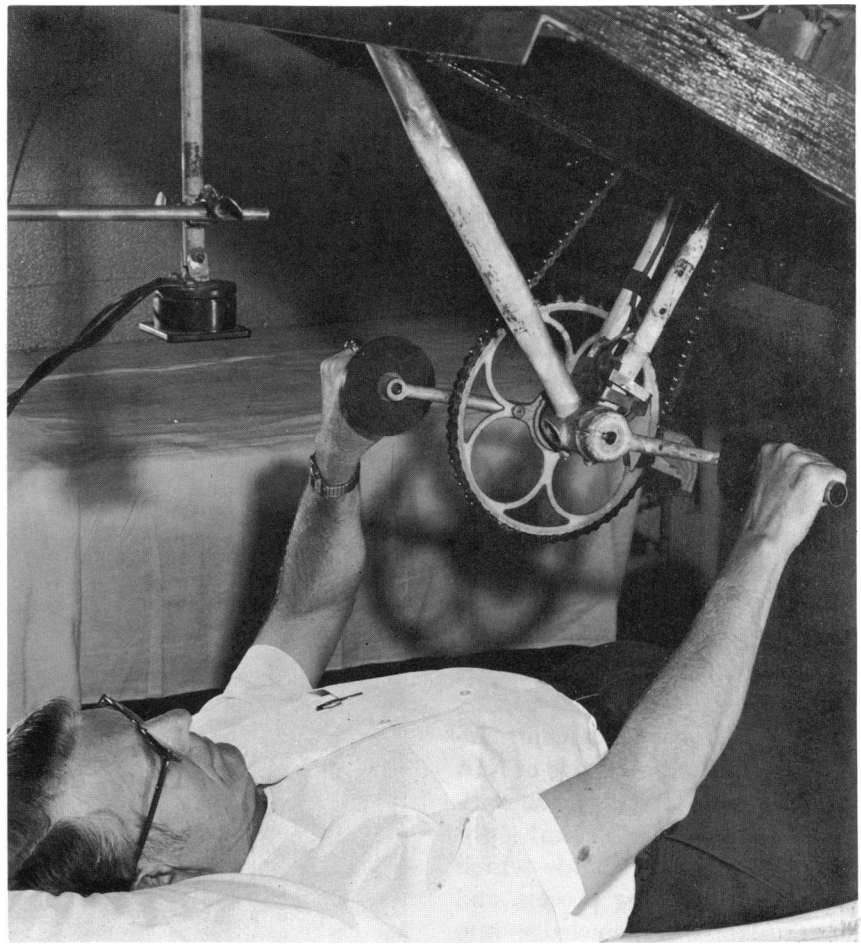
Research Programs of the National Institute on Aging

ROBERT N. BUTLER, MD



A volunteer who periodically visits the Gerontology Research Center cranks a bicycle ergometer to determine the effects of aging on maximum arm work output.

FOR UNTOLD CENTURIES man, realizing the immutability of death, has searched for the elusive "fountain of youth," in order to prolong not just life but what he believed to be the best part of life. This bias toward youth continues and is especially strong in our culture today. Television, movies, and magazines portray young adults living "the good life." Modern-day fountains of youth—vitamin E, for example—are promoted quite successfully, although their effectiveness in maintaining or returning youthfulness is doubtful.

Science has succeeded in prolonging life. The average American life expectancy at the turn of this century was 47 years; now it is 70.4 years. The elderly, espe-

☐ *Tearsheet requests to Robert N. Butler, MD, Director, National Institute on Aging, National Institutes of Health, Bldg. 31, Rm. 4B–59, 9000 Rockville Pike, Bethesda, Md. 20014.*

cially those over 85 years of age, are the fastest growing age group in the country. Thus, unlike cancer or even heart disease, which only a certain percentage of Americans will ever suffer, aging will affect every one of us who lives long enough. Nevertheless, scientists know little about the aging process and about improving the lives we have lengthened.

To too many, old age appears to be a time of chronic illness, failing mental abilities, dwindling bank accounts, and stagnation. Clearly, the extension of life has brought many problems, but perhaps the largest single issue is that of looking realistically at aging and not trying to pretend that it does not occur.

