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New Horizons for the Clinical Specialty of Anti-Aging Medicine: The Future with Biomedical Technologies

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Abstract

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. Because it embraces the utilization of biomedical technologies, anti-aging medicine offers a hopeful model of healthcare in which healthy human lifespans of 120 years and longer may be achieved — if we employ anti-aging therapeutics today, and encourage the continued expansion of biomedical technologies to prevent, treat, and cure diseases.

Keywords: anti-aging medicine; biomedical technologies; biotech; life enhancement; life extension; human lifespan

Introduction to Anti-Aging Medicine

Historian Alan Kan remarked that "The best way to predict the future is to invent it." Anti-aging medicine — its thirteen-year long history, as well as its future horizons — is a case study on future-forward innovative thinking that benefits humankind and future generations.

In 1992, a group of one dozen pioneering physicians and scientists 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, this group 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, this group 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 dysfunctions, disorders, and diseases. "Anti-aging medicine," and the American Academy of Anti-Aging Medicine (A4M), were born.

In the years that have since followed, anti-medicine has achieved international recognition. Anti-aging medicine is now practiced by thousands of physicians in private medical offices, as well as at some of the most prestigious teaching hospitals around the world.

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 human lifespan. 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. In its September-October 2001 issue, 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 -- anti-aging medicine was heralded as an effective solution to the growing aging population worldwide. In "Aging versus antiaging: Geriatrics is in trouble while antiaging medicine takes off," the World Future Society states that "geriatrics may … be suffering from competition arising in a new health-care subspecialty: antiaging."[1] 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." [1] The publication also notes the steady rise in the number of members of the A4M and certified anti-aging physicians and health practitioners, while the number of certified geriatricians is on the decline.

Similarly, the highly respected Global Aging Initiative of the Center for Strategic and International Studies issued its support of anti-aging medicine in its "Summary Report of the Co-chairmen and Findings and Recommendations of the CSIS Commission on Global Aging." Among its conclusions, the Center for Strategic and International Studies stated in its Economic Restructuring and Labor Policy section that governments should "pursue an integrated strategy designed to raise productivity by … providing financial support, and creating a favorable tax and regulatory environment for research and development in the industrial, new services and health sectors, including disease prevention, anti-aging medicine, and other innovative technology."[2]

As it has remained since 1992, the A4M is a non-profit educational medical organization dedicated to the scientific premise that diseases and disabilities of human aging are largely preventable, treatable, and perhaps even reversible. The A4M is an international body of physicians, scientists, academicians, and government- and university-affiliated officials. A4M's membership numbers 14,500 in over 78 nations worldwide. The A4M serves as an advocate for the new clinical specialty of anti-aging medical science and acts as a conduit to physicians, scientists, and the educated public who wish to benefit from the almost daily breakthroughs in biotechnology which promise both a greater quality as well as quantity of life.

Demographics of Global Aging

One of humankind's greatest achievements is the extension of the human lifespan. Since 1950, average life expectancy worldwide has increased by twenty years, to stand at 66 years.[3] Over the next fifty years, the UN projects steady increase in life expectancies for all countries, regardless of the extent of their economic development. While more developed regions experience the lowest mortality and have higher levels of life expectancy at birth than less developed regions (and lest developed countries), the gains in life expectancy will result with a worldwide life expectancy of 76.0 by the year 2050. [3]

According to the Population Reference Bureau, "the world's older population has been growing more numerous for centuries, but the pace of growth has accelerated." Observe PRB statisticians: "The global population age 65 or older was estimated at 461 million in 2004, an increase of 10.3 million just since 2003. Projections suggest that the annual net gain will continue to exceed 10 million over the next decade ─ more than 850,000 each month. In 1990, 26 nations had older populations of at least 2 million, and by 2000, older populations in 31 countries had reached the 2 million mark."[4] By 2030, the PRB predicts that "more than 60 countries will have at least 2 million people age 65 or older." [4]

