An Overview of Research on Aging and the Status of Gerontology Today

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LTHOUGH THE SEARCH FOR IMMORTALITY AND THE "fountain of youth" is perhaps as old as our species, the significance of research on aging has only recently been recognized by scientists, Congress, and the public. "Gerontology" is a twentiethcentury term despite its Greek roots. Metchnikoff (1901), the 1903 Nobel Prize winner, used it for the first time in his remarkable book, *The Nature of Man: Studies in Optimistic Philosophy.*

Gerontology is broadly defined as the study of aging from biological, psychological, and social perspectives. I see gerontology as developmental biology, seeking a fundamental understanding of the mechanisms of senescence or, with somewhat different emphasis, the mechanisms of longevity; it is concerned with the involutionary counterpart of the fundamental biology of growth and differentiation. Thus, gerontology is a critical component of the biology of the human lifecycle. (Geriatrics, on the other hand, is the application of the knowledge of gerontology to prevention, diagnosis, care, and treatment of older persons and their illnesses through medicine, nursing, and the allied health professions.)

It is a field that is necessarily derivative and interdisciplinary. It is ready to prosper from the new concepts and techniques of the "new biology": recombinant DNA; hybridoma technology; and the flourishing

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neurosciences. Moreover, it is prepared to use certain new methodological developments, from noninvasive techniques such as CAT scanning and Nuclear Magnetic Resonance (NMR) to statistical methods that make it possible to examine the impact of multiple variables upon multiple outcomes, thereby permitting new understandings of socialhistorical analyses, specifically cohort and longitudinal studies.

The goal of gerontology is to maintain the maximum integrity and efficiency of the organism over time or, as the National Institute on Aging's A National Plan for Research on Aging (1982, vii) put it, to promote "health and well-being by extending the vigorous and productive years of life." Research on aging must, therefore, address the agerelated progressive loss of reserve function and the decline in homeostasis or homeostatic competence or, to put it differently, the increasing vulnerability to diseases, disabilities, and conditions.

To approach these goals and address these issues, the gerontologist must straddle the gray area between normal aging and disease. The excellent work of Reubin Andres and his colleagues (Andres and Tobin 1977) on glucose metabolism has helped reshape our view of diabetes and old age. One can make similar points about the borderline between aging and disease in connection with osteoporosis and other conditions. From this perspective, as from others, it is possible to say that gerontology is practical and potentially cost-effective in its application. It offers multiple payoffs compared with, say, the examination of one disease at a time. Consider the immune system. If we are able to reduce immune senescence and the autoimmune phenomena that also develop with age, we would be having multiple effects upon multiple diseases. Nonetheless, to demonstrate how extremely complex gerontology is, immune senescence, as Schimke (1981) has pointed out, may have an important biological survival advantage by delaying or reducing autoimmune phenomena.

Research emphasizing variables of aging as well as those associated with disease-oriented research remarkably enhances the power of the biomedical-behavioral research enterprise. Already, there is evidence (for instance, in pharmacology) that research guided by the perspective of aging influences both the quality and the quantity of life. And, the retardation of deteriorative aging phenomena, especially in certain of the critically sensitive mediating and integrative systems (central nervous system, endocrine, immune), provides us with the opportunity to promote the actual achievement of the inherent, natural, genetically determined human life span potential. Ę

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. مما Most commonly, research on aging is the work of nongerontologists. Yet, this may not be true often enough. Biologists do not take advantage of opportunities to include aging variables in many of their studies on a range of animal models. Human developmentalists have left an enormous gap in creating a comprehensive portrait of the human life cycle. There are few studies of the biomedical and psychosocial aspects of early adulthood, middle age, and old age (Butler 1975). Very few scientists actually spend extensive and intensive time with persons representing various socioeconomic classes and ethnic and racial groups at various stages of life. An exceptionally small amount of time is actually spent in collaboration with older persons themselves in direct psychosocial study.

When gerontology emerged in the mid-1940s and 1950s, it began in a descriptive manner generating a litany of decrements, such as Nathan Shock's chart of biomedical changes over time-less muscle mass, a weaker hand grip, altered enzymes, changing blood flow in various organs. But even these "obvious" findings have been revised as, for example, in the finding from the Baltimore Longitudinal Study (Shock 1977) that both free and bound testosterone levels do not alter in relationship to normal aging per se, but only in connection with chronic disease and alcoholism. Unfortunately, there have been few such longitudinal studies oriented toward and conceived from the perspective of aging-those developed in 1955 at Duke (Palmore 1970), the National Institute of Mental Health in 1955 (Birren et al. 1963), and at Baltimore (Shock 1977) in 1958. When one compares the larger context of studies of pathology and of organ disease, one sees what a small investment indeed has been made in adult development, including old age.

