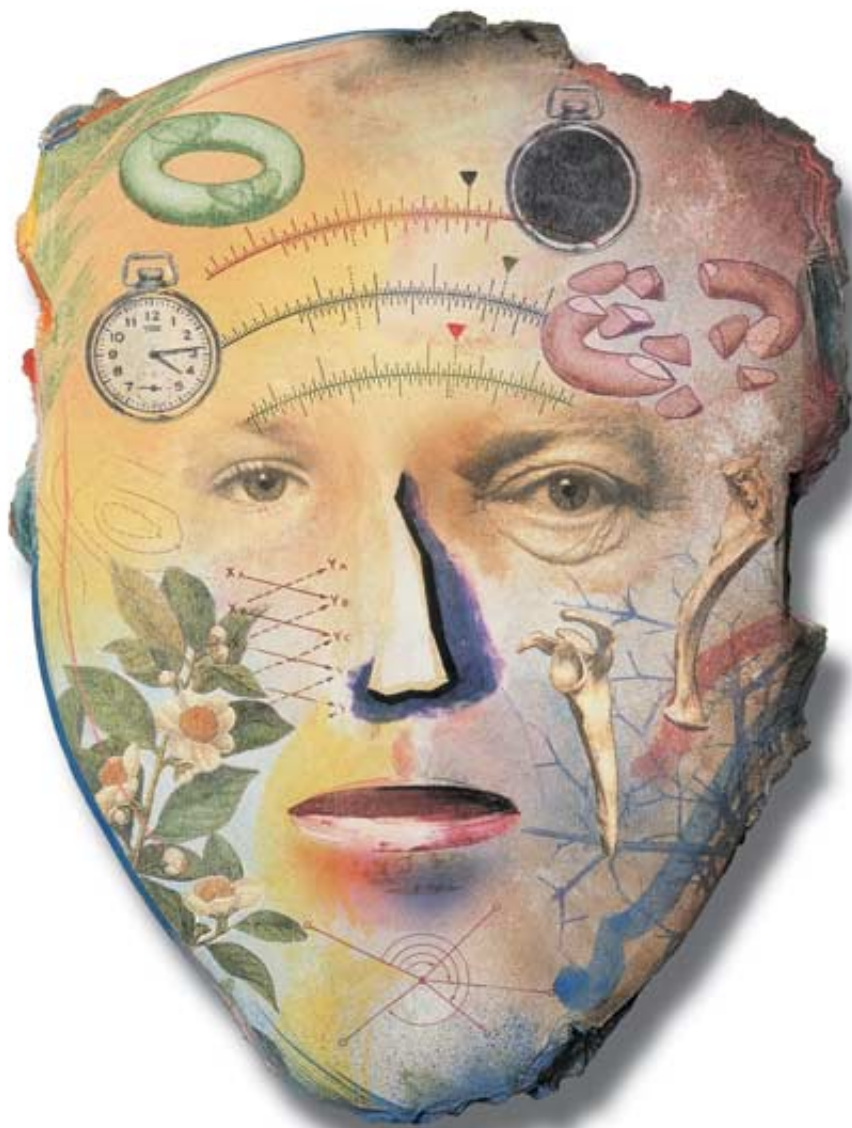


No Truth to the Fountain of Youth

Fifty-one scientists who study aging have issued a warning to the public: no anti-aging remedy on the market today has been proved effective. Here's why they are speaking up

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Efforts to combat aging and extend human life date at least as far back as 3500 B.C., and self-proclaimed experts have touted anti-aging elixirs ever since. Indeed, the prospect of immortality has always had universal appeal, spurring Alexander the Great and Ponce de León to search for the legendary Fountain of Youth and feeding alchemists' desire to manufacture gold (once believed to be the most potent anti-aging substance in existence). But the hawking of anti-aging "therapies" has taken a particularly troubling turn of late. Disturbingly large numbers of entrepreneurs are luring gullible and frequently desperate customers of all ages to "longevity" clinics, claiming a scientific basis for the anti-aging products they recommend and, often, sell. At the same time, the Internet has enabled those who seek lucre from supposed anti-aging products to reach new consumers with ease.

