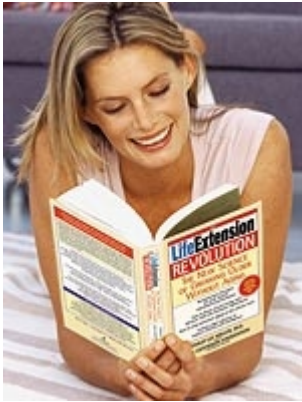


LE Magazine June 2005

COVER STORY

The Life Extension Revolution

By Matt Sizing



Published by Bantam Books in association with the Life Extension Foundation and due to arrive in bookstores nationwide this May, *The Life Extension Revolution* distills 25 years of advanced disease-prevention and anti-aging science.

In this new book, anti-aging physician Philip Lee Miller, MD, teams with respected health author Monica Reinagel to offer a comprehensive guide to the “new science of growing older without aging.”

The Life Extension Revolution contains hundreds of invaluable insights into the modern science of achieving optimal health while avoiding cancer, heart disease, diabetes, Alzheimer’s, and other increasingly common diseases of aging. This wealth of information, along with the book’s step-by-step recommendations for developing and implementing your own customized anti-aging program, will appeal to millions of increasingly health-conscious Americans who are interested in leading longer, richer, and more productive lives.

With *The Life Extension Revolution*, Dr. Miller and his colleagues at the Life Extension Foundation hope to introduce the life extension philosophy and practice of optimal health and longevity to a new audience of millions around the world.

Like most doctors, Dr. Philip Lee Miller did not begin his medical career intending to practice anti-aging medicine. But after years of treating sick and dying patients in the emergency room, he was burned out and ready for a change. A conference for the newly formed American Academy of Anti-Aging Medicine would change the course of Dr. Miller’s professional career for good:

“Here was a group of outspoken doctors and scientists who were no longer willing to accept the conventional approach to medicine but had a much different vision—one in which common diseases are obsolete, eighty-year-olds are fit and healthy, and the outer limit of human life span is measured in centuries rather than decades. It was—and still is—a radical vision, but one that is fueled by stunning recent advances in our understanding of the mechanisms of aging, right down to the molecular level.”

It was there that Dr. Miller first encountered the Life Extension Foundation, a group of researchers and advocates for anti-aging and life extension medicine. Life Extension was formed in 1980 to radically challenge the prevailing conventional wisdom, a calcified medical establishment, profiteering pharmaceutical companies, the FDA, and other leaden government bureaucracies. The Foundation’s ammunition in this fight: fresh, provocative, yet scientifically based ideas about how health, nutrition, and lifestyle choices can redefine the limits of the healthy human life span.

AHEAD OF THE CURVE

Life Extension rapidly established a reputation for identifying important yet overlooked medical research from around the world, and advocating controversial positions years before they were discovered and accepted by conventional medicine. In the 1980s, for example, Life Extension was virtually alone in advocating the importance of lowering homocysteine levels to reduce heart attack and stroke risk, the value of aspirin therapy in avoiding heart attacks, and the benefits of little-known nutrients like coenzyme Q10 and lycopene in preventing chronic diseases and even slowing the growth of cancer.



“Science has repeatedly ratified the many controversial positions [Life Extension] has advanced,” notes Dr. Miller. “Over the years, the Foundation’s careful, rigorous, and responsible approach has made it well regarded by even the most conventional of physicians.”

From the beginning, Life Extension’s mission has included advocating for the right of patients and doctors to access the best information and most novel lifesaving disease treatments available. The Foundation has challenged the FDA and powerful drug companies in the US Congress and the nation’s courts on behalf of Americans’ right to import lower-cost prescription drugs from

abroad. And Life Extension has and continues to fund cutting-edge research on disease and aging through its nonprofit Foundation. “The Life Extension Foundation not only provides its members with the latest health-promoting research, but also donates millions of dollars each year to world-class scientists conducting such research,” notes Saul Kent, a Director of the Life Extension Foundation.

Today, the Life Extension Foundation is the largest and most successful organization of its kind in the world. Life Extension counts among its members world-renowned anti-aging scientists, medical researchers, and physicians, along with more than 100,000 people from all walks of life—all united by a common desire to live longer lives in optimal health.

Through the Foundation’s exhaustively researched disease treatment and prevention protocols, the monthly Life Extension magazine, email newsletters and bulletins, an extensive and constantly updated website, and other resources, Life Extension members have unparalleled access to continuously updated, groundbreaking research on preventing disease and optimizing health.

LAUNCHING THE LIFE EXTENSION REVOLUTION

With *The Life Extension Revolution*, the Foundation and New York-based Bantam Books have joined to bring the life extension philosophy and lifestyle to a new, broad-based audience.

According to Saul Kent, Life Extension was contacted by Bantam executives “who were interested in publishing a new book about the best ways to maintain health and extend longevity, a book that also contains the cutting-edge research that will lead to revolutionary breakthroughs in the future.” As discussions on the proposed book advanced, Life Extension began looking for an author—ideally, a physician already active in the practice of anti-aging medicine. The search quickly led to Dr. Miller.

