

Position Statement on Human Aging

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A large number of products are currently being sold by antiaging entrepreneurs who claim that it is now possible to slow, stop, or reverse human aging. The business of what has become known as antiaging medicine has grown in recent years in the United States and abroad into a multimillion-dollar industry. The products being sold have no scientifically demonstrated efficacy, in some cases they may be harmful, and those selling them often misrepresent the science upon which they are based. In the position statement that follows, 52 researchers in the field of aging have collaborated to inform the public of the distinction between the pseudoscientific antiaging industry, and the genuine science of aging that has progressed rapidly in recent years.

IN the past century, a combination of successful public health campaigns, changes in living environments, and advances in medicine has led to a dramatic increase in human life expectancy. Long lives experienced by unprecedented numbers of people in developed countries are a triumph of human ingenuity. This remarkable achievement has produced economic, political, and societal changes that are both positive and negative. Although there is every reason to be optimistic that continuing progress in public health and the biomedical sciences will contribute to even longer and healthier lives in the future, a disturbing and potentially dangerous trend has also emerged in recent years. There has been a resurgence and proliferation of health care providers and entrepreneurs who are promoting antiaging products and lifestyle changes that they claim will slow, stop, or reverse the processes of aging. Even though in most cases there is little or no scientific basis for these claims (1), the public is spending vast sums of money on these products and lifestyle changes, some of which may be harmful (2). Scientists are unwittingly contributing to the proliferation of these pseudoscientific antiaging products by failing to participate in the public dialogue about the genuine science of aging research. The purpose of this document is to warn the public against the use of ineffective and potentially harmful antiaging interventions, and to provide a brief but authoritative consensus statement from 52 internationally recognized scientists in the field of what we know and do not know about intervening in human aging. What follows is a list of issues related to aging that are prominent in both the lay and scientific literature, and the consensus statements about these issues that grew out of debates and discussions among the 51 scientists associated with this article.

LIFE SPAN

Life span is defined as the observed age at death of an individual, whereas maximum life span is the highest documented age at death for a species. From time to time, we are

told of a new highest documented age at death, as in the celebrated case of Madame Jeanne Calment of France, who died at the age of 122 (3). Although such an extreme age at death is exceedingly rare, the maximum life span of humans has continued to increase because world records for longevity can move in only one direction—higher. However, despite this trend, it is almost certainly true that, at least since recorded history, people could have lived as long as those alive today if similar technologies, lifestyles, and population sizes had been present. It is not people that have changed; it is the protected environments in which we live, and the advances made in biomedical sciences and other human institutions, that have permitted more people to attain, or more closely approach, their life-span potential (4). Although longevity records are entertaining, they have little relevance to our own lives because genetic, environmental, and lifestyle diversity (5) guarantees that an overwhelming majority of the population will die long before attaining the age of the longest-lived individual.

LIFE EXPECTANCY

Life expectancy in humans is the average number of years of life remaining for people of a given age, assuming everyone will experience, for the remainder of their lives, the risk of death based on a current life table. For newborns in the United States today, life expectancy is approximately 77 years (6). Rapid declines in infant, child, maternal, and late-life mortality during the 20th century led to an unprecedented 30-year increase in human life expectancy at birth from the 47 years that it was in developed countries in 1900. Repeating this feat during the lifetimes of people alive today is unlikely. Most of the prior advances in life expectancy at birth reflect dramatic declines in mortality risks in childhood and early adult life. Because the young can only be saved once and because these risks are now so close to zero, further improvements, even if they occurred, would have little effect on life expectancy (7–9). Future gains in

life expectancy will, therefore, require adding decades of life to people who have already survived seven decades or more. Even with precipitous declines in mortality at middle and older ages from those present today, life expectancy at birth is unlikely to exceed 90 years (males and females combined) in the 21st century without scientific advances that permit the modification of the fundamental processes of aging (10). In fact, even eliminating all aging-related causes of death currently written on the death certificates of the elderly population will not increase human life expectancy by more than 15 years. In order for this limit to be exceeded, the underlying processes of aging that increase vulnerability to all common causes of death currently appearing on death certificates will have to be modified.

IMMORTALITY

Eliminating all of the aging-related (11) causes of death presently written on death certificates would still not make humans immortal (12). Accidents, homicides, suicide, and the biological processes of aging would continue to take their toll. The prospect of humans living forever is as unlikely today as it has always been, and discussions of such an impossible scenario have no place in a scientific discourse.

GERIATRIC MEDICINE VERSUS AGING

Geriatric medicine is a critically important specialty in a world where population aging is already a demographic reality in many countries and a future certainty in others. Past and anticipated advances in geriatric medicine will continue to save lives and help to manage the degenerative diseases associated with growing older (13,14), but these 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. Until we better understand the aging processes and discover how to manipulate them, these intrinsic and currently immutable forces will continue to lead to increasing losses in physiological capacity and death, even if age-associated diseases could be totally eliminated (15–20).

