-year-old humans increased survival by 36 percent and in early human clinical trials appears to act similarly for antiaging.

- **CRISPR:** Currently the simplest, most versatile, and most precise method of genetic manipulation, CRISPR is a technology that enables geneticists to edit parts of the genome by removing, adding, or altering sections of the DNA sequence. The company Editas Medicine focuses on translating CRISPR systems into treatments for people with serious diseases. At the time of this writing, they have received FDA approval for a genome-editing trial—although research currently shows that CRISPR is somewhat risky in terms of its potential to wreak havoc on DNA.
- **AI-based drug discovery:** The goal of AI-based drug discovery is to shorten the research, discovery, and preclinical stages, from three to four years to just a few months. This could save time and financial resources in the development stage of antiaging drugs, as well as provide stronger drug candidates for approval. The company Insilico Medicine is working on an AI engine that covers the entire drug discovery process, from hypothesis generation and target identification to real-world evidence collection.
- **mRNA:** Messenger RNA (mRNA) transfers instructions stored in the DNA to make the proteins required for cells. The company Moderna is developing mRNA medicines that teach your own cells to produce proteins that could prevent, treat, or cure diseases.
- **Isotopically fortified organic compounds:** Instead of preventing oxidative stress, isotopically fortified molecules do not get damaged by oxidative stress and can be consumed to replace the natural organic compounds that do, making the body more resilient. The company Retrotope has demonstrated the safety and efficacy of isotopically fortified organic compounds for several pediatric diseases.
- **Machine vision and sensing:** Advances in AI now allow laser-like accuracy in disease detection from easily accessible data like images. For example, Google Brain has developed accurate predictors for multiple diseases using basic retinal scans. Another company, Haut.AI, uses machine vision to monitor skin health and personalize interventions.
- **Wnt pathways:** One of primary signaling pathways that regulate the self-renewal and differentiation of adult stem cells are the Wnt pathways, which play a role in the formation of new tissues as well as repair and regeneration. The company Samumed has identified novel biological targets and developed drugs that that modulate Wnt activity.
- **New organs:** 3-D bioprinting of tissues and organs presents a new way to restore lost tissue structure and function. The company United Therapeutics has developed a range of products to address cardiovascular disease, infectious diseases, and cancer.

To stay up-to-date on these more advanced concepts, subscribe to my free podcast at BenGreenfieldFitness.com and read the books *Juvenescence* by Jim Mellon and *The Kaufmann Protocol* by Dr. Sandra Kaufmann, and follow the work of Peter Diamandis and his A360 organization.

Antiaging Condensed

In case your head is spinning from all the information in this chapter, here's how you can systematize everything you have just read about:

- Don't smoke.
- Minimize your intake of processed and packaged foods.
- Be able to clearly identify and succinctly state your life's purpose.
- Set aside time for friends and family.
- Set aside time to attend to your spiritual disciplines, such as silence and solitude, meditation, gratitude, fasting, or breathwork.
- Have sex regularly.
- Incorporate low-level physical activity throughout your day, and take it outdoors as much as possible.
- Follow a diet low in sugar and vegetable oils and rich in wild plants, dark berries, tannic beverages, herbs, spices, sulfur-rich foods, organ meats, healthy fats, and low-glycemic-index carbohydrates such as legumes and tubers. If you carry genetic factors that predispose you to excess fat storage, an inflammatory response to fats, or difficulty digesting fats, continue to incorporate regular periods of fasting and manage your blood glucose, but shift toward a more Mediterranean approach higher in monounsaturated fats (see chapter 13 for more on this).
- Perform a twelve-to-sixteen-hour intermittent fast every day, a twenty-four-hour dinner-to-dinner fast one to four times per month, and a caloric-restricted or zero-calorie three-to-five-day water fast two to four times a year.
- Drink pure, clean, filtered water and add liquid trace minerals, sea salt, or Celtic salt to it. Also include hydrogen tablets or some other form of hydrogen-rich water at least twice a day, in the morning and evening, if your budget permits.
- Each day, expose your body to a variety of hormetic stressors, most notably cold, heat, sunlight, wild plants, herbs, hyperoxia, and hypoxia (use a hyperbaric chamber or LiveO2 if either fit your budget). Consider supplementing with ketone esters or ketone salts, particularly for long fasting periods, before or after airline travel, or before or during long workouts.
- Prior to any carbohydrate-containing meal, consume insulin-stabilizing compounds such as bitter melon extract, Ceylon cinnamon, apple cider vinegar, berberine, rosemary, turmeric, ginger, fenugreek, *Gymnema sylvestre*, or cayenne.
- If you are up for the task and like the flavor, consume a variety of shellfish and organ meats, including sweetbreads, liver, heart, and kidneys, at least four times a month. If you wind up leaving out the sweetbreads, consider using the peptide epithalon, the peptide thymosin-alpha, or thymus injections.
- If your budget permits, consume a morning or midday smoothie that contains rhodiola, colostrum, chlorella, spirulina, marine phytoplankton, aloe vera, coffeeberry fruit extract, frozen broccoli sprouts, and moringa. You can also include other sirtuin-supporting foods in the smoothie, such as blueberries, cacao powder or cacao nibs, black currant powder, turmeric, quercetin, chamomile, or green tea extract. (See a list of possible ingredients at BenGreenfieldFitness.com/antiagingsmoothie.)
- Increase telomerase activity by consuming one packet of TianChi on an empty stomach at some point in the afternoon, or by supplementing with astragalus or TA-65 and TAM-818.
- If your budget permits, supplement each morning with carnitine, alpha lipoic acid, CoQ10, PQQ, glutathione, pterostilbene, MitoQ, astragalus, vitamin D, fish oil, C60, SkQs, and a good multivitamin/mineral complex, and then supplement each evening with magnesium, melatonin, and, if you are not breastfeeding or having regular sex, oxytocin. Also try to use a daily probiotic that contains pomegranate seed and skin extract (such as the brand SEED).
- The prescription drugs rapamycin, metformin, and deprenyl can also be used but are not, in my opinion, necessary or, in many cases, even recommended.
- If your budget permits, at some point during the day, consume a serving of ketone salts or ketone esters.
- If your budget permits, regularly drink Dr. Mercola's autophagy tea or put the ingredients into one of your smoothies (see page 325 for the recipe).
- If your budget permits, utilize my full peptides protocol from the peptides section of this chapter.
- If your budget permits, purchase and regularly use a Vielight, Joovv light, and a low-EMF infrared sauna.
- If your budget permits, get an NAD IV once a month and sustain levels with daily NR or NMN intake or NAD patches between IVs. Alternatively, and especially for an affordable solution, prepare and drink pau d'arco tea daily.
- If your budget permits, harvest and bank your stem cells and, one to two times per year, have them injected into any ailing joints or into your bloodstream, preferably combined with PRP and exosomes.
- If your budget permits, visit an antiaging or wellness clinic monthly or quarterly for thymus and placental injections, along with a test of your hormones so you can consider bioidentical hormone replacement therapy if needed.

HOW TO QUANTIFY AGING

Of course, the elephant in the room and the million-dollar question is, *How can I actually know whether any of these tactics are even working for me to reverse aging and enhance my health?* So let's finish with a handful of simple techniques as well as more advanced tests that you can use to measure the efficacy of your efforts to increase longevity, reduce the rate at which telomeres shorten, and stave off the aging processes discussed in this chapter.

Resting Heart Rate

In 2018, the body-metric-tracking company Fitbit released over 150 billion hours of heart data. Among a host of interesting conclusions that can be drawn from this data, including the law of diminishing returns with excessive exercise and the extreme importance of regular walking, is the significant suggestion that a high resting heart rate (RHR) is a very strong predictor of early death. If your RHR is 80, for instance, you're twice as likely to die from heart problems than someone whose RHR is below 50, and you're three times more likely to die if your RHR is over 90.