“After speaking with Dr. Miller, it became clear his philosophy of anti-aging medicine was a good fit with the approach and program of the Life Extension Foundation,” says Kent. Bantam Vice-President Toni Burbank, who acquired and helped bring the book from concept to reality, recalls an early meeting with Dr. Miller: “We were impressed with Dr. Miller’s knowledge, the way he talked about his patients, and his genuine conviction about the importance of this medical approach.” Veteran health writer Monica Reinagel was recruited to assist with the book.



COMBINING SCIENCE AND PRACTICE

In addition to sharing the latest anti-aging research, *The Life Extension Revolution* draws on Dr. Miller’s own experience and unique practice of anti-aging medicine to offer advanced therapies and protocols that will enable millions of people to fashion their own individualized anti-aging and disease-prevention programs. According to Burbank, the book’s combination of cutting-edge research and sound, practical advice makes *The Life Extension Revolution* unlike any other health book on the market.

“Most ‘live longer’ books on the market tell you to stop smoking, eat your veggies, stay mentally active, exercise regularly, and wear your seatbelt,” explains Burbank. “All good advice, but people know all this already. *The Life Extension Revolution* goes way beyond that, to address aging at the cellular level.” Among the things Burbank finds particularly notable about the book is its comprehensive discussion of male and female hormone replacement, “which explains the various issues people are concerned about more clearly than any other text I’ve seen.”

Life Extension’s Kent agrees that the book’s combination of anti-aging science and real-life medical practice makes it unique. “*The Life Extension Revolution* presents groundbreaking research and therapies for preventing and reversing aging, along with recommendations that are backed by studies published in peer-reviewed scientific journals,” says Kent. “Yet it also illuminates this science with simple, real-life case studies written by a doctor who has been practicing anti-aging medicine for years.”

Indeed, the book charts the progress of a number of patients from Dr. Miller’s practice. Despite their varying backgrounds, medical concerns, and health goals, these individuals all come to experience the life-transforming power of developing and actively practicing an anti-aging lifestyle.

“Dr. Miller told us most of his patients are middle-aged, highly productive people who feel they are losing their zest for life and are troubled by early-warning health signs like high cholesterol,” says Burbank. “The treatments he describes in the book put those patients back on track, so they can enjoy peak performance indefinitely. I think that’s the major promise this book offers.”

And that is exactly the promise laid out by Dr. Miller in the book’s introduction. “Your customized anti-aging and life extension program will give you a more youthful, energetic, and disease-proof body and mind,” he writes. “More importantly, it will help to

ensure that you'll be there to take full advantage of all that the ever-expanding future holds.”

A NEW ROLE FOR MEDICINE

The night-and-day difference between how conventional and anti-aging medical practitioners approach the problem of aging can be simply put: “Whereas the focus of conventional medicine is on the diagnosis and treatment of disease, the goal of anti-aging medicine is to promote optimal health and wellness throughout every phase of the human life span.”

To this end, anti-aging medicine is built on four principles. It is:

- functional, or concerned with improving every function of the body in health as well as disease states;
- preventive, using aggressive nutritional and metabolic theories to thwart disease before it occurs;
- holistic, considering each aspect of health and how it relates to the whole person; and
- integrative, in seeking to combine traditional and alternative therapies. “By remaining open-minded but science-based,” Dr. Miller explains, “we can combine the best and most effective therapies from conventional and alternative approaches.”

Here the book introduces the concepts of cellular “programming,” biochemistry, environmental influences, heredity, and lifestyle factors. Each plays a role in the “cascading and compounding” effects of normal aging—just as correcting age-related hormone deficiencies, introducing health-promoting nutrient protocols, and avoiding unnecessary exposure to environmental toxins have similarly cumulative effects in arresting and even reversing the ravages of aging.

Overcoming the Aging Effects of Stress

Excess cortisol, produced by the body in reaction to stress, exerts myriad dangerous effects. “If you have a chronic imbalance of stress hormones (too much cortisol and too little DHEA),” says Dr. Miller, “you are aging faster than you need to, and opening the door for diseases from heart disease to diabetes to depression.”

Anti-aging medicine offers therapies to correct stress-induced hormone imbalances. Chronic stress elevates levels of dangerous cortisol while depressing levels of beneficial DHEA (dehydroepiandrosterone). Excess cortisol not only promotes heart disease, obesity, and diabetes, but also impairs immune response and neurological function. By contrast, DHEA has been shown to protect against bone loss and osteoporosis, limit skin aging, reduce body fat, increase lean body mass, enhance mood, improve sexual performance, boost immune function, and relieve menopausal symptoms.

Although DHEA is produced in abundance in the body, its levels peak in our twenties and thereafter decline dramatically, making supplementation desirable. Dr. Miller strongly advocates DHEA replacement therapy and offers detailed advice on how to work with an anti-aging practitioner to determine your cortisol and DHEA levels through blood testing, distinguish “normal” versus “optimal” DHEA levels, and monitor your progress with follow-up testing. Precautions for DHEA use, as by men with prostate cancer, are also included.

According to Dr. Miller, “Restoring a balance between cortisol and DHEA is the first important step in creating a more youthful hormone profile.”

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Restoring Youthful Hormone Levels

Because “hormonal decline is a primary factor in the aging process,” separate chapters are devoted to sex hormones (such as progesterone, estrogen, estradiol, and testosterone) and to thyroid and growth hormone.