From all perspectives—biological, psychological, and social—we know even less about healthy aging than we know about pathological aging, and we know little enough about that. Elusive, difficult-tomeasure elements in human character, judgment, wisdom, and creativity have only minimally been studied. It should be noted that National Institutes of Health study sections and foundation review groups are not enthusiastic about supporting descriptive studies. They are not too interested in descriptive biological studies at the cellular level, nor in the examination of patterns of late-life personality change. This reality poses difficulties for a field which has developed recently and unevenly.

Nonetheless, there has been some movement beyond description to

explanation, to the experimental elucidation of underlying mechanisms (for example, the relationship of DNA repair to life span). Moreover, investigators are identifying various agents and strategies that can be employed to intervene in the aging processes (here again, I include interventions applied by scientists and clinicians other than gerontologists).

Thus, there are the beginnings of a "new" gerontology, including pharmacological, immune, hormonal, and social interventions, which are both prophylactic and therapeutic. Osteoporosis and bereavement are illustrative of conditions which can be actively dealt with to some degree. Exercise, calcium, and estrogen are useful in the prevention of osteoporosis. Social support systems (such as the widow-to-widow program) can reduce morbidity and mortality among the bereaved.

Although there has been some private support for the field, it has been the federal government, primarily through the National Institute on Aging (NIA), that has fostered, supported, and conducted research on aging. For an overview of this research, I refer to several key documents resulting from profound efforts by the NIA leadership in coordination with advisers and consultants throughout the country to build an infrastructure for future payoff irrespective of immediate clinical application.

First, the very fine book, *Mammalian Models for Research on Aging* (Committee on Animal Models for Research on Aging 1981) explores appropriate and relevant aging-animal models which can be employed for a variety of studies on aging and age-related diseases. This work was done in collaboration with the Institute of Laboratory Animal Resources of the National Academy of Sciences.

Second, *Biological Markers of Aging* (Reff and Schneider 1982) investigates various biological markers related to the processes of aging. Any effort to investigate strategies for intervention requires nonlethal markers, one example of which is forced ventilatory capacity. One must conclude, however, that we do not at this stage have finely tuned measures of functional or biological aging.

Third, Biological Mechanisms in Aging (Schimke 1981) examines contemporary theories and hypotheses which can be grouped under genetic, DNA, protein synthesis, post-translational changes, immune system, and neuroendocrine aspects. Let me elaborate on some key issues that are covered in this book, to which George Martin and Caleb Finch made significant contributions. ð

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There is no single, universal aging process, even at the cellular level. It is critical to learn how to experimentally manipulate the variable of time. (Note Hayflick's "suspended animation" by way of frozen cells after different doubling times. Hayflick's cells can be preserved for extended periods of time and cell replication recommenced.) Equally compelling is the need for mutant models with specific biochemical defects that have hypothesized relations to aging, for example, altered superoxide dismutase and altered alpha DNA polymerase. Such specific biochemical defects may open the door to our understanding of the profound changes of aging. In this regard, Martin has often asked: "How do underlying genetic determinants set the stage for selective, differential expression of various aspects of the senescent phenotype in man?" It is essential to discover the fundamental mechanisms underlying the expression of abiotrophic genes, those with delayed expression. How can we alter the immune deficiency of aging by influencing the patterns of cyclic nucleotides or by DNA repair in lymphocyte populations? Evidence is cited in this work of the positive correlation between efficiency of certain forms of DNA repair and species-specific maximal life spans.

Finch has considered issues of transplantation of neural cells to the aging brain to restore function of lost or damaged tissue, the use of transplanted fetal neurons, the estimation of dopaminergic activities in the basal ganglia after developing lesions in the substantia nigra, and the role of glucocorticoids in modulating the rate of some aspects of brain aging. What exciting territory is this central nervous system and its role as pacemaker in aging; how important to look at issues of redundancy and neuroplasticity; how interesting such facts as reactive synaptogenesis, even in aging rodent brains with new conductivity of healthy neurons next to damaged or deceased ones. And how extremely promising the findings related to senile dementia of the Alzheimer's type, which can be catalogued as cholinergic neuron deficiency.

