

Anti-Aging Medicine: The Future is NOW

Dr. Robert Goldman, Chairman

American Academy of Anti-Aging Medicine (A4M)



Abstract

In 1993, a group of one dozen future-forward physicians was convened to discuss the wide-ranging ramifications of rapidly emerging important discoveries towards identifying the mechanisms of deterioration and vulnerability to age-related diseases. As such, we introduced a new definition of aging. In this new perspective, the frailties and physical and mental failures associated with normal aging are caused by physiological dysfunctions that, in many cases, can be altered by appropriate medical interventions. As an extension of this redefinition, we proposed an innovative model for healthcare that focused on the application of advanced scientific and medical technologies for the early detection, prevention, treatment, and reversal of age-related dysfunction, disorders, and diseases. "Anti-aging medicine" was born.

In the decade that since followed, anti-aging medicine has achieved international recognition. Anti-aging medicine is now practiced by thousands of physicians in private medical offices as well as some of the most prestigious teaching hospitals around the world. Many medical schools now include anti-aging in their programs and physicians have clocked hundreds of thousands of hours of advanced medical education to train in this new medical specialty. Acknowledging the social, economic, and medical dilemmas anticipated to arrive with a rapidly growing aging population worldwide, anti-aging medicine has also garnered important recognition from leading public policy groups and members of academia. Universally, those involved in healthcare or those whose fields of expertise intersect with healthcare issues support anti-aging medicine as a healthcare model promoting innovative science and research to prolong the healthy lifespan in humans. Public policy organizations and government agencies are now embracing anti-aging medicine as a viable solution to alleviate the mounting social, economic, and medical woes otherwise anticipated to arrive with the aging of nearly every nation on the planet. The A4M's membership is comprised of 12,500 physicians, health practitioners, and scientists from 75 countries, and our education, training, and advocacy efforts continue to establish this clinical science around the world. Each of us alive today has reaped the benefits of the innovative science created by the A4M.

As we begin the second decade of the anti-aging medical movement, in this paper we will explore the history of anti-aging medicine, its explosive and rapid international growth and adoption, and the future of this exciting scientific specialty.

Introduction

Anti-aging medicine is a medical specialty founded on the application of advanced scientific and medical technologies for the early detection, prevention, treatment, and reversal of age-related dysfunction, disorders, and diseases. It is a healthcare model promoting innovative science and research to prolong the healthy lifespan in humans. As such, anti-aging medicine is based on principles of sound and responsible medical care that are consistent with those applied in other preventive health specialties.

The American Academy of Anti-Aging Medicine (A4M) is the world's leading professional medical society involved in addressing the issues of global aging. Our member physicians and scientists are an important subset of the preventive healthcare sector. While A4M members come from different medical training backgrounds, have different focuses in their clinical practices or research efforts, and represent every major nation, we are united in a single pursuit to eradicate the debilitating and disabling diseases of aging. As stated in *Geriatrics*, "many of us do not tune in on the oldest persons when we read articles on prevention. ... What I am finding is that much of what we prevent in midlife is also preventable in late life" (Sherman). The specific enhancement to preventive health that those involved in anti-aging bring is a focus on the use of high-tech diagnostic and treatment biomedical technologies for the very earliest detection and most aggressive care of disease. Thus, supporting anti-aging medicine is equivalent to supporting preventive healthcare; conversely, opposition against anti-aging medicine equates to a vote against preventive health and all the society-wide benefits with which it is associated.

Those involved in anti-aging medical research and clinical care are keenly focused on intervention to prevent or reverse dysfunction, disorders, and diseases involved in degenerative biological processes in aging. The savings in disease-related costs of such an approach are clear. In the United States alone, as Table 1 reflects, eliminating the number of deaths from just six diseases would result in hundreds of billions of dollars returned to the economy (not including the savings in medical costs) (Funding First):

<i>Disease</i>	<i>Savings</i>
Cancer	\$46.5 trillion
Heart disease	\$48.5 trillion
Stroke	\$7.7 trillion
Circulatory disease	\$5.8 trillion
Influenza	\$3.5 trillion
AIDS	\$7.6 trillion

TABLE 1. Healthcare Savings with Elimination of Diseases

Moreover, Kevin Murphy and Robert Topel of the University of Chicago Business School (Murphy *et al*) used a value per-life of \$5 million (extrapolated from accident payouts by insurers) to calculate what the six years' gain in average life expectancy during 1970-1990 alone were worth across the total U.S. population. Their calculations produced the astounding discovery that the change in life expectancy over the twenty-year period was worth \$57 trillion in 1992 dollars. Converted into a yearly valuation, the Murphy and Topel study assigns a \$2.4 trillion a year value on longevity for the U.S. alone. Reducing the death rate from either heart disease or cancer by 20%, argue Murphy and Topel, would be worth around \$10 trillion to Americans -- more than one year's U.S. Gross Domestic Product.

Anti-Aging Medicine Is Based in, and Validated by, Independent Scientific Evidence

No one should mistake anti-aging medicine for alternative medicine. According to the US National Center for Complementary and Alternative Medicine, a division of the National Institutes of Health, "Complementary and alternative medicine (CAM) covers a broad range of healing philosophies, approaches, and therapies. Generally, it is defined as those treatments and health care practices not taught widely in medical schools, not generally used in hospitals, and not usually reimbursed by medical insurance companies. ... Therapies are used alone (often referred to as alternative), in combination with other alternative therapies, or in addition to conventional therapies (sometimes referred to as complementary)."

In distinct contrast to alternative medicine, the diagnostic and treatment methods accepted by the A4M and utilized in anti-aging medicine are consistent with principles of conventional Western medicine. Anti-aging medicine embraces biomedical and technological advances to deliver cutting-edge assessments and therapies for disease. High-tech non-invasive diagnostics including CT scans, early-detection screenings via ultrasound and PET, stem cell research, genetic engineering, and more, are integral components of this fast-growing specialty of preventive medicine.

The Safety of Anti-Aging Medicine

The foundations of anti-aging medicine are very early detection via high-tech, non-invasive screenings and evaluations, administration of nutrients and biological agents in physiological doses, and lifestyle changes. Of these elements, in the United States the first two fall directly under the jurisdiction of the Food and Drug Administration (FDA).

In the United States, the FDA's Center for Drug Evaluation and Research (CDER) monitors the safety of approved drug and therapeutic biologic products through the Adverse Event Reporting System (AERS), a computerized information database that receives adverse drug reaction reports from manufacturers. Health care professionals and consumers send reports voluntarily through the MedWatch program. The reports in AERS are then evaluated by clinical reviewers at CDER and the Center for Biologics Evaluation and Research (CBER) to detect safety signals and to monitor drug safety. To-date, there are no filings of safety problems with any anti-aging drugs or therapeutic biologic products at the CDER website (<http://www.fda.gov/cder>).

In the January 11, 2003 issue of *The Lancet*, a study by Palmer et al reported on a survey of adverse events reported to poison control centers (PCC) in the United States. The results included:

- 2,332 calls in total received
- 1,466 pertained to the ingestion of dietary supplements
- 784 people experiencing symptoms
- 489 cases selected for this study
- 250 Fifty-percent certainty that negative effects were associated with supplements use
- 83 One-third of events occurred were of severity that was greater than mild
- 0 Deaths

Timeline of Anti-Aging Scientific Research

In the short three years from 2000 to 2002, scientific researchers have made remarkable progress in lifespan research in animal models. These projects have tremendous implications for near-term application to humans. In animal models of longevity, researchers have extended healthy lifespan by 30 to 300% depending on the species and the degree of intervention.

MAY 2000: Lexicon Genetics Inc. of Texas published research in *Molecular and Cellular Biology* describing a gene that controls how quickly mice age, and its relationship to a pathway of cancer suppression in humans. In knocking out the Ku80 gene in mice (mouse and human Ku80 are 85% identical and have the same biochemical function, researchers produced mice that aged more than twice as fast as normal mice, manifesting age-related problems triggered by loss of the gene's normal function. The team determined that the Ku80 gene functions as part of a cellular senescence pathway controlled by the p53 tumor suppression gene -- one of the most commonly mutated genes in human cancers.

SEPTEMBER 2000: Sandhu *et al* from the University of Ottawa (Canada) publish findings in *Journal of the National Cancer Institute* resulting from studies of effect of vitamin E on cancer-cell mutations in laboratory mice. The team found that, as an antioxidant, vitamin E protects against cell mutations through two mechanisms: one, by scavenging nitric oxide free radicals (previously shown to cause mutations) and two, by reducing the infiltration of white blood cells into tumors (which may generate free radicals and lead to further cancer cell mutations).

SEPTEMBER 2000: Melov *et al* of The Buck Institute for Age Research publishes findings in *Science* demonstrating the use of a drug in lengthening an animal's normal lifespan. Mimicking enzymes found in most animals, Eukaryon Inc. of Massachusetts developed two drugs -- synthetic forms of the natural enzymes catalase and superoxide dismutase -- that could, like their natural counterparts, defuse free radicals and counter their deleterious effects on DNA, thereby extending the lifespan of worms by more than 50%. Except in very high doses, the drugs did not have any adverse effects in mice or worms. Melov remarked that: "It was only 5 years ago that I heard a very prominent gerontologist at a major aging meeting say there would never be any drug that extends lifespan in any organism."