Although bioidentical hormone replacement therapy offers extraordinary benefits for men and women entering middle age, the public at large remains shockingly ignorant about the readily correctable effects of age-diminished hormone levels. Dr. Miller clearly distinguishes between desirable bioidentical hormones and thoroughly discredited, side effect-prone synthetic versions. It is important to work with an anti-aging doctor to develop and periodically reevaluate individually customized dosages, thus ensuring a natural and optimal balance between various hormones.

Detailed female and male protocols for bioidentical sex hormone replacement are included, as well as a discussion of the benefits of hormone-modulating herbs and phyto-estrogens for women and of prostate-protecting nutrients for men. The book clarifies common misconceptions about anti-aging treatments (such as the overlooked role of testosterone in women and progesterone in men), as well as those concerning the causes of and remedies for estrogen dominance in men. Precautions for those with hormone-sensitive cancers are noted, as are recommended nutrients and herbs for relieving menopausal symptoms (black cohosh, licorice root extract, dong quai) and protecting prostate health (nettle extract, pygeum extract, and lycopene).

Thyroid and Growth Hormone

Two other hormone systems merit evaluation in a comprehensive anti-aging program: the familiar but largely misunderstood thyroid hormone, and the somewhat more mysterious and controversial human growth hormone. “Both thyroid and growth hormone are fundamental to maintaining a youthful, healthy body as you grow older,” says Dr. Miller.

Symptoms of underactive thyroid function include weight gain, constipation, insomnia, fatigue, susceptibility to colds and flu, cold hands and feet, sleepiness, and dry or flaky skin. Yet suboptimal thyroid function is frighteningly common, under-diagnosed, and under-treated. Endocrinologists estimate that one in five women and one in 10 men over 60 suffer from underactive thyroid. Astonishingly, one study found that 40% of patients who were already taking thyroid medication still had abnormally high levels of TSH (thyroid stimulating hormone), an indicator of low thyroid function. Because even “normal” TSH levels increase heart disease risk, Dr. Miller advises testing for TSH and other blood markers of thyroid function, and working with an anti-aging doctor to bring these values into the “optimal” range signifying peak thyroid function.

Human growth hormone (HGH) is responsible for the remarkable growth spurts seen in childhood, and later for repair and regeneration of tissues and organs in grown adults. According to Dr. Miller, “Growth hormone also works throughout life to maintain bone strength, muscle tone, brain function, and the integrity of the hair and skin.” Signs associated with diminished HGH include thinning bones, decreased muscle strength, fat accumulation, impaired heart and immune function, wrinkled skin, and thinning hair. Like other hormones, HGH declines with age; by the age of 60, HGH levels are just 25% of youthful levels. Although supplementing with injectable exogenous (outside the body) HGH remains somewhat controversial, Dr. Miller argues strongly in favor of considering it as part of a comprehensive anti-aging program. Alternatively, nutrients such as L-arginine, L-glutamine, L-ornithine, lysine, glycine, and niacin are known to increase the body’s endogenous (internal) release of growth hormone, as are activities such as regular exercise.

Strategies for Maximizing Brainpower

Developing “maximum brainpower for life” concludes the discussion of body- and mind-rejuvenating therapies in *The Life Extension Revolution*. As Dr. Miller notes, “Even a minor loss of cognitive function is a serious matter, and one that can cause a great deal of emotional distress. Our minds are the thing that makes us most uniquely us, the means by which we interact with the world around us and make our mark in that world. The thought that this might somehow slip away from us as we get older is very disturbing.”

Growing knowledge of the biochemical and energy-producing processes that underlie brain function affords us the opportunity to support those processes through a strategy of lifestyle and behavioral changes, diet, and supplements. Six critical ways to support optimal brain function are: increasing circulation and oxygenation to the brain; enhancing energy production in the brain;

promoting neurotransmitter production; maintaining the structural integrity of the neuronal membranes; increasing the size and complexity of the neuronal network; and protecting the brain from oxidative damage.

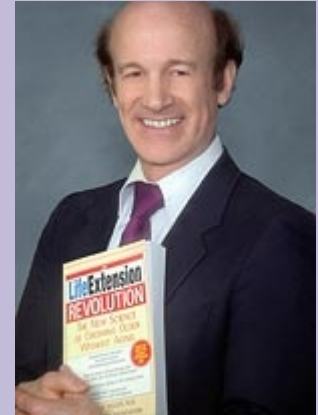
Along with a program of basic nutritional support and “targeted” brain nutrients such as phosphatidylcholine, ginkgo biloba extract, and acetyl-L-carnitine, Dr. Miller incorporates critical elements such as physical exercise, hormone balancing, mental exercise, and stress reduction in his comprehensive program for promoting brain health. Also included is a discussion of so-called “smart drugs.” While virtually ignored in the US, these drugs are widely used in Europe to treat neurodegenerative disorders and improve brain function. Some, such as L-deprenyl and hydergine, are approved for off-label use in the US, while others, such as piracetam, adrafinil, and modafinil, have yet to gain FDA approval. Dr. Miller offers advice, cautions, and strategies for those interested in obtaining these drugs.

Q&A: PHILIP LEE MILLER, MD

In more than 33 years of medical practice, Philip Lee Miller, MD, has traversed the vastly different worlds of conventional and anti-aging medicine. Trained in emergency medicine and neurology, Dr. Miller was a board-certified ER physician before transitioning to anti-aging medicine following a close one-year association with Dr. Julian Whitaker of the Whitaker Wellness Institute in Newport Beach, CA.

