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The Longevity Dividend: Geroscience Meets Geropolitics

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From the Editor

The Longevity Dividend: Geroscience Meets Geropolitics

Robert B. Hudson, Editor

Can 1 year of clock time be matched by less than 1 year of biological time? That is the intriguing question posed by S. Jay Olshansky and the other authors contributing to this issue of *Public Policy & Aging Report*, which is devoted to the longevity dividend. Multifaceted research in the natural and behavioral sciences is focused on whether the period of healthy life can be extended by slowing the biological processes of aging. Dan Perry, president of the Alliance for Aging Research, refers to this approach as nothing less than a "moon-shot effort to harness the underlying processes of aging as a new model for health promotion and disease prevention." Were the promising findings of a growing number of laboratory and animal-based studies to be borne out in human trials, authors here speak of a paradigmatic breakthrough that would rival those of public health in the 19th century and medicine in the 20th century.

The challenge is both diagnostic and political. Can scientists such as those reporting here convince skeptics within the biomedical community, public and private funders of such research, and the general public that attacking aging is a viable and more efficient approach to reducing the risk of all fatal and disabling diseases and improving well-being across the life cycle? Moreover, beyond skeptics, those advancing scientifically based longevity research must overcome historical and contemporary so-called antiaging efforts promoted by those, charlatans or otherwise, pursuing a fast buck based on life's most basic question: How to avoid death?

Science and politics come together when juxtaposing longevity initiatives against the disease-specific research and therapy that have garnered the lion's share of biomedical research funding in the post–World War II years. Biogerontologists initially faced a challenge of research in age and aging not being perceived as a legitimate arena when placed against other professions, disciplines, and concerns. Accompanying that stigma was the growing political appeal (uncontested) and scientific justification (more controversial) of disease-specific agencies and protocols in which the payoff between research and results seemed more straightforward. The political appeal of disease-based research is captured in political scientist Harold Seidman's recounting of a classic bureaucratic encounter from the 1950s: "[I]n 1955 the National Microbiological Institute was renamed the National Institute of Allergy and Infectious Diseases. As was explained [by a Senate staffer] at the time, the Institute had been

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Articulating the Case for the Longevity Dividend

S. Jay Olshansky

The benefits of most public-health interventions that are now well established, as well as the recognized harmful health consequences of some behavioral risk factors, were rarely considered as accepted doctrine when first identified. In fact, some unassailable public-health interventions are still rejected by some, and almost every major discovery in the history of public health initially faced disbelief, vehement skepticism, and even scorn. The scientific study of aging is leading researchers in the direction of a major breakthrough that has the potential to revolutionize public health in our aging world—but obstacles once again stand in the way.

In this essay, I describe the Longevity Dividend Initiative—a contemporary effort to extend the period of healthy life by slowing the biological processes of aging (Olshansky, Perry, Miller, & Butler, 2006)—and some of the obstacles that stand in the way of what many consider to be one of the most exciting breakthroughs in the history of science and public health.

Healthy Life Extension

The most precious of all commodities is life itself, and if there is one attribute most of us share, it is the desire to remain alive. The yearning for healthy life is equally important—perhaps even more so—especially for those struggling to regain health that has been lost. One would think, therefore, that the case for extending our healthy years would be universally accepted and easy to make, regardless of how it is achieved. Sadly, this is not the case.

In public health, examples of interventions that in the past had a profound influence on the length and quality of life include the development and dissemination of clean water, sanitation, indoor living and working environments, and refrigeration (although there is still plenty of room for lessening disparities in health and longevity and the factors that contribute to them). During the last century, epidemiologists raised public awareness of the life-shortening effects of smoking and other harmful risk factors, as well as the life-extending effects of proper diet and exercise, among other lifestyle choices.

In the modern world of medicine and medical technology, a trip to the doctor, dentist, or other health professional is justified as a form of primary prevention. When a health issue arises—such as a serious infection, cancer, or heart disease—the routine for most is to seek out and trust modern medical treatment as the best approach to regaining one's health. In fact, a strong endorsement for the efficacy of medicine's ability to extend healthy life comes from its validation by the insurance industry.

These three pillars of healthy life extension have earned people's trust, and deservedly so, but concerns are being raised about how much more healthy life can be manufactured using these approaches. The reason is the biological aging of our bodies.

In the last half-century, a combination of public health and medicine enabled most people born in the developed world to live past age 65, and for them, a large percentage live past age 85. As appealing as this scenario is, the problem that arises with extended survival is that a less tractable risk factor has emerged—the biological aging of our bodies. Public health can manufacture only so much survival time through lifestyle modification, after which medical technology has an important life-extending impact, but even these methods of life extension eventually leave the survivors facing biological aging.

Think of the effect of aging on the body as the same as the effect of miles on an automobile. Very few things go wrong with most cars during the first 3 years and 36,000 miles, and for some automobiles the warranty period has been extended to 10 years and 100,000 miles. Operate these cars beyond their warranty period, and a cluster of problems emerges. These problems are an inevitable by-product of the passage of time and the accumulation of damage that arises from operating the machine—they are not programmed to occur at a set time by the auto manufacturers. Although planned obsolescence is part of the manufacturing ethos for some companies, what I mean here is that automobile manufacturers do not build a specific death time into a car.

The same principles hold true for human bodies. Once we operate our bodies beyond the equivalent of their biological warranty period, a large number of health issues begin to emerge and cluster tightly into later regions of the life span. Among scientists who track these events, this phenomenon is known as competing causes, which is another way of saying that a large number of lethal and disabling conditions accumulate in aging bodies. Ameliorating any one lethal condition independent of all others leaves the person with a high risk from all other remaining conditions. With time (and age), the treatments

devised through medicine (which tend to focus on one disease at a time) and risk factor modification then become progressively less effective as survivors move further into older age windows where aging-related diseases cluster ever more tightly together. Keep in mind that, just like automobiles, our bodies are not programmed with aging or death genes that are set off at a predetermined age. Aging is best thought of as an inadvertent by-product of fixed genetic programs that evolved under the direct force of natural selection for early-life developmental events; aging is a product of evolutionary neglect, not evolutionary intent.

Science has now demonstrated that aging is inherently modifiable.

Recognizing the fact that competing causes places a damper on the future effectiveness of disease-oriented medical interventions, scientists in the field of aging have proposed that the next big step in public health and healthy life extension is to attack the seeds of aging rather than just its consequences. The idea is to slow the aging of our bodies such that 1 year of clock time is matched by less than 1 year of biological time. This approach would allow people to retain their youthful vigor for a longer time period and, if delayed-aging interventions work the way researchers hope they do, compress the infirmities of old age into a shorter time frame at the end of life. Delaying biological aging is the only viable approach to addressing the increasing importance of competing causes and the rise of aging as an ever more important risk factor for disease. This effort to transform aging science into a new paradigm for combating disease and extending the period of healthy life is referred to as the Longevity Dividend Initiative.

It is at this juncture where one of the main problems occurs. The contemporary proposal to slow aging as a means to extend healthy life has historical linkages to medical deception, charlatanism, and greed (Gruman, 1966). Historically, the quest for immortality was couched within a prolongevity message suggesting that ingesting or injecting substances with alleged antiaging properties could manufacture youth. One of the most famous among these is the alchemist's dream of transmuting lead into gold, a process thought to confer immortality to those who ingested minute quantities.

In the late 19th century, French physiologist Charles-Edouard Brown-Sequard claimed to have discovered the secret to rejuvenation. Brown-Sequard crushed the testicles of domesticated animals, extracted what he called vital substances from them, and then inoculated older people against what he termed the aging disease. Modern versions of these ancient antiaging potions have been described as posing the "potential for physical and economic harm" (United States Government Accounting Office, 2001).

Finally, some scientists in the field of aging have formed companies designed to attract outside investors interested in cashing in on a possible breakthrough in the field of aging (Anton, 2013). Although this approach enables some aging science to occur that would not otherwise be funded, it can and has led to exaggerated claims and unproven interventions that reach the marketplace before they are fully evaluated using the tools of science. This, too, creates suspicion among members of the public, who already have a difficult time distinguishing between medical fraud and genuine public-health interventions.

Taken together, these historical and contemporary roadblocks to legitimacy have delayed the entrance of aging science into the realm of accepted discourse as a legitimate and, quite frankly, valuable and needed public-health intervention. However, these aren't the only roadblocks.

Religious Arguments

Religious objections are sometimes posed in response to proposals to enhance public health by modulation of aging. The objection usually starts from the assertion that tampering with aging is equivalent to tampering with God's plan for us—an effort that should not be pursued. However, this argument loses its power when those proposing it admit that both they and their children have been vaccinated against lethal childhood diseases. It is hard to imagine that God's plan is to kill most children from communicable diseases before they reach the age of 10, but up until the 19th century that was humanity's fate. Most people who make this argument also admit that they would seek medical attention if they (or their loved ones) experience heart disease or cancer. Why is one form of disease prevention acceptable while another is not?

Population Growth

When delayed aging was first proposed as a public-health intervention in the 1950s, rapid population growth was a concern because the growth rate in the post–World War II era was about 3 percent (see Table 1). To place this growth rate into perspective, consider that, at 3 percent growth, the population would double in 26 years. Thus, both demographers and environmentalists, among others, were for good reason alarmed about the population growth rate during most of the last half of the 20th century. Although the rate of population growth has attenuated considerably since 1950, the momentum for population growth will remain through the middle of this century, and

environmental concerns have escalated considerably. Population growth and resource depletion definitely should be on our minds, and these issues are appropriate to raise when discussing healthy-life extension.

The thing is, those making this argument believe that delayed aging will dramatically accelerate population growth, wipe out the reductions in the growth rate achieved in recent decades, further challenge resource depletion, and generate a new set of population and environmental headaches. As it turns out, none of these concerns are valid.