Alarmed by these trends, scientists who study aging, including the three of us, have issued a position statement containing this warning: no currently marketed inter-

vention—none—has yet been proved to slow, stop or reverse human aging, and some can be downright dangerous. While the public is bombarded by hype and lies, many biologists are intensively studying the underlying nature of aging in the belief that their research will eventually suggest ways to slow its progression and to thereby postpone infirmity and improve quality of life. But anyone purporting to offer an anti-aging product today is either mistaken or lying. The full position statement, drafted and endorsed by 51 internationally recognized investigators, can be found on the *Scientific American* Web site [see bottom of page 95]. Here we state the case as we see it, speaking for ourselves.

What Aging Is ... and Isn't

ANY DISCUSSION OF AGING should first clarify its terms. Various definitions have been proposed, but we think of aging as the accumulation of random damage to the building blocks of life—especially to DNA, certain proteins, carbohydrates and lipids (fats)—that begins early in life and eventually exceeds the body's self-repair capabilities. This damage gradually impairs the functioning of cells, tissues, organs and organ systems, thereby increasing vulnerability to disease and giving rise to the characteristic manifestations of aging, such as a loss of muscle and bone mass, a decline in reaction time, compromised hearing and vision, and reduced elasticity of the skin.

This accretion of molecular damage comes from many sources, including, ironically, the life-sustaining processes involved in converting the food we eat into usable energy. As the energy generators of cells (mitochondria) operate, they emit destructive, oxidizing molecules known as free radicals. Most of the damage caused by these reactive molecules gets repaired, but not all. Biologists suspect that the oxidative assaults ultimately cause irreparable injury to the mitochondria, thereby impeding the cell's ability to maintain the integrity of the countless molecules needed to keep the body operating properly. The free radicals may also disrupt other parts of cells directly.

Aging, in our view, makes us ever more susceptible to such ills as heart disease, Alzheimer's disease, stroke and cancer, but these age-related conditions are superimposed on aging, not equivalent to it. Therefore, even if science could eliminate today's leading killers of older individuals, aging would continue to occur, ensuring that different maladies would take their place. In addition, it would guarantee that one crucial body component or another—say, the cardiovascular system—would

eventually experience a catastrophic failure. It is an inescapable biological reality that once the engine of life switches on, the body inevitably sows the seeds of its own destruction.

Men and women in the developed world typically live longer now (75 and 80 years, respectively) than they did throughout much of history (about 25 years) because human ingenuity—which brought us sanitation systems, vaccines, antibiotics and so on—has had phenomenal success in thwarting the infectious and parasitic diseases responsible for a great deal of premature death. We live longer now not because we have altered the way we age but because we have altered the way we live.

Though inevitable, aging is not, as some might think, a genetically programmed process, playing itself out on a rigidly predetermined time schedule. The way evolution works makes it impossible for us to possess genes that are specifically designed to cause physiological de-

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cline with age or to control how long we live. Just as an automobile does not have a built-in plan for decline written in its blueprints, we do not possess genetic instructions that tell our bodies how to age or when to die.

The logic behind this assertion goes basically like this: Genes perpetuate themselves by orchestrating the transformation of a fertilized egg into a sexually mature adult that produces offspring. Clearly, any genetic variant that compromises this developmental process would be self-eliminating. Conversely, evolution is totally blind to the consequences of gene action (whether good, bad or indifferent) after reproduction is achieved. Genes or genetic variants that prove detrimental in the postreproductive part of the life span can become commonplace, but only if they participate in important processes early on. For

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example, several genes that contribute to cancer in the later years are known to participate in growth and development early in life.