Dr. Miller founded and today serves as medical director of the Los Gatos Longevity Institute, where he maintains an active anti-aging medical practice. He is a charter member of the American Academy of Anti-Aging Medicine and a fully certified diplomate of the American Board on Anti-Aging Medicine.

Life Extension sat down with Dr. Miller to discuss *The Life Extension Revolution*, his views on the current state of conventional and anti-aging medicine, and what lies ahead in the future.



Life Extension: Which, if any, personal experiences compelled you to write *The Life Extension Revolution*?

Dr. Miller: My own temporary ill health started me on my journey. As I note in the book, I developed a severe lipid imbalance that sent my cholesterol and triglycerides soaring—a condition I was able to correct not with drugs, but with a regimen of vitamins and antioxidants, dietary changes, and stress reduction. But anti-aging medicine is as much about improving many lives as it is about changing one patient’s life. This book is an opportunity to reach a wider audience and affect a greater number of lives.

LE: As far as individuals are concerned, what did you hope to accomplish by writing *The Life Extension Revolution*? What impact is the book likely to have on readers in terms of their own practice of life extension?

Dr. Miller: While I hope to make the practice of anti-aging medicine more accessible and understandable to a wider audience, the book is also intended to be a guide in developing, implementing, and maintaining a customized anti-aging plan. Anti-aging medicine already is a patient-driven phenomenon, and I hope the book motivates readers to demand more of their physicians in helping to prevent disease and optimize health.

LE: In the book, you describe how embracing an anti-aging lifestyle transformed the health and lives of many of your real-life patients. Does any one patient success story stand out?

Dr. Miller: It’s hard to cite one success story, simply because so many patients have been able to move to higher levels of wellness, energy, and motivation. My practice has been more like an accumulation of wonderful people whose lives have changed greatly for the better.

LE: How has your association with the Life Extension Foundation influenced your everyday practice of anti-aging medicine? How did your clinical practice influence the book’s content and overall message?

Dr. Miller: First, my relationship with the Foundation has strengthened my belief that dedicated, tenacious organizations like Life Extension can make a huge difference in both individual lives and how medicine is practiced on a broader level. There are very few organizations like Life Extension that are fighting for freedom of choice and a greater array of therapeutic approaches in health and nutrition, and that makes the Foundation all the more invaluable.

Second, Life Extension provides the scientifically based research and information needed for a rigorous, structured approach to anti-aging medicine. I combine that with a mastery of experience and intuition: the practice of objectively based medicine combined with art and compassion. I approach lab testing, for example, somewhat like a grand master might approach a

game of chess: I try to see beyond the first move to the entire board, with a sense of purpose and strategy. My approach is goal oriented, not disease based.

LE: What impact do you hope *The Life Extension Revolution* will have on medicine as it is practiced today?

Dr. Miller: Medicine today is in a state of great transition. It truly is a revolution. What we know as modern medicine is being reshaped and redefined, from a focus on disease and pathology to functional medicine that is goal oriented and rejuvenating. Restoring function, energy, performance, and joy will be the goals of medicine in the future.

LE: What effect do you think the book will have on conventional physicians who are interested in practicing anti-aging medicine? What hurdles must be overcome to change how medicine is practiced today?

Dr. Miller: Change is not easy or welcomed. Today's physicians are constrained by algorithm-based policies, bureaucracies, forms, and rules that restrict their very sense of autonomy. It will take great courage to change. But anti-aging medicine is liberating; it rekindles a sense of wonder and excitement among physicians when they realize that so much more can be done for patients than is currently allowed.

LE: On a broader societal level, what needs to happen before the anti-aging lifestyle can become mainstream? Do you think the life extension philosophy and lifestyle can prevent or minimize looming epidemics such as obesity and diabetes?

Dr. Miller: We must begin, first and foremost, with a sense of personal responsibility. We are not a society that generally accepts responsibility for our actions and circumstances. Once we change this mindset, the physician-patient relationship needs to be redefined as something like that of a coach and student—not the infantilizing parent-child type of relationship that so frequently characterizes physician-patient interactions today.

There are great social forces in play as well. Medicare is running out of money just as the first baby boomers begin to turn 65. Social and economic pressures will begin to force the change in mindset I've just described. My advice is to begin taking care of yourself, because the government and "the system" may not be able to do so in the future. Prepare yourself by maintaining your sense of self-sufficiency and independence. The process of nutritional medicine, supplementation, hormone restoration, and cognitive enhancement can help keep the entire population more energetic, productive, and happy. And these changes cut to the very heart of what defines a healthy, sustainable society.

COVER STORY

The Life Extension Revolution

By Matt Sizing

STOPPING DISEASE AT THE CELLULAR LEVEL

“To maintain our youthful vitality as we get older, we also want to take care that the bright future is not dimmed or diminished by disease,” says Dr. Miller. Thus, the second part of *The Life Extension Revolution* presents a multifactorial approach to disease prevention extending all the way down to the human cells, the smallest units of living matter capable of functioning independently. Separate chapters are devoted to four key molecular or biochemical processes—oxidation, inflammation, methylation, and glycation—that are central to aging and many diseases of aging.