Global greying is intrinsically tied to human longevity, for the demographic shift described in the preceding paragraph directly impacts the health status across the population. In short, people are living longer, and the health needs of this booming older population are now drawing much attention. All diseases fall into four categories. The first three—inherited genetic disease, infectious disease, and trauma—account for only 10% of the cost for treating all disease in most nations. Ninety percent of all healthcare dollars are spent on extraordinary care in the last two to three years of life, specifically to treat aging-related diseases. As observed by Wilmoth *et al*, whereas in the early 1900s, deaths were primarily attributable to infectious disease and sanitation-related diseases, by the late 1900s, a much different list of the leading causes of death emerged. Wilmoth and colleagues conclude from their case study of Swedish men and women dating from 1861 to 1999, that the continued upward trend in longevity in the 21st century will rely on the ability of science to "prevent and cure ailments such as coronary heart disease, stroke, and cancer."[5]

Concurrent to the longevity revolution, we are experiencing the technology revolution. New medical technologies are continually being innovated or refined such that we can improve healthcare, increase its accessibility, encourage independent living, and promote extended productivity and vitality. Emerging biotechnologies are leading the way to innovations including plentiful sources for replacement organs and tissues, interventions that help us to maintain our physical strength and mental acuity, and the end of today's incurable diseases with nanochips or genetic therapies. By embracing the adoption and utilization of technology, we foster both quantity and quality of life.

As such, anti-aging medicine has become the focal point of the new biotechnological revolution: anti-aging medical technologies have the potential to halt the degenerative physiology we now call "normal human aging." In the following section, we present a timeline of key anti-aging biotechnologies making recent headlines.

Anti-Aging Biotech in the Headlines

In the realm of clinical anti-aging medicine, there are four key biotechnologies with near-term implications for the extension of the healthy human lifespan, namely:

- *Regenerative medicine,* innovations to regrow damaged or diseased tissues and organs
- *Stem cells,* technology to permit development of a supply source for human cells, tissues, and organs for use in acute emergency care as well as treatment of chronic, debilitating disease
- *Genetic engineering,* advancements that allow scientists to alter genetic make-up to eradicate disease
- *Nanotechnology,* enabling scientists to use tiny tools to manipulate human biology at its most basic levels

With regard to these aforementioned biotechnologies, newsworthy advancements have included:

- Immature neural stem cells were induced to mature into adult brain cells. This new technique, conducted by the McKnight Brain Institute, successfully replicates the actual process of brain cell maturation with such precision as never before accomplished. Lead researcher Dr. Bjorn Scheffler commented that "We can basically take these cells and freeze them until we need them. Then we thaw them, begin a cell-generating process, and produce a ton of new neurons." This advancement has tremendous potential for neurodegenerative dieseases, such as Parkinson's Disease and Huntington's Disease, in that regeneration of parts of the brain will soon be possible. . (Scheffler *et al*, *Proc National Acad Sci*, June 14, 2005)[6]
- A Japanese woman was cured of diabetes via a donor transplant of insulin-producing islet cells from her mother; no rejection occurred. (Matsumoto *et al*; *The Lancet*, May 2005)[7]
- In the latest follow-up of 8 Alzheimer's patients in whom injections of genetically modified tissue designed to boost nerve growth factor (NGF) took place in 2001 and 2002, researchers report that in 6 of the 8 patients, the implants "have successfully slowed their disease." Memory tests suggest that gene therapy slowed cognitive decline by as much has 50%, and brain scans showed that the patients' brains were more active than before. In addition, and most interestingly, in the one patient that died (hemorrhaged during the operation), a post-mortem found that "some of the brain tissue that had been dying off as result of AD had started to rejuvenate" — with tissue regeneration located precisely surrounding the site of the injected cells). (Tuszynski *et al*, *Nature Medicine*, June 2005)[8]
- Clemson University scientists have modified ink-jet printers to deposit a "bio ink" of cells, growth factors, and degradable gel (acts as scaffold for growth) to form 3D tubes of living tissue. With the current research now focused on incorporating functional blood vessels into organs as they are "printed," future prospects include the large-scale mass production of organs such as human hearts, livers, kidneys, and other organs, along with the essential nutrients they need to survive. (Xu *et al*, *Biomaterials*, May 2005)[9]
- Researchers from University of South Florida found that stem cells from human umbilical cord blood reduced heart attack damage in rats. Injected directly into rats' hearts after suffering induced heart attacks, the stem cells greatly reduced the amount of heart damage and restored heart pumping function to near normal. Drugs were not needed to prevent rejection. Predicts Dr. Robert Henning, lead researcher: "Umbilical cord blood stem cells could offer a new way to limit or repair heart attack damage in people." (Henning *et al*, *Cell Transplantation*, January 2005)[10]
- At the Hospital de Egas Moniz (Lisbon, Portugal), doctors have performed a total of 41 procedures in which tissue from a patient's nasal cavity — rich in stem cells — were implanted in the spinal cord at the site of injury causing the paralysis. Dr. Carlos Lima and colleagues report that 10% of patients now able to walk, and all patients have reported some degree of increased feeling in paralyzed limbs since their surgery. No infections or deaths were reported.[11]
- Dr. Seung Kim and colleagues at Stamford University coaxed immature brain cells to develop into insulin-producing islet cells that are lacking in diabetes. They added a "cocktail" of brain chemicals to brain stem cells, thereby coaxing them to become ones that were able to produce insulin in response to blood sugar levels. Transplants of modified stem cells into kidneys in mice were found to release insulin in response to rising blood sugar levels. After 4 weeks, the cells remained alive and continued to produce insulin, and none had turned cancerous (Hori *et al*, *PloS Medicine*, April 2005).[12]