In most cases—outside of extremely overtrained athletes and those with a history of diseases that damage the heart's electrical system, such as coronary artery disease, heart attack, and infections such as endocarditis and myocarditis—the lower the heart rate, the better. On BoundlessBook.com/19 you'll find links to more of this fascinating data, but ultimately, if you begin to track RHR and see it rising over time, that could indicate accelerated aging.

Telomere Testing

Relatively new laboratory technology can measure the rate at which telomeres shorten, along with mitochondrial aging, white blood cell count, cellular damage, and more. At-home testing companies such as TeloYears, SpectraCell, Repeat Diagnostics, and Life Length can use this technology to measure your average telomere length (ATL). ATL is the mean length of all telomeres in a given sample of leukocytes or white blood cells found in a single drop of blood (blood is the standard sample collection method used for telomere measurement because it is typically more reliable than saliva). You can then compare your results to those of other people of your age and gender, and you can even compare your biological age to your chronological age. One caveat is that the accuracy and reliability of most telomere tests appears weak at best. But when I interviewed Dr. Bill Andrews of Sierra Sciences, he recommended Life Length and Repeat Diagnostics because they use a more accurate form of telomere testing referred to as FISH. Another company, SpectraCell, uses a more accurate form of telomere testing referred to as TCR technology.

Another intriguing age-tracking company called Osiris Green works differently: it offers an Epigenetic Age Analysis service that provides you with a biological predictor of age by measuring several different areas of DNA from saliva and then observing what types of changes in the DNA occur over time. According to Osiris Green, over a person's lifetime, DNA undergoes repeated chemical changes, referred to as epigenetic changes, and these epigenetic changes can potentially alter the way genes function, which can have physiological consequences. Many of these epigenetic changes appear random, but some regions of DNA experience consistent and predictable epigenetic changes that progress with age like the ticking of a clock. Their service looks specifically at several of these areas and uses the observed changes to predict your biological age.

White Blood Cell Count

White blood cells are the primary immune system cells that ward off pathogens. But you may be surprised to learn that higher circulating levels of white blood cells are not necessarily indicative of a healthier immune system—quite the opposite, in fact. White blood cell counts on the lower end of normal can predict a better chance of a long life. This seems to be true primarily in healthy individuals, and people who are generally unhealthy or have a compromised immune system should not use low white blood cell counts to predict longevity.

The normal range for white blood cells is 4,000 to 10,000 cells per microliter of blood. You can request a white blood cell count test from your doctor or medical provider, as it is often included in a complete blood count (CBC) test.

Handgrip Strength

Grip strength is known to predict all-cause mortality risk in middle-aged and elderly people even better than blood pressure. Even when controlling for disease status, inflammatory load, inactivity, nutritional status, and depression, grip strength predicts all-cause mortality in older disabled women, and poor grip strength is an independent risk factor for type 2 diabetes.

Aside from mentally tracking whether you can give a firm handshake, the easiest way to test your grip strength is with a simple home device called a digital dynamometer, although you can also track your grip strength with your dead-hang time from a pull-up bar, a farmer's walk for time, or how long you can clutch a weighted barbell or hex bar in your hands.

Walking Speed

People who walk the fastest tend to die later. A study performed in 2013 revealed that out of seven thousand men and thirty-one thousand women who walked recreationally, those with the highest frequent natural walking speed were less likely to die than others. Conversely, a rapid decline in walking speed has been shown to predict death.

To track and test your walking speed, you can use any GPS or wristwatch with speed-measurement capabilities designed for runners, triathletes, or adventure racers. Good brands include Garmin, Suunto, and Timex. I personally find that when I walk, it is best to simply focus on fast foot turnover and to force myself to walk at a slightly faster pace than what I would consider to be a leisurely amble.