Curtailing Oxidation

More than 50 years ago, Dr. Denham Harman’s “free radical theory of aging” dramatically altered how people think about aging. In studying radiation sickness in laboratory mice, Dr. Harman noticed that radiation exposure produced an onslaught of unstable molecules known as free radicals. Over time, free radicals can disrupt the functioning of cells and tissues, causing severe symptoms and even death. Oxidation caused by free radicals can impair the functioning of cell membranes, DNA, enzymes, protein synthesis, and mitochondrial function. Poor diet, aging, intense exercise, exposure to toxins, and illness all increase the risk of oxidative stress. In the last half-century, countless studies have implicated cumulative free radical damage in the development of common diseases of aging such as cancer, heart disease, diabetes, and Alzheimer’s.

Preventing free radical damage is a cornerstone of any program to prevent disease and forestall the aging process. Key strategies to reduce oxidative stress include consuming chemical-free foods and liquids, and limiting exposure to ultraviolet radiation and other environmental toxins. An overlooked yet essential tool in counteracting free radical damage is to increase the body’s store of antioxidants, which quench free radicals before they can cause harm. Supplementing with potent doses of gamma tocopherol, lycopene, and green tea, with minerals such as selenium, zinc, and manganese, and with mitochondrial energizing agents such as coenzyme Q10, lipoic acid, and acetyl-L-carnitine, is essential to counteracting free radicals. Antioxidant phytochemicals such as resveratrol, grape seed, lutein, and zeaxanthin afford additional protection against free radicals. While these phytochemicals are contained in fruits and vegetables, most people cannot possibly hope to derive from dietary sources the amounts required for optimal antioxidant protection. Thus, Dr. Miller offers a compendium of antioxidants and the recommended dosages of each needed to “rust-proof” your cells and provide the best possible protection against the damaging effects of cellular oxidation.

Cooling Inflammation

Life Extension has long warned its members about the lethal dangers of systemic inflammation, yet this precipitator of diseases such as cancer, Alzheimer’s, heart disease, and even arthritis is only now gaining widespread attention. Controlling inflammation is central to disease prevention and life extension. The good news is, inflammation itself is a highly treatable, correctable condition.

Keeping inflammation in check requires careful and ongoing monitoring of critical blood markers such as C-reactive protein and fibrinogen. Undisputed yet often ignored research shows that even slightly elevated levels of these blood markers can double heart disease risk, even in those with no other risk factors such as high cholesterol. A comprehensive program for controlling inflammation has as its foundation regular blood testing to assess and monitor these and other important markers of inflammation. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin can play a critical role in reducing inflammation and lowering risks for inflammation-implicated cancers of the colon, prostate, breast, and esophagus by a remarkable 50-90%. With about 150,000 Americans dying each year from these four cancers alone, the cancer-preventive effects of these NSAIDs cannot be underestimated.

After examining the benefits and potentially lethal side effects associated with controversial COX-2 inhibitors and statin drugs, Dr. Miller offers supplemental and dietary strategies demonstrated to markedly reduce inflammation. Supplements such as omega-3 fatty acids, bromelain, ginger, curcumin, DHEA, vitamin K, and ginkgo biloba all have shown powerful anti-inflammatory effects. Likewise, a diet that emphasizes monounsaturated fats (such as those found in fish and olive oil) and low-glycemic foods (such as whole grains and vegetables), while limiting foods that are high in arachidonic acid (such as fatty cuts of red meat), can provide powerful protection against the insidious consequences of chronic inflammation.

Enhancing Methylation

Until recently, few outside the field of molecular biology were familiar with the process of methylation, which involves the transfer of a methyl group (one atom of carbon attached to three atoms of hydrogen) from one molecule to another. Today, every health-conscious adult has good reason to be familiar with it. "Your body depends on methylation to detoxify carcinogens and other poisons, to repair damaged DNA, to form new cells, and to manufacture important anti-aging hormones," explains Dr. Miller. "Inadequate methylation is one of the primary preventable causes of premature aging and disease." For example, when healthy methylation patterns are disrupted, homocysteine levels increase. Fortunately, we can greatly enhance methylation by arming our bodies with several nutrients that support this critically important process.

All the way back in 1981, Life Extension advised its members to take steps to lower blood levels of an amino acid called homocysteine. Overlooked research begun in the late 1960s by Harvard pathologist Kilmer McCully argued that elevated homocysteine is a more accurate, meaningful predictor of heart attack and stroke risk than is cholesterol. Homocysteine provokes chemical reactions that damage the endothelial cells lining arterial walls, thus encouraging the formation of cholesterol deposits. As Dr. Miller deftly explains:

"McCully pointed out that cholesterol begins to build up inside blood vessels only if the blood vessel walls have been damaged. Lowering cholesterol may slow the accumulation of cholesterol deposits on the walls of the damaged arteries, but it does nothing to stop the initial damage from occurring. As such, focusing heart disease prevention efforts on lowering cholesterol is like trying to prevent rain with an umbrella."

