

Anti-aging medicine

I recently returned from a meeting of the American Academy of Anti-Aging Medicine (AAM) where I delivered a paper entitled "Endocrine Aspects of Aging." Here, I will share with you some of the high points of this most interesting conference.—Dr. Hoffman

There is no question that the horizons of longevity have already been extended. This has come about largely through the efforts not of doctors but of plumbers. By this I mean that improvements in sanitation over the past few centuries have vastly reduced the incidence of infectious diseases that used to dispatch many individuals in the prime of life. The average life span of people during the Middle Ages in Europe was around 40 years. Today, it is around 75 years. According to *Scientific American* magazine, "the centenarian population grew by 160 percent in the U.S. during the 1980s. Many demographers predict that 20 million to 40 million people will be aged 85 or older in the year 2040, and 500,000 to four million will be centenarians in 2050. The economic burden of caring for people older than 85 could be vast, especially if a huge percentage of them need special care."

The concern, of course, is that while longevity has been extended, quality of life, by and large, has not. Far too many Americans are living well beyond the medieval life expectancy only to encounter decades of chronic pain, immobilization, mental deterioration and prescription drug dependency.

The approach to life extension has been, until lately, one of targeting the major killer diseases for eradication. Thus the search for hi-tech approaches to heart disease and cancer have dominated the arena of medical research, consuming billions annually. At first, this may seem a logical way of promoting longevity, but biostatisticians have pinpointed a remarkable fact: Even as dramatic an innovation as a universally

successful cancer cure would have a minimal impact on life span. Remarkably, eliminating cancer as a cause of death would extend the average longevity by a mere 2 years!

Evidently, the conclusion to be drawn is that it is not disease but the aging process itself that is responsible for the death of most Americans. Yet the National Institutes of Health allocate to cancer research twenty times the amount of money that they allocate to anti-aging research. A rebalancing of national priorities is clearly in order.

Perhaps part of the problem is a lack of rational resolve. Policy-makers in this area lack a clear vision of what enhanced longevity might bring. Perhaps they fear that active promotion of anti-aging research might threaten the fabric of society by creating a huge elderly population, sustained only via expensive technological support, inundating Social Security and Medicare, and devastating pension programs. A vast army of disabled and senescent oldsters would prove an unacceptable burden to 21st century America.

While partly justified, fears of this scenario may be exaggerated. First, our approach to longevity need not prioritize just numerical survival; it also must emphasize quality aging. Languishing for years on sophisticated life-support systems in the critical care unit of the hospital of the future just does not constitute acceptable life extension.

Secondly, the anti-aging movement, while embracing sophisticated high-tech innovations, aligns itself mostly with economical lifestyle modifications such as diet, exercise, modest stress reduction and the use of anti-aging "nutraceuticals." Drugs and hormone therapies are envisioned as low-cost interventions to forestall more costly medical and surgical catastrophes.

Finally, research suggests that if critical barriers to longevity are removed, older individuals can remain healthy

and unencumbered by serious debility well past ninety, until they naturally “drop off the end of the aging curve.” There is evidence that the incidence of medically costly and debilitating illness actually decreases once an individual surpasses certain key aging milestones. According to Thomas T. Perls, M.D., a geriatrician at Harvard: “People in their late nineties or older are often healthier and more robust than those 20 years younger. Traditional views of aging may need rethinking.”

What actually is aging? Here, a distinction must be made between chronological and biological aging. A person’s age in years correlates only roughly with the rate at which his or her bodily systems age. In the rare hereditary medical condition argyria, for example, aging is markedly accelerated, to the point where children afflicted with the disease take on the appearance of elderly dwarves.

Conversely, others seem to cheat Father Time by maintaining youthful appearance and vitality well into their mature years.

Consequently, anti-aging researchers have proposed a series of “biomarkers” to better delineate the aging process. A few of these appear below:

- Muscle mass
- Muscle strength
- Post-exercise time
- Reflex speed
- Joint mobility
- Breathing capacity
- Endurance
- Short-term memory
- Problem-solving skills
- Balance
- Liver function
- Skin elasticity
- Wound healing capability

- Hormone levels
- Sleep quality
- Immune function
- Cancer markers
- Free radical defenses
- Fat to lean ratio
- Glucose/insulin tolerance
- Lipid profile
- Susceptibility to blood clots

No doubt, other biomarkers may merit inclusion in this list. The routine preventive physical exam of the future may derive more relevance from a biological age assessment based on such objective parameters. The technology is already here.