With regard to population growth, I have estimated how the growth rate (GR) would change with the hypothetical extreme scenario of immortality (i.e., no more deaths). The data in Table 1 demonstrate that under the extreme scenario of immortality, the GR would be about 1.5 percent (i.e., the GR would be defined by the birth rate because the death rate would be zero)—which is three times faster than the current GR of about 0.5 percent. However, longer lives tend to be accompanied by lower fertility, so I estimate a GR under conditions of hypothetical immortality of about 0.9 percent—still twice the current GR. Because immortality is not likely to happen anytime soon, and because the longevity dividend associated with delayed aging would yield only marginal increases in life expectancy, the actual population GR would rise only slightly if the longevity dividend is achieved.

In fact, the population GR would also rise marginally with a hypothetical cure for cancer or heart disease. I have yet to hear anyone argue that cures for these diseases should not be pursued because success would be accompanied by accelerated population growth and resource depletion. The bottom line is that the Longevity Dividend Initiative will have a negligible effect on population growth and the environment, but it will have a dramatically positive impact on work, retirement, health care financing and costs, and physical and psychological well-being.

Delayed Aging Means Increased Infirmity

Perhaps the most common misconception and fear about aging science and the Longevity Dividend Initiative is the belief that delayed aging will extend the period of infirmity at the end of life—the fear that most people have as they approach older ages. This view is ironic because although the scientists involved may disagree on exactly how to accomplish the goals we researchers have set, the one thing we all have in common is the final and most important goal of extending the period of healthy life. An intervention that does not meet the test of extending the health and functionality of both body and mind together would not be pursued—in fact, such an intervention would be seen as harmful.

Articulating the Case for the Longevity Dividend

The case for the longevity dividend is extremely compelling and, in theory, should be easy to make to funders, public-health professionals, and the general public. Here is the line of reasoning:

1. Treating diseases worked well in the past to extend healthy life, but aging has emerged as the primary risk factor for the most common fatal and disabling diseases.

Table 1. Population Growth Rates With and Without Immortality

Year	Birth rate (per thousand)	Death rate (per thousand)	Growth rate (percent)	Population doubling time (years)
1000*	~ 70	~ 69.5	~ 0.1	~ 800–1,000
1900	50	30	2.0	35
1950	45	15	3.0	26
2000	15	10	0.5	140
Immortality	~ 15	0	1.5	~ 53
Immortality**	~ 10	~ 0.1	~ 0.9	~ 80

* The birth rate and death rate in the year 1000 cannot be known with certainty. These numbers are used to illustrate that vital rates were extremely high by comparison with today, and that the birth rate throughout most of human history hovered, on average, just above the death rate.
** Birth rates would likely decline if immortality was achieved. The estimated birth rate of 10 per thousand is speculation, and perhaps even an overestimate. A death rate of zero is impossible to achieve in the real world, where accidents, homicide, and suicide are present. The difference between the vital rates under the more realistic demographic conditions that might occur in the presence of immortality would lead to a growth rate of less than 1 percent and a population doubling time of approximately 80 years.

2. The longer individuals live, the greater the influence of aging on disease expression.
3. Aging science offers medicine and public health a new and potentially far more effective weapon for preventing disease, extending healthy life, and avoiding the infirmities associated with old age (Butler et al., 2008).
4. Failing to take this new approach could leave people who reach older ages in the future even more vulnerable to rising disability than they are now.
5. Aging science represents a new paradigm of public health that has the potential to yield more effective methods of delaying most fatal and disabling diseases, extending healthy life, and reducing the prevalence of infirmities more commonly experienced at older ages (Sierra, Hadley, Suzman, & Hodes, 2009).

Reductions in the infirmities of old age and increased economic value to individuals and societies would accrue from the extension of healthy life.

The language of the longevity dividend must be unambiguous. Much like the introduction of antibiotics in the mid–20th century and the broad dissemination of basic measures of public health a century ago, humanity is once again fortunate enough to witness the rise of a new paradigm in human health. Aging science has successfully turned the spotlight on the origins of the aging of people's bodies and minds and the fatal and disabling diseases that accompany us in our later years. What the scientific study of aging reveals shakes up a long-held assumption that aging is an inevitable and immutable by-product of the passage of time (Miller, 2002), and these new discoveries fundamentally challenge the fatalistic view that aging and death are nature's way of removing the old to make way for the young.

Science has now demonstrated that aging is inherently modifiable. Furthermore, there is now reason to believe that aging science can be translated into new, more effective medical and public-health interventions that will be able to combat fatal and disabling diseases far more effectively than any intervention available today—yielding an extension of the period of healthy life in ways that could not even be imagined just a few years ago.

Although people who benefit from advances in aging science will probably live longer, the extension of healthy life is the primary goal. In addition, reductions in the infirmities of old age and increased economic value to individuals and societies would accrue from the extension of healthy life.

It is only a matter of time before aging science acquires the same level of prestige and confidence that medicine and public health now enjoy, and when that time comes, a new era in human health will emerge. An abundance of formidable obstacles are standing in the way, including strongly held views of how to proceed, a history of association with dubious aging interventions, and misconceptions about the goals in mind and the impact of success on population growth and the environment. Once the air clears and aging science is translated into effective and safe interventions that can be measured and documented to extend our healthy years, the 21st century will bear witness to one of the most important new developments in the history of medicine.

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Geroscience Offers a New Model for Investigating the Links Between Aging Biology and Susceptibility to Aging-Related Chronic Diseases

Felipe Sierra • Ronald A. Kohanski

The proportion of elders in the human population across the globe is higher than at any time in history, and improving and maintaining their health represent new frontiers of modern medicine. From the point of view of gerontologists, everyone who is in late life has experienced aging, the progressive decline of physical and mental abilities. Geriatricians, who study the diseases of older adults, stress that aging is itself the major risk factor for most of those diseases. Geroscientists, who research the underlying molecular and cellular processes of aging and age-related disease, believe that this basic biology of aging is the potential missing link between aging as the major risk factor and the chronic diseases prevalent in the older population. Accordingly, the Geroscience Interest Group (GSIG) at the National Institutes of Health (NIH) promotes innovative approaches to better understand the relationships between the biological processes of aging and age-related chronic diseases and disabilities.

When the NIH was founded in 1930, the average human life expectancy from birth was about 60 years in the United States (see, e.g., University of Oregon Mapping History Project, n.d.). By the turn of the last century, life expectancy from birth had increased to about 77 years (see, e.g., University of Oregon Mapping History Project). The earliest achievements in life expectancy resulted from improvements in sanitation and treatments for infectious diseases—parts of the original mission of the NIH when it was formally created from the Hygienic Laboratory. The NIH has been extremely successful in recognizing and responding to the emergent health issues of each era while also supporting fundamental advances in basic biological research. Addressing public-health issues and therapies designed to counteract the effects of infectious and acute diseases, which were the major scourges of an earlier time, also led to dramatic decreases in mortality at young ages.

However, in part because of the success of NIH-led programs that have increased life expectancy, the burden of diseases affecting the U.S. population has also changed. As stated on the occasion of the 100th anniversary of the American Cancer Society, "Back in 1913 . . . cancer was a lesser threat for most Americans. The biggest killers then were flu, pneumonia, tuberculosis, and stomach bugs. At a time when average life expectancy was 47, few lived long enough to get cancer" (Associated Press, 2013, ¶ 2). Now, the biggest killers in the United States and worldwide are heart disease and cancer, and the major causes of disability are chronic diseases and conditions—including diabetes, obesity, sarcopenia, osteoporosis, and dementias (among others)—that are found most often in elders.

Since its inception, the NIH has responded to the shifting landscape of health concerns and diseases by establishing and reorganizing institutes and centers that are capable of responding forcefully both to widespread diseases and to rare illnesses. The NIH has supported, in parallel, fundamental research in basic biology and application of these findings in clinics and clinical trials. What, then, are the current and future challenges of aging that the NIH could address, given that aging is not a disease but encompasses all parts of the body while putting that body at greater risk of disease and death?

For the NIH, the challenges of aging are not new. The National Institute on Aging (NIA) was established in 1974 as a component of the NIH. From its inception, the mission of the NIA has encompassed many aspects of aging, including physiological, behavioral, social, and economic factors (in essence, gerontology); clinical approaches to the diseases of aging (in essence, geriatrics); and the basic biology of the processes and molecular mechanisms of aging, as well as the basis for understanding age-related disease (geroscience). Two fundamental discoveries in geroscience have occurred over the past 2 decades that may underpin innovative approaches to aging across the NIH: Life spans

Interventions yielding longer life have been coupled with improvements in health at older ages.

are influenced by genetics, and life spans can be altered pharmacologically. Moving forward from these two discoveries is a third important (but still tentative) observation: Life spans that have been increased by interventions or by genotypes appear to coincide with improved health.

Basic research and clinical studies both support the potential for improved health during aging.

For centuries, people have known that life span could be extended (probably within limits) simply by adopting a moderate diet and exercise. Basic research and clinical studies both support very strongly the potential for improved health during aging, even when faced with chronic diseases (see, e.g., National Institute on Aging, 2013). In an extreme approach—more suitable to experimental systems with laboratory animals than would be practical on a large scale for human populations—substantially reduced caloric intake extends life span. Generally, these behavioral interventions yielding longer life have been coupled with improvements in health at older ages. As described in some studies of human centenarians and their kindred, survival to old age may coincide with a lower burden of disease—an outcome that is encouraging (Atzmon et al., 2004). However, knowledge about the extent to which any given intervention that extends life span reduces the burden of disease or increases the tolerance for disease remains incomplete. For example, despite recent successes for encouraging behavioral interventions that improve health—most notably a reduction in smoking tobacco and an increase in wearing seatbelts in cars—reversing the trends from immoderate diets and too little exercise are still works in progress for most people.