Clearly, works such as *Biological Mechanisms in Aging* urge us to continue to move gerontology beyond simple notions to more defined hypotheses so couched that they can be examined experimentally with as likely an opportunity for refutation as confirmation.

Aging in Society (Riley, Hess, and Bond 1983) summarizes much of contemporary social-historical aspects of aging and points the way to new hypotheses. I personally predict that the impact of individual and population aging upon societal and industrial productivity already a concern in Japan which is experiencing rapid population aging—will soon be one of the most potent scientific and even political issues of our time.

A final key document is the above-mentioned A National Plan for Research on Aging, with the more popular and descriptive subtitle of Toward an Independent Old Age, the work of 29 scientific advisors and 210 consultants to the NIA, as well as of its leadership. Comprehensive and interdisciplinary, it deals with basic mechanisms of aging, clinical manifestations of aging, interactions involving older people and society, and increasing productivity among older people. The report is a major, invaluable summary of our present state of knowledge—a kind of overview/review and a summary of research needs and opportunities. But it is not yet a plan for implementation with necessary budgets for resources, funds, and personnel (including research training) that can be staged in a rational manner over time. This remains to be developed.

Pressure for Life Span Extension

All of this research on aging is conducted by scientists representing numerous disciplines and widely disparate aims and interests. There are, as mentioned, nongerontologists contributing deliberately, or as a byproduct, to the understanding of senescence and longevity. There are those whose primary interest is longevity—that is, extension of the life-span—for whom interest in the mechanisms of senescence is secondary. For this group of researchers, physician-historian Gerald Gruman's (1966) term "prolongevity" is useful: "the belief that it is possible and desirable to extend significantly the length of life by human action." No doubt longevity researchers would agree with George Bernard Shaw who stated in *Back to Methuselab* that "men do not live long enough. They are, for all purposes of high civilization, mere children when they die."

Still others, including behavioral and social scientists, are interested above all in the quality-of-life issues, that is, in extending the vigorous productive years of effective functioning. Geriatricians can be included here, some of whom conduct clinical investigations helping us to understand the differentiation/interaction of aging and disease and 6

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means of preventing or ameliorating clinical manifestations of aging. Finally, there are the scientists who wish to foster our understanding of the biological and behavioral aspects of aging without ideology or clinical application necessarily in mind.

But it would appear that some of the very goals of these research efforts have sparked outright resistance to their progress. During my tenure as director of the NIA, I encountered persons in policy-making positions who fear, and even to some degree oppose, research which they perceive primarily as extending the life span. They associate extending life with prolonging decrepitude, senility, and unbearable social costs; they see such issues as the solvency of Social Security as unsolvable. In other words, they fear that research on aging might actually succeed. Opposition also comes from the "Gloomy Gus" camp—those who are certain that we can never meet the challenges posed by the extraordinary increase in average life expectancy and by the absolute number and relative proportion of older persons within the population.

In my efforts to gain support for research on aging, I emphasized that our objective is quality of life as well as quantity of years. I reminded policy makers that it always takes time for societies to adapt to great social change. Society has still not fully adjusted to the industrial revolution; note slums, structural unemployment, separation of family from workplace, industrial pollution. I did and continue to argue that humankind can and already does, to some extent, enjoy the triumph of survivorship that has characterized our century—the 26-year gain in average life expectancy since 1900. Compare this with the 29-year gain achieved in the preceding 4,900 years—i.e., since 3,000 years before Christ when, in the Bronze Age, average life expectancy was 18.

I believe that we can adapt: through new social arrangements; through different work, education, and retirement patterns; by conquering senility; and by enhancing late-life productivity. In the view of life-span extension researchers, such an adaptation to a more mature society could offer great advantage; they see young societies as less creative than old ones and believe that the maturing of society would make it possible to preserve more effectively and utilize investments already made by important contributors.

The public is intrigued with the issue of longevity—witness the popularity of books such as Walford's Maximum Life Span (1983).

Although among the public, scientists, and policy makers, most accept the premise of the federal Research on Aging Act of 1974—that the task is to promote vigorous and extended life, not one or the other all "behind the scenes" dynamic forces must be considered in any serious overview of research on aging and of its future.

Thus, one must also consider, first, the long-held perception that the quality of gerontology or research on aging, and its practitioners, are not equal in quality to other fields of science, and, second, the historical sense of futility—that there is not much anyone can do about aging. I believe that both of these notions have begun to change.