- Dr. Woo Suk Hwang and colleagues from Seoul National University, who cloned the first human embryo to use for research, report they have used the same technology to create batches of embryonic stem cells from 9 patients (6 adults and 3 children, with spinal cord injuries, juvenile diabetes, and a rare immune disorder). Their work demonstrates that ESCs "can be derived using nuclear transfer from patients with illness, regardless of sex or age." It also shows that it is possible to provides a source for tailored tissue to cure various diseases, in that stem cells can now be matched to patients and their medical conditions.[13]
- Dr. Alison Murdoch and colleagues from Newcastle University (UK) cloned the country's first human embryo. In their study, 3 clones survived and grew in the lab for 3 days, 1 clone survived for 5 days. In Great Britain, therapeutic cloning is allowed, where there is also a non-binding ban on human cloning; supporters of therapeutic cloning point to its potential future applications in fighting disease. (Reported in *Reproductive & BioMedicine Online*, May 2005)[14]
- RNA interference (RNAi) is a technology for silencing genes gone awry: scientists correct defective RNA splices that, when expressed, cause disease. It is estimated that about 30% of all human genetic diseases involve RNA splicing errors, and other diseases, such as cancer, involve defective genes that may be targeted and silenced through RNAi. Dr. Norbert Perrimon and colleagues at Harvard University attached modified RNA molecules to an altered cholesterol molecule readily absorbed by cells. The modified RNA-carrying cells cut total cholesterol levels by 37%. (Wohlbold *et al*, *Leukemia*, May 2005)[15]

The Arrival at Practical Immortality

To summarize the importance of the above profiled biotechnological advancements in medicine, we cite the speculations produced in a study of the next fifty years of cardiology, released by the American College of Cardiology at its annual meeting of 2000. Their prediction:

> 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.[16]

The value of biotechnology and its application to human health and longevity has been well stated by the Board of Editors of *Scientific American*. In the magazine's March 2001 issue, the editors remark that "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."[17]

Dr. Jim Oeppen of Cambridge University (United Kingdom) and Dr. James Vaupel of the Max Planck Institute for Demographic Research (Germany) have observed that maximum life expectancy has risen by a quarter of a year, each year, for the past 160 years. Commenting on their demographic analysis, Drs. Oeppen and Vaupel remarked, "If life expectancy were close to a maximum, then the increase in the record expectation of life should be slowing. *It is not*."[18]

Indeed, practical immortality — healthy human lifespans of 120 years and longer — may be achieved if we employ anti-aging therapeutics today, and encourage the continued expansion of biomedical technologies to prevent, treat, and cure diseases. Medical knowledge and technology doubles every 3.5 years, and gains in human longevity are directly proportional to the cumulative sum of advancements in the biotech fields.

Innovative Vision of the Future of Medicine

As this paper presents, we are amidst an exciting period in the accelerating biotech revolution. In order to effectively deliver the biomedical and biotechnological advancements that comprise the anti-aging medical clinical specialty to patients, it is therefore necessary to establish a premier, world class facility at which pioneering discoveries in clinical and research objectives in life enhancement and life extension may be freely pursued by leading anti-aging scientists and physicians in the field.