Furthermore, longevity has long been known to run in families, and geroscience has identified many of the genes and biochemical pathways that can increase life span. Much of this knowledge is based on work done primarily in model experimental systems (laboratory animals) whose genes can be manipulated, but it also comes from studies of long-lived human families and populations. Indeed, multiple animal studies (Bartke, 2011; Kenyon, 2010; Selman & Withers, 2011) have shown that life span is quite malleable and can be extended significantly by manipulation of one or more among a few hundred genes linked to aging (most of which belong to three or four well-defined molecular pathways).

In addition, this type of research has shown that some behavioral modifications that extend life span, such as caloric restriction, function through one or more of these pathways (Fontana, Partridge, & Longo, 2010). In concert with these findings on the genetics of life span are studies on whether life span can be extended by pharmacological agents known to interact with one or more of the molecular pathways linked to life span (Chung, Manganiello, & Dyck, 2012; Fernández & Fraga, 2011; Harrison et al., 2009; Lam, Peterson, & Ravussin, 2013; Park et al., 2012). Thus, a handful of pharmacological agents—including sirtuin activators, rapamycin, and others—have been shown to alter life span in tests using laboratory animals. Prominent among this research is the work done by the NIA-supported Interventions Testing Program (Nadon et al., 2008), which has been critical in producing a turning point in thinking about health in relation to interventions that increase life span.

A recent discovery is the extent to which targeting specific molecular processes that increase life span are also important in the development of most chronic diseases (Baker et al., 2011; Jeck, Siebold, & Sharpless, 2012). In searching for ways to translate basic research into treatments that can meet the major health challenges of an aging population, the NIA has been the lead institute for Alzheimer's disease, in particular, and dementias and cognitive declines in general, with substantial involvement from the National Institute of Neurological Disorders and Stroke and the National Institute of Nursing Research. Other NIH institutes have been leaders focused on specific diseases and conditions; because many of these diseases are found predominantly in elders, the NIA also supports research in these areas.

As their names indicate, many NIH institutes have been developed in response to emerging health needs identified by specific diseases. For example, the National Institute of Allergies and Infectious Diseases takes the lead on research about allergies and infectious diseases, but also on declining immunity with age; the National Heart, Lung, and Blood Institute takes the lead on studies of heart failure; the National Cancer Institute takes the lead on cancer research; and so forth. However, because one or another aspect of biology affects more than one disease or condition, NIH institutes sometimes work in parallel, and often together, to address specific shared interests. Several examples of research areas—categorized as important in the basic biology of aging—are illustrative: cellular senescence is one important process by which cells lose vigor and increase the risk of tumor formation, and at least four institutes of the NIH deal with this area of research (although the main ones are the National Cancer Institute and the NIA). Another facet

As the increase in survival to older ages becomes more an expectation than a dream, there is a greater need to understand how to improve and maintain health during aging.

of the biology of aging involves regeneration of damaged tissue, which declines with aging in most but not all animals. One broadly shared goal is to translate knowledge of the biology of regeneration (in animals that do versus do not retain this capacity) to improve regeneration in humans (whose regenerative capacity diminishes with aging); 13 institutes of the NIH are involved in this area. Likewise, 16 institutes of the NIH support research on inflammation, which can be both acute and chronic; the two forms of inflammation serve seemingly contradictory functions in health, on the one hand promoting healing but on the other hand increasing the risk for disease.

As the increase in survival to older ages becomes more an expectation than a dream, there is a greater need to understand how to improve and maintain health during aging. The NIH has always promoted and supported turning discovery into health via translating research to practice. The trans-NIH GSIG, for example, seeks to apply this credo to promote healthier aging. With an aim toward efficiency, members of the GSIG from 20 NIH institutes and centers work together, seeking innovative approaches to better identify the relationships between the biological processes of aging and the biological processes of age-related chronic diseases and disabilities. The underlying understanding is that these processes are likely to be the same, or to influence each other if they are not the same. We and others involved in this effort hope to meet the current and future challenges of aging and the age-related burden of disease through research supported by the diverse institutes and centers comprising the NIH.

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Origins of Geroscience

Gordon J. Lithgow

Before the outbreak of World War II, a group of physicians and biologists found themselves at a conference in the traditional biologist's retreat at Woods Hole on beautiful Cape Cod. The conversation turned to aging. With incredible vision, they recognized that studying aging would be vital for future human health and formed the Club for Research on Ageing. This club was the precursor to The Gerontological Society of America (GSA), founded in 1945. From its inception, GSA recognized the value of cross-disciplinary exchange. In its certificate of incorporation, the founders stated that one purpose of GSA was "to afford a common meeting ground for representation of the various scientific fields interested in such problems and those responsible for care and treatment of the aged." Over the years, many researchers have valued the interdisciplinary nature of the field but, during the rapid growth of the aging field between 1990 and 2000, some degree of balkanization emerged. The new geroscience initiative addresses this need to return to the vision of the GSA founders and strive for an interdisciplinary, research-focused approach to combat age-related disease.

Aging is the single greatest challenge for biomedicine in the 21st century, and statistics from numerous sources highlight the fact that age-related diseases increasingly represent a true national emergency. This state of affairs is particularly disturbing given the shortage of resources available to study aging processes and their relationship to disease. Two general approaches can be employed when facing this challenge, the first being the traditional approach of investigating single disease conditions in isolation. The single-disease model describes the vast majority of biomedical research, in which classes of diseases (cancer, neurological disease, metabolic disease, and so on) define laboratories, university departments, and institutes—even the structure of the National Institutes of Health (NIH). This model pretty much guarantees that, for example, a cancer biologist rarely encounters researchers interested in Alzheimer's disease or Parkinson's. Although this traditional approach will undoubtedly continue to yield important information, it appears to focus on combating downstream symptoms rather than upstream causes.

The observation that aging itself is the most important common risk factor for many of the world's socially and economically important diseases suggests a second approach, one that employs the methodology and organization of interdisciplinary science and perceives chronic disease as a spectrum of conditions that arise from a common cause: aging itself. In this way of looking at chronic disease, a neuroscientist is just as likely to provide critical information to a cancer biologist as anyone within the cancer field. This approach places aging processes at the center of disease research and strives to identify the features of normal aging that contribute to the origins of multiple disease states.

For much of the 20th century, research in the biology of aging remained outside the mainstream of serious science. Partly as a result of a series of false claims about so-called elixirs that originated from the early years of endocrinology, this sidelining was mainly due to a lack of any valid experimental approach demonstrating that the process of normal aging could be manipulated for research purposes. The comparison between aging and developmental biology is striking. Great strides were made in developmental biology throughout the second half of the 20th century, due primarily to the discovery of homeotic genes, the emergence of developmental programs, and the demonstration of sequential, tissue-specific gene action. During this period, aging research lacked any widely accepted paradigm, and experiments were generally confined to cataloguing changes at the functional, physiological, and tissue levels.

The application of genetics to the study of aging (or, more precisely, *longevity*) in the late 1980s provided an enormous impetus to the field and essentially ushered aging biology into the mainstream of biomedical research. The first clues to the genetic basis of longevity emerged from breeding experiments with the fruit fly *Drosophila* and the nematode *C. elegans.* Laboratory evolution experiments were conducted on *Drosophila*, and long-lived populations were developed by selecting for late reproduction. At the same time, recombinant inbred lines of *C. elegans* were created with very different life expectancies. Both of these approaches pointed to a hitherto unexplored genetic architecture of life span and aging, but the major conceptual breakthrough came with the discovery of single gene mutations that have profound effects on the *C. elegans* life span. Such mutations extended the mean and maximum life span 70 percent to

100 percent, with minor effects on the animal's growth and reproduction.

An entire subfield emerged from these discoveries, with hundreds of scientists finding hundreds of genes over the last 20 years. These genes encode a great variety of biological functions, including intracellular signaling pathways that are the subject of considerable current research. During this time, a problem emerged: An artificial distinction has been made between science aimed at understanding normal aging and research looking at disease. For the most part, some biologists seemed to focus only on longevity, doing everything possible to exclude disease from their models. This approach made sense because the experiments were designed to understand the determinates of the underlying aging rate—but a whole generation of scientists emerged who had no training in general gerontology, never joined GSA, and had little appreciation of the role of aging in disease pathology.

By the middle of the last decade, it became apparent that the mechanisms determining longevity in laboratory animals were very much related to the mechanisms being investigated in studies of cancer, cardiovascular disease, neurodegenerative disease, and so forth. Many of the major modifiers of longevity, such as insulin and TOR signaling pathways, were also under investigation as drug targets. Moreover, scientists studying neurological disease were focusing on age-associated molecular damage, such as a loss of protein homeostasis. It became clear that modulating the aging rate could be combined with disease models; interventions that slow aging appear also to postpone or eradicate age-related disease pathology. This observation was made previously in calorie-restricted rodents and suggests that much progress could be made if such interventions were available for humans.

Despite the fact that these observations suggested a new approach to aging and disease, scientists have been very slow to adopt it—in part because such science cuts across established disciplines. Current funding for aging research is primarily aimed at understanding individual age-related disease, with much less attention paid to aging itself as a possible cause. Individual laboratories often study individual diseases, sometimes even ignoring the aging component completely. It is startling that both individual laboratories and entire institutes devoted to age-related diseases ignore the single most important risk factor for age-related diseases. It is tempting to speculate that this failure to take aging into account has contributed to the massive failures in Alzheimer's disease clinical trials. This silo-like model likely will continue if the barriers between disciplines are not challenged and the biology of aging is not brought into mainstream biomedical research.