ANTIAGING MEDICINE

Advocates of what has become known as antiaging medicine claim that it is now possible to slow, stop, or reverse aging through existing medical and scientific interventions (21–26). Claims of this kind have been made for thousands of years (27), and they are as false today as they were in the past (28–31). Preventive measures make up an important part of public health and geriatric medicine, and careful adherence to advice on nutrition, exercise, and smoking can increase one's chances of living a long and healthy life, even though lifestyle changes based on these precautions do not affect the processes of aging (32,33). The more dramatic claims made by those who advocate antiaging medicine in the form of specific drugs, vitamin cocktails, or esoteric hormone mixtures are, however, 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 (34). The misleading marketing and the public acceptance of antiaging medicine is not only

a waste of health dollars; it has also made it far more difficult to inform the public about legitimate scientific research on aging and disease (35). Medical interventions for age-related diseases do result in an increase in life expectancy, but none have been proven to modify the underlying processes of aging. The use of cosmetics, cosmetic surgery, hair dyes, and similar means for covering up manifestations of aging may be effective in masking age changes, but they do not slow, stop, or reverse aging. At present, there is no such thing as an antiaging intervention.

ANTIOXIDANTS

The scientifically respected free-radical theory of aging (36) serves as a basis for the prominent role that antioxidants have in the antiaging movement. The claim that ingesting supplements containing antioxidants can influence aging is often used to sell antiaging formulations. The logic used by their proponents reflects a misunderstanding of how cells detect and repair the damage caused by free radicals and the important role that free radicals play in normal physiological processes (e.g., the immune response and cell communication) (37–39). Nevertheless, there is little doubt that ingesting fruits and vegetables (which contain antioxidants) can reduce the risk of having a number of age-associated diseases such as cancer (40), heart disease (41,42), macular degeneration, and cataracts (43,44). At present, there is relatively little evidence from human studies that supplements containing antioxidants lead to a reduction in either the risk of these conditions or the rate of aging, but there are a number of ongoing randomized trials that address the possible role of supplements in a range of age-related conditions (45–49), the results of which will be reported in the coming years. In the meantime, possible adverse effects of single dose supplements, such as beta-carotene (50), caution against their indiscriminate use. As such, antioxidant supplements may have some health benefits for some people, but so far there is no scientific evidence to justify the claim that they have any effect on human aging (51,52).

TELOMERES

Telomeres, the repeated sequence found at the ends of chromosomes, shorten in many normal human cells with increased cell divisions. Statistically, older people have shorter telomeres in their skin and blood cells than do younger people (53,54). However, in the animal kingdom, long-lived species often have shorter telomeres than do short-lived species, indicating that telomere length probably does not determine life span (55–57). Solid scientific evidence has shown that telomere length plays a role in determining cellular life span in normal human fibroblasts and some other normal cell types (58). However, increasing the number of times a cell can divide may predispose cells to tumor formation (59,60). Thus, although telomere shortening may play a role in limiting cellular life span, there is no evidence that telomere shortening plays a role in the determination of human longevity.

HORMONES

A number of hormones, including growth hormone, testosterone, estrogen, and progesterone, have been shown in

clinical trials to improve some of the physiological changes associated with human aging (61,62). Under the careful supervision of physicians, some hormone supplements can be beneficial to the health of some people. However, no hormone has been proven to slow, stop, or reverse aging. Instances of negative side effects associated with some of these products have already been observed, and recent animal studies suggest that the use of growth hormone could have a life-shortening effect (63–65). Hormone supplements now being sold under the guise of antiaging medicine should not be used by anyone unless they are prescribed for approved medical uses.

CALORIC RESTRICTION

The widespread observation that caloric restriction will increase longevity must be tempered with the recognition that it has progressively less effect the later in life it is begun (66), as well as with the possibility that the control animals used in these studies feed more than wild animals, predisposing them to an earlier death. Although caloric restriction might extend the longevity of humans because it does so in many other animal species (67–69), there is no study in humans that has proven that it will work. A few people have subjected themselves to a calorically restricted diet, which, in order to be effective, must approach levels that most people would find intolerable. The fact that so few people have attempted caloric restriction since the phenomenon was discovered more than 60 years ago suggests that, for most people, quality of life seems to be preferred to quantity of life. The unknown mechanisms involved in the reduced risk of disease associated with caloric restriction are of great interest (70), and they deserve further study because they could lead to treatments with pharmacological mimetics of caloric restriction that might postpone all age-related diseases simultaneously (71).

DETERMINING BIOLOGICAL AGE

Scientists believe that random damage that occurs within cells and among extracellular molecules is responsible for many of the age-related changes that are observed in organisms (72–74). In addition, for organisms that reproduce sexually, such as humans, each individual is genetically unique. Therefore, the rate of aging also varies from individual to individual (75). Despite intensive study, scientists have not been able to discover reliable measures of the processes that contribute to aging (76). For these reasons, any claim that a person's biological or "real age" (77) can currently be measured, let alone modified, by any means must be regarded as entertainment (78), not science.

ARE THERE GENES THAT GOVERN AGING PROCESSES?