Aging is an organism's progressive and presently irreversible loss of ability, after maturity, to function optimally within its environment. This is a natural phenomenon which, as far as is known, affects all higher forms of life and perhaps all living things. However, the establishment of the National Institute on Aging (NIA) supports the concept that the study of aging is not just an examination of decline, loss, and decrement—which do accompany aging—and not just the study of disabilities or diseases which may in part be due to social adversities. Rather, it is an exploration of the normal processes of development that are fundamental to life and continue into old age, and about which we know too little. These processes include creativity, life experience, perspective, and judgment. Indeed, the overall objective of NIA research is to examine the variety of factors—biological, psychological, and social—which constitute the aging process, and to translate this knowledge into ways of preventing, promoting, modifying, or reversing these factors so that life is better and more dignified in the later years.

Research on aging may be divided into two general areas—the disease processes that characterize old age and the biomedical, behavioral, and societal changes that comprise the aging process. The diseases of old age have received—and still receive—research attention from the various components of the National Institutes of Health (NIH), but NIH interest in the aging process itself truly began following the establishment of the National Institute of Child Health and Human Development (NICHD) in 1962. The NICHD program on aging was quite small, and public and congressional pressures began to push for the establishment of an institute on aging. This activity culminated in the Research on Aging Act (Public Law 93–296), signed into law on May 31, 1974, authorizing the establishment of the National Institute on Aging. On July 1, 1975, NIA was separated from its parent Institute, NICHD, and 6 months later was functioning as an independent research organization.

According to the Research on Aging Act:

> The Congress finds and declares that—
> (1) the study of the aging process, the one biological condition common to all, has not received research support commensurate with its effects on the lives of every individual;
>
> (2) in addition to the physical infirmities resulting from advanced age, the economic, social, and psychological factors associated with aging operate to exclude millions of older Americans from the full life and the place in our society to which their years of service and experience entitle them;

A healthy volunteer from the community takes test to measure sensory and motor nerve conduction velocities at the Gerontology Research Center. This test can detect nerve dysfunction, which may be related to diabetes.

(3) recent research efforts point the way toward alleviation of the problems of old age by extending the healthy middle years of life;

(4) there is no American institution that has undertaken comprehensive systematic and intensive studies of the biomedical and behavioral aspects of aging and the related training of necessary personnel;

(5) the establishment of a National Institute on Aging within the National Institutes of Health will meet the need for such an institution.

The questions which the NIA might pursue are almost endless. But some problems of the elderly are, by definition, out of the Institute's power, such as the actual delivery of service, including health services. Yet, even here, research performed or supported by NIA could provide fundamental information on which to base decisions about service activities.

The Institute's research program is being addressed to many questions of concern to both the lay and scientific communities. Furthermore, some of these projects have already yielded promising results. Most of NIA's current research efforts are in the biomedical aspects of aging, a bias inherited from NICHD. However, now—and in the future—as the Institute interacts with the rest of the scientific community, the American public, and other special-interest groups, the NIA program will achieve a better balance of biomedical, behavioral, and social aspects of aging.

Biomedical Aspects of Aging

Why do old people experience more illness than young people? Can the treatment of the elderly be improved? Why do people age? These are some of the questions the NIA is trying to answer.

For almost 50 years scientists have known that the humoral immune response grows less effective with increasing age, and now the same effect is recognized in the cellular immune system. Several changes in the immune system are responsible for this, including tissue changes and a reduction in the number of cells that precede antibody formation. This decreased immune response is probably a major factor in the apparent increased susceptibility of the elderly to infectious diseases.

In 1975, scientists in the Laboratory of Cellular and Comparative Physiology of the NIA Intramural Program (commonly called the Gerontology Research Center) discovered another reason for this loss of immunity in the elderly. They found that older animals have an increased number of cells that inhibit the protective activities of the body's immune response.

As one of the most exciting and promising fields in biomedical research today, immunology holds a key to improving the health of people of all ages. Immunologists are actively searching for means to enhance the activity of the immune system in people of all ages. An NIA grantee at the University of California, Los Angeles, placed mice on diets moderately restricted in calories or proteins and not only increased resistance to some viral infections, but also prolonged the animals' lifespan and improved their resistance to certain tumors. Evidently, the immune systems of the mice on special diets stayed "younger" longer than the systems of control animals.

Immunology may also play a major role in a devastating and frightening disease of old age—senile dementia, which destroys a person's memory and personality. Autoimmunity, in which the immune response attacks tissues in one's own body, has been theorized to be one cause of senile dementia. "Senility" is a lay term that is medically known as organic brain syndrome. There may be as many as 100 causes of senility. When the underlying cause is recognized and treated, there is an excellent chance of reversing the state.