SEPTEMBER 2000: Lin *et al* at the Massachusetts Institute of Technology report in *Science* that caloric restriction in yeast by physiological or genetic means showed a substantial extension in lifespan. The team identified that activation of the protein Sir2p by the oxidized form of nicotinamide adenine dinucleotide induced by calorie restriction results in the increased longevity.

OCTOBER 2000: Wolkow *et al* at Massachusetts General Hospital and Department of Genetics, Harvard Medical School in Massachusetts experimented with two genes -- daf-2 and age-1 -- present in nerve, muscle, and intestine cells. The team removed and then replaced these genes in each of the various cell types in worms. Replacing either gene in nerve cells restored the long lifespan of worms. Restoring the gene activity in muscle or intestine cells overcame certain functional defects in the cells, but failed to increase the lifespan of the worm. Further experiments showed that higher levels of the genes prolong life by activating certain pathways in nerve cells. The team proposes that activation of these gene pathways controls the health of nerve cells that secrete a variety of hormone

signals, some of which regulate the lifespan of other tissues. The team concludes that because animals from worms to mammals probably share a common system for controlling lifespan, "these findings point to the nervous system as a central regulator of animal longevity."

DECEMBER 2000: Phillips *et al* from University of Guelph (Canada) report that fruit flies lived 40% longer when given a healthy human gene that fights oxidative cell damage. Reactive oxygen species metabolism -- as results from oxidation -- has significant impact on aging and lifespan determination. The team inserted the human SOD1 gene -- vital for cells to fight free radical damage -- into nerve cells of the fruit fly. The human gene and the fruit flies' version combined to offer super-protection against oxidation.

DECEMBER 2000: Fabrizio *et al* from University of Connecticut Health Center reported in *Science* reveals that mutations in a metabolism-related gene called 'Indy' can double the lifespan of the fruit fly. In addition, the flies retained the majority of their physical faculties (determined by their ability to fly and successfully breed). The 'Indy' gene, which is involved in nutrient transport, is expressed in both fruit flies and mammals. Study co-author Reenan believes that Indy mutations increase life span by altering the metabolism and "mimicking calorie restriction." He also speculated that it might be possible to develop a drug that limits the effect of the Indy gene, therefore extending the human life span.

APRIL 2001: Tatar *et al* from Brown University report in *Science* that female fruit flies with defective copies of insulin-like receptor (InR) live up to 85% longer than wild-type controls. Treatment with a juvenile hormone analog restores lifespan to normal. Dr. Tatar's research shows that juvenile hormone deficiency, which results from an InR mutation, is largely responsible for extended longevity in InR mutants. Dr. Tatar believes the insulin signaling system is likely to regulate aging in humans and may act through secondary hormones such as growth hormone, thyroid hormone, or insulin growth factor.

APRIL 2001: Longo *et al* from Andrus Gerontology Center at University of Southern California in Los Angeles report that a mutation in the gene Sch9 in yeast allows it to live up to three times its normal lifespan. The mammalian analog of the Sch9 gene is the protein kinase Akt/ protein kinase B, which is implicated in insulin signaling and functions in a pathway that regulates longevity and stress resistance in worms. Comments lead researcher Dr. Longo, Akt/PKB "may be a candidate for gene-based manipulations to improve health [in humans]."

AUGUST 2001: Hamilton *et al* from the University of Texas Health Science Center report in the *Proceedings of the National Academy of Sciences* that oxidative stress increases in age. This team observed significant increase in levels of 8-oxo-2-deoxyguanosine (oxo8dG) in DNA isolated from tissues of older rodents. Dietary restriction was shown to significantly reduce the age-related accumulation of oxo8dG levels in DNA in all tissues of the mice studied.

AUGUST 2001: Zanesi *et al* from Jefferson Medical College in Philadelphia report in the *Proceedings of the National Academy of Sciences* on the successful use of gene therapy to prevent cancer in mice. The team targeted the FHIT gene, which is damaged in many forms of cancer: FHIT causes damaged cells to terminate before they can start the uncontrolled growth of cancer. Cells in which this gene is damaged, by carcinogens for

example, do not die the way they normally would. When mice were engineered to lack a working copy of the FHIT gene, they became vulnerable to conditions leading to cancer. The researchers conclude that "FHIT may be a one-hit tumor suppressor gene in some tissues."

SEPTEMBER 2001: Cao *et al* from University of California at Riverside published findings in *Nature* indicating that elderly mice fed a low-calorie regime demonstrated reversals of changes in several genes that were altered in aging animals. Furthermore, 70% of the anti-aging effects of long-term caloric restriction also occurred in old mice put on a short-term low-calorie diet.

SEPTEMBER 2001: Wang *et al* from University of Illinois at Chicago College of Medicine report in the *Proceedings of the National Academy of Sciences* that in aging mice they could promote expression of the Forkhead box M1B (FoxM1B) gene, a ubiquitously expressed member of the Fox transcription factor family whose expression is restricted to proliferating cells and that mediates hepatocyte entry into DNA synthesis and mitosis during liver regeneration. By promoting the increased expression of FoxM1B, then removing a portion of the liver, the mice rapidly regenerated new tissue -- unlike typical aged mice. The DNA in the regenerating liver cells replicated normally, and cells divided as they do in livers of injured young mice. Furthermore, lab studies showed that increasing expression of FoxM1B restored the activity of numerous other genes involved in cell division. Importantly, lead researcher Dr. Costa notes that the FoxM1B gene controls exit from cell division, without which cells would retain too many copies of DNA -- a defect commonly seen in cancer. Because in humans the FoxM1B gene exists not only in the liver but throughout the body., the team believes their discovery might one day be used in gene therapy to replace old cells and organs in the elderly.

NOVEMBER 2001: In ongoing continuation of research, Melov *et al* from the Buck Institute for Age Research report that treatment of mice with antioxidant drugs quadrupled their lifespan. The study shows for the first time that antioxidant drugs are capable of extending mammalian lifespan, specifically by reversing oxidation that typically arises in the aging process. The antioxidant drugs mobilized into cell mitochondria to counter the aging effects of free radicals. Says Melov, "these new findings suggest novel therapeutic approaches to neurodegenerative diseases associated with oxidative stress, such as ... Alzheimer's and Parkinson's diseases, in which chronic oxidative damage to the brain has been implicated."

JANUARY 2002: Tyner *et al* from Baylor College of Medicine in Houston report in *Nature* that a critical protein that protects animals from cancer in their early years appears, in later life, to cause much of the deterioration associated with aging. Conducting their research on mice, the team mutated the animals to demonstrate enhanced resistance to spontaneous tumors; as these altered mice aged, they displayed an early onset of reduced longevity, osteoporosis, organ atrophy, and a diminished stress tolerance. The team concluded that the p53 protein -- integral in the cancer-fighting armament of animals including humans -- eventually shuts of the body's ability to renew its organs and tissues, producing bone and muscle deterioration and other hallmarks of aging. According to lead researcher Dr. Donehower, the results "raise the shocking possibility that aging may be a side effect of the natural safeguards that protect us from cancer."

JANUARY 2002: Larson *et al* from the University of California Los Angeles report in *Science* that they more than doubled the lifespan of worms by simply depriving them of a micronutrient called coenzyme Q. Drs. Pamela L Larsen and Catherine F Clarke found that adult worms fed on a coenzyme Q diet lived 59% longer than those fed a normal diet. Coenzyme Q is an antioxidant that helps to transport electrons during cellular respiration, however Larsen and Clarke say that their results suggest that the substance may also have a “pro-oxidant” effect. If this is true, reducing the animals’ consumption of coenzyme Q may extend lifespan by lowering oxidative damage to cells.

JANUARY 2002: Arantes-Oliveira *et al* from the University of California San Francisco report in *Science* that stem cells may play an important role in determining how long we live. Researchers studying germ-line stem cells in nematode worms discovered that the stem cells appear to regulate a system that speeds up aging. The team was already aware that germ-line cells had an impact on lifespan, however in their most recent study they found that they could extend the worms' lifespan by destroying specific germ-line precursor cells that develop from stem cells. Destroying these cells has also been shown to have the same effect on fruit flies.

JANUARY 2002: Kang *et al* from the US National Institute of Neurological Disorders and Stroke, a division of the National Institutes of Health, report in the *Proceedings of the National Academy of Sciences* that feeding fruit flies throughout adulthood with the drug 4-phenylbutyrate (PBA) can significantly increase lifespan, without diminution of mobility, stress resistance, or reproductive ability. Moreover, treatment for a limited period, either early or late in adult life, was also found to be effective. PBA extended the maximum lifespan of fruit flies by over 50% and their average lifespan by one-third.

Timeline of Research Advancing Human Longevity

As with animal models for longevity, there are recent advances that indicate we are close to practical medical interventions to modify the metabolism of aging in humans.

AUGUST 2001: Pucca *et al* Howard Hughes Medical Institute at Children's Hospital/Harvard Medical School report that they have identified a group of genes that appears to determine an individual’s lifespan. Scientists examining the genetic code of 308 siblings of people who had lived until they were at least 90-years-old discovered that many of the siblings had inherited a specific set of genes on chromosome 4. The region that the scientists have identified contains approximately 500 genes, thus the team are now trying to pinpoint the gene that grants longevity. Although anyone has yet to attempt to alter human lifespan by genetic modification, scientists have already extended the lifespan of lower-organisms such as nematode worms and fruit flies using genetic techniques. The researchers believe that people who live to a ripe old age have had the fortune to inherit genes that extend the lifespan but possibly more importantly, have also managed to avoid inheriting genes that are associated with diseases such as cancer, heart disease, and Alzheimer’s disease. Study leader Kunkel, remarked: “It is clear to us that longevity has a genetic component.”