No genetic instructions are required to age animals, just as no instructions on how to age inanimate machines are included in their blueprints (72,79). Molecular disorder occurs and accumulates within cells and their products because the energy required for maintenance and repair processes to maintain functional integrity for an indefinite time is unnecessary after reproductive success. Survival beyond the reproductive years and, in some cases, raising progeny to independence, is not favored by evolution because limited

resources are better spent on strategies that enhance reproductive success to sexual maturity rather than longevity (80). Although genes certainly influence longevity determination, the processes of aging are not genetically programmed. Overengineered systems and redundant physiological capacities are essential for surviving long enough to reproduce in environments that are invariably hostile to life. Because humans have learned how to reduce environmental threats to life, the presence of redundant physiological capacity permits them and the domesticated animals they protect to survive beyond reproductive ages. Studies in lower animals that have led to the view that genes are involved in aging have demonstrated that significant declines in mortality rates and large increases in average and maximum life span can be achieved experimentally (81–84). However, without exception, these genes have never produced a reversal or arrest of the inexorable increase in mortality rate that is one important hallmark of aging. The apparent effects of such genes on aging therefore appear to be inadvertent consequences of changes in other stages of life, such as growth and development, rather than a modification of underlying aging processes. Indeed, the evolutionary arguments presented herein suggest that a unitary programmed aging process is unlikely to even exist, and that such studies are more accurately interpreted to have an impact on longevity determination, not the various biological processes that contribute to aging. From this perspective, longevity determination is under genetic control only indirectly (15,85). Thus, aging is a product of evolutionary *neglect*, not evolutionary *intent* (86–89).

CAN WE GROW YOUNGER?

Although it is possible to reduce the risk of aging-related diseases and to mask the signs of aging, it is not possible for individuals to grow younger. This would require reversing the degradation of molecular integrity that is one of the hallmarks of aging in both animate and inanimate objects. Other than performing the impossible feat of replacing all of the cells, tissues, or organs in biological material as a means of circumventing aging processes, growing younger is a phenomenon that is currently not possible.

GENETIC ENGINEERING

Following the publication of the human genome sequences, there have been assertions that this new knowledge will reveal genes whose manipulation may permit us to intervene directly in the processes of aging. Although it is likely that advances in molecular genetics will soon lead to effective treatments for inherited and age-related diseases, it is unlikely that scientists will be able to influence aging directly through genetic engineering (90,91) because, as already stated, there are no genes directly responsible for the processes of aging. Centuries of selective breeding experience (e.g., agricultural, domesticated, and experimental plants and animals) have revealed that genetic manipulations designed to enhance one or only a few biological characteristics of an organism frequently have adverse consequences for health and vigor. Therefore, there is a very real danger that enhancing biological attributes associated with extended

survival late in life might compromise biological properties important to growth and development early in life.

REPLACING BODY PARTS

Suggestions have been made that the complete replacement of all body parts with more youthful components could increase longevity. Although possible in theory, it is highly improbable that this would ever become a practical strategy to extend length of life. Advances in cloning and embryonic stem cell technology may make the replacement of tissues and organs possible (92–97) and will likely have an important positive impact on public health in the future through the treatment of age-related diseases and disorders. However, replacing and reprogramming the brain, which defines who we are as individuals, is, in our view, more the subject of science fiction than likely science fact.

LIFESTYLE MODIFICATION AND AGING

Optimum lifestyles, exercise, and diets 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. However, there is no scientific evidence to support the claim that these practices increase longevity by modifying the processes of aging.

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. Our language on this matter must be unambiguous: 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 (98,99). We strongly urge the general public to avoid buying or using products or other interventions from anyone claiming that they will slow, stop, or reverse aging. If people, on average, are going to live much longer than is currently possible, then it can only happen by adding decades of life to people who are already likely to live for 70 years or more. This “manufactured survival time” (100) will require modifications to all of the processes that contribute to aging—a technological feat that, although theoretically possible, has not yet been achieved. What medical science can tell us is that because aging and death are not programmed into our genes, health and fitness can be enhanced at any age, primarily through the avoidance of behaviors (e.g., smoking, excessive alcohol consumption, excessive exposure to sun, and obesity) that accelerate the expression of age-related diseases, and by the adoption of lifestyles (e.g., exercise and diet) that take advantage of a physiology that is inherently modifiable (101).

CONCLUSION

We enthusiastically support research in genetic engineering, stem cells, geriatric medicine, and therapeutic pharmaceuticals, technologies that promise to revolutionize medicine as we know it. Most biogerontologists believe that our rapidly expanding scientific knowledge holds the promise that means may eventually be discovered to slow the rate of aging. If successful, these interventions are likely to postpone age-related diseases and disorders and extend the pe-

riod of healthy life. Although the degree to which such interventions might extend length of life is uncertain, we believe this is the only way another quantum leap in life expectancy is even possible. Our concern is that when proponents of antiaging medicine claim that the fountain of youth has already been discovered, it negatively affects the credibility of serious scientific research efforts on aging. Because aging is the greatest risk factor for the leading causes of death and other age-related pathologies, more attention must be paid to the study of these universally underlying processes. Successful efforts to slow the rate of aging would certainly have dramatic health benefits for the population, by far exceeding the anticipated changes in health and length of life that would result from the complete elimination of heart disease, cancer, stroke, and other age-associated diseases and disorders.

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