

Antiaging Therapy: A Boom in Sustaining Human Quest for Youth

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Antiaging therapy, a recent medical discipline, aims high quality of health for people in second half of their lives. Advocates of antiaging therapy claim that it is now possible to slow or reverse aging through medical and scientific interventions. Preventive measures make up an important part of antiaging program. Careful adherence to nutrition, hormonal and cell based therapies, genetic manipulations, other medications and supplements can increase one's chances of living a healthy life.

Key words: Aging, antiaging, caloric restriction, antioxidant

People have been searching for the fountain of youth for ages. The lure of advertisements for antiaging products can be hard to resist. But researchers have learned that aging is an intricate, complex process that involves many areas of our body (<http://www.mayoclinic.com>; accessed 15 Jul. 2005). Many people have seen aging as a time of cognitive and physical decline. For past three decades most scientists and the general public have accepted this negative age-stereotype as the norm, but fortunately this view is now challenged. New findings show that well-being and a positive view of aging are major protective factors against the effects of age on the organism¹. This forms the basis of antiaging.

Antiaging refers exclusively to slowing, preventing or reversing the aging process (<http://www.longevitymemo.org>; accessed 20 Jul. 2005). Antiaging medicine seeks strategies in order to maintain a high quality of health for people in second half of their lives i.e., without chronic damage to their health². The development of specific antiaging treatment and the emergence of the practice of antiaging medicine have created new ethical and legal issues. Current therapies carry many doubts about their safety and effectiveness, which makes the practice of antiaging medicine with the prescription of these therapies a challenging issue from both a legal and ethical perspective³. Age management programs including use of growth hormone, other medications and supplements are widely reported for the treatment of aging⁴. Following

antiaging strategies as estimated by the World Health Organization, the percentage of people aged over 85 will increase dramatically from the year 2010 on. In the light of these data, antiaging medicine or preventive medicine can no longer be neglected².

MEMOIRS

As we are celebrating 21st century, it would be fun and interesting to trace the history of reversing the effects of aging. The new buzz word for 21st century may be antiaging but the concept of stopping the clock; living forever is far from new. Human quest for youth begins from ancient times and continues from the twentieth century until today. Prescientific beliefs were governed by animistic forms of thoughts leading to attempts to control aging, disease and death through magic and supernatural agencies⁵. Ebers papyrus (one of oldest known medical works from ancient Egypt) recommended suggestion for ingesting internal organs of young animals. *Shushruta Samhita* described a mountain plant *Soma* for altering mental functioning caused by aging. The concept of restorative waters of the pool of youth, healing waters, rejuvenation by injection of fluids and processed sex glands of young animals, all emphasize the human quest for youth⁶.

THE COMPLEX INTRICATE PROCESS OF AGING

Scientists believe that random damage which occurs within cells and among extra cellular molecules are responsible for many of the age-related changes that are observed in

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organisms⁷. Body reaches peak efficiency at the age of 30. Taking 30 as reflective of 100% performance, the pumping efficiency of heart is reduced by 20% when person reaches the age of 55. Kidney function is reduced to about 25% at 55 y of age. Maximum breathing capacity declines by about 40% by 55 and 60% by 75 y. Basal metabolism rate goes down by about 10% (<http://www.therubins.com>; accessed 28 Jul. 2005). Hair pigmentation dilution results primarily from a reduction in tyrosinase activity resulting true gray and white hair⁸. Human aging is associated with declining activity of growth hormone and changes in body composition, function and metabolism⁹. Aging imparts a variety of physiologic changes in the oropharynx, esophagus and stomach. It increases the risk for esophageal and gastrointestinal disorders¹⁰. The aging immune system is characterized by the progressive decline in the antibody and T-cell mediated responses to antigen¹¹. Age-related impairment of hearing, vision and smell is due to both decreased efficacy of the parts of brain concerned and disorders of sensory receptors. Unsaturated fatty acids especially omega 3 fatty acid and alpha-linoleic acid (major component of omega 3) play a major role¹².

No genetic instructions are required to age^{7,12}. Although genes certainly influence longevity determination, the process of aging is not genetically programmed. Studies in lower animals have led to view that genes are involved in aging¹³. However these genes have never produced a reversal or arrest of inexorable increase in mortality rate, which is one important hallmark of aging. From this perspective longevity determination is under genetic control only indirectly¹⁴.

Longevity research does provide many theories. Theories of aging are almost as old as human civilization. Philosophers argue that one is born with predetermined amounts of vital substance. Once that vital substance is consumed in course of living, we die. Two broad views exist today, one group of theories argues that aging results from random or stochastic events- unpredictable insults from environment or from day-to-day metabolic processes. Other group sees aging as a result of programmed or non-stochastic events (<http://www.infoaging.org>; accessed 10 Aug. 2005). Major theories of aging as a consequence of random events are described below

Cross-linking theory of aging:

Based on the observation that with age, our proteins, DNA and other structural molecules develop

inappropriate attachments or cross links to one another. Researchers speculate that when brain tissue from young animals is treated with cross-link inducing compounds brain tissue soon looked quite similar to older brain tissue¹⁵.