The World Center for Anti-Aging Medicine in an innovative vision of the future of medicine. The World Research Center functions as a world-class, university affiliated research and treatment facility unique in its focus on the investigation and application of diagnostic and treatment protocols that extend the length, and enhance the quality, of the human lifespan. Researchers yielding discoveries that will revolutionize the very early detection, treatment, and rejuvenation of aging-related disorders will work alongside clinicians delivering multi-therapeutic interventions designed to slow, stop, and/or reverse the process of human aging. As a test-bed for the most promising and innovative biotechnological advancements pertaining to aging intervention, the World Research Center will be the undisputed pinnacle of cutting-edge medicine.

The World Center for Anti-Aging Medicine features state-of-the-art clinical applications for diagnostics:

- Assessment of Biomarkers of Aging: various technologies to ascertain "biological age" — the performance of the body's cells, tissues, and organs
- Early detection of cancers and infectious disease, some of the most costly and burdensome illnesses today

As well as technologically advanced therapeutics such as:

- Bio-Identical Hormone Replacement Therapy (BHRT), aimed at arresting age-related declines in hormone levels such that the natural peaks achieved in youth are maintained through life
- Dietary supplementation, to improve or maintain peak physical performance and mental acuity as we age
- Natural detoxification, to cleanse toxins from the body
- Intravenous chelation, to remove heavy metals from the body
- Aesthetic procedures, including Botox® injections, cosmetic fillers, dermabrasion, and mesotherapy, to reverse the physical signs of aging
- Hyperbaric oxygen therapy, to promote oxygen levels available to tissues and retard premature cellular death
- Immune restoration, including reversal therapies for stimulation of the thymus gland, which becomes involuted as we age and thereby contributes to a weakening of the immune system
- Stem cell therapeutics: to replace cells in the skin, organs, sex glands, immune system, blood-forming system, muscles, and other systems, that decline due to age-related changes and thereby progressively weaken such cells and cause cell death
- DNA breakdown repair: gene therapies, along with DNA and RNA repair techniques, to counteract the otherwise immutable onset of aging-related diseases
- Sports medicine rehabilitation, spinal and musculoskeletal rehabilitation, and physical therapy, to counteract the cumulative wear-and-tear on muscles and bone as we age
- High-tech surgical robotics, employed for invasive therapies to reduce human errors and enhance post-surgical recovery

Combined, this multi-disciplinary approach towards multi-modal medical care will yield invaluable insights and permit the deployment of the latest interventions to slow — and even stop, and quite possibly, reverse — aging.

Concluding Remarks

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%.[19]

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. [19]

With a worldwide life expectancy now standing at 78.59 years (weighted average),[20] and a projected world population exceeding 9 billion by the year 2050,[21] the field of anti-aging medicine is witnessing unprecedented growth and acceptance. 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 human lifespan. 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 phrase "anti-aging" is, as such,

a euphemism for the application of advanced biomedical technologies focused on the early detection, prevention, and treatment of aging-related disease. Anti-aging medicine is:

- *Scientific.* Anti-aging diagnostic and treatment practices are supported by scientific evidence and therefore cannot be branded as anecdotal.
- *Evidence-based.* Anti-aging medicine is based on an orderly process for acquiring data in order to formulate a scientific and objective assessment upon which effective treatment is assigned.
- *Holistic.* Anti-aging medicine utilizes an organized framework for the head-to-toe diagnostic assessment, and subsequent design of a treatment regimen.
- *Synergistic.* Anti-aging medicine recognizes that oftentimes, a multi-modal, multi-therapeutic approach (including nutritional supplements) may deliver greater rejuvenative effects than by administering single therapies alone.
- *Well-documented* by peer-reviewed journals including *Aging, American Journal of Cardiology, Journal of the American Geriatrics Society, Journal of the American Medical Association, Lancet,* and many others.