Facial Appearance

According to research, the perceived age of your face is likely a better predictor of your risk of mortality than your actual age, cognitive function, or health markers. The obvious way to track this variable is to pay close attention to your "mirror, mirror on the wall." For example, every Wednesday, after administering my clay mask and skin serum, I lean forward to inspect my face for signs of oxidative damage or excessive wrinkling—or the opposite, which I would expect if I, say, added a high dose of astaxanthin or stepped up my sweating protocol in an infrared sauna.

Subjective Evaluation of Your Quality of Life

Chances are, if you are content with your physical and psychological health, social relationships, and immediate environment, you may end up living longer. On the other hand, being discontent or having a poor opinion of your current situation may lead to an early death. A positive subjective opinion of your life is even a better predictor of longevity than objective measurements.

To measure your subjective quality of life, you can take tests or use questionnaires, such as the Quality of Life Scale, to determine how satisfied you are with your current circumstances. On BoundlessBook.com/19 you'll find links to online tests and questionnaires.

Muscle Quantity (with a Caveat) and Quality

Since muscle produces proteins and metabolites that directly regulate your recovery from trauma and injury, lean muscle mass can serve as a metabolic reservoir for healthy aging. Some research suggests that the more muscle you have, at least to a certain extent, the better you can recover from surgeries, burns, falls, breaks, and punctures, and the longer you can stave off sarcopenia (age-related muscle loss). Of course, as you learned in chapter 9, muscle is also directly correlated to longevity because the expression of a longevity-enhancing protein known as kiotho depends on skeletal muscle strength. The only caveat is that the muscle can't be useless, extra body mass that your body has to carry and cool—it must be high-quality, functional, powerful muscle.

So what is the best way to test your muscle quantity and quality? You may be familiar with the body mass index (BMI), which measures your total body mass. But this is not necessarily the best scale to use to determine how much high-quality, functional muscle you have because it measures all of the mass on your whole frame. Instead, the fat-free mass index (FFMI) is an excellent measure of muscularity. Your FFMI is equivalent to your lean body mass in kilograms divided by your height in meters squared. The equation looks like this:

$$\text{FFMI} = (\text{lean body mass in kg}) \div (\text{height in m})^2$$

The average FFMI score for men is about 19 (in between a slight build with low musculature and a normal build with average musculature), and the average score for women is about 15.

Several wearable tracker devices now use noninvasive tendon-force measurement tools to track muscle speed and power during movement, including the M-Power and the Moxy.

Life Purpose

Time and time again, evidence has shown that having a strong life purpose predicts your allostatic load, which is a fancy term for age-related wear and tear, and that people with a stronger life purpose tend to live longer than those who have no clear direction or purpose in life. Make sure that you can express your purpose in one succinct sentence, and if you need help figuring it out, check out Mastin Kipp's book *Claim Your Power.*

Intelligence

It may not seem very fair, but intelligent people live longer. It has been shown that across all causes of mortality, a higher IQ can protect you. Some have suggested that this is due to the faster reaction times that accompany higher IQs. In other words, if you are smarter and have a quicker brain, you will likely react faster to an incoming car. This may be part of it, but it is not the full picture. Another aspect of intelligence-induced longevity may be that more intelligent people make more intelligent decisions regarding their health, choosing healthy behaviors over self-destructive ones. Basically, the smarter you are, the less likely you are to drink too much, not exercise, overeat fast food, or smoke. Research backs up this theory as well. For example, one recent paper published in the journal *Intelligence* reveals that the more intelligent you are in your late teens and early twenties, the younger you can feel in your seventies!

Although some aspects of intelligence cannot be measured, you can indeed test your IQ. The most reliable, accurate, and accepted results come from tests administered by licensed professionals using validated methods. But it can still be fun to test yourself with apps and online quizzes. The best apps for testing your IQ (and for increasing it via training) are IQ Test Pro Edition, Mensa Brain Training, and IQ Test Free. You'll find links on BoundlessBook.com/19.