By studying both aging cells and animals, investigators hope to learn why people age and exactly what happens when they age. Many changes occur in body cells as these cells age, but scientists must yet determine which cellular changes are directly related to aging in tissues and organs and, in turn, in the body as a whole. Furthermore, scientists must determine if cellular changes are intrinsic or environmentally induced.

Research on cellular and subcellular aging is underway in NIA's Laboratory of Molecular Aging and Laboratory of Cellular and Comparative Physiology. The Laboratory of Molecular Aging pursues the causes of changes in structure and function that occur with age at the molecular, enzymatic, and intracellular levels. This work will contribute directly to an understanding of age-dependent changes in kidney and heart function, muscle activity, and metabolism.

The Laboratory of Cellular and Comparative Physiology is examining the nature of the age-related deterioration of certain cells of the immune and related systems and the underlying cellular and molecular mechanisms responsible for this deterioration. The results of this work will provide a basis for two other areas of interest to this Laboratory—the development of methods for the early detection of signs of cellular aging and the

control or reversal of these changes. Already, LCCP investigators are evaluating the potential immunological effects of chemicals, such as 2-mercaptoethanol, transplanted cells, and diet manipulation in mice.

Better treatment for the elderly is essential to improving the quality of their later years, but many factors are involved. Too often today, the physician and family settle for an incomplete diagnosis or course of therapy for an old person because he is old and must "expect" to be ill. Or, perhaps the treatment would have to be extended over time and the family assumes that the older person might not live long anyway. (An elderly volunteer in NIH's Human Aging Study (1955–66) went to his physician about a pain in his left leg. The physician declared, "Sam, for Pete's sake, what do you expect at 102?" Sam retorted, "Look, my right leg is also 102, but it doesn't hurt a bit. Now explain that.") The elderly are entitled to the best medicine available, if only to allow them to enjoy their little time left as comfortably as possible.

Improved diagnosis and treatment depend, however, on more extensive knowledge about the aging body—what is normal for it and how it reacts to drugs, for example. Gerontologists realize, for instance, that glucose tolerance tests or leukocyte counts in the aging person cannot be evaluated against the "normal" standards established in younger people. The National Institute on Aging proposes that new normal values for diagnostic procedures be established for the elderly.

Further, chemotherapy represents another area where our knowledge must be adapted to the elderly. Aged Americans use 25 percent of the drugs prescribed, although they represent only 10 percent of the population. In fact, drugs constitute the largest single medical expenditure which the elderly must meet almost entirely on their own. Medications are prescribed for the aged in much the same manner as they are for younger adults. Yet, pharmacologists know that infants and young children require special dosages. Likewise, more research is essential to determine optimal dosages for the elderly and to define possible toxic, as well as short- and long-term side effects. Our lack of knowledge in this area means that we must monitor closely an elderly patient who is receiving medication. For example, there is a greater risk of bleeding when heparin is administered to older women; there may be a link between reserpine and breast cancer in women; and diazepam causes excessive drowsiness with age. Wise prescription guidelines for the elderly will be based on fundamental research within the purview of the National Institute on Aging.

The psychologist (center) tests a volunteer's ability to recall and recognize figures and letters as part of the Gerontology Research Center's behavioral studies of aging.

Behavioral Aspects of Aging

Why is there a decline in mental abilities in late adult life? How can the elderly be helped to cope with the many changes they encounter—retirement, death of friends and relatives, reduced income, dependence, and illness, for example—as well as their own approaching death? When are people ready to retire?

People over 65 years of age commit 25 percent of the suicides in the United States. Obviously, therefore, the "golden years" appear quite tarnished to many. Gerontologists need a better understanding of the psychological changes and problems these people face in order to make elderly persons' last years happier and more fulfilling.

Failing memory is embarrassing to the aged person, worrisome to his family, and it contributes to myriad problems in day-to-day living. NIA scientists have found, however, that mnemonics learned by older people can be quite helpful in enabling them to store and retrieve information. Mnemonics is a classic memory

improvement technique which involves associating items to be learned with stops on an imaginary journey.

NIA grantees, using rats, are studying changes in brain chemistry and tissue in an attempt to correlate such changes to declining memory and learning functions. These investigations indicate that the rat may be a good model for the study of human senility.