By 2005, researchers at the Buck Institute for Aging Research had come to the conclusion that progress could be made in combating chronic disease by modifying the course of aging. They coined the term *geroscience* to describe the science emerging at the interface of the biology of aging and age-related disease. At the Buck Institute, the term described the interrelated activities of molecular biologists, neuroscientists, protein chemists, cell biologists, geneticists, endocrinologists, pharmacologists, mathematicians, and others. NIH adopted the term for a Common Fund initiative, and the first Interdisciplinary Center on Geroscience was formed in 2007 to optimize interactions and create synergy between the field of biogerontology, numerous age-related diseases, and technology development. Now, more and more institutions are embarking on interdisciplinary approaches to aging; it will be exciting to see what emerges.

Aging is the single greatest challenge for biomedicine in the 21st century.

Perhaps researchers should be looking at the diseases of aging the way they once looked at major infectious childhood diseases. These terrifying diseases were brought under control because scientists understood that the diseases essentially had a single cause: microbes. The development of two general classes of interventions (antibiotics and vaccines) were sufficient to control a large number of distinct conditions. If the diseases of late life also have a single cause (aging itself), then researchers should be able to develop classes of therapeutics by targeting aging mechanisms in a way similar to targeting microbial infection.

Geroscience is not really a new approach; the scientists who incorporated GSA had the same idea. However, geroscience does describe a series of new discoveries linking aging to disease and, as such, offers a novel set of targets for the biomedical community. A new generation of scientists who have seen how easy it is to alter aging rates in the laboratory is maturing and applying that experience to investigating disease. These scientists are comfortable working in interdisciplinary teams and do not see or understand the need for traditional boundaries between disciplines, particularly between basic and clinical science. This group of researchers comprises a first generation of geroscientists—for the sake of us all, the scientific community needs to support their endeavors.

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Inflammation and Cellular Senescence: Potential Contribution to Chronic Diseases and Disabilities With Aging

James L. Kirkland

Introduction

Aging predisposes to most of the chronic diseases that drive morbidity and health costs—including atherosclerosis (leading to heart attacks, strokes, and peripheral vascular disease), diabetes, dementias, cancers, arthritis, and blindness—as well as frailty, age-related muscle dysfunction (sarcopenia), and loss of resilience. These conditions, as well as aging tissues, are associated with inflammation that is chronic, low grade, and sterile—indicating absence of detectable pathogens (Chung et al., 2009).

Cellular senescence, a process associated with chronic inflammation, is induced by a range of stresses, including DNA damage, reactive metabolites, and toxins (Tchkonia, Zhu, van Deursen, Campisi, & Kirkland, 2013; Waaijer et al., 2012). Although senescent cells cannot divide, they actively secrete multiple inflammatory mediators, including cytokines, chemokines, and proteases, termed the senescence-associated secretory phenotype, or SASP (Coppé et al., 2010). Senescent cell burden and SASP components increase in many tissues with aging (Freund, Orjalo, Desprez, & Campisi, 2010).

The immune system, especially macrophages, can clear senescent cells (Hoenicke & Zender, 2012; Yevsa, Kang, & Zender, 2012). Chemokines that attract macrophages are part of the SASP (Freund et al., 2010). However, with aging, macrophage responses become compromised (Sebastian, Lloberas, & Celada, 2009), potentially contributing to senescent cell accumulation. Furthermore, high senescent cell burden can interfere with immune function, with such SASP components as interleukin-6 (IL-6) inhibiting macrophage responsiveness (Guerrero et al., 2012). Because senescence could contribute to both age-related and chronic disease-related inflammation, selectively targeting senescent cells might interrupt links among aging, immune dysfunction, and disease, potentially delaying age-related chronic conditions as a group, instead of one at a time.

Cellular Senescence and Healthspan

My laboratory hypothesized that senescent cell removal could enhance healthspan. This hypothesis was based on the observation that senescent cell accumulation is delayed in fat tissue of long-lived mouse models, findings from the Sharpless laboratory that $p16^{INK4a}$ (a protein that promotes cellular senescence) increases with aging and is lower in mice with delayed age-related dysfunction due to caloric restriction (Krishnamurthy et al., 2004), and communications with the Campisi laboratory about the SASP (Coppé et al., 2008).

To test this hypothesis, we decided to make a mouse with a senescence-induced promoter driving a drug-inducible suicide gene (the AP20187-activated caspase-8 ATTAC construct, which we obtained from the Scherer laboratory; Pajvani et al., 2005), and a green fluorescent protein (GFP) reporter. This procedure would allow selective removal of senescent cells by treating mice with AP20187, a drug with little effect on normal cells, and tracking or isolating senescent cells in untreated animals based on GFP fluorescence.

We proposed using an accelerated aging strategy before turning to studies of chronological aging and characterizing the healthspan of the mice. We then worked with the van Deursen laboratory, which made mice with a transgene comprising a senescence-activated $p16^{INK4a}$ promoter element driving the suicide and tracking constructs. To accomplish the accelerated aging strategy, the mice were bred onto a progeroid background (BubR1 hypomorphic mice). In animals treated with AP20187, senescent cells were reduced and age-related cataracts and losses in fat tissue, muscle mass, and physical function were delayed compared with untreated genetically identical mice (Baker et al., 2011). These and related animals are being used to test if removing senescent cells delays onset of age-related chronic diseases.

Cellular Senescence and Age-Related Conditions

Inflammation and accumulation of senescent cells have been associated with several age-related conditions, some of which are considered here.

Frailty. *Frailty* refers to the muscle weakness, physical dysfunction, and decreases in mobility, endurance, and resilience that can occur in association with chronic disease and advanced old age. Frailty is related to systemic inflammation and, potentially, the SASP (Tchkonia et al., 2013; Walston et al., 2002). We envisage trials of agents that reduce inflammation or target senescent cells in borderline

frail subjects who are about to undergo such medical procedures as chemotherapy, radiotherapy, anesthesia, or elective surgery, which can push these subjects into overt frailty or delirium. After initial laboratory studies in animal models, such as old *INK-ATTAC* mice, clinical trials can be implemented of agents that target senescent cells on time to recovery of symptom scores, strength, or cognition after medical interventions.

Diabetes. Type 2 diabetes predisposes to coronary artery disease, stroke, neuropathy, retinopathy, kidney dysfunction, infections, and other conditions. Aging and obesity are risk factors for diabetes. Aging, obesity, and diabetes, in turn, are associated with senescent cell accumulation and increased circulating SASP-related cytokines that cause insulin resistance (Minamino et al., 2009; Tchkonia et al., 2010). Consistent with the possibility that targeting senescent cells could ameliorate diabetes, inhibiting p53-related cellular senescence reduced inflammation and enhanced insulin responsiveness in obese mice.

Cardiovascular diseases. Increased age is a leading risk factor for atherosclerosis, which predisposes to heart attacks, strokes, and peripheral vascular disease—leading causes of death and of health care costs. Atherosclerotic lesions are associated with focal senescent cell accumulation (Holdt et al., 2011; Minamino et al., 2002). Inflammatory cytokines produced by senescent cells contribute to the inflammatory microenvironment in blood vessels that predisposes to atherosclerosis (Wang & Bennett, 2012). Senescence-related fat tissue dysfunction may also contribute through increasing circulating atherogenic lipids (Tchkonia et al., 2010). Targeting senescent cells might reduce blood lipids and blood vessel dysfunction, potentially slowing or preventing progression of atherosclerosis.

Aging is associated with hypertension, a risk factor for cardiovascular disease, stroke, and kidney disease. Hypertension is associated with cellular senescence in the kidney and heart, which are among the end organs damaged by hypertension, suggesting a role for senescence in hypertension-induced morbidity (Westhoff et al., 2008). SASP factors that affect tissue regeneration and fibrosis might contribute to hypertension-related end organ dysfunction, a hypothesis that merits testing.

Lung disease. Aging and smoking, major risk factors for chronic obstructive pulmonary disease, are associated with elevated lung tissue $p16^{INK4a}$ (Aoshiba & Nagai 2009; Tsuji, Aoshiba, & Nagai, 2009), suggesting involvement of cellular senescence. Senescence and SASP-related cytokines may also contribute to idiopathic pulmonary fibrosis (Minagawa et al., 2011), another lung condition for which aging is a leading risk factor.

Dementias. Alzheimer's disease and other dementias, which are leading drivers of age-related disability, are associated with senescent cell accumulation at sites of brain pathology (reviewed in Golde & Miller, 2009). Tangles and plaques in brains of patients with Alzheimer's disease express $p16^{INK4a}$, a mediator of cellular senescence. Perhaps senescent cell removal can ameliorate a range of age-related neurodegenerative diseases.

Eye disease. Blindness and common major eye disorders, including cataract, glaucoma, and macular degeneration, are associated with aging. Removing senescent cells from *INK-ATTAC;BubR1*$^{H/H}$ mice delayed cataract development (Baker et al., 2011). Prevalence of glaucoma, which involves raised intraocular pressure, increases with aging. Cellular senescence has been noted in parts of the eye involved in fluid outflow in glaucoma patients (Liton et al., 2005). Macular degeneration is the commonest cause of blindness in elders. Retinal pigment epithelial cell senescence has been proposed to contribute to macular degeneration (Kozlowski, 2012). Thus, cellular senescence is at least associated with the major eye diseases. Perhaps targeting senescent cells will prevent or ameliorate these diseases.