JANUARY 2002: Arking *et al* from Johns Hopkins University report in the *Proceedings of the National Academy of Sciences* that they discovered a gene that appears to have an important role in determining a person’s lifespan. The gene, which has been named Klotho after the Greek Fate who spun the thread of life, was discovered when the scientists were studying the genes of adults aged 65 and above and comparing them with

those of infants. Results showed that 3% of the infants had the Klotho gene variant, compared with just 1% of those aged 65 and older. According to the researchers, these findings suggest that infants possessing two copies of the Klotho gene variant are more than twice as likely to die before they reach 65.

FEBRUARY 2002: Dalton *et al* announce they have isolated a gene which they believe could lead to the development of drugs enabling people to live longer. Scientists at DeCode Genetics in Iceland have given the gene the name of the Methuselah gene, for which they know the location and soon they predict to discover the exact DNA sequence and how it works in the body. The researchers discovered that those who lived longer appeared to have inherited a single gene that protected them against old age, rather than being born into families which did not inherit genes that made them vulnerable to illnesses.

OCTOBER 2002: Shults *et al* from the University of California in San Diego report that the food supplement coenzyme Q10 could slow down the progression of Parkinson's disease. Enrolling 80 Parkinson's patients for the trial, all of whom were in early-stage PD and did not yet need levodopa, were treated with coenzyme Q10. After 8 months of treatment with coenzyme Q10, patients who had received the highest dose of Q10 exhibited a 44% reduction in disease progression, compared with the placebo group. Even patients treated with the lowest dose the supplement were more able at carrying out simple daily activities, for example dressing and washing, and demonstrated better mental functioning and mood. The authors conclude that their findings: "are supportive of the view that mitochondrial dysfunction does play a role in the pathogenesis of sporadic Parkinson's disease."

OCTOBER 2002: Blood pressure drugs called ACE inhibitors, which help diabetics to lower their risk of developing complications, have been suggested to be of value in developing drugs that delay the effects of aging. Part of the reason why diabetics tend to age faster than non-diabetics is that their high-blood sugar levels encourages the body to produce complex proteins called advanced glycation end products (AGEs). These proteins interfere with cell functioning, accumulate in skin making it look wrinkly, and stiffen blood vessels. Now researchers at the Baker Institute in Melbourne, Australia have found that ACE inhibitors appear to exert their anti-aging effects by preventing the build-up of AGE's. ACE inhibitors work by blocking the production of the enzyme angiotensin II, which is thought to encourage the production of cell-damaging free radicals that stimulate the production of AGE's. According to the *New Scientist* magazine, "ACE inhibitors are unlikely to become an elixir of youth because they cause unpleasant side effects such as coughing and irregular heartbeat." However, there is hope that drugs designed to have a similar effect on AGE's without the adverse effects of current ACE inhibitors could provide us with a new class of age-delaying drugs.

Perspectives on the Maximum Human Lifespan

The A4M submits that human life expectancy is not predetermined, finite, or immutable. We offer as documentation a study conducted by demographers J. R. Wilmoth and L. J. Deegan of the University of California/Berkeley along with H. Lundström, and S. Horiuchi and appearing in a recent issue of *Science*. In this report, the team finds that in Sweden, the maximum age at death has risen from 100 years during the 1860s to about 108 years during the 1990s. The team cites "an intensification of efforts ... to prevent or even cure ailments such as coronary heart disease, stroke, and cancer" has profoundly contributed to "the more rapid rise in the maximum age since 1969" [Wilmoth JR, Deegan LJ, Lundstrom H, Horiuchi S, "Increase in Maximum Life-Span in Sweden, 1861-1999," *Science* Sep 29 2000; 2366-2368].

Gerontologists have long been mired by calculating maximum human longevity by solely focusing on mortality rates. The Gompertz mortality model, in which maximal longevity is based on constants reflecting solely the variables of population sizes and mortality rate, and other similar linear models, completely ignore the enormous potential for technology to function as the quantum leap accelerating the extent and achievement of scientific discovery leading to practical human immortality. It is time to incorporate the variable of technological knowledge in order to shed the very small, linear perspective of the potential human lifespan that scientists have held steadfastly for the past 100 years.

Thus, it is the position of A4M that life expectancy projections based on pastcast models will be quickly abandoned in favor of a new forecasting projection of longevity. In our model of technodemography, five near-term biotechnological interventions could bridge the timeframe for many Baby Boomers of today to capitalize on the biomedical advancements of tomorrow. By living to reap the benefits of the future's biomedical achievements, the human species will achieve a maximum lifespan of 150 to 200 years.

As such, A4M submits that five key biomedical technologies will profoundly increase the healthy human lifespan, namely:

- *stem cells*, giving rise to a supply of human cells, tissues, and organs for use in acute emergency care as well as treatment of chronic, debilitating disease
- *cloning*, a technique holding tremendous promise in producing consistent organs, tissues, and proteins for biomedical use and transplant in humans
- *nanotechnology*, enabling scientists to use tiny tools to manipulate human biology at its most basic levels
- *artificial organs*, making plentiful replacement body parts available
- *nerve impulse continuity (brain/spinal cord)*, enabling nerve signal transmission to be maintained without interruption despite physical trauma

The Anti-Aging Healthcare Model Protects Seniors

The elderly population in the US will double in size over the next quarter-century, as Baby Boomers reach retirement age. Eight in ten Americans will be age 65 or over by the year 2025. Today, Boomers now represent 28% of the U.S. population and are the largest single sustained growth of the population in the history of the United States. Their mass alone has had an enormous impact on the national psyche, political arena and social fabric. By many measures, the Baby Boomer generation has redefined every life-cycle stage as they pass through it. In the 1960s and 1970s, they created a youth culture of rock n' rollers and hippies, who grew up to become the young urban professionals of the 1980s.

As a group, today's fifty-somethings control 70% of the wealth in the U.S., own 77% of the financial assets, represent 66% of stockholders, and own 80% of the money in savings and loans. As the oldest of the Baby Boomers approaches later adulthood, they are again poised to redefine the next life stage -- retirement. The Baby Boomers are not willing to part with their tangible achievements of success prematurely: their seemingly universal yearn to retain their lean

and mean mental and physical stature with each birthday they celebrate pushes anti-aging health care to the forefront of clinical medicine.

Anti-aging medicine serves to fill a void in quality, wellness-oriented preventive healthcare that is sought specifically by Baby Boomers. Baby Boomers across this nation are, at this very moment, seeking the medical expertise of anti-aging physicians to provide very early detection, as well as the aggressive yet gentle treatment of disease, to help them live long and fulfilling lives. A recent medical study suggests that 60% of people over the age of 65 are going outside the confines of disease-based medicine and seeking options to help them with enhancing their quality of life as they extend the quantity of life. As such, anti-aging medicine does not prey on the aging population; rather, this medical specialty protects the health and well-being of Baby Boomers and the elderly.

Costs and Burdens of Disease

In order to grasp the vast potential positive benefit of anti-aging medicine, it is important to understand the current financial costs and socioeconomic burdens of disease.

- Raeburn estimates that the treatment of heart disease alone -- not including stroke and other cardiovascular diseases -- cost \$102 billion in 1999, and could climb to \$143.9 billion (a 41% increase) by 2010.
- The American Diabetes Association estimates that diabetes costs over \$137 billion a year.
- The US National Vital Statistics Reports estimates that Alzheimer's Disease, the number of cases of which will triple to 10.22 million in the US in 2050, costs \$80 - \$100 billion annually in healthcare and lost wages.
- The US Centers for Disease Control & Prevention state that arthritis is the leading cause of disability in the U.S. The number of cases is increasing by 750,000 each year, with a projected 60 million cases by 2020. This condition will cost \$65 billion per year in medical care and lost productivity.
- The American Obesity Association reports that about 69 million Americans are overweight and 51 million are obese. These numbers have been rising steadily, translating to 61% of U.S. adults of the age 20 years and over are overweight, and 26% are obese. Annually, overweight/obesity causes at least 300,000 excess deaths annually in the US, burdening the nation with a healthcare tab of more than \$100 billion each year.

Clearly, the continuation of aging-related diseases with a rapidly greying population will be unsupportable from a financial and social standpoint. It is incumbent upon public policymakers and the healthcare sector to encourage means of early diagnosis and effective early interventions as embraced by anti-aging medicine to address this situation.

Today in the United States, the federal government spends \$350 billion, or 3.5% of Gross Domestic Product (GDP), on healthcare for the elderly population. That will double in just two decades. According to Gleckman, within 40 years, Washington will be spending 50% more on healthcare than on Social security. By 2075, experts are estimating the expenditure to double and stand at 14.5% of GDP. Actuaries project that by 2010, per-capita spending on healthcare for Americans 65+ will be \$10,000. With the widespread adoption of anti-aging medicine, more of the nation's population will receive early screenings to detect illness. This is expected to cut the treatment side of disease by reducing the costs of having to treat full-blown illness in a greater segment of the population. Early detection and treatment will also lead to extended healthy lifespans absent of debilitating or disabling medical conditions.