Mandatory retirement—often at the age of 65 or 70—is a common practice in this country. This, coupled with the unwillingness of many firms to hire people who are in late middle age, means that a large segment of our population is forced into retirement or jobs requiring less skill than they possess before they want to discontinue working. Furthermore, the Social Security limit of $2,700 annually on other income further inhibits those elderly who would like to continue working in some capacity.

Since mandatory retirement may well be declared unconstitutional in the future, we must be able to assess who is ready for retirement and who is not—based on factors such as competence, economic needs, and personal desires. The National Institute on Aging is interested in the effects of mandatory retirement and in developing effective retirement test patterns.

Social Aspects of Aging

Why do young people fear old age? What effect will the growing elderly segment of our population have on our society? Does aging differ in various groups in our country?

I have termed the negative attitude toward aging held by much of our society "ageism." We need research to determine the reasons for this as well as how to teach respect for the elderly and to reconcile our fears of death and dying. Improving the physical and mental health and the economic well-being of our older citizens will do much to enhance the attitudes of the rest of society toward aging.

The National Institute on Aging is also supporting investigations on the effects on society of differential mortality rates in various subsets of our population and the impact of changes in population age structure on employment, retirement, widowhood, transportation systems, and housing, for example. While other Federal Government agencies will be responsible for actually adjusting social systems to changing population demands, NIA-supported research can provide the basic information they need to determine the direction of these adjustments.

There are rather significant differences in life expectancies for some subgroups in our society. Black, Mexican-American, and American Indian persons have noticeably shorter life expectancies than white persons in this country, most probably because of socioeconomic disadvantages. Many of these people cannot expect to live long enough to benefit from Social Security and Medicare. Besides taking steps to improve the life expectancy for future generations of these groups, we should take measures now to enable more minority-group elderly to share the benefits available to white Americans after the age of 65 years.

Baltimore Study of Aging

Psychological and social factors of aging, as well as the biological aspects, are under evaluation in the Baltimore Longitudinal Study of Aging, conducted by NIA's Clinical Physiology Branch. Begun in 1958, this study periodically examines 650 men to monitor cardiac, renal, and pulmonary function, body composition, exercise, physiology, carbohydrate and lipid metabolism, drug pharmacokinetics, nutrition and endocrine factors, and behavioral and social variables.

The combination of these disciplines in the study of aging should provide scientists with ways to prevent or ameliorate the debilitating effects of old age. Already, data from this longitudinal study suggest that exercise may lead to a longer life. In addition, risk factors may also be identified which, if nullified, could do much toward controlling the chronic noninfectious diseases of such importance in this country and of such devastating effect on our elderly.

In 1977 the National Institute on Aging plans to make this longitudinal study much more comprehensive and valid for the general population by preparing to add women to the study. This enlarged population, along with other clinical, behavioral, and social research projects, will round out the NIA research program after 1977.

Other Aspects of Research

Basic to all future research on aging is an adequate supply of trained investigators and sufficient animal resources. Gerontology and geriatric medicine are simply not recognized by many in the scientific and medical worlds. Thus, there is a shortage of trained manpower now and few people to interest young investigators in the field. Furthermore, scientists who are beginning their careers in gerontology often have difficulty in funding

their projects. Other, more-established researchers in different fields may wish to change the direction of their studies toward aging research, but are unable to get support for the training necessary to give them skills in that field.

Recognizing these obstacles to the development of a trained cadre of investigators in the field of aging, the National Institute on Aging is taking several steps to rectify these problems. The Institute has a special research grant program designed to provide funds to young scientists to enable them to pursue independent investigations during the formative stages of their research careers. In addition, the National Research Service Award Act provides for individual and institutional type fellowships to support training of pre- and post-doctoral scientists. Some type of senior fellowship is also needed to enable those interested in mid-career changes to pursue a new career in aging research.

Animal models form the basis for research in almost any area of biomedicine. Suitable laboratory animals on which aging experiments might be performed or in which the aging process might be systematically observed are needed. Until recently, investigators throughout the country were unable to acquire adequate supplies of shorter-lived species, such as rats and mice, at all age levels. Even these animals are expensive to raise and are often in a fragile condition if they reach old age. A 26-month-old rat costs $80, and a kennel-maintained beagle, 10 to 12 years old, $1,500.

The National Institute on Aging has established and is maintaining, under contract, a germ-free colony of laboratory rats and mice, of known genealogy, at different ages, and in numbers presently sufficient for aging research. NIA hopes to insure a growing supply of such animals for future use and to encourage the development of other models, including invertebrates, such as the roundworm, and subhuman primates.

Physiological