Cancers. Accumulation of mutations in genes that predispose to cancer could contribute to increasing cancer incidence with aging. Cancer development also requires a permissive tissue microenvironment (Gupta & Massague, 2006). Cellular senescence may defend against cancer in younger individuals, because senescence of potentially cancerous cells stops their proliferation and SASP components may destroy adjacent precancerous cell collections. In younger individuals with limited numbers of senescent cells and an intact immune system, senescent cells might be removed soon after their appearance. However, in older individuals, the SASP could contribute to a cancer-permissive microenvironment owing to both increased senescent cell accumulation and reduced senescent cell clearance due to compromised immune function (Campisi & d'Adda di Fagagna, 2007). Indeed, injecting senescent fibroblasts together with precancerous cells into mice promotes tumor formation (Liu & Hornsby, 2007). Studies to test if removing senescent cells reduces cancer initiation or spread in mice are underway.

Radiation and certain chemotherapeutic drugs can increase senescent cell burden, suggesting that senescence and the SASP might contribute to complications after cancer therapy (Le et al., 2010; Roninson, 2003). Patients treated for cancer as children frequently develop diseases that have been associated with cellular senescence, including coronary artery disease, strokes, cognitive dysfunction, and other types of cancer, earlier than siblings who had not been treated for cancer (Oeffinger et al., 2006). Furthermore, IL-6,

a prominent SASP component, increases following cancer treatment (Cesari et al., 2004). Drugs that reduce effects of IL-6 ameliorate frailty-like symptoms in patients with pre-malignant hematologic disease (Verstovsek et al., 2010). Thus, targeting senescent cells might reduce short-term and long-term effects of cancer treatment.

Bone and joint diseases. Osteoarthritis is the most common cause of disability in elders. In osteoarthritis, inflammatory cytokines and proteases that are SASP components are present in synovial fluid (Freund et al., 2010) and senescent cells accumulate in cartilage (Price et al., 2002). Focal senescent cell accumulation can occur in cases of fracture nonunion (Bajada, Marshall, Wright, Richardson, & Johnson, 2009). Osteoporosis has been associated with cellular senescence in mice (Chen et al., 2013). Thus, cellular senescence could play a role in age-related bone and joint disease.

Other diseases and disabilities. Several other chronic conditions appear to be associated with both aging and cellular senescence, such as prostatic hypertrophy (Castro, Giri, Lamb, & Ittmann, 2003). Senescent cells can also accumulate in young individuals with progeroid, accelerated aging-like syndromes (Benson, Lee, & Aaronson, 2010). Although in general senescent cell abundance is higher in tissues from older subjects than in those from younger subjects, these cells can appear at any point during life, especially at sites of disease.

Conclusions

Chronic inflammation, cellular senescence, or other fundamental aging mechanisms could be at the nexus between chronological aging and many of the chronic diseases that are responsible for the bulk of deaths, morbidity, and health costs in modern society. Much work remains to be done to test if these associations are causal and, particularly, if interventions that target basic aging mechanisms ameliorate age-related diseases. Such interventions need to be thoroughly tested in disease-specific animal models (preferably old animals with an aging tissue microenvironment) and subsequently in clinical trials. If these interventions indeed delay age-related chronic diseases as a group and compress morbidity, health care as we know it could be transformed.

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Delayed Aging Versus Delayed Disease: A New Paradigm for Public Health

Dana P. Goldman • S. Jay Olshansky

Health Investment

Life expectancy has increased dramatically since the beginning of the 20th century, and many people are now living decades longer than their ancestors did just three or four generations ago. Most of the rise in longevity has been driven by basic advances in public health and better nutrition but, more recently, improved behavioral risk factors (e.g., reduced smoking) and treatments for specific diseases have extended life further.

More recent declines in death rates, especially at middle and older ages, are largely a product of a successful disease model in which physicians and scientists have found ways to either delay the onset and progression of fatal diseases or extend the lives of those who have them. The contemporary disease model is an outgrowth of the approach to infectious diseases that arose centuries ago in which each disorder is treated as it arises—as if independent of all other conditions.

The longer lives we enjoy have come with both desirable and undesirable side effects. On the positive side, healthy life span has risen rapidly for many during the last century—offering individuals and societies unique opportunities to benefit from many more healthy, active, and productive older people then ever before in history. In fact, in one of our forthcoming publications (Lowsky, Olshansky, Bhattacharya, & Goldman, in press), we demonstrate that even in the oldest region of the life span (those ages 85-plus) in the United States, a surprisingly large percentage of people are in nearly perfect mental and physical health. In many important ways, a segment of the oldest old is not much different than people decades younger. In addition, the absolute number of healthy older people will rise rapidly due to population aging in the coming decades, and there is reason to be optimistic that the healthy lifestyles adhered to by many will pay off in even further extensions of healthy life.

Longer lives also have been accompanied by a Faustian trade—the rise of chronic fatal and disabling conditions at unprecedented rates in recent decades. Keep in mind that children saved from dying of communicable diseases, which killed many before the age of 10 throughout human history, now live long enough to experience the complications that accompany aging bodies. Although the good news is that a much longer portion of our total life spans are lived in relatively good health, the rise of cardiovascular disease, cancer, Alzheimer's, and a host of other conditions is largely a product of living long enough to experience them.

An additional complication of longer lives is that many more people are now qualifying for old-age entitlement programs, such as Social Security and Medicare, and they will remain in these programs longer. These social programs were not originally designed with this level of extended survival in mind.

There may be considerable debate about the future course of health and longevity, but one important factor that influences them both has not changed: The approach to fatal diseases remains firmly entrenched in the disease model. We tend to wait until a health condition arises, treat it, and then live on until another health hurdle gets in the way. Proactive primary prevention is relatively rare.

Although advances in attacking diseases have extended life, evidence suggests they may not continue to extend healthy life at older ages—especially not at the levels witnessed in recent decades. Demographic

Recent research has shown that decades of improvement in the functional status of older Americans has halted since 2002.

modeling has shown that increased disability rates are now accompanying increases in life expectancy in the United States—or, at best, leaving healthy life span unchanged. The rise of adult-onset and childhood obesity suggests that future cohorts of older people may face even more health challenges than cohorts reaching older ages today.

As people age, they are much less likely to fall victim to a single, isolated disease. Instead, competing causes of death more directly associated with biological aging cluster within individuals as they approach later ages. These conditions elevate mortality risk, as well as create the frailty and disability profile that can accompany old age.

A new form of aging science is beginning to emerge (described in greater detail in this issue of *Public Policy & Aging Report*) that has the potential to extend healthy life and simultaneously reduce the prevalence of comorbidities over the entire lifetime. In deciding whether and how much society should invest in this new delayed-aging model, three questions arise:

1. What are the relative health and economic benefits and costs of delayed aging versus the delayed-disease model?
2. Can we afford to continue with the delayed-disease model given the large demographic shifts that are forthcoming and the anticipated diminishing returns from investments that treat diseases after they arise rather than proactively delaying their occurrence?
3. Can society afford to invest in the science that would lead to accelerated development of interventions that extend healthy life?

A newly published white paper (Goldman et al., in press) answers these questions. Here, we provide a brief summary of the findings.

Using the Future Elderly Model (a microsimulation that tracks cohorts of people age 51 or 52 and older through time based on the Health and Retirement Survey), we predicted medical spending, health conditions, functional status, and employment given initial demographic and health conditions. In addition, we developed five scenarios about the future course of mortality (projected to 2060) and compared them along health and medical spending dimensions.

Two disease-specific scenarios represented continuations of the status quo in medical research, disease treatment, and improvements in behavioral risk factors (e.g., attacking diseases either individually through treatments or systemically through behavior modification). A delayed-aging scenario was designed to be a hypothetical assessment of a successful effort to translate research on the biology of aging into therapeutic interventions that reduce and compress both morbidity and mortality into a shorter duration of time at the end of life. We then added in delayed-cancer and delayed–heart disease scenarios to represent realistic improvements in death rates from both major causes of death in the coming decades. The published manuscript contains details of the data, microsimulation model, and all related assumptions.

Our results demonstrate, first, that the number of people ages 65 and older in the United States is expected to more than double over the next 50 years under current optimistic scenarios about major fatal diseases, rising from 43 million in 2010 to 106 million by 2060. However, if delayed aging comes to pass, there would be just under 7 percent more people ages 65-plus in the United States in 2060. More important, under the delayed-aging scenario, a significantly larger number of people who reach ages 65 and older between now and 2060 would be healthy relative to conditions that would exist under the other scenarios. Additional evidence of the health benefits of delayed aging is that per capita Medicare spending is shown to be lower in the delayed-aging scenario.

Delayed aging would also yield a larger 65-plus population between now and 2060, which means more people would qualify for federal entitlement programs—thus raising their costs. A hypothetical increase in the age of eligibility for Medicare would fix this problem, but it is uncertain whether this fix or some other modification to Medicare would be most appropriate to handle the larger, healthier older population that would result from delayed aging.

Competing health risks limit the impact of major clinical breakthroughs for specific diseases.

Our results demonstrate that shifting the focus of medical investment to delayed aging would lead to a unique set of desirable but economically challenging circumstances. The potential gains are significant. Although the disease model has reduced mortality from lethal conditions dramatically in the past century, its influence is now waning because of competing risks. As people live longer, they are more likely to experience

multiple diseases. Our simulations of reduced incidence of cardiovascular disease and cancer suggest incrementally smaller gains in longevity going forward by continuing to attack these diseases independently.

More generally, the focus on healthy aging should also be emphasized. Recent research has shown that decades of improvement in the functional status of older Americans has halted since 2002 (Bhattacharya et al., 2004; Crimmins & Beltran-Sanchez, 2011; Hulsegge et al., 2013; Lakdawalla, Bhattacharya, & Goldman, 2004). This trend suggests that many of the historical drivers of better health in older adults will not continue, so we now need to look elsewhere. Declining disability buttresses the case for research on slowing aging by compressing morbidity and extending healthy life, because it will provide an adequate workforce for the goods and services the future aging society will use.