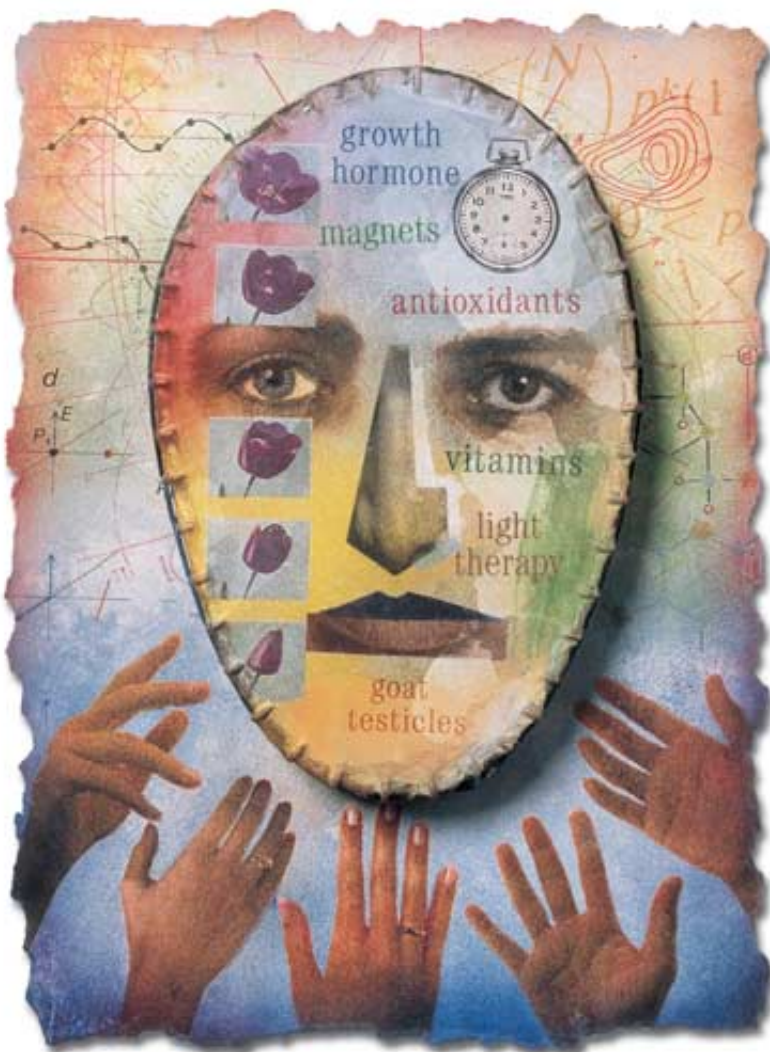
Without a doubt, a host of our genes influence aging, but they do so indirectly, as an inadvertent by-product of processes involved in growth, development, and the maintenance of health and vigor. The lack of a specific genetic program for aging and death means that there are no quick fixes that will permit us to treat aging as if it were a disease. A single genetic intervention in an organism as complex as a human being would have little chance of combating the probably vast array of genes and biological activities that play subtle, unpredictable parts in the timing of our ultimate demise.

False Claims

DESPITE THIS COMPLEXITY, some researchers believe that they may manage to find ways to slow the rate of human aging. If they succeed, many people will live longer than would otherwise be expected, and a few people might even surpass the modern longevity record of 122 years. But the primary goal of biomedical research and efforts to slow aging should not be the mere extension of life. It should be to prolong the duration of *healthy* life. Slowing the rate of aging could help postpone the onset of age-related diseases and infirmities, essentially enabling people to stay younger longer.

On what grounds do we assert so vehemently that no purported anti-aging intervention has been proved to modify aging? To assess whether an intervention has affected a biological process, researchers need a yardstick for measuring that process. In this case, no single or aggregate age-related phenomenon has proved to be a reliable indicator of the rate of aging in humans or other species. Without a yardstick, there can be no measurements, and without measurements there can be no assurance that an intervention was successful.

People eager to retain or restore their youthful biology might well recognize the paucity of proof but decide to try a putative anti-aging intervention anyway, thinking they have little to lose. They should think again. For instance, the U.S. Food and Drug Administration does not require products sold as dietary supplements to undergo the rigorous tests of safety and effectiveness that medicines must pass before they can be sold to the public. Consequently, these supplements come with no guarantees of purity or potency, no established guidelines on dosage, and



often no warnings about side effects that may result when the products are taken along with approved medications.

Antioxidants constitute one popular class of supplements touted to have anti-aging powers. Such chemicals occur naturally in the body and in fruits and vegetables and are believed to neutralize free radicals. Proponents claim that if taken in sufficient quantities, antioxidant supplements will sop up the radicals and slow down or stop the processes responsible for aging. But eliminating all free radicals would kill us, because they perform certain necessary intermediary steps in biochemical reactions. Further, although epidemiological studies have demonstrated that the antioxidant vitamins E and C contained within the foods we eat may reduce the risk of cancer, macular degeneration and other disorders, no one has established that vitamin supplements containing antioxidants limit oxidative damage in the body or influence aging.