Countless clinical studies over the last two decades have borne out McCully's research and Life Extension's pioneering advocacy. Today we know that elevated homocysteine not only elevates cardiovascular risk factors, but also is linked to Alzheimer's disease, osteoporosis, Parkinson's disease, depression, and other potentially lethal conditions. The first step in controlling homocysteine is to have your blood tested for it. While low homocysteine indicates healthy methylation, high homocysteine signals impaired methylation and elevated disease risk. Even so-called "normal" levels of homocysteine elevate risk; in fact, a person with a "normal" homocysteine level of 10 $\mu\text{mol/L}$ of blood has twice the risk of heart disease as someone with an optimal level of 6.3 $\mu\text{mol/L}$ or lower.

Aggressive supplementation with folic acid and vitamins B6 and B12 is usually enough to keep homocysteine from posing an extreme risk. To bring your levels into the optimal range, Dr. Miller recommends an "advanced pro-methylation protocol" including trimethylglycine (TMG), a methyl donor that helps to remethylate homocysteine back into methionine. After debunking common myths about cholesterol and cholesterol-lowering drugs propagated by pharmaceutical companies, Dr. Miller demonstrates how nutrients can safely and effectively optimize levels of total cholesterol, LDL (low-density lipoprotein), and other blood lipids without the potentially harmful side effects of prescription drugs.

Preventing Glycation

Glycation is another overlooked biochemical process that, like methylation, is critical in determining how quickly our bodies age and their ability to stave off the diseases of aging. Specifically, glycation "is a chemical reaction in which molecules of sugar and protein get tangled up, resulting in deformed and nonfunctioning molecules." Glycated proteins then fuse together in a process known as cross-linking. As more glycated proteins cross-link, body tissues become increasingly stiff and tough. Glycation damages organs such as the heart, eyes, and skin, which require flexibility for optimal functioning.



"Glycation is now known to be a primary factor in the development of many age-related diseases, including atherosclerosis, heart failure, Alzheimer's disease, complications of diabetes, cataract formation, and premature aging of the skin," explains Dr. Miller. While glycation can never be entirely prevented, the overconsumption of sugary foods that typifies the modern American diet "promotes glycation like pouring gasoline on a fire, directly contributing to the modern epidemics of obesity, heart disease, and [type II] diabetes."

In addition to avoiding sugary foods and refined carbohydrates, we can protect against glycation by supplementing with nutrients such as carnosine. By offering itself as a target for glucose molecules that normally would cross-link to proteins in the process of glycation, carnosine may be one of the most-effective anti-aging nutrients available today. Carnosine protects proteins in the eye against glycation, shields tiny blood vessels in the brain from damage that can lead to Alzheimer's disease, relaxes and dilates blood vessels leading to the heart (thus increasing blood flow and enhancing the heart's ability to contract and pump blood), and prevents skin aging and wrinkling by inhibiting the cross-linking of collagen, thus preserving the skin's elasticity. Carnosine is also a strong antioxidant, and particularly potent against the destructive hydroxyl radical. Also addressed are anti-glycation drug therapies such as aminoguanidine, which inhibits glycation and is approved for use in Europe, and alagebrium (formerly known as ALT 7111), a newer drug under development.

Dr. Miller concludes his discussion of glycation and other correctable risk factors by pointing out that “these silent cellular mechanisms can undermine the body’s function and erode your health. By taking steps now to prevent oxidation, reduce inflammation, enhance methylation, and prevent glycation, you can improve your chances of living a long and healthy life.”

INDIVIDUALIZING YOUR ANTI-AGING PROGRAM

This section of *The Life Extension Revolution* integrates the anti-aging and disease-prevention therapies discussed earlier into “a complete program of supplements, dietary recommendations, and lifestyle habits that will help you grow old without aging.” Detailed testing protocols, supplement regimens, and lifestyle recommendations provide a foundation that will enable every reader to develop a customized anti-aging program: “your passport to a long and vibrantly healthy life.”

Medical Testing for Aging and Risk Factors

Medical testing is an integral part of a successful anti-aging program. “Testing allows us to assess your aging status and identify risk factors for disease, customize your protocols, and monitor your ongoing progress and the effectiveness of your program,” explains Dr. Miller. “To implement an anti-aging program without benefit of this information is like driving with a blindfold on.”

Detailed testing protocols are organized into three categories:

- hormone profiles (thyroid function, adrenal function, DHEA, and male and female hormone profiles and ratios)
- reversible risk factors (including inflammatory markers such as C-reactive protein and fibrinogen, homocysteine to assess methylation, and blood lipids such as total cholesterol, LDL, HDL [high-density lipoprotein], and triglycerides)
- blood chemistry (similar to Life Extension’s Complete Blood Count/Chemistry Profile, these tests measure blood glucose, liver and kidney function, red and white blood cell profile, and iron and mineral levels).

For each testing protocol, “normal” reference ranges (used by conventional medicine to signify the absence of disease) and “optimal” ranges (used by anti-aging medicine to promote and preserve health) are provided. “The goal of this program is for you to enjoy vibrant good health throughout a long lifetime,” explains Dr. Miller. “That means that most of the standard reference ranges must be discarded in favor of optimal ranges.”

Working with a qualified physician to measure, assess, and correct your medical tests is strongly recommended. This emphasis, Dr. Miller says, “is not meant to discourage or disempower you—quite the opposite”; obtaining the best results from your anti-aging program simply means working “with a doctor who understands the difference between normal and optimal and is willing to take preemptive action against aging.”

Also included is valuable information on when to have your testing done (to establish a baseline, during the implementation phase to fine tune protocols, and annually to monitor your progress). Because different testing laboratories use different reference ranges, information is provided on how to make sure that you are comparing “apples to apples” in interpreting your test results.

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Designing Your Supplement Program

An aggressive nutritional supplementation program is another cornerstone of any comprehensive anti-aging and life extension program. Even if we were to eat a precisely balanced diet comprising only highly nutritious foods, it would still be impossible to consume the variety and amounts of nutrients needed for optimal health.

The Life Extension Revolution's step-by-step guide to building a customized dietary supplementation program begins with a "comprehensive regimen of vitamins, minerals, and essential fatty acids." The vast majority of daily multi-vitamin/mineral formulas conform to nutritional guidelines propagated by the federal government and thus fail to offer adequate nutritional support. "Instead of trying to determine what amount of nutrients will maximize health, the government instead has determined the minimal level of nutrition required to prevent overt disease," says Dr. Miller. Moreover, most one-per-day formulas use cheaper, synthetic vitamins and poorly absorbed mineral salts. Therefore, a true high-potency, pharmaceutical-grade multi-vitamin/mineral formula that promotes health and fights disease may supply nutrients in amounts that are 10-50 times those in the government's inadequate recommendations. Rounding out a daily nutritional foundation are antioxidants such as gamma tocopherol, omega-3 fatty acids such as those contained in EPA/DHA formulas, carnosine to minimize glycation, bone-building nutrients such as calcium and magnesium, and vitamin K. Much overlooked, vitamin K directs calcium into the bones and away from blood vessel walls and other organs, adding to the body's defenses against both osteoporosis and heart disease.

Step two is enhancing brain power with nutrients such as ginkgo biloba, acetyl-L-carnitine, phosphatidylcholine, phosphatidylserine, and DMAE. Step three entails testing hormone levels and, if needed, beginning a program to restore youthful levels of crucial hormones such as DHEA, testosterone, estrogen(s), and progesterone. Finally, step four proactively corrects reversible risk factors, with specific nutrients for lowering dangerous homocysteine and reducing inflammation and cholesterol as necessary.

While some readers may find such a program somewhat daunting, Dr. Miller reminds us that "we are attempting nothing less than to forestall the aging process itself—to grow older without aging."

The Anti-Aging Lifestyle

A customized anti-aging and disease-prevention program also incorporates four essential components of the anti-aging lifestyle: diet, exercise, sleep, and stress reduction. "The foods you eat, the amount and quality of exercise and rest you get, and even your mental attitude about life make an enormous difference in your health and vitality," Dr. Miller remarks. "More to the point, they all affect the rate at which your body is aging."

Rather than count calories or carbohydrates or fat grams, the anti-aging diet stresses consuming roughly equal parts of lean protein, complex carbohydrates, and healthful fats. More important than quantity is the quality of the protein, carbohydrates, and fats consumed. The anti-aging diet, like other elements of the anti-aging program, naturally promotes fat and weight loss, if needed. Four basic principles characterize the anti-aging diet:

- Eliminating sugar and refined carbohydrates, which promote high blood sugar and insulin surges, provoking a cascade of debilitating effects throughout the body.
- Replacing unhealthy saturated fats and trans fats (which promote heart disease and increase the incidence of obesity, diabetes, and cancer) with foods containing healthy monounsaturated fats (such as olive oil and nuts) and essential fatty acids (such as omega-3-rich salmon and other fatty fish).
- Increasing consumption of the high-quality protein your body requires to build cells, tissues, and organs. At least one third of calories consumed should be in the form of high-quality lean proteins such as fish, egg whites, lean cuts of organically raised beef and poultry, low-fat organic dairy products, and beans and legumes.
- Eating more red, yellow, and green foods, particularly fresh vegetables that, calorie for calorie, contain more nutrients than any other kind of food. Consuming the widest possible variety of brightly colored fruits and vegetables ensures the most comprehensive intake of health-promoting phytochemicals.

Countless studies have demonstrated and confirmed the disease-preventing, anti-aging benefits of regular exercise. These include improved heart and lung function, increased bone density, reduced body fat, decreased joint pain, improved muscle

strength and tone, reduced blood pressure, improved glucose tolerance and stress, and improved libido and sexual function. One example of exercising “smarter, not harder” is interval training, which alternates short bursts of intense exercise with short periods of recovery. Because of the body’s adaptive responses—what Dr. Miller calls the “efficiency trap”—long-duration exercise such as long-distance running or biking actually increases the production and storage of fat. By avoiding the efficiency trap, interval training maximizes both calorie and fat burning.

In addition to aerobic exercise, strength or resistance training should be incorporated in your exercise regimen. Strength training helps to build and maintain muscle strength, lower blood sugar, improve insulin, and maintain bone density and mass, among other benefits. Improving your flexibility by doing simple stretches at the end of your exercise regimen will help you reduce the risk of injury and discomfort from exercise and other daily activities.

Meaningful changes in lifestyle habits can have a countervailing influence on the aging and disease-promoting effects of everyday stress. While many Americans consider watching television to be a form of “relaxation,” it has no beneficial effects on stress hormones and may even adversely affect brain function and hormone levels. “The type of relaxation that has beneficial effects on the body,” Dr. Miller says, “is usually achieved through a focused and intentional practice such as meditation, yoga, or breathing exercises.” Studies have confirmed that meditation and yoga lower cortisol and raise DHEA levels, improve immune response, decrease pain, alleviate depression, and lower blood pressure.