Wear and tear theory of aging:

It suggests that years of damage to cells, tissues and organs eventually wears them out, killing them and then the body. Telomerase, the cap of DNA shortens with each cell division and reaches critical short length such that cells no longer divide but become senescent¹⁶. Increased cortisol levels in circulation¹⁷ also prove this theory.

Free radical theory of aging:

Free radicals cause DNA damage, cross linking of proteins¹⁸ and formation of age-pigments¹⁹. They cause much irreversible damage^{20,21}. Mitochondria also suffer damage, which accumulates and is responsible for derangement of energy production and thus aging²².

Somatic mutation theory of aging:

Most of somatic mutations will be corrected and eliminated but some will not. Those will accumulate eventually causing cell to malfunction and die (<http://www.nia.nih.gov/health/pubs/secrets-of-antiaging/p6.htm>; accessed 14 Aug. 2005). Many scientists believe that mitochondrial aging is important contributor to aging²³. Theories of aging based on programmed events include;

The pacemaker theory of aging:

It is based on the notion of biological clocks. The two bodily systems most often suggested, as biological clocks are neuroendocrine system and the immune system¹¹. These systems are set at birth to run for specified period of time.

Genetic theory of aging:

Life span determined by genes we inherit are called as longevity assurance genes. It includes gene for a protein called apolipoprotein E and certain versions of gene for immune proteins²⁴. Long life is tied to three genes-CETP, apo C-III and APM 1 (<http://anti-ageing.us/2005/03/long-life-tied-to-3-genes.htm>; accessed 16 Aug. 2005). Verification of all these above theories is based on survival, mortality curves, biomarkers of aging and batteries of biological age²⁵.

Biological markers of aging:

Biological markers are measurable indicators of aging in living organisms²⁶. Potential biomarkers that are

applicable to human aging include *in vitro* proliferative capacity of fibroblast, glycation of collagen and DNA unwinding rate²⁷.

ANTIAGING THERAPY

Today antiaging therapy is one of the fastest growing segments of medicine. It is a combination of different therapies used to slow and reverse human aging. The methods show scientific promise in slowing the aging process and extending the lifespan in mammals.

Factors involved with antiaging therapy:

Fig. 1 represents the antiaging pyramid illustrating the various factors involved with antiaging medicine (<http://www.genmedsys.com>; accessed 17 Aug. 2005). At the base of the pyramid are antioxidants. At the cellular level, antioxidants serve to deactivate certain free radicals in turn helping to decrease inflammation²⁸. The best sources for antioxidants are fruits and vegetables. Vitamins, minerals used therapeutically, can be of immense help in fighting diseases and spreading recovery. This is the cornerstone of antiaging program. As one gets older one's ability to absorb many vitamins and minerals drop considerably. The problem is compounded in people who eat poorly, drink alcohol, smoke and take some prescription medications (<http://www.peacefulmind.com>; accessed 16 Aug. 2005). Youthful hormone levels preserve vigor and stave off degenerative diseases. Major hormones that decrease with aging are human growth hormone (hGH), dehydroepiandrosterone (DHEA), testosterone²⁹, estrogen, progesterone and melatonin³⁰. Aging precipitates progressive decline in overall cognitive function. It causes loss of ability to store and retrieve from short-term memory and to learn new

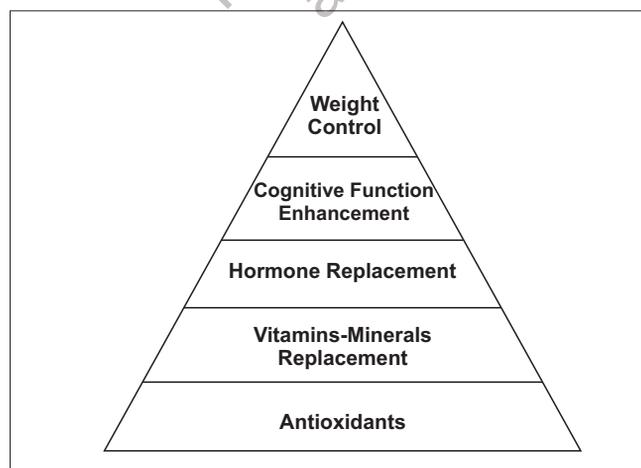


Figure 1: Antiaging pyramid

informations. Potent brain boosting nutrients include antioxidants, pharmacological, nutritional supplements and memory-enhancing nutrients like *Gingko biloba*, acetyl carnitine and vinpocetine. The percentage of adults who are obese has been rising for a decade. Antiaging efforts without weight control are irrational (<http://www.peacefulmind.com>; accessed 16 Aug. 2005).