Anti-aging medicine unites physicians and scientists from around the world to forge a model for clinical healthcare that advances life enhancing, life extending technologies. As the founding organization in the world's fastest growing medical specialty, the American Academy of Anti-Aging Medicine (A4M) is committed to the pursuit of excellence in all aspects of leadership in the anti-aging medical field that it provides to 14,500 members in 78 nations around the world. The flagship World Center for Anti-Aging Medicine serves as a microcosm for a hopeful, helpful vision of life enhancing, life extending clinical healthcare and medical research that creates a better world for every man, woman, and child. We welcome your participation in this project, which will directly and indirectly improve the lives of hundreds of thousands of people around the globe.

References

1. Wagner C. Aging versus antiaging: Geriatrics is in trouble while antiaging medicine takes off, *The Futurist,* September-October 2001, 8-9.
2. Summary Report of the Co-chairmen and Findings and Recommendations of the CSIS Commission on Global Aging," August 29, 2001. Washington, DC: Global Aging Initiative, Center for Strategic and International Studies.
3. World Population Prospects: The 2000 Revision--Highlights (ESA/P/WP.165), Population Division, Department of Economic and Social Affairs, United Nations, 28 February 2001.
4. Kinsella K and Phillips DR, Global Aging: The Challenge of Success, *Population Bulletin* 60, no. 1 (Washington, DC: Population Reference Bureau, 2005).
5. Wilmoth JR, Deegan LJ, Lundstrom H, Horiuchi S. Increase of maximum lifespan in Sweden, 1861-1999, Science, Sept. 29, 2000.
6. "Brain cells are matured in lab," BBCNews.com, June 14, 2005.
7. Matsumoto S, Okitsu T, Iwanaga Y, Noguchi H, Nagata H, Yonekawa Y, Yamada Y, Fukuda K, Tsukiyama K, Suzuki H, Kawasaki Y, Shimodaira M, Matsuoka K, Shibata T, Kasai Y, Maekawa T, Shapiro J, Tanaka K. Insulin independence after living-donor distal pancreatectomy and islet allotransplantation. Lancet. 2005 May 7;365(9471):1642-4.
8. Tuszynski MH, Thal L, Pay M, Salmon DP, U HS, Bakay R, Patel P, Blesch A, Vahlsing HL, Ho G, Tong G, Potkin SG, Fallon J, Hansen L, Mufson EJ, Kordower JH, Gall C, Conner J. A phase 1 clinical trial of nerve growth factor gene therapy for Alzheimer disease. Nat Med. 2005 Jun;11(6):551-5. Epub 2005 Apr 24.
9. Xu T, Jin J, Gregory C, Hickman JJ, Boland T. Inkjet printing of viable mammalian cells. Biomaterials 26 93-99 (2005).
10. Henning RJ, Abu-Ali H, Balis JU, Morgan MB, Willing AE, Sanberg PR. Human umbilical cord blood mononuclear cells for the treatment of acute myocardial infarction. Cell Transplant. 2004;13(7-8):729-39.
11. "Experimental Portuguese stem cell procedure offers hope to paralyzed," Agence France-Presse, Feb. 7, 2005.
12. Hori Y, Gu X, Xie X, Kim SK. Differentiation of Insulin-Producing Cells from Human Neural Progenitor Cells. PLoS Med. 2005 Apr;2(4):e103. Epub 2005 Apr 26.
13. "Scientists clone human stem cells from patients," Reuters, May 20, 2005.
14. "UK scientists clone human embryo," BBC News, May 20, 2005.
15. Wohlbold L, van der Kuip H, Moehring A, Granot G, Oren M, Vornlocher HP, Aulitzky WE. All common p210 and p190 Bcr-abl variants can be targeted by RNA interference. Leukemia 19, 290-292 (01 Feb 2005) Correspondence
16. Raeburn R, "Oh, so you have a pig's heart too," *Business Week*, March 27, 2000.
17. Board of Editors, "The Future of Human Evolution," *Scientific American*, March 2001.
18. Oeppen J and Vaupel J, "Broken Limits to Life Expectancy," *Science*, May 10, 2002, 296 (5570), pp. 1029-103.
19. World Health Organization's Ageing & Health, www.who.int/ageing/scope.html; accessed Oct 18, 2000.
20. CIA World Factbook, March 2005.
21. World Population 1950 to 2050. US Census Bureau, International Data Base, April 2005.