Indeed, if we are to save public programs for seniors, an integral focus must be on adoption of anti-aging medicine in the preventive healthcare setting. By cutting the spending on healthcare, there will be more funds to appropriate to other public programs. Observes McCauhey Ross in his article in *US News & World Report*:

While politicians are debating how to ration healthcare, scientists are focused on a more promising endeavor alleviating the diseases that commonly come with old age. ... [W]hile there will be many more elderly people, there will not be an increase in chronically disabled elderly. Dying old is generally cheaper than dying young. A 70-year old consumes almost three times as much health care in the last two years of life as a 101-year old receives. What is expensive is older people living through years of chronic dependence. ... [Government]-funded programs will reap these savings and reduce their tab.

That's just it -- A4M believes in finding solutions to eliminate or, at least, alleviate the disorders that lead to chronic dependence and disability.

How Anti-Aging Medicine Is Changing the Healthcare Landscape

Aging is a global dilemma. While the world's total population grows at an annual rate of 1.7%, the segment over age 65 increases by 2.5% per year. Developed nations, thanks in large part to their adoption of diagnostic techniques affording screening and early detection of disease, have experienced a profound transformation of their demographics: nearly 20% of the developed world is age 60+. In the next 20 to 30 years, The World Health Organization projects that elderly populations in developed countries will increase by 30 to 140%, and in developing countries this bracket will grow by 200 to 400%.

The World Health Organization's Ageing and Health section states that "in the absence of appropriate policies to deal with population ageing, resources are often ill spent." Worldwide, in developed and developing nations, public policy as well as resource allocation fail to provide for the medical, social, and economic needs of a rapidly expanding group of older citizens.

The American Academy of Anti-Aging Medicine (A4M) continues its substantial commitment to encourage nations in Europe, South America, and Asia, as well as our neighbors Mexico and Canada, to institute innovative public policy initiatives and implement academic and professional physician training in order to adequately address the challenges relating to the aging populations that governments worldwide now face.

In expanding the reach of anti-aging medicine, we have adopted the Olympic model for global expansion by developing strong international partnerships with individuals placed in prominent positions in their respective medical commissions, governmental bodies, and academic and research-based affiliates and universities. In doing so, we have garnered strong participation in Asia, South America, and Europe. Indeed, a significant portion of the A4M's membership, standing now at 12,500, is garnered from outside the US borders.

With the momentum of the past four years of international development, the A4M projects that our presence on the global front will reach critical mass by 2004, where the Academy -- and our valued members -- are recognized as the leading scientists and physicians in the most exciting clinical specialty of this decade and well beyond. As the world's leading nonprofit medical organization dedicated to the exploration and application of innovative diagnostics and therapeutic interventions that aim to detect, prevent, and treat aging related diseases, the 25,000+ medical professional trained by A4M in the anti-aging medical specialty look to us as their authoritative source on cutting-edge health promotion and longevity.

The Future is NOW

We are, as many now describe, "Winning the War Against Aging." Dr. Joao Pedro Magalhaes at the University of Namur (Belgium) authored this such-titled article, in which he reports that "many advances in antiaging science have been made at the cellular level," and suggests that "aging may soon become nothing more than a scary bedtime story." Commenting on Dr. Magalhaes article, Dr. Steven Austad, biology professor at the University of Idaho remarked that "the prospects of dramatically increasing human longevity are excellent." Dr. Austad is one of anti-aging's most ardent independent supporters, previously expressing that by January 1, 2150 it will be documented that a human has reached the age of 150 or more. His confidence in this prediction is so steadfast that he's wagered \$500 million dollars to that effect.

Concurrently, we are making unprecedented gains in extending the maximum human lifespan, and enhancing its quality. Time magazine convened a forum in February 2003 on "The Future of Life." Four hundred scientists, academics, artists, clerics and business executives espoused on a "coming century of startling advances — in personalized medicine, including life spans well beyond 100 years [and] increasingly smart computer programs that will emulate biological processes." When asked how long he expected to live given the realized and soon-forthcoming biological and technological advances, technology innovator Raymond Kurzweil replied unhesitatingly, "1,000 years. My kids, too."

Remarkably, Millennium Man may be a short-lived concept, edged out by the arrival of Multi-Millennium Man. University of Cambridge scientist Aubrey de Grey has remarked that aging is a "barbaric phenomenon that shouldn't be tolerated in polite society." He submits that humans will live an average lifespan of 1,000 years by eliminating age-related diseases and maintaining the body's vitality — effectively rewriting the equation for lifespan calculation by removing age-related mortality altogether. Further, de Grey predicts that human life expectancy at birth in the year 2100 will be 5,000 years, factoring in "not only anti-aging discoveries, but also changes in technology."

The A4M's optimism for the extension of the maximum human lifespan has become contagious, as Dr. Kurzweil and Dr. de Grey's predictions make our vision of a healthy human lifespan of 120 to 200 years seem conservative. Thanks to the dialogue opened by the A4M on the subject of how long and well humans will live, A4M has inspired one of the most thought-provoking and awe-inspiring scientific discussions.

As humankind advances closer and closer to the realization of the Ageless Society, A4M invites you to join us in ushering in this exciting era of human history. Often now imitated by those referring to "longevity medicine," "successful aging," "healthy aging," "optimal aging," and "age management," and other sound-alike phrases, make no mistake: the American Academy of Anti-Aging Medicine established the concept and original definition of "anti-aging medicine" for which various synonyms have failingly attempted to rebrand. The anti-aging revolution is scientific innovation that cannot be denied.

Concluding Remarks

The A4M remains committed to this future-forward perspective. Our 12,500 members are united by a universal dedication to promote innovative science and research to prolong the healthy human lifespan. As A4M enters its second decade, the next ten years of anti-aging science promises to be filled with innovation and insight that will fuel the best and brightest minds in this medical specialty to help humankind achieve long, productive, vital lives.

The improvement of the human condition heralded by the anti-aging medical movement and spearheaded by the A4M ensures a bright future for us all. To paraphrase the Swedish political leader and former secretary-general of the United Nations, Dag Hjalmar Agne Carl Hammar skjold (1905-1961), "Never look [back] to test the ground before taking your next step; only he who keeps his eye fixed on the far horizon will find the right road."

Resources: Useful Internet Websites

Accessible 24/7/365, we can avail ourselves of the latest information pertaining to aging, aging intervention, preventive health, and biotechnological advancements via the Internet. Table 2 is a representative list of the diversity of relevant websites on these subjects; inclusion is not to be construed as endorsement by the author or the A4M. It is the responsibility of the reader to conduct diligence concerning the information presented in these websites.

RESOURCE	WEBSITE URL
The World Health Network, the Internet's leading anti-aging portal	http://www.worldhealth.net
The A4M's Special Information Center ? Publishing & Media Showcase	http://www.a4minfo.net
LEXCORE, The Life Extension Core of Information: the online repository warehousing data on A4M's longitudinal study of aging and aging interventions	http://www.lexcorelink.net
Administration on Aging Statistical Information on Older Persons	http://www.aoa.dhhs.gov/aoa/stats/statpage.html
Alzheimer's Disease Education and Referral (ADEAR) Center	http://www.alzheimers.org
American Nutraceutical Association	http://www.americanutra.com
Baby Boomer Headquarters	http://www.bbhq.com/
CenterWatch Clinical Trials Listing	http://www.medscape.com/misc/swatchindex.cfm
CliniWeb	http://www.phsu.edu/clinweb
Combined Health Information Database	http://chid.nih.gov
Healthfinder Gateway	http://www.healthfinder.org/default.htm
Healthy People 2010	http://www.health.gov/healthypeople/
InteliHealth	http://www.intelihealth.com/
International Society for Aging and Physical Activity	http://www.isapa.org/
Internet Grateful Med	http://igm.nlm.nih.gov/
MDChoice	http://www.mdchoice.com/index.asp
Medscape	http://www.medscape.com/
Mental Health Infosource	http://www.mhsource.com
National Academy of Sports Medicine	http://www.nasm.org
National Academy on an Aging Society	http://www.agingsociety.org/
National Aging Information Center	http://www.aoa.dhhs.gov/naic/default.htm
National Center for Complementary & Alternative Medicine	http://nccam.nih.gov
National Center for Health Statistics	http://www.cdc.gov/nchs/default.htm
National Council on the Aging	http://www.ncoa.org/
National Library of Medicine	http://www.nlm.nih.gov/
National Osteoporosis Foundation	http://www.nof.org
NIH Office of Dietary Supplements--IBIDS Database	http://ods.od.nih.gov/databases/ibids.html
Reuters Health Information	http://www.reutershealth.com/
ScienceDaily Magazine	http://www.sciencedaily.com/
US Census Age Data	http://www.census.gov/population/www/socdemo/age.html#elderly
US Food & Drug Administration	http://www.fda.gov/
World Health Organization, Ageing & Health	http://www.who.int/ageing/
Virtual Hospital	http://www.vh.org/Providers/ClinRef/FPHandbook/FPContents.html