Whether the current focus of medical research and investment should be shifted from the disease model to delayed aging depends on whether the potential gains can be realized and the adverse consequences allayed.

Still, the fact remains that longer lives mean that Social Security and other income-support programs have greater fiscal burdens, and total Medicare and Medicaid expenditures increase even as per capita medical costs decline. An unequivocal answer to the question of whether the current focus of medical research and investment should be shifted from the disease model to delayed aging depends on whether the potential gains can be realized and the adverse consequences allayed.

It is clear that competing health risks limit the impact of major clinical breakthroughs for specific diseases—that is, making progress in one disease means another one will eventually emerge in its place. This state of affairs makes research and investment to delay aging quite valuable, given the evidence suggesting that all fatal and disabling disease risks are lowered simultaneously. Not surprisingly, we see extremely large population health benefits in our delayed-aging scenario. The major challenges of delayed aging appear to be of a fiscal nature, although these are manageable. In any case, benefits to societies from delayed aging would accrue rapidly and extend to all future generations.

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Biogerontology in the Public Arena: 'Its Hour Come Round at Last'

Dan Perry

Like the rough beast of the famous poem by W. B. Yeats, a scientific consensus that aging might be slowed to avert chronic diseases in older people is slouching toward serious consideration in public policy.

Aging populations on the rise worldwide prefigure drastic increases in age-related disabilities (Alliance for Aging Research, 2013; United Nations Population Fund & HelpAge International, 2012). Responding to this looming public health crisis, biogerontologists and their allies are proposing a moon-shot effort to harness the underlying processes of aging as a new model for health promotion and disease prevention in the 21st century (Butler et al., 2008).

Aging has long been recognized as the leading risk factor for chronic diseases and infirmities of old age, ranging from cancer to Alzheimer's disease to physical frailty. Recent research using mammalian models has fueled speculation that aging is potentially modifiable as a source of infirmities of aging in humans as well (Carnes, Staats, & Sonntag, 2008; Kirkland, 2013; Miller, 2009; Rae et al., 2010).

Among putative interventions to blunt disease risks are antiaging dietary and pharmaceutical interventions, as well as strategies to extend youthful health by removal of senescent cells from living tissues (Accili, de Cabo, & Sinclair, 2011; Colman et al., 2009; Harrison et al., 2009; Tchkonia, Zhu, van Deursen, Campisi, & Kirkland, 2013). Encouraged by high-level support for a multi-institute mechanism at the National Institutes of Health (NIH) promoting research collaborations into the underlying biology of aging, advocates are primed to press for increased funding from both federal sources and private philanthropy (Olshansky, Perry, Miller, & Butler, 2006).

The belief that aging itself, rather than the separate health issues of old age, is a proper target for interventional science has been attracting adherents for decades.

Forty years ago, when Congress created the National Institute on Aging (NIA), leading scientific authorities touted lengthened lives with vigor in old age as a primary goal of the new agency. Lawmakers including the venerable Claude Pepper embraced the goal of life extension with an enthusiasm rarely heard today among political figures or from the NIH.

With unbridled optimism, Pepper (who at the time chaired the House Aging Committee) regaled his colleagues that understanding aging would transform healthcare: "With the incredible potential of worldwide technology and invention, it won't surprise me to learn—I hope!—that people are living regularly to 150 and 200 years old if they are born in the middle of the next century" (United States House of Representatives Select Committee on Aging, 1978, p. 15).

In the decades since, it has been easy to ignore those who champion medical interventions slowing aging as a strategy to prevent and postpone the chronic diseases that affect older people.

Richard Miller addressed a scientific audience a few years ago with an only slightly tongue-in-cheek assessment of why biogerontology has failed to be embraced as a panacea for age-related diseases and disability among the older population. Miller assessed the obstacles to finding a cure for aging as 85 percent political and 15 percent scientific. Among the political obstacles Miller (2006) noted:

- Aging is viewed (incorrectly) as unalterable.
- Drugs that actually slow aging cannot be tested in time to show a profit within the CEO's lifetime; whereas drugs *purported* to slow aging are highly profitable even though they don't work.
- A politician who wants to "conquer cancer" is a hero. A politician who wants to "slow aging" is a nut-case.

Regardless of which of Miller's hurdles are most daunting, the fact remains that federal funding of biomedical research continues to pursue cures and better treatments for specific diseases, especially for those with vocal constituencies. Recent developments, however, including congressional interest and creation of the trans-NIH Geroscience Interest Group (GSIG), are setting the stage for a determined push for increased federal support for age-modifying research with clinical potential.

If the creation of the GSIG and its starring role in the high-level 2013 Geroscience Summit Conference leads to a bolder emphasis on interventional aging studies in the United States, the success will have a long and distinguished pedigree.

In the early 1970s, scientists studying the underpinnings of aging, along with their supporters, agitated for establishment of a separate gerontological institute to be added to the NIH. The greatest advocate for this new institute was the indomitable Florence Mahoney, a society matron with close ties to the Cox publishing empire. Mahoney employed intimate dinner parties in her home in the fashionable Georgetown district in Washington, D.C.,

as an instrument for forging political alliances for her favorite causes. In 1974, she told a reporter:

> I'm working now for a bill that would create another institute for the National Institutes of Health. This one would serve as a center for research into aging. I am convinced that if we get one, within a few years—with drugs and knowledge—we would prevent or slow down the disease of aging. (Robinson, 2001, p. 236)

Mrs. Mahoney lobbied Senator Thomas Eagleton (who introduced the Research on Aging Act of 1974), declaring, "Basic research in the process of aging is widely recognized in the scientific community as an idea whose time is come" (Robinson, 2001, p. 243).

Congressional records show that lawmakers expected positive returns for extended health and vitality for older Americans to come from deep probes into the basic mechanisms of aging (United States House of Representatives Select Committee on Aging, 1978). The Gerontological Society of America and the American Geriatrics Society in a joint statement declared that "the study of the aging process, the one biological condition common to all, has not received research support commensurate with its effects on the life of every individual" (United States Senate Special Committee on Aging, 1974, p. 51)

Biochemist and author Bernard Strehler was another influential proponent of research that might alter the human experience of aging. Moving from the NIH Gerontological Center in Baltimore in 1967, Strehler took charge of the Ethel Percy Andrus Gerontology Center at the University of Southern California. He wasted no time in introducing himself to California's newly elected U.S. senator, Alan Cranston. Under Strehler's tutelage, Cranston became an ardent champion of research into aging while serving on the Senate authorizing committee that oversaw the NIH.

Strehler told senators,

> Those of us who are directly involved in research on the origins and effects of aging believe that the new Institute is the first step toward the understanding of the origins, impairments and eventually . . . retardation and perhaps even reversal of at least certain aspects of this most universal enemy of mankind's health, in mind and body. (United States Senate Special Committee on Aging, 1974, p. 54)

While testifying at a congressional hearing, Richard Greulich, the NIA's first scientific director, outlined efforts to establish a body of research that might ultimately "reverse, delay, or in some other way ameliorate the deleterious effects of human aging" (United States House of Representatives Select Committee on Aging, 1978, p. 4).

In an echo of today's advocates for extended health span through research, British gerontologist Alex Comfort told a House committee, "We are talking about making it take 70 years to reach 60 or possibly if we are lucky taking 80 years to reach 60" (United States House of Representatives Select Committee on Aging, 1978, p. 17).

Not every lawmaker who heard these bold statements from scientists was enthusiastic. One member of the House committee said, "There is growing biomedical evidence that by the year 2000, aging will be understood and possibly overcome. While this would fulfill mankind's fondest dream—the possibility of life without death—it would also disrupt our society thoroughly" (United States House of Representatives Select Committee on Aging, 1978, p. 3).

An influential 1977 dialogue under the auspices of the National Science Foundation conference led by University of Chicago professors Bernice Neugarten and Robert Havighurst also reflected concern for the ethical and social consequences of extended longevity (Neugarten & Havighurst, 1977). Conference-goers—including lawmakers and staff, economists, legal and medical authorities, and heads of think tanks and senior citizens organizations, along with officials of the Johnson administration—debated whether the federal government should mount a concerted scientific research effort to control the underlying processes of aging in order to extend years of health. Proceedings were subsequently shared with Congress and government staff. The Neugarten and Havinghurst report sparked a burst of intellectual energy that became a rallying point for a new generation of biogerontologists (Olshansky & Hayflick, 2011).

Among the participants at the National Science Foundation conference, the strongest proponent for pursuing the slowing of the rate of aging as a national goal was James L. Goddard, former commissioner of the Food & Drug Administration. He told the group that gerontology had reached a point where, if coupled with "a sophisticated body of experimental data and a highly sophisticated technology," it would allow science to move rapidly toward "fulfilling man's age-old dream of extending life" (Neugarten & Havighurst, 1977, p. 21).

As a former federal official, Goddard bemoaned that research in aging was relatively trivial compared with the moneys invested in specific diseases of aging. He judged that the disparity was due to the lobbying power of disease-specific support groups and medical professions active in those fields.

Goddard described what is needed to mobilize a national research drive to slow aging. His list might be profitably studied by today's advocates on behalf of the same goal. A national project on the scale of the space

Aging has long been recognized as the leading risk factor for chronic diseases and infirmities of old age.

program or the Manhattan Project, he said, "requires a coalition of outstanding leadership, strong political support, the presence of strong vested interests, political support, the economic wherewithal, and . . . a capability which can reasonably be expected to lead to a successful outcome" (Neugarten & Havighurst, 1977, p. 22).