Several scientific theories attempt to explain the aging process and provide insights into how we might retard it. Among the most popular is the Free Radical Theory of Aging, first promulgated by Denham Harmon. This concept has recently gained influence from an ingenious experiment comparing fruit flies with or without bioengineered adoptive antioxidant protection: the free radical-shielded flies lived up to 20 percent longer and remained physically active far longer into old age. The implication for humans is that, via consumption of antioxidant-rich supplements or foods, aging can be delayed.

Indeed, lifestyle influences have been linked to a variety of disease processes that curtail longevity. Smoking, poor diet, excessive (but not moderate) alcohol consumption, illegal drug use, unsafe sex, reckless driving, exposure to environmental and occupational pollutants, and firearms hasten the demise of many Americans who should otherwise reach an advanced age. Therefore, a rational approach to life extension is predicted on fundamental lifestyle intervention.

Another mechanism of aging is via a process called "protein cross-linking." A simple analogy is the way foods "brown"

while baking: heat induces changes in protein structure called cross-links, which render the food cooked. Similarly, in biological systems, the aging process results in a steady accumulation of dysfunctional cross-linked proteins, culminating in deterioration and death. Ingenious strategies are being investigated that slow the cross-linking cascade.

Other theories hold that human aging results from fundamental changes in immune function. Immune surveillance declines with age, resulting in greater susceptibility to cancer, infectious disease and autoimmune conditions. Administration of thymic extracts or specifically bioengineered monoclonal antibodies might help buttress a flagging immune function.

Maladaptive reactions to stress also have been shown to accelerate the aging process. They do so by increasing the production of catecholamines, stress hormones that include adrenaline, the well-known "fight-or-flight" hormone. Elevated levels of catecholamines have been shown to impair immunity, promote high blood pressure, diabetes and heart disease as well as to impair memory and worsen allergic diseases. Most individuals who survive into their 80s or 90s embody personal traits of resilience and stress-coping that have sheltered them from the adverse effects of rampaging catecholamines.

Evidence also suggests a role for hormones in the process of aging. Deft manipulation of estrogen, progesterone, testosterone, thyroid, growth hormone and melatonin—all of which decline with age—may preserve certain aspects of youthful vigor. By contrast, levels of insulin tend to rise in response to dietary excess and sedentary lifestyle. The resultant "Syndrome X" is a major precipitant of premature disease.

It also is clear that certain aspects of aging are genetically programmed. For example, the presence of a gene called Apo-E4 predicts susceptibility to Alzheimer's disease. Through the genetic engineering of the future, doctors may be able to

selectively “edit out” deleterious genes or modify the expression of genes already encoded. Specific growth factors may be available to “turn on” the mechanisms for organ repair or “turn off” the harmful proliferation of tissue that occurs in certain degenerative diseases such as arthritis, arteriosclerosis or cancer.

“Smart drugs” already are available that crudely modulate levels of neurotransmitters in the brain. Among the most popular is Deprenyl, a prescription medication used to slow the progression of Parkinson’s disease. It is held by some anti-aging researchers that Deprenyl and other drugs can be used to halt the decline in mental functioning that is the hallmark of aging. The advent of better “smart drugs” may provide a breakthrough in enhancing the quality of our later years.

Cosmetic aspects of rejuvenation deserve attention here, too. Conscientious application of improved techniques of dermatology and plastic surgery (always used in conjunction with appropriate lifestyle modification) can create a meaningful anti-aging “makeover.” Newer, less invasive techniques such as laser surgery and natural skin treatments now enhance the repertoire of longevity specialists.

Finally, high-tech advances such as exquisitely modeled miniature microprocessor seeing and hearing devices may eventually reduce the debilitation now suffered by many of the aging. New techniques of locomotion utilizing robotics and virtual reality could eventually resuscitate failing motor skills. Remarkable progress in organ transplantation and artificial organ technology also may ultimately transform the search for longevity.

Nevertheless, the zeal for life extension must be tempered with a healthy recognition of our ultimate limitations. We live in a dazzlingly youth-oriented culture that places a premium on beauty, fitness, hedonistic indulgence and

sexuality. We need to acknowledge the importance of maturity, even debility, illness, pain and death. Our efforts to extend life and to improve the quality of our newly-attained longevity must be tempered with respect for our humble biological origins and the spiritual connectedness that our lives embody.