TABLE 2. Helpful Website Resources

References

- "1.7 billion — the numbers of obese worldwide," NutraIngredients.com, March 17, 2003.
- "Ace inhibitors and anti-aging drug development," reported by www.bbc.uk, October 2, 2002.
- Arantes-Oliveira N, Apfeld J, Dillin A, Kenyon C. "Regulation of life-span by germ-line stem cells in *Caenorhabditis elegans*," *Science*. 2002 Jan 18; 295(5554): 502-5.
- Arking DE, Krebsova A, Macek M Sr, Macek M Jr, Arking A, Mian IS, Fried L, Hamosh A, Dey S, McIntosh I, Dietz HC, "Association of human aging with a functional variant of *klotho*," *Proc Natl Acad Sci U S A*. 2002 Jan 22; 99(2): 856-861.
- Board of Editors, "The Future of Human Evolution," *Scientific American*, March 2001.
- Brand M., *Nature* 2002 Jan 3; 415(6867): 96-9.
- British Journal of Cancer* 2001; 85:1311-1316.
- Can we prevent aging?, MSNBC, Jan. 21, 2001.
- Canadian Medical Association Journal* 2001; 165:1495-1498.
- Cao SX, Dhabhi JM, Mote PL, Spindler SR, "Genomic profiling of short- and long-term caloric restriction effects in the liver of aging mice," *Proc Natl Acad Sci U S A*. 2001 Sep 11; 98(19): 10630-5.
- Chandra RK. "Effect of vitamin and trace-element supplementation on cognitive function in elderly subjects." *Nutrition*. 2001 Sep;17(9):709-12.
- Dalton A, "Scientists find key to eternal life," *The Scotsman*, Feb. 4, 2002.
- deMagalhaes JP. "Winning the war against aging," *The Futurist*, March-April 2003, 48-50.
- Diabetes* 2002 Feb; 51(2): 347-355.
- European Journal of Clinical Nutrition* 2001; 55:1053-1058.
- Fabrizio P, Pozza F, Pletcher SD, Gendron CM, Longo VD, "Regulation of longevity and stress resistance by *Sch9* in yeast," *Science*. 2001 Apr 13; 292(5515): 288-90.
- Funding First, reported by *Mass High Tech*, July 10, 2000, 18(28); 1
- Giugliano D., *Circulation* 2002; 105.
- Gleckman H, "Social Security isn't the only surplus-buster," *Business Week*, May 21, 2001.
- Global Aging Initiative, Center for Strategic and International Studies], "Summary Report of the Co-chairmen and Findings and Recommendations of the CSIS Commission on Global Aging," August 29, 2001.
- Golden F. "Day 3: Living to 1,000?" *Time Inc.*, <http://www.time.com/time/health/printout/0,8816,421979,00.html>, accessed March 21, 2003.
- Gut* 2002;50:61-64.
- Hamilton ML, Van Remmen H, Drake JA, Yang H, Guo ZM, Kewitt K, Walter CA, Richardson A, "Does oxidative damage to DNA increase with age?," *Proc Natl Acad Sci U S A*. 2001 Aug 28; 98(18): 10469-74.
- High KP, *Clinical Infectious Diseases* 2001; 33:1892-1900.
- Hsing A., *Journal of the National Cancer Institute* 2002; 94: 1648-1651.
- Huang GT, "Mind-Machine Merger," *Technology Review*, May 2003.
- Huang HY, *American Journal of Clinical Nutrition* 2002; 76:549-555.
- Jiang R, *J Amer Med Assn (JAMA)* 2002; 288:2554-256.
- Kang HL, Benzer S, Min KT, "Life extension in *Drosophila* by feeding a drug," *Proc Natl Acad Sci U S A*. 2002 Jan 22; 99(2): 838-43.
- Larsen PL, Clarke CF, "Extension of life-span in *Caenorhabditis elegans* by a diet lacking coenzyme Q," *Science*. 2002 Jan 4; 295(5552): 120-3.
- Lexicon Genetics Discovers Gene Controlling Onset of Aging in Mice Press Release, Lexicon Genetics Inc., May 10, 2000.
- Lin SJ, Defossez PA, Guarente L, "Requirement of NAD and SIR2 for life-span extension by calorie restriction in *Saccharomyces cerevisiae*," *Science*. 2000 Sep 22; 289(5487): 2126-8.
- Martin GM, LaMarco K, Strauss E, Kelner KL. "Research on aging: the end of the beginning," *Science*, Feb. 28, 2003.
- McCaughey Ross B, "Almost a fountain of youth," *US News & World Report*, April 12, 1999.
- Melov S, Doctrow SR, Schneider JA, Haberson J, Patel M, Coskun PE, Huffman K, Wallace DC, Malfroy B, "Lifespan extension and rescue of spongiform encephalopathy in superoxide dismutase 2 nullizygous mice treated with superoxide dismutase-catalase mimetics," *J Neurosci*. 2001 Nov 1; 21(21): 8348-53.
- Minsky M. "Will Robots Inherit the Earth?," *Scientific American*, October 1994.
- Mitchell S. "Scientists developing drugs to extend life," *NewsFactor Sci-Tech*, Feb. 28, 2003.
- Murphy K, Topel R. "The health effect," *The Economist*, June 3, 2000, p. 78.
- National Vital Statistics Reports*, Vol. 47 No. 20, June 30, 1999.
- Oeppen J and Vaupel J, "Broken Limits to Life Expectancy," *Science*, May 10, 2002, 296 (5570), pp. 1029-103.
- Palmer ME, Haller C, et al. "Adverse events associated with dietary supplements: an observational study," *Lancet*, Jan, 11, 2003; 361:101-106;
- Phillips JP, Parkes TL, Hilliker AJ, "Targeted neuronal gene expression and longevity in *Drosophila*," *Exp Gerontol*. 2000 Dec; 35(9-10); 1157-64.

Puca AA, Daly MJ, Brewster SJ, Matisse TC, Barrett J, Shea-Drinkwater M, Kang S, Joyce E, Nicoli J, Benson E, Kunkel LM, Perls T, " A genome-wide scan for linkage to human exceptional longevity identifies a locus on chromosome 4," *Proc Natl Acad Sci U S A*. 2001 Aug 28; 98(18); 10505-8.

Raeburn R, "Oh, so you have a pig's heart too," *Business Week*, March 27, 2000.

Richman S, "Testimony on The International Population Stabilization and Reproductive Health Act (S. 1029), July 20, 1995.

Rogina B, Reenan RA, Nilsen SP, Helfand SL, "Extended life-span conferred by cotransporter gene mutations in *Drosophila*," *Science*. 2000 Dec 15; 290(5499): 2137-40.

Sandhu JK, Haqqani AS, Birnboim HC, "Effect of dietary vitamin E on spontaneous or nitric oxide donor-induced mutations in a mouse tumor model," *J Natl Cancer Inst.*, 2000 Sept. 6; 92(17); 1429-33.

Schults C., *Archives of Neurology* 2002; 59:1541-1550.

Science News, Oct. 7, 2000, Vol. 158, p. 238.

Sherman FT, "Our Prevention Dilemma," *Geriatrics*, April 2001, 56(4), 3-4] *Stroke* 2001; 32.

Tatar M, Kopelman A, Epstein D, Tu MP, Yin CM, Garofalo RS, "A mutant *Drosophila* insulin receptor homolog that extends life-span and impairs neuroendocrine function," *Science*. 2001 Apr 6; 292(5514); 107-10.

The Human Genome Project, *Anti-Aging Medical News*, Spring 2002, p. 13.

Tyner SD, Venkatachalam S, Choi J, Jones S, Ghebranious N, Igelmann H, Lu X, Soron G, Cooper B, Brayton C, Hee Park S, Thompson T, Karsenty G, Bradley A, Donehower LA., "p53 mutant mice that display early ageing-associated phenotypes," *Nature* 2002 Jan 3; 415(6867); 45-53.

U.S. Centers for Disease Control and Prevention, reported by webmd.com on May 3, 2001.

Wagner C, "Aging versus antiaging: Geriatrics is in trouble while antiaging medicine takes off," *The Futurist*, September-October 2001, 8-9.

Wang X, Quail E, Hung NJ, Tan Y, Ye H, Costa RH, "Increased levels of forkhead box M1B transcription factor in transgenic mouse hepatocytes prevent age-related proliferation defects in regenerating liver," *Proc Natl Acad Sci U S A*. 2001 Sep 25; 98(20); 11468-73.

Wolkow CA, Kimura KD, Lee MS, Ruvkun G, "Regulation of *C. elegans* life-span by insulinlike signaling in the nervous system," *Science*. 2000 Oct 6; 290(5489); 147-50.

Zanesi N, Fianza V, Fong LY, Mancini R, Druck T, Valtieri M, Rudiger T, McCue PA, Croce CM, Huebner K, "The tumor spectrum in FHIT-deficient mice," *Proc Natl Acad Sci U S A*. 2001 Aug 28;98(18):10250-5.

Anti-Aging Medicine: Independent Recognition & Endorsement



The 12,500 physicians, health practitioners, and scientists representing 75 countries worldwide who are A4M members are an important subset of the preventive healthcare sector.

While A4M members come from different medical training and backgrounds, have different focuses in their clinical practices or research efforts, and represent every major developed nation across the globe, A4M members are united in a single pursuit to eradicate the debilitating and disabling diseases of aging. Focusing on detection screenings, nutrition monitoring and education, risk factor management, and patient education and counseling, clinical anti-aging medical care is committed to health promotion.