For more than a half-century, the federal investment in medical research has focused on a proliferating number of new categorical institutes named for specific diseases and constituencies. Earlier in its history, the NIH was a laboratory for studying bacteriology and promoting public hygiene. Somewhat later, it focused on basic biology and the production of vaccines and antitoxins. Following World War II, the tradition of using scientific names for major divisions of the NIH came to an end. With a flood of new moneys approved by Congress, institutes now were named for diseases—cancer, diabetes, heart disease, stroke—to ensure continued congressional largess (Harden, 2013).

Established in 1974, the NIA was not immune from the imperative to identify its work with a specific disease and constituency. Robert Butler, the first director of the NIA, understood how political support grows from "the health politics of anguish" (Robinson, 2001, p. 249). Given voice by interest groups, this dynamic has shaped the modern NIH, disease by disease.

Moreover, Butler realized that he needed to identify a disease of aging the NIA could call its own. He told a biographer that

> we really had to do what the other institutes had done to survive—they had "disease missions." The ordinary person didn't think you could do anything about aging. I thought we needed a terrible disease to publicize, and picked Alzheimer's. (Robinson, 2001, p. 249)

During most of the NIA's funding history, grants and centers aimed at Alzheimer's disease have occupied approximately half of the institute's budget. Some researchers disdained the trend as the Alzheimerization of aging (Adelman, 1998). Even Butler, who defended a large investment for Alzheimer's, also spoke out for greater balance and a broader research mission for the NIA (Benowitz, 1996).

Butler later teamed with colleagues in the field of aging to call for pursuing a longevity dividend (Olshansky et al., 2006), referring to the health, economic, and social benefits that might result from retarding aging processes to postpone diseases of middle age and late life. The Alliance for Aging Research brought the theme to Capitol Hill in 2006 and drove the point home in presentations aimed at senators and their staffs (Alliance for Aging Research, 2006).

Months later, a newly adopted Senate appropriations bill instructed the NIH that

> new discoveries have led many scientists to believe that it may become possible to postpone the onset of a wide range of fatal and disabling diseases, in a coordinated fashion, by retardation of the aging processes. . . . to alleviate this financial burden [of diseases of aging] and to develop interventions that can extend health and longevity, the Committee urges the NIH to increase dramatically its annual investment in the biological basis of aging. (United States Senate Committee on Appropriations, 2007, p. 138)

Senate appropriations language again, in 2012, further solidified congressional support for the formation of the GSIG, which would focus on the relationships between aging and age-related disease and disability (United States Senate Committee on Appropriations, 2012). In record time, the GSIG won endorsements from heads of 20 separate NIH institutes and centers. According to the director of communications at the NIH Office of Intramural Research, "GSIG is the most exciting and dynamic interest group to emerge at the NIH in recent years" (C. Wanjek, personal communication, July 18, 2013).

Advances in Geroscience: Impact on Healthspan and Chronic Disease, a 3-day geroscience summit slated for October 31, 2013, through November 1, 2013, will explore how mechanisms that drive aging constitute the common predisposing steps for virtually all chronic disease and are the shared targets of NIH research in laboratories throughout the United States. NIH director Francis Collins plans to lead off the sessions. Some 50 scientists will highlight research on inflammation, adaption to stress, stem cells and regeneration, metabolism, epigenetics, and macromolecular damage—all common drivers of aging and chronic disease.

If this gathering and related activities succeed in heightened recognition (especially across the NIH and in the nation's academic research centers) of research and medical modification of aging as the common road to healthier aging, the dreams of champions past—Claude Pepper, Florence Mahoney, Alex Comfort, Bernard Strehler, Robert

Butler, and others—will be validated and brought to wider national attention at long last.

Dan Perry is president of the Alliance for Aging Research in Washington, D.C.

Mechanisms that drive aging constitute the predisposing steps for virtually all chronic disease.

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Beyond Medicare Reform: Strategies to Enhance Health and Well-Being in Older Persons

John W. Rowe • Linda P. Fried

One of our society's greatest accomplishments, the dramatic progressive increases in life expectancy, also presents one of its greatest challenges as we struggle to develop effective approaches to the design, delivery, and financing social and health care services for the rapidly increasing numbers of older persons. Much of the current debate regarding health care for the elderly relates to payment reform in Medicare, including a variety of valuable initiatives relating to enhancements in quality, reductions in waste, and increases in value. But these efforts, even if successful, will fall short of creating a system of services that meet the needs of older persons.

As geriatricians/gerontologists, we and other members of the MacArthur Network on an Aging Society have developed a set of recommendations that go beyond the current Medicare reform discussion and that we believe can strengthen our capacity to enhance the well-being of our growing elderly population. In this brief article, we highlight our thoughts regarding three of the critical areas: the health care workforce, social and community supports and efforts to enhance engagement of older persons, and public health and prevention. The background documents regarding the organization's analysis and complete set of recommendations regarding health care can be found at www.agingsocietynetwork.org.

Workforce Issues

From the perspective of the competence of the health care workforce, we are ill prepared to meet the demand for health care services of the future elderly population. The United States has two simultaneous major health care workforce challenges. The first is the inadequate numbers of health care providers available to provide basic primary care services, especially in light of health care reform legislation, which will provide health insurance to over 30 million previously uninsured individuals. There is currently broad debate regarding whether the best strategy to enhance our primary care capacity should be to train more primary care providers, rely more on interdisciplinary teams, or enable advanced practice nurses to provide core primary care services without direct physician supervision. The strategy latter has been recommended by the Institute of Medicine (2010) but resisted by some physician organizations on the stated grounds that the quality of care may suffer.

A second and equally serious problem is the general lack of expertise in geriatric medicine in the U.S. health care workforce, including physicians, nurses, social workers, and others. This issue has been addressed in *Retooling for an Aging America*, a report from the US National Academy of Sciences (Institute of Medicine, 2008). Although evidence shows elderly people benefit from health caregivers who understand the needs of their age group, less than 1 percent of doctors and nurses have training in geriatric care.

Even fewer physician general practitioners have training in geriatric care. A focus on expanding the numbers of geriatricians is critical. Geriatricians are in extremely short supply. As of 2012, there was one 1 geriatrician for every 2,551 Americans age 75 or older. Given the projected increase in the number of older Americans, this ratio is expected to drop to 1 geriatrician for every 3,798 older Americans by 2030 (American Geriatrics Society, 2013). Earlier studies predicted that 36,000 additional geriatricians would be needed by 2030, but a more recent study (Peterson, Bazemore, Bragg, Xierali, & Warshaw, 2011) has called that estimate "impossible and unrealistic" (p.701).

The Institute of Medicine made several specific recommendations, including a strengthened effort to ensure that all physicians and nurses, as well as specialists, receive training in the basic principles of geriatric care, including the diagnosis and management of not only so-called noncommunicable, chronic diseases that are increasingly common with advanced age, such as diabetes, cancer, heart disease, and stroke, but also dementia, frailty, polypharmacy, incontinence, and other common geriatric syndromes. The focus must be on both quantity and quality of health care staff—not only having adequate numbers but also ensuring their competence in geriatrics.

Social and Community Support, Care, and Engagement

The health of a population is supported not only by obvious medical and public health efforts but also by the social supports, networks, and community that bind people to one another and prevent social isolation. Social

From the perspective of the competence of the health care workforce, we are ill prepared to meet the demand for health care services of the future elderly population.

isolation is an important predictor of health, and disengagement in late life is a very significant public health problem.

In the United States, the family has served as the primary safety net for the social, psychological, and financial needs of older persons, while government—in the form of social insurance, medical insurance, and community services—has played a supportive but secondary role. Family caregivers are an important source of support for an aging population, and informal caregivers—either relatives or friends—care for the vast majority of older adults with disabilities. The estimated economic value of their unpaid contributions was approximately $450 billion in 2009 (Feinberg, Reinhard, Houser, & Choula, 2011). The magnitude of informal caregiving services is such that, if such unpaid care were not available, the costs would overwhelm our health care system. With increased life expectancy and the arrival, in 2011, of the first of the baby boomers to age 65, the need for home-based care provided by informal caregivers will continue to grow.

Important changes in the structure and function of the family are threatening the capacity of the family to serve this traditional safety-net role. Simultaneous increases in life expectancy and decreases in fertility are leading to more elders with fewer younger family members to support them. For instance, in the year 1900, 21 percent of the U.S. population had living grandparents at birth; in the year 2000, 76 percent had living grandparents when they reached age 30 (Gonyea, 2013). Increases in women's participation in the workforce and the fact that as the oldest old reach into their 90s and beyond, their children are also becoming old and have problems of their own further aggravate the difficulty. It is, of course, important to note that all evidence suggests that families wish to care for their elders; the problem is not intent, but capacity.

The risks for older persons from these changes in family structure and function are both financial and social. Those who see themselves on the bottom rung of social connectedness are more likely to have poorer health and shorter lives. As Laura Carstensen (2009) has writes in *A Long Bright Future*, these findings suggest that "health isn't just predicted by how many resources people have, but by how they relate to other people" (p. 101).

Being part of a community, having friends, and getting out of the house are all predictors of better health. For older adults, the threat of social isolation grows with time as friends and spouses die and life becomes more restricted. Active and productive engagement is associated with better physical health, lower rates of depression, and less use of medical services (Seeman et al., 1995). As volunteers, older adults can fulfill important social and economic needs while reaping the very real mental and physical health benefits of social contribution. In "Building Communities That Promote Successful Aging," Fried, Freedman, Endres, and Wasik (1997) and colleagues write that while many older adults have a great deal of time available to them, they are "in the main, marginalized from productivity . . . even though being able to make a contribution has been described as an essential element of 'successful aging'" (p. 216).