Aging Clock Analysis

Finally, researchers are now investigating a new way to quantify aging via a method that looks at your "aging clock." This method analyzes the nucleolus, which is the part of the cell's nucleus where the protein-building ribosomes are located. Part of the nucleolus is occupied by ribosomal DNA (rDNA), which encodes for RNA. There appears to be a direct link between nucleolus aging and markers of accelerated aging in humans, and researchers now hypothesize that measuring the amount of methylation on the rDNA may turn out to be a very accurate way to determine true biological age. But at this point, rDNA measurements aren't widely available or cost effective.

The Bottom Line

If all of that tracking information seemed a little overwhelming on top of everything else I've already covered in this chapter, here is a quick summary and explanation of how you can habitually weave these antiaging measurements into your life:

- Track your resting heart rate daily.
- Get a telomere test, CBC, and mitochondrial profile test annually.
- Get a body fat test quarterly.
- Test your handgrip strength weekly.
- Pay attention to the way your face looks in the mirror weekly.
- Perform a treadmill walking speed test weekly (you can do this as a warm-up or cool-down for any of the workouts from chapter 12).

- If you own a device that tracks muscle speed and power, choose one strength training workout from chapter 12 during which you can measure muscle speed production, or simply keep mental or written track of your strength progressions for specific exercises, and try to track on a monthly basis.
- Take a subjective quality-of-life questionnaire.
- Create a clear, short, succinct, one-sentence purpose-of-life statement, memorize it, and put it into action.

Finally, here's one bonus tip for you. A study entitled "Ability to Sit and Rise from the Floor as a Predictor of All-Cause Mortality" investigated 2002 men and women aged fifty-one to eighty who performed a sitting-standing test to and from the floor, which was scored from 0 to 5: one point was subtracted from 5 for each support used (for example, using both hands and one knee to get up would result in a score of 2, while being able to simply pop up using just one leg would result in a score of 4). The ability to sit down and stand up efficiently and with minimal assistance was directly correlated with a decrease in mortality.

After reading this study, I began making it a goal most days to do a quick two-minute burst of sitting on the floor, extending my legs in front of me, then standing up as many times as I can, using my arms and any other support as little as possible. Try it. It's harder than you may think.

THE LAST WORD

The world's longevity all-stars live longer, but they live better too, with strong connections to family and friends; active lifestyles; clean air, light, and water; a distinct life purpose; an avoidance of smoking; an overwhelmingly plant-based diet that includes fasting; moderate, daily physical activity; and a sprinkling of the other natural practices outlined in this chapter. When asked, centenarians also attribute their long lives to mild amounts of good stress—meaning spartan conditions combined with a life of manual labor, along with a strong sense of community.

In addition, modern biohackers and longevity gurus and scientists are increasingly turning to a host of better-living-through-science tools, technologies, and tactics, with a strong focus on mitochondrial and stem cell support, caloric-restriction and fasting strategies, supplements, IVs, and injections.

ONE THING YOU CAN DO THIS WEEK

One prevailing characteristic of many Blue Zones residents is that their diets include wild and often bitter plants. Our modern produce is fluffy, beautiful, and sugary, far unlike wild nettles growing in the countryside or root shavings collected from a forest floor. But from rosemary to dandelion to clovers, it is not that difficult to either grow or find wild plants and herbs just about anywhere. Your task this week is to use a field guide or an app such as FlowerChecker or PlantSnap to identify one edible wild plant that grows near you and figure out how to harvest it and include it in a recipe.

In addition, most of the longest-lived fit and happy people I know have figured out how to hack their environment to allow them to engage in low-level physical activity all day long, rather than being sedentary and then doing a brutal exercise session at the beginning or end of the day. From keeping a pull-up bar or kettlebell in the office to taking daily walks or using treadmill workstations, the sky's the limit as to how this can be accomplished. This week, choose one way that you can change your environment to allow for more movement, such as only using a chair or a sitting position when you're eating or driving.

For citations for all the research studies mentioned in this chapter and a deeper dive into the topics of this chapter—including links to podcasts, blog posts, recommended tools and supplements, and much more—visit BoundlessBook.com/19.