Like antioxidants, another fashionable anti-aging intervention, hormone replacement, has a plausible rationale. This strategy was first popularized early in the 20th century, when older men occasionally submitted to the

grafting of testicles from goats or monkeys or received injections of macerated testicles. Today pure forms of hormones can be administered. The replacement strategy seems logical in principle because the blood levels of most hormones—among them melatonin, growth hormone, testosterone and dehydroepiandrosterone (DHEA)—commonly decrease with age. Also, experiments on older men have demonstrated that some physical and physiological attributes that show declines over time, notably muscle mass and skin elasticity, respond favorably in the short term to growth hormone replacement.

On the other hand, hormones can cause worrisome side effects. In mice, for instance, delivery of melatonin increases the risk of tumor development, and the overproduction of growth hormone leads to kidney problems, premature heart and lung failure, and an increased probability of early death. Human adults given growth hormone have suffered from acromegaly (excess bone growth) and carpal tunnel syndrome. Estrogen replacement therapy may offer health benefits to some postmenopausal women; however, this form of therapy has recently been challenged and has risks of its own, such as breast cancer and blood clots. In short, hormone replacement therapy has a place in the treatment of specific age-associated disorders, but evidence that it affects the rate of aging is lacking.

Some people might wonder whether following today's public health recommendations for diet and exercise can serve as a more natural Fountain of Youth. Good nutrition and regular exercise do reduce the risk of various diseases and, in that way, may extend the duration of life for many people—thereby serving as the best current prescription for a long and healthy life. As is true of other interventions, though, no one has shown that diet or exercise, or both, directly influences aging.

What Science Says

WE FIND IT IRONIC that a phony anti-aging industry is proliferating today, because serious efforts to understand aging have advanced greatly in recent years. Biologists who work with yeast, roundworms, fruit flies and mice have extended life by manipulating the genes of those species. These genetic alterations did not affect what is believed to be an important hallmark of aging in a population (an exponential increase in the risk of dying with time after puberty), which means that the longevity extensions in those experiments cannot safely be interpreted as resulting from an intervention in the aging process. Nevertheless, further study of those genes could offer clues to the influences on longevity and to approaches that might postpone infirmity and age-related disorders.

Another avenue of research may also lead to true aging interventions. Investigators have known for decades that caloric restriction extends life and the duration of good health in all species in which it has been studied, as long as the diet includes enough nutrition for routine maintenance of the body. These findings suggest that caloric restriction might have similar effects in humans. Given that few people would ever reduce their food intake enough to lengthen their lives, biologists are now trying to discover the mechanism that underlies the benefits of caloric restriction and to find agents that might mimic those helpful effects in people without forcing them to go hungry.

A number of scientists look at current research trends and feel hopeful. They can envision a time when treatments based on an understanding of aging can help slow its progression and when not yet specialized (stem) cells can be coaxed to repair and rejuvenate damaged tissues, enabling people to remain vigorous longer than they

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would without medical assistance. Not all researchers share that optimism, though. Some assert that aging's complexity will forever militate against the development of anti-aging therapies.

One thing is indisputable: the number of elderly people is growing worldwide, and opportunists stand ready to cash in on the burgeoning market for anti-aging products. The researchers who wrote and endorsed the position paper appearing on *Scientific American's* Web site do not necessarily agree on every word written there, but everyone realized that we had to set aside our minor differences to raise awareness of the growing scam. The public needs to know that the products sold as anti-aging remedies at longevity clinics and elsewhere have no scientifically proven efficacy and may at times be harmful. Systematic investigations into aging and its modification are in progress and could one day provide methods to slow our inevitable decline and extend health and longevity. That day, however, has not dawned yet. ■

On the Web...

To read the full position statement on aging and its extensive list of references, follow this link to the "Explorations" part of the *Scientific American* Web site: www.sciam.com/explorations/2002/051302aging/