ANTIAGING ENEMIES

Increased sugar level in blood results in formation of C reactive proteins (CRP) since its level in body strongly influenced by diet. Body makes CRP from interleukin-6, a powerful inflammatory chemical. High CRP levels are turned up in people who are overweight³¹. Staying away from sugar and high-glycemic (simple) carbohydrates, which the body rapidly converts to sugar, is one of the best ways to decrease inflammation. Excessive dietary intake of saturated fats can significantly raise the blood cholesterol level, especially the level of low density lipoproteins or bad cholesterol. Guidelines issued by National Cholesterol Education Program (NCEP) recommend that the daily intake of saturated fats should be kept below 10% of total caloric intake. Intervention strategies have generally focused on lowering bad cholesterol³². Excess sun exposure without a sunscreen can damage skin by starting inflammation process, a significant factor contributing to aging³³. This inflammation is due to free radicals, which produce oxidative stress that damages cell membranes³⁴. Hypertension eventually leads damage to heart, arteries, kidneys and other organs. Alcohol stimulates the inflammatory process within body. Intake of alcohol should be in moderation. High cholesterol levels are detrimental. Increased high density lipoprotein levels prove to be a negative predictor of premature coronary heart disease and a potential antiatherogenic agent. A cardiovascular workout is imperative in order to maintain weight and oxygenation of red blood cells³¹. No supplements can counter-act the negative effects of smoking on health and longevity. Abstinence from smoking is the best.

MAJOR CATEGORIES OF ANTIAGING STRATEGIES: CURRENT ASPECTS

Today's researchers are exploring caloric restriction, cell-based therapies, hormonal therapies and genetic manipulation. So far, caloric restriction has the soundest basis and estrogen replacement is among the interventions most commonly used (<http://www.antiagingny.com>; accessed 9 Sept. 2005).

Caloric restriction:

Caloric Restriction (CR), i.e., under nutrition without malnutrition, remains the only experimental paradigm that has been shown consistently to extend lifespan and slow aging in short-lived species. Intramural Research Program of the National Institute on Aging began a study of CR in nonhuman primates. Emerging data's strongly support physiological responses to CR³⁵. The possible biological mechanisms that underlie antiaging action include attenuation of oxidative damage, modulation of glycemia, insulinemia and hormesis³⁶. Caloric restriction may slow down many age-dependent processes and extend life span. Recent evidence has shown that autophagy is involved in aging. CR prevents the age-dependent decline of autophagic proteolysis³⁷. Dietary restriction was found to delay the onset of age-related neoplastic diseases³⁸. One of the working hypotheses is that dietary restriction alters nervous and/or endocrine functions that influence the characteristics of fuel use; this modulation in fuel-use characteristics is proposed to retard the aging process³⁹. Leptin signaling is a substantial pathway involved in antieffects of CR⁴⁰.

Cell-based therapies:

Cell transplantation continued throughout 20th century. Clinical trials are investigating the effects of differentiated cells such as adrenal cells as auto or allotransplants into the brains of patients with Parkinson's. The recent identification of preneuronal stem cells in primates has raised hope of restoring neurologic function in conditions ranging from paralysis to dementia (<http://www.hosprract.com>; accessed 20 Aug. 2005). Stem cells are programmed cells in the human body that can continue dividing forever and change into other types of cells. They have the potential to treat many diseases including Parkinson's, Alzheimer's⁴¹, diabetes⁴² and cancer. Additionally, the scientific methodology known as therapeutic cloning has come under attack. US has attempted to push for a global ban on the therapeutic cloning, fortunately this initiative was defeated in late 2004 (<http://www.longevitymemo.org>; accessed 20 Jul. 2005).

Hormone therapy:

Numerous hormonal changes occur during human aging. Andropause, the age-related decline of testosterone production is an area of ongoing research. Production of many other hormones including growth hormone decreases with aging too. Growth hormone replacement therapy has been approved by FDA (<http://www.usdoctor.com>; accessed 2 Sept. 2005). Replacement therapy has resulted in improved muscle/fat ratio,

increased lipolysis, bone density changes and improved exercise capacity (<http://www.maxsportsmag.com>; accessed 8 Sept. 2005). Melatonin an antistress agent is a chronobiotic with antiaging properties. Melatonin replacement also proves to be an effective antiaging strategy³⁰. Dehydroepiandrosterone (DHEA) replacement therapy has attracted considerable attention over recent years. DHEA deficiency includes effects on well-being, energy levels, mood and libido. DHEA exert its action via downstream metabolism to sex steroids⁴³. In contrast to other hormones of aging circulating level of insulin increase in individuals as they age. This occurs because the tissues that respond to insulin to lower blood sugar levels become resistant to its action. This lead pancreas to secrete more and more insulin resulting 'pseudo-diabetes of aging'. Replacing estradiol, testosterone, growth hormone and reducing cortisol-raising stress are strategies employed to maintain insulin sensitivity (<http://www.antiagingny.com>; accessed 9 Sept. 2005).