As reported by Health Promotion International, such efforts result in direct improvements of population-wide health status ["WHO is making a difference through health promotion, Health Promotion International, 1999, 14(1)]. With the appointment of Dr. Gro Harlem Brundtland as World Health Organization (WHO) Director General in 1998, the organization ushered in a "novel era ... that see[s] health promotion ... as an essential approach for health gain." In its health promotion initiative, the WHO identified "ten global health targets for the 21st century. The goals are "to achieve an increase in life expectancy and in the quality of life for all; to improve equity in health between and within countries; and to ensure access for all to sustainable health systems and services." As such, the life-enhancing, life-extending pursuits of the A4M are synchronous to the WHO initiative.

Anti-aging medicine has matured into a prestigious medical field that has become recognized by independent public policy organizations. The World Future Society (a nonprofit educational and scientific organization founded in 1966 as a neutral clearinghouse exploring the impact of social and technological developments on the future) praised anti-aging medicine as an effective solution to the growing aging population worldwide. Citing an "aging baby-boom generation [that] is bringing a potential medical crisis to the fore: a critical lack of doctors who specialize in treating elderly patients," the World Future Society refers to antiaging medicine as embracing "a realignment of priorities from the problems of the elderly to the opportunities of longer lives." [Wagner C, "Aging versus antiaging: Geriatrics is in trouble while antiaging medicine takes off," *The Futurist*, Sept.-Oct. 2001, 8-9].

Similarly, the highly respected Global Aging Initiative of the Center for Strategic and International Studies recommended that governments should "pursue an integrated strategy ... for research and development in ... new health sectors, including ... anti-aging medicine and other innovative technology." ["Summary Report of the Co-chairmen and Findings and Recommendations of the CSIS Commission on Global Aging," Global Aging Initiative/Center for Strategic and International Studies, August 29, 2001.]



The Truth About Human Aging Intervention

A4M Official Position Statement

Issued June 2002 and November 2002;

with Excerpts from "Anti-Aging Medicine at Ten Years,"

Anti-Aging Medical News, Summer 2003

Introduction

In June 2002, a group of 51 gerontologists and biogerontologists published a "Position Statement on Human Aging" in *Scientific American* (primary authors Olshansky SJ, Hayflick L, and Carnes B.).

In response to the aforementioned article, and other assorted commentary from the gerontological establishment, the 12,500 members of the A4M issues its Official Position Statement on "The Truth on Human Aging Intervention," representing the position of clinical practitioners around the world who are involved in delivering advancing safe and efficacious anti-aging medical care.

Fallacies and Facts

GERONTOLOGICAL FALLACY*: "Past and anticipated advances in [aging] interventions only influence the manifestations of aging--not aging itself. The biomedical knowledge required to modify the processes of aging that lead to age-associated pathologies confronted by geriatricians does not currently exist."

A4M FACTUAL RESPONSE: In the April 10th issue of the *Journal of the American Medical Association*, the Alliance for Aging Research reports that "There is little research on the aging process itself: less than 1% of the entire budget of the National Institutes of Health (NIH) is devoted to studying the biology of aging." [Mitka M, "As Americans Age, Geriatricians Go Missing," *JAMA*, 287(14); April 10, 2002.] Over the next five years, the NIH's budget will be doubling: in 2003, the NIH will receive \$27.3 billion. Of this \$3.7 billion increase over fiscal year 2002, zero dollars have been earmarked for clinical anti-aging research. Moreover, the National Institute on Aging (NIA), the NIH branch tasked with "understanding the nature of aging," has received over \$10.3 billion since its creation in 1974, yet NIA admits that "despite increasing funds to make awards, the Institute has experienced a decline in success rate [ie, the payoff of research versus cost of project awards]." ["Overall Funding Policies, National Institute on Aging, www.nia.nih.gov/funding;/policies/gfunding.html].

We propose that the NIA rethink its funding strategy in order to welcome eager, independent anti-aging researchers who lack the bloated-budget thinking of their gerontology counterparts. At an "average NIA grant of \$345,000 to \$370,000," A4M submits that over 2,000 anti-aging research projects -- yielding near-term, applicable results for aging intervention -- could be funded by the \$880 million appropriated to NIA for 2002.

* Statement as published in Olshansky SJ, Hayflick L, and Carnes B., "The Truth About Human Aging," *Scientific American*, June 2002.

GERONTOLOGICAL FALLACY*: "Eliminating all aging-related causes of death currently written on the death certificates of the elderly will not increase human life expectancy by more than 15 years."

A4M FACTUAL RESPONSE: In 1900, the leading causes of death, namely tuberculosis, pneumonia, and diarrhea/enteritis, reflected lack of sanitation and effective infection control. Life expectancy in 1900 stood at just 47.3 years. In 1997, the leading causes of death, namely heart disease, cancer, and stroke -- collectively, the "degenerative diseases of aging," Life expectancy in 1997 stood at 79 years (women) and 74 years (men). The US Department of Health and Human Services projects that life expectancy in 2050 will be 84.3 years for women and 79.7 years for men. ["Healthy People 2010," U.S. Department of Health and Human Services. Washington DC: January 2000.] A4M believes that at least another ten years can be added to life expectancy when factoring in the impact of biotechnology. This position is supported by the Global Business Network (GBN), a worldwide membership organization engaged in a collaborative exploration of the future. GBN Chairman Peter Schwartz has remarked that " Science and medicine will not only extend more people's lives to ... 120 years, but advances in biology will lengthen human life even beyond that. If we look at the current work on stem cells and phenomena like telomerase ... we find we're learning a great deal about the control mechanisms for aging. It's very likely that over the next 25 years, society will see serious and effective medical intervention in the aging process -- people undergoing such therapy will keep looking and feeling and acting younger than their calendar age. The prospect of individuals living significantly longer than the current norm will begin to open up. In fact, looking at historical trends, one finds that over the past century, we nearly doubled our lifespan, the average having gone from about 45 to 85. There's no reason to imagine that we won't do at least as much in the next century. If you double 85, you're at 170 -- so my bet is actually conservative." ["Wanna Bet?," *Wired* May 2002, p. 131.]

GERONTOLOGICAL FALLACY*: "Relatively little evidence from human studies that supplements ... lead to a reduction in either the risk of these conditions or the rate of aging."

A4M FACTUAL RESPONSE: In April 2002, Dr. Bruce Ames et al of the University of California/Berkeley reported in *The American Journal of Clinical Nutrition* that they were able to treat more than 50 genetic diseases with high doses of vitamins. The team also believes that there may be many more diseases similarly treatable -- including aging, because the process involves biochemical deficiencies that may be modulated with vitamin therapy. The researchers suggest that vitamins, which are converted to coenzymes, team up with enzymes to perform various essential metabolic functions. Saturating the body with vitamins increases coenzyme levels and provides the necessary nutrients to conduct cellular processes properly. Commenting on the findings, Dr. Ames states that "there is potentially much benefit ... in trying high-dose nutrient therapy, because of the nominal cost, ease of application, and low level of risk." Dr. Ames adds that he "suspect[s] the big impact [of dietary supplementation] is going to be in aging." [Ames BN, Elson-Schwab I, Silver I, *Am J Clinical Nutrition*, April 2002, 75: 616-658.]

GERONTOLOGICAL FALLACY*: "No product currently sold has been demonstrated to reverse aging. No hormone, has been proved to slow, stop or reverse aging. Growing younger is a phenomenon that is currently not possible."

A4M FACTUAL RESPONSE: We reference the 1990 landmark study on growth hormone by Daniel Rudman et al, in which the researchers state "the effects of six months of human growth hormone on lean body mass and adipose-tissue mass were equivalent in magnitude to the changes incurred during 10 to 20 years of aging." [Rudman D, Feller AG, Nagraj HS, Lalitha PY, Goldberg AF, Schlenker RA, Cohn L, Rudman IW, Mattson DE, "Effects of human growth hormone in men over 60 years old," *N Engl J Med* 1990 Jul 5; 323(1): 1-6]. More recently, in April of this year, scientists from the US National Institute of Neurological Disorders and Stroke, a division of the National Institutes of Health, reported earlier this year in the *Proceedings of the National Academy of Sciences* that feeding fruit flies throughout adulthood with the drug 4-phenylbutyrate (PBA) can significantly increase lifespan, without diminution of mobility, stress resistance, or reproductive ability. Moreover, treatment for a limited period, either early or late in adult life, was also found to be effective. PBA extended the maximum lifespan of fruit flies by over 50% and their average lifespan by one-third. [Kang HL, Benzer S, Min KT, "Life extension in *Drosophila* by feeding a drug," *Proc Natl Acad Sci U S A*. 2002 Jan 22; 99(2): 838-43]

GERONTOLOGICAL FALLACY*: "It is unlikely that scientists will be able to influence aging directly through genetic engineering because ... there are no genes directly responsible for the processes of aging."

A4M FACTUAL RESPONSE: In February 2002, Icelandic biotechnologists announced that they had isolated the Methuselah gene, a stretch of DNA that offers a protective defense against old age. The researchers located the gene after comparing the records of 1,200 people who lived for 90 years or longer with that of a similar number of people with average lifespans. Results showed that those who lived longest were more closely related than those who lived for an average lifetime, and that a single gene appeared to be responsible for protecting the nonagenarians from the ravages of old age. Kari Stefansson, the Chief Executive of DeCode Genetics, the company behind the discovery, believes that the discovery will help scientists to develop life-lengthening drugs, saying: "There is no reason why we cannot do this. We know the location of this gene. Soon we will study its exact DNA sequence and work out how it works in the body. You can then think of making drugs that could replicate its action."