The Research Agenda

Research on aging has, of course, come into being at a very difficult time. In this period of austerity it has not enjoyed the support for research, research training, and clinical training that other biomedical and behavioral research areas experienced during their formative years. There is, at present, only token clinical investigation in geriatrics; only a few major programs devoted to such important subjects as senile dementia, despite the pervasive, devastating, and expensive aspects of that disease; fewer autopsies performed on older persons (and almost never in nursing homes where the population is primarily elderly) at a time when we could profit so much from developing the pathology of aging. Death certificates remain an uncertain source of data, and the diagnostic data of multiple pathologies so characteristic of geriatrics are not even collected. Only a few centers of psychosocial research, and not one national population laboratory, are to be found. Various demographic and epidemiological investigations wait to be conducted. There is all too little work in measuring biological and behavioral changes that occur in human performance over time, despite the likelihood of an increasingly graving work force, especially after 1990.

The extraordinary sex difference in life expectancy—which is expanding—provides opportunities for studies of genetic, hormonal, immune, social, and psychosocial factors; yet, there is virtually no work underway.

In the domain of "real world" research, there are very few servicerelated research activities to improve the health and social service delivery in efficiency, cost, and quality. Considering the enormity of the nation's health costs, this is a most important point. We have a long way to go in developing assessment methodology for proper placement, to understand health predictors and risk factors. Little has been done in the way of health maintenance studies in later years; elements in rehabilitation and cost-effective approaches using paraprofessionals and interdisciplinary teams remain unexplored. The new proposals of the Secretary of Health and Human Services based upon the Yale studies of the diagnosis-related groups (DRG) require us to ask how they will fit with the multiple pathology characteristic of the geriatric patient. These are "glamorous" areas of investigation. Our needs are as great in such unglamorous research areas as incontinence, decubiti, and falls (accidents are the number five cause of death among older persons).

Research on aging has clear tasks ahead. It will have to be unusually imaginative, taking advantage of all sorts of collaborations in endeavoring to telescope its natural development. Call it "operation catch-up." It must receive special emphasis now, not only from government but also from the private sector—from foundations and corporations—in order to meet the truly awesome challenge posed by the demographic changes immediately in front of us. When the twenty-first century begins, the post-World War II baby boom will be going gray. By then it will be too late to begin to find ways to prevent and treat their senile dementia, to promote their late-life effective functioning, to understand the aging body's changed responses to various medications.

Individual aging is not the only issue; science must help prepare us for population aging. We all seek the time when, as James Fries (1980) predicts, "the number of very old persons will not increase. The average period of diminished physical vigor will decrease, chronic disease will occupy a small proportion of the typical life span and the need for medical care in later life will decrease." These may be our distant goals, but they are not the present facts. The number of old age persons *is* increasing. The 85-plus age group is the fastest growing age group in the United States. Rosenwaike, Yaffe, and Sagi (1980) describe a 26 percent decline in mortality rates among the extreme aged between 1966 and 1977.

The average period of diminished physical vigor has not yet decreased; indeed, the National Center of Health Statistics reports increased disability and morbidity for all age groups. Chronic disease does not yet occupy a smaller proportion of the typical life span. Only 14 percent of people over 65 are free of chronic disease. Mahler (1981) estimates that 10 percent of a lifetime is spent in disease and disability. The National Center of Health Statistics introduced the concept of "average disability-free life expectancy"; the latest count was 68. So far the need for medical care has not decreased; one measure of need, cost, is rising. Sicker and sicker and older and older patients are now coming to nursing homes. Forty percent of all nursing home residents are over 80, and 20 percent of people over 80 are nursing home residents. (Imprudent and insensitive budgetary cutbacks in Medicare and Medicaid may reduce medical care provided in old age, however.)

In its short life, gerontology has justified itself sufficiently to deserve support for its potential contributions. It is time to offer that support and, for scientists, it is time to enter the field. You will never get bored in gerontology. It is exceptionally cross-cutting. It stimulates emotional, ideological, even political responses, if not passions. It speaks to the life cycle as a whole, for aging is a life-long matter. It calls for broad-based national, cultural, and socioeconomic responses from public and private sectors. It expects us to question deeply held premises, break down stereotypes, and alter mind sets. It calls forth humaneness from policy makers, to match the possible "mischief" that could be wrought by those behavioral and biomedical scientists who try to unravel the mysteries of aging and to understand better and contribute more to the relations of aging to society.

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