Genetic manipulations:

Ribonucleic acid (RNA) based research is directed at damaged nucleic acid. The cosmetic industry is already marketing skin preparations supplemented with RNA in hope of restoring the RNA content of aged skin. Deoxyribonucleic acid (DNA) based research is directed partly at genes and partly at other chromosomal features such as telomeres, which may serve as a biologic clock. More than 60 genes seem to be involved in aging have been identified. A recent discovery of p21 gene may regulate other genes affecting aging (<http://www.hosprract.com>; accessed 20 Aug. 2005).

Other strategies:

A strategy for Engineered Negligible Senescence (SENS) is a detailed plan for curing human aging. The key to SENS is appreciation that aging is best viewed as a set of progressive changes in body composition at the molecular and cellular level, caused as side effects of essential metabolic processes. SENS strategy does not interfere with metabolism but to repair or obviate the accumulating damage. Senescence marker protein-30 (SMP-30) has been proposed as an important aging marker shown to blunt death caused by intracellular Ca²⁺ accumulation (<http://www.gen.com>; accessed 10 Sept. 2005). Free radicals aid in development of atherosclerosis and many other degenerative diseases of aging. Chelation therapy can bring profound improvement to many essential metabolic and physiologic functions of the body (<http://www.antiagingny.com>; accessed 11 Sept. 2005). Medical Massage Therapy is therapeutic bodywork delivered in a

TABLE 1: ANTIAGING SUPPLEMENTS: THE MAJOR PLAYERS

	Functions	Research finding	Possible side effects
Vitamin A (Retinol)	Antioxidant needed for vision, bone development, reproduction and immune function	Enhances learning, memory, and immune system function.	Headache, fatigue, joint pain
Vitamin C (Ascorbic acid)	Antioxidant needed for growth and repair of connective tissue, bone and teeth	Protects against cancer, enhances immune system function	Diarrhea, headache, redness of skin
Beta-carotene	Antioxidant	Deficiency linked to heart disease	Increased risk of lung cancer
Selenium	Antioxidant	Protects against cancer and AIDS-related illnesses	Irritability, fatigue, nerve damage, GI upset
Coenzyme Q 10	Antioxidant, protects against reperfusion damage, congestive heart failure, muscular dystrophy	Protects against cancer and gum disease	Serious allergic reactions, mild GI discomfort
Estrogen	Improves bone mineral density and lipid profile, promotes vaginal epithelial growth and lubrication	Enhances cognition	Increased risk of breast and other cancers, gall bladder disease, thromboembolism
Testosterone	Improves bone mineral density, stimulates libido, increases red cell mass and strength	Increase lean muscle mass and bone density, enhances cognition	Hepatic toxicity, polycythemia, impotence

medical setting and effective treatment for a number of conditions like sprain, osteoarthritis, neck pain and insomnia (<http://www.antiaginggroup.com>; accessed 12 Sept. 2005). ProCyte Corporation has come up with a new patented technology for antiaging skin care. Its Neova™ copper peptide therapy utilizes collagen and elastin promoting capabilities of copper to revive dull, lifeless skin, remedy fine lines, wrinkles, restore moisture and firmness (<http://www.skincancerx.com>; accessed Sept. 2005).

ANTIAGING SUPPLEMENTS: THE MAJOR PLAYERS

The current antiaging supplements used today are listed in Table 1 (<http://www.mayoclinic.com>; accessed 15 Jul. 2005).

Ethical assessment of antiaging therapy:

Four ethical arguments in favor of anti aging medicine are beneficence, efficiency, limited autonomy and improved quality of life⁴⁴.

Tips for antiaging:

Tips for antiaging given by the Harvard study of adult development translating into a happy and healthy longevity include, avoiding cigarettes, keeping a healthy weight, wearing sunscreen, proper diet, regular exercises, developing good adjustment and coping skills, maintaining strong social relationships, reduced anxiety, laughter the best medicine, and pursuing education (<http://www.peacefulmind.com>; accessed 16 Aug. 2005).

CONCLUSIONS

Since recorded history, individuals have been, and are continuing to be victimized by promises of extended youth or increased longevity by using unproven methods that allegedly slow, stop or reverse aging. Research in genetic engineering, stem cells, geriatric medicine, and therapeutic pharmaceuticals hold promise for postponement of age-related diseases and extension of the period of healthy life.

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