This discovery follows new data released by the Harvard Centenarian Study, which recently found that 100% of the centenarians they studied had Methuselah-type genes, which appeared to protect them from age-related conditions such as cancer, dementia and heart disease. Many had also inherited a gene dubbed the longevity gene. The researchers also found that the children of centenarians were likely to live 10 to 15 years longer than the norm, and their siblings were four times more likely than average to live to see their 90th birthday. Remarks Thomas Perls of the Harvard study, "An average set of genes will allow you to live to your mid to late eighties. To get another 20 healthy years, you have these disease-resistant genes." [Dalton A, "Scientists find key to eternal life," *The Scotsman*, February 4, 2002.]

GERONTOLOGICAL FALLACY*: "Suggestions have been made that the complete replacement of all body parts with more youthful components could increase longevity. Though possible in theory, it is highly improbable that this would ever become a practical strategy to extend length of life."

A4M FACTUAL RESPONSE: Replacement parts for worn out or damaged human organs are presently helping people to extend both total and healthy lifespan. In the not-so-distant future, refinement of today's organ replacement technologies will extend total lifespan even farther. The A4M is not the only medical organization putting forth this position. At its annual meeting in 2000, the American College of Cardiology predicted: "It is the year 2024. You are 75 years old, and you discover that a man next to you on an airplane has a pig heart, and his arteries are swarming with "smart dust" that sends continuous reports on his condition to his doctor's computer. That's not so strange, because you have a pig heart, too. And by 2049, when you are 100, many of your organs will be replaced. Plus you'll feel better than you did at 50 because "nanolabs" in your blood can manufacture and supply drugs whenever they are needed." [Raeburn R, "Oh, so you have a pig's heart too," *Business Week*, March 27, 2000].

GERONTOLOGICAL FALLACY*: "Optimum lifestyles, including exercise and a balanced diet along with other proven methods for maintaining good health, contribute to increases in life expectancy by delaying or preventing the occurrence of age-related diseases. There is no scientific evidence, however, to support the claim that these practices increase longevity by modifying the processes of aging."

A4M FACTUAL RESPONSE: In an important study of 6,2000 men by researchers from the Veterans Affairs Palo Alto Health Care System/Stanford University published in 2002, physical fitness was determined to be more important a factor in longevity than high blood pressure, sky-high cholesterol levels, or bad habits such as smoking. In fact, the researchers found that men with the lowest exercise capacity were roughly four times more likely to die during the study than the fittest participants. Altogether, physical fitness was shown to have a bigger impact on the risk of death than all of the well-publicized heart disease risk factors. [*New England Journal of Medicine* 2002; 346:793-801, 852-853.]

The net result of risk factor intervention or biotechnological applications from genetic engineering to stem cell research is the same: a prolonged disease-free lifespan. Anti-aging medicine is a medical specialty founded on the application of advanced scientific and medical technologies for the early detection, prevention, treatment, and reversal of age-related dysfunction, disorders, and diseases. Thus, anti-aging medicine considers the disabilities associated with normal aging to be caused by physiological dysfunction which in many cases are amenable to medical treatment. Whether it is by delaying or preventing the occurrence of age-related diseases, or modifying the processes of aging, the net result of anti-aging medicine is to increase the healthy human lifespan.

GERONTOLOGICAL FALLACY*: "Despite intensive study, scientists have not been able to discover reliable measures of the processes that contribute to aging. For these reasons, any claim that a person's biological or "real age" can currently be measured, let alone modified, by any means must be regarded as entertainment, not science."

A4M FACTUAL RESPONSE: With a major mission objective to "support and conduct high-quality research on aging processes and age-related diseases," is it not requisite that NIA elucidates the markers of biological age? In 1999, the A4M launched the LEXCORE research study (www.lexcorelink.net). LEXCORE is an independently-funded longitudinal study of aging that employs a large-scale, cross-population data acquisition strategy in order to obtain a depth and breadth of data collection harvesting key indicators of health. Sixty-five sites around the world are participating in this research effort. A4M anticipates that LEXCORE will yield clear definitions for the parameters of biological age within a very short period once critical mass of data is achieved. Once these markers are established, correlations to efficacious interventions for aging may readily be established.

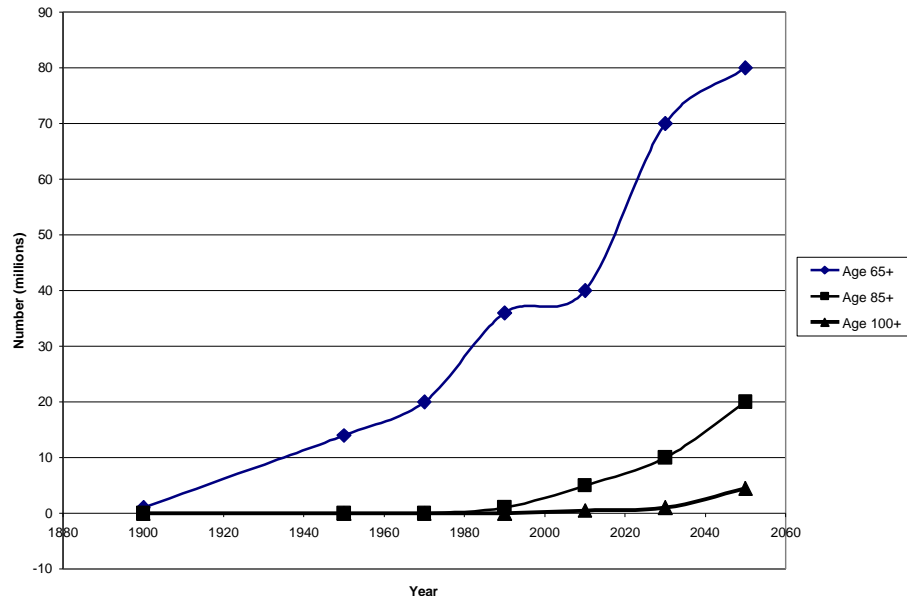
GERONTOLOGICAL FALLACY*: "Dramatic claims made by those who advocate antiaging medicine ... are ... not supported by scientific evidence, and it is difficult to avoid the conclusion that these claims are intentionally false, misleading or exaggerated for commercial reasons."

A4M FACTUAL RESPONSE: A4M is a non-profit organization, and does not promote or endorse any specific treatment nor does it sell or endorse any commercial product. A4M agrees that there are a few less-than-reputable vendors involved in the anti-aging industry. To-date, A4M has launched three important initiatives to combat this problem:

- In 1999, the A4M created the Consumer Education & Research Council, which seeks to expose anti-aging product marketing practices that may be misleading or deceptive and educate consumers about what they should expect from anti-aging healthcare products.
- In an ongoing effort to warn the public of dubious marketing efforts of fraudulent and unscrupulous vendors, the A4M regularly issues advisories at our website (www.worldhealth.net). In July 2001, A4M issued an alert titled "Beware Bait-and-Switch Nutritionals Marketing that Misrepresents Scientific Growth Hormone Research," to warn the public of misleading claims being made by nutritional HGH manufacturers and vendors attempting to confuse research documenting injectable HGH replacement therapy as validating nutritional products.
- In 2002, the A4M established the Panel to Establish Guidelines for Anti-Aging Product Marketing, a committee of medical ethicists, physicians, scientists, and business leaders who will promulgate ethical guidelines for self-regulation of the anti-aging marketplace.

GERONTOLOGICAL FALLACY*: "There are no lifestyle changes, surgical procedures, vitamins, antioxidants, hormones or techniques of genetic engineering available today that have been demonstrated to influence the processes of aging."

A4M FACTUAL RESPONSE: If we are to believe the gerontological propaganda that nothing whatsoever has influenced the processes of aging, how can the following trends in the growth of the population brackets age 65+, 85+, and 100+ be explained:



Created from data from Federal Interagency Forum on Aging-Related Statistics, "Older Americans 2000: Key Indicators of Well-Being," at www.agingstats.gov/chartbook2000; *Centenarians in the United States -- Current Population Reports 1990: Special Studies, Publication P23-199RV*, U.S. Department of Health and Human Services, July 1999.

Moreover, the United Nations Second World Assembly on Ageing that took place in April 2002 predicts that:

- One out of every ten persons is now 60 years or older; by 2050, one out of every three persons will be age 60+.
- The oldest old (age 80 and over) is the fastest growing segment of the older population. Currently making up 100% of the 60+ age group, this segment will grow to 19% by 2050.
- The number of centenarians (aged 100 years or more) is projected to increase fifteen-fold, from approximately 145,000 in 1999 to 2.2 million by 2050.

[UN Press Release, April 9, 2002, at www.irna.com]

If -- as the gerontological establishment purports -- nothing whatsoever influences the processes of aging, how are millions of people around the world living longer and healthier extended lifespans, and why would the United Nations make these predictions for fifty years from now?

GERONTOLOGICAL FALLACY: "What we anticipate is that everyone alive today will be long dead before a life expectancy of 100 is achieved -- if it ever is."