There are many approaches possible for creating societal win-wins that support the contributions that older adults seek to make. For this discussion, we highlight social programs that support grandparents with a significant amount of responsibility for their grandchildren, programs that both protect the children and ease stress on the grandparents. In addition, these programs can support the caregivers responsible for older adults. Federal policy should both directly support these goals and encourage states to do so as well.

Prevention and Public Health

Much of the trend driving health care spending today is the result of an epidemic in chronic conditions, including heart disease, hypertension, and diabetes, which has origins in changing patterns of diet and physical inactivity. Chronic disease has been estimated to account for 75 percent of health system costs, and more than two thirds of Medicare beneficiaries in 2008 had at least two chronic conditions (Centers for Medicare & Medicaid Services, 2010). Many of these conditions can be prevented or the disease progressions slowed through intensive lifestyle interventions. The results of research into the most effective prevention and screening tools for these conditions, specifically in older individuals, should inform prevention efforts and the coverage and cost sharing associated with their use.

Health economist Dana Goldman, a member of the MacArthur Network on an Aging Society, has studied the value of investments in longer lives of better quality of preventing disease in the first place, rather than treating it later (Goldman et al., 2009). He examined, for example, the

costs and benefits of preventing cardiovascular risk factors such as diabetes, hypertension, obesity, and smoking and finds that prevention—even at older ages—has great social value and would be cost-effective if the right interventions are adopted. Goldman and his colleagues found, for example, that a person age 51 or 52 who was effectively treated for diabetes would add 3.1 years and 1.6 quality-adjusted years to life and would save $34,483 in lifetime medical expenses. Quality-adjusted years are defined as years with minimal impediments to mobility and daily activities, as well as minimal pain and depression. Results were similar, though with smaller effects, for other conditions. The bottom line is that these chronic diseases could be prevented and could add significantly to quality of life without increasing average lifetime medical spending.

The creation of the Prevention and Public Health Fund by the Affordable Care Act was a first step toward this goal. The fund, according to the U.S. Department of Health and Human Services, is "an unprecedented investment in promoting wellness, preventing disease, and protecting against public health emergencies" (U.S. Department of Health and Human Services, 2013, ¶ 1). The fund helps the states tackle and prevent the leading causes of death and root causes of costly, preventable chronic disease, detect and respond rapidly to health security threats, and prevent accidents and injuries. In addition, the Affordable Care Act creates a National Prevention, Health Promotion, and Public Health Council, composed of senior officials across the government, to elevate and coordinate prevention activities and design a focused strategy across departments to promote the nation's health.

Unfortunately, ongoing use of funds from the Prevention and Public Health Fund in order to offset spending in other areas threatens to undermine the preventive capacity of the entire health care system. This problem is exacerbated by the fact that, although the fund was intended to supplement, not supplant, existing public health funding, this has not necessarily been the case in the face of current budget restrictions.

While the ongoing efforts to improve the effectiveness and efficiency of Medicare are important, and likely necessary to preserve the availability of this landmark program, the intense focus on Medicare reform has been to the neglect of other areas, as described above, which must be advanced if we are to establish a truly effective approach to enhancing well-being and managing chronic disease in older persons.

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handicapped in making its case to the Appropriations Committee because 'no one had ever died of microbiology.'"

The articles in this issue of *PP&AR* revolve mostly around the GeroScience Interest Group (GSIG) at the National Institutes of Health (NIH), an initiative involving multiple institutes and centers that is actively promoted by biologists and others, many affiliated with The Gerontological Society of America and the American Geriatrics Society. The group's aim is to establish first-order recognition of aging itself as a major risk factor for a host of physically, mentally, and economically devastating diseases that mark much of contemporary old age. Authors argue here that the cancers, heart disease, and dementias central to health-related concerns are, to a significant degree, a product of living long enough to experience them. Longevity research holds the promise of primary prevention, rather than remediation after disease has struck. To the degree that primary prevention can be demonstrated, geroscience and the longevity dividend could assume the paradigmatic stature of 19th-century public health.

The lead article by S. Jay Olshansky, who played a central role in organizing this issue of *PP&AR*, lays out the promise and the challenge of what slowing the biological processes of aging might mean. He notes that "a large number of health issues begin to emerge and cluster tightly into later regions of the life span," a phenomenon known as competing causes—that is, lethal and disabling conditions that accumulate in aging bodies. Olshansky also counters the principal misconception associated with the Longevity Dividend initiative: that delayed aging will only extend the period of infirmity at the end of life; no scientist, he offers, would engage in research and intervention that would not result in an extended period of *healthy* life. More positively, he concludes that longevity-dividend research would centrally address the reality that aging is the principal risk factor for a host of diseases and that, in the absence of research addressing this truth, advanced old age will be increasingly problematic. In a companion piece, Olshansky and Dana Goldman acknowledge that delayed-aging research might lead to a "unique set of desirable but economically challenging circumstances." Healthier late life would clearly be all to the good on its own terms, but the authors acknowledge that Social Security, Medicare, and Medicaid might face additional fiscal burdens even if per capita medical costs were to decline. On balance, they suggest that extremely large population health benefits would outweigh the fiscal challenges.

Felipe Sierra and Ronald Kohanski of the National Institute on Aging (NIA) speak to steps being taken at the NIA and the NIH to promote research into the basic biology of aging, identifying aging as the major risk factor for the chronic diseases prevalent in the older population. In particular, they review the work that GSIG is currently promoting. For example, geroscience can identify many of the genes and biochemical pathways that can increase life span; animal studies have shown that life span is quite malleable and can be extended by manipulation of a set of genes linked to aging. Within the NIH, new cooperative ventures involving an array of institutes and centers are underway.

Gordon Lithgow addresses the work of physicians and biologists who early on saw and continue to see that the study of aging is vital to the future of human health. Yet, disease-specific research and the evolution of a disease-specific structure at the NIH impeded the steps that an aging-first approach might have generated over the years. As one source of division, Lithgow points to an artificial distinction having been made between science aimed at understanding normal aging and science aimed at studying disease. He mentions individual laboratories that have ignored the aging component completely, and he goes on to speculate that the shortcomings of many Alzheimer's disease clinical trials may have resulted from a failure to take aging effects adequately into account. He and colleagues at the Buck Institute coined the term *geroscience* to describe the interface of the biology of aging and age-related disease, work that an emerging generation of biogerontologists is now pursuing.

James Kirkland turns to one element of aging as a major risk factor in late-life diseases: cellular senescence, a process associated with chronic inflammation. Because senescent cells secrete multiple inflammatory mediators, senescent cell burden and inflammatory components increase in many bodily tissues with aging. Thus, selectively targeting senescent cells might interrupt links among aging, immune dysfunction, and disease, "potentially delaying age-related chronic conditions as a group, instead of one at a time." Kirkland enumerates a series of diseases and disabling conditions that might be alleviated through successfully addressing cellular senescence and concludes, "If these interventions indeed delay age-related chronic diseases as a group and compress morbidity, health care as we know it could be transformed."

The final two contributions to this issue turn more directly to the policy and political issues raised by the Longevity Dividend research initiative. The enthusiasm of this emerging body of research in undeniable, but the fact remains that in both funding and organizational terms, disease-specific and profession-specific agencies control much of center stage across aging research—whether biological, medical, or behavioral. Dan Perry confronts this reality head-on, citing Richard Miller's partially tongue-in-cheek assessment of why slowing aging has been slow to catch on: Aging is seen (incorrectly) as unalterable; drugs that slow aging cannot be tested and validated in a pharmaceutical executive's lifetime; and a politician who wants to "conquer cancer" is a hero, but one who wishes to "slow aging" is a nutcase. In a more serious vein, Perry traces the birth and rise of the NIA and speaks to key actors over the years who helped establish aging's legitimacy in a world of more established science pathways. Slowing the rate of aging

raised critical ethical and economic issues that had to be countered if not completely overcome before this field of study was validated. Furthermore, aging was perennially up against the lobbying power of disease-specific researchers and advocates. Even the legendary first director of the NIA, Robert Butler, realized he had to have a specific age-related disease to hang his budgetary hat on and, with some reluctance, he chose Alzheimer's. That Alzheimer's disease occupied roughly half of the NIA's budget has long been a contentious property of the NIA, one condemned some years ago by Richard Adelman as "the Alzheimerization of aging." Yet Butler went on, with others, to call for greater balance and for pursuing a longevity dividend. Recently, a Senate appropriations bill endorsed the approach, urging "the NIH to increase dramatically its annual investment in the biological basis of aging." In 2012, GSIG won endorsements from 20 separate NIH institutes and centers. A culminating event is Advances in Geroscience: Impact on Healthspan and Chronic Disease, a summit being held at the NIH in late October 2013. NIH director Francis Collins will kick off the conference, with participation from some 50 scientists presenting research on key drivers of aging and chronic disease.

A more direct policy piece by Jack Rowe and Linda Fried concludes the issue. Rowe has chaired the MacArthur Network on an Aging Society, which among other initiatives, has developed a set of recommendations regarding how Medicare can be reformed and strengthened to enhance the health-related needs of an aging population. In keeping with the other articles in this issue, Rowe and Fried's piece identifies one area of great concern in public health and prevention—what the authors label "an epidemic in chronic conditions." MacArthur has supported the work of Dana Goldman and his concern with preventing rather than treating these conditions; his findings suggest that effective treatment would extend life, including quality-adjusted years, and potentially result in notable cost savings to Medicare and other health programs. Rowe and Fried also highlight the need for enhancement of the geriatric workforce and improvement of informal supports on behalf of elders with chronic illness. As with the longevity dividend, such interventions might result in relative—if not absolute—cost savings, but policymakers will want to see supporting evidence in each of these arenas.

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