Getting sufficient sleep should also be a priority in any serious anti-aging program. As Dr. Miller reminds us, while “you may feel that you can fit more into every day by sleeping less . . . ultimately you will fit more into your life by living longer.” Steps to better sleep include taking vitamins (which tend to be stimulating) in the morning while consuming any additional mineral supplements (which are lightly sedating) at night. Avoid exercising at night, as this can create a surge of stimulating hormones. Additionally, research has demonstrated that melatonin, a hormone produced by the pineal gland, helps people fall asleep faster, and improves the duration and quality of sleep.



THE FUTURE OF LIFE EXTENSION SCIENCE

As noted earlier, the Life Extension Foundation has several important missions. These include informing and educating medical professionals and the public about the state of life extension and anti-aging science, and fighting anti-consumer legislation and government bureaucracies such as the FDA that seek to deny or block access to information and novel new therapies. A third important mission is actively supporting and funding the most promising anti-aging and life extension research.

The Life Extension Revolution concludes with a look at some of the most novel anti-aging technologies currently under development, as well as a preview of therapies that many life extension scientists believe could revolutionize the practice of medicine within our lifetimes.

- **Caloric restriction.** In laboratory experiments involving mice, rats, and dogs, animals fed a restricted yet highly nutritious diet lived much longer than did those allowed to eat as much as they want. On average, life expectancy was increased by about one third. Caloric restriction not only increased average life expectancy but also maximum life span, by as much as 40-60%. These effects were seen even in aged animals fed a calorie-restricted diet.

Ongoing, multi-decade studies at the University of Wisconsin and the National Institute on Aging are examining caloric restriction’s effects on rhesus monkeys, which have a maximum life span of 30 years. While it is too early to know whether caloric restriction will extend the monkeys’ maximum life span (though researchers expect this to be the case), it is clear that by preventing the onset of age-related diseases such as cancer and diabetes, caloric restriction has already extended the monkeys’ average life span.

Caloric restriction appears to accomplish these effects by retarding aging and the onset of disease—the very goals of the anti-aging and disease-prevention program outlined in *The Life Extension Revolution*. While no data exist on the long-term effects of caloric restriction in humans, these remarkable animal studies have led some people to adopt calorie-restricted diets, and have spawned research into modified caloric-restriction regimens such as fasting and intermittent fasting.

According to Dr. Miller, some research findings suggest that caloric restriction “may actually be able to reverse some of the genetic changes of aging, effectively rejuvenating the elderly.” New areas of research such as epigenetics, which focuses on the factors affecting genetic expression, and gene chip technology, which can analyze the genetic expression of thousands of genes at once, may enable scientists to evaluate how therapies such as caloric restriction affect genetic expression, thus bringing us closer to true anti-aging therapies.

- **Nuclear transfer.** The process of “nuclear transfer”—commonly referred to as cloning—offers the prospect of a world in which healthy new cells, tissues, and organs could be created as needed from each individual’s very own cells, with that person’s

unique genetic identity intact.

“Nuclear transfer technology can transform a mature cell into a very special and powerful type of cell called an embryonic stem cell,” notes Dr. Miller. Unlike normal cells, embryonic stem cells are immortal in the sense that they can continue to divide indefinitely and thus create infinite generations of new cells; they likewise differ from normal cells in having the potential to develop into any type of cell in the body.

Eminent scientists and leading health and medical organizations are adamant in their support for embryonic stem cell research as “our best and brightest hope for cures for today’s incurable diseases and conditions (including aging),” says Dr. Miller; however, “the future of this research is threatened because of a highly emotional and political debate over the ethics and morality of human cloning.” In exploring both the scientific intricacies of embryonic stem cell research and the political controversy surrounding it, Dr. Miller makes a compelling, clearly reasoned case for proceeding with therapeutic cloning (the cloning of very early-stage human cells, rather than human beings,) while noting “widespread scientific and popular support for regulations that would prohibit reproductive cloning of humans.”

• **Cryonic suspension.** The “ultimate time-buying strategy,” cryonic suspension is an often-misunderstood technology in which blood and fluids are removed from the body and replaced with solutions of cryopreservation agents that protect the body against freezing damage. The body is then cooled to subzero temperatures to arrest physical decay indefinitely.

In recent years, an advanced technique known as vitrification has enabled researchers to transform cryogenically preserved tissue into a “hard, glassy solid as it cools, with little or no ice formation.” By avoiding the formation of ice crystals that can damage cells and

tissues cooled to very low temperatures, vitrification allows scientists to preserve cellular structure virtually intact, greatly increasing the chances that organs will function normally once rewarmed. “Although it may sound like pure science fiction,” remarks Dr. Miller, “human cryonic suspension has actually been in practice since the 1960s.” Cryonic suspension involves complex philosophical and ethical issues, and several major scientific hurdles must be overcome before the successful reanimation and repair of cryonically preserved patients.

Dr. Miller concludes by noting that long-term cryopreservation, like other life extension technologies that are still in their infancy, “may be only a temporary stopgap, a bridge that may allow a generation or two of pioneers to cross from the technologically limited shores of the present to the brighter beaches of a future in which disease and aging are no longer.”

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