S. Jay Olshansky, in "100-Year Life Expectancy May Be 500 Years Off," *Chicago Tribune*, Feb. 19, 2001

"In research published in *Science* in 1990, Olshansky et al ... concluded that the practical upper limit to life expectancy is 85 years -- 88 for women and 82 for men."

Press Release from University of Illinois at Chicago Feb. 18, 2001 on S. Jay Olshansky, *Science*, Feb. 23, 2001

A4M FACTUAL RESPONSE:

Olshansky, who since 1990 has presented historical statistical analyses in which it is purported that the elimination of cancer, heart disease, and diabetes would increase life expectancy only to about age 85 -- and would thereby proliferate disabling conditions such as arthritis, Alzheimer's disease, and vision and hearing losses in advanced age, we remind our colleagues of a scientific study published by the same publication in which Olshansky's February report appears. In "Increase in Maximum Life-Span in Sweden, 1861-1999" (*Science* Sep 29 2000: 2366-2368), the study's authoring team, demographers J. R. Wilmoth and L. J. Deegan of the University of California/Berkeley along with H. Lundström, and S. Horiuchi, shares that in Sweden, **the maximum age at death has risen from 100 years during the 1860s to about 108 years during the 1990s.** The team cites "an intensification of efforts ... to prevent or even cure ailments such as coronary heart disease, stroke, and cancer" has profoundly contributed to "the more rapid rise in the maximum age since 1969."

GERONTOLOGICAL FALLACY: "Regardless of how many lifestyle improvements we make, vitamins we ingest, or hormones we inject, the changes of life expectancy at birth rising to 100 years or beyond are slim to nil."

Press Release from University of Illinois at Chicago Feb. 18, 2001 on S. Jay Olshansky, *Science*, Feb. 23, 2001

A4M FACTUAL RESPONSE:

"Researchers used to believe the older you get, the sicker you get,' says Harvard Medical School physician Thomas T. Perls. 'That's completely wrong.' **Starting healthy habits now can add years later on. Do you smoke? Keep a positive attitude? Limit red meat? The answers to such questions may affect your likely expiration date.**" Those of us with **average genes and healthy habits can expect to live until about 85.**"

"How long have you got," *Scientific American--The Quest to Beat Aging*, Summer 2000

"Antiaging therapies may soon add even more candles to the cake, says zoologist Steven N. Austad of the University of Idaho. 'The first 150-year-old person is probably alive right now,'" Austad predicts."

"How long have you got," *Scientific American--The Quest to Beat Aging*, Summer 2000

GERONTOLOGICAL FALLACY:

"Our [human] bodies evolved to survive long enough to reproduce and raise our young. 'Had our bodies been crafted for extended operation, we would have fewer flaws capable of making us miserable in our later days."

Press Release from University of Illinois at Chicago "UIC Expert Tinkers with Evolution to Create 'Built-to-Last' Human, Feb. 9, 2001

A4M FACTUAL RESPONSE:

"Thanks to modern technology and medicine, people have taken much more control over their differential survival. Ills are not the barriers they once were. Our technology may exert the greatest influence."

Board of Editors, "The Future of Human Evolution," *Scientific American*, March 2001

GERONTOLOGICAL FALLACY: "Future gains in life expectancy will ... be measured in days or months rather than years. The next quantum leap in life expectancy ... can occur only if 'biomedical researchers can discover how to modify the aging process and make such a discovery widely available to the entire population."

Press Release from University of Illinois at Chicago Feb. 18, 2001 on S. Jay Olshansky, *Science*, Feb. 23, 2001

A4M FACTUAL RESPONSE:

The American Academy of Anti-Aging Medicine offers a hopeful and attainable model for medicine in the new millennium founded on the dramatic advancements offered by the biotech revolution delivering a continued and expanding arena of discovery and advancement in our understanding of ways to mitigate age-related disability and disease. Conceived by A4M, **technodemography is the application of modern biotechnology to the issues of aging diagnosis, sprevention, and intervention, such that one may extrapolate future progress in human aging based on the application of innovative medical interventions on aging.** This concept may be illustrated by The Longevity Link, a novel representation of the impact of five key biomedical technologies on gains in human longevity:

$$I \propto \sum_{k=1}^5 T_k^{\frac{t}{3.5}}$$

where:

λ = human longevity

$T_k = \{$

stem cells, giving rise to a supply of human cells, tissues, and organs for use in acute emergency care as well as treatment of chronic, debilitating disease

cloning, a technique holding tremendous promise in producing consistent organs, tissues, and proteins for biomedical use and transplant in humans

nanotechnology, enabling scientists to use tiny tools to manipulate human biology at its most basic levels

artificial organs, making plentiful replacement body parts available

nerve impulse continuity (brain/spinal cord), enabling nerve signal transmission to be maintained without interruption despite physical trauma

$\}$ technological knowledge

and τ = year (after 2000 A.D.), where

the exponent $\tau/3.5$ represents the doubling time of medical knowledge and technology every 3.5 years

A4M's technodemographers predict that these advancements will receive widespread application and availability by the year 2029.

Today, medicine is at its most important crossroads it has encountered. An artificial impasse constructed by a traditional, antiquated gerontological establishment seeks to obfuscate truth and science with politics and propaganda. Remember:

FACT: No lawsuits for wrongful death have been confirmed, determined, directly proven, or associated with a physician for practicing anti-aging medicine.

FACT: State licensing boards perceive innovative physicians – such as those practicing anti-aging medicine, as ripe targets for administrative actions, to-date being unsuccessful in proving any actual medical practices of harm to patients.

FACT: Hormone replacement therapy, performed judiciously and administered in physiological doses by a qualified anti-aging physicians, is well researched and scientifically documented to improve health and has not been directly confirmed to cause any unhealthy adverse effects, such as cancer.

FACT: Anti-aging medicine is a multi-disciplinary model for wellness-based healthcare, uniting physicians and scientists across specialties in a spirit of cooperative research and application to promote a scientifically-validated whole-body approach to individual medical care.

FACT: Anti-aging medical therapeutics and interventions are taught as part of postgraduate medical education at many medical universities around the world.

FACT: Anti-aging medical education qualifies as Continuing Medical Education (CME) by the American Medical Association (AMA), the American Osteopathic Association (AOA), Medical Media Communications, and overseas medical societies such as the German Endocrinological Society.

Concluding Remarks

As the goal of achieving healthy, productive, extended human lifespans grows near, those clinicians and scientists who have dedicated their professional lives to the pursuit of anti-aging in the form of safe, effective, and progressive interventions as advanced by the A4M have drawn much attention from the "biogerontologists" – biologists who research the processes of aging. As described by Dr. Robert Binstock and colleagues from the School of Medicine's Aging, Health, and Society Department at Case Western Reserve University, the contemporary prominence of the anti-aging movement "threaten[s] biogerontological researchers and practitioners." [Binstock RH. "The war on 'anti-aging medicine,'" *The Gerontologist*, 43(1), 4-14.] According to Dr. Binstock, much of biogerontology's territorialism towards the study of aging stems from "the marginal status" of that field that required a dozen years of political lobbying in the 1970s and 1980s to overcome. Yet, Dr. Binstock warns that "through their attack on anti-aging medicine, [biogerontologists] may be shooting themselves in the foot." Instead, Dr. Binstock advocates "public dialogue ... to ensure that everyone benefits from [aging interventions]."

A4M agrees that dialogue, not diatribe, will collectively advance the pursuit of the healthy extended human lifespan in a much more productive fashion. The mechanisms of aging intervention and clinical methods to attack aging-related disorders are degenerative metabolic processes that lead inevitably to disease and, finally, to death. Were intellectual honesty to prevail, all those involved in aging research and policymaking would admit that aging is a treatable condition. It is together, in a spirit of cooperation, that the all researchers and clinicians

interested in improving the condition of the aging human population can move forward to the ultimate mutual goal of eliminating aging-related diseases within our lifetime.

History is replete with examples of medical pioneers whose innovations and foresight were trivialized, ignored, challenged, or violently opposed by the establishment, only to ultimately become accepted by society at-large. Leopold Auenbrugger was ridiculed for percussing and auscultating his patients' chests; Ignaz Semmelweis' recommendation for doctors to wash their hands before each patient landed him in a mental asylum; and more recently, cardiologists denied Nathan Pritikin's program for dietary modification to modulate cardiovascular risk until after his death. Given time and objective, undeniable evidence, scientific truths are ultimately borne out. In the words of Dr. Augenbrugger, "It has always been the fate of those who have illustrated the arts and sciences by their discoveries to be beset by envy, malice, hatred, destruction, and calumny."

The American Academy of Anti-Aging Medicine (A4M) is a not-for-profit medical society dedicated to the advancement of technology to detect, prevent, and treat aging related disease and to promote research into methods to retard and optimize the human aging process. A4M is also dedicated to educating physicians, scientists, and members of the public on anti-aging issues. A4M believes that the disabilities associated with normal aging are caused by physiological dysfunction which in many cases are amenable to medical treatment, such that the human lifespan can be increased, and the quality of one's life improved as one grows chronologically older. A4M seeks to disseminate information concerning innovative science and research as well as treatment modalities designed to prolong the human lifespan. Anti-Aging Medicine is based on the scientific principles of responsible medical care consistent with those of other healthcare specialties. Although A4M seeks to disseminate information on many types of medical treatments, it does not promote or endorse any specific treatment nor does it sell or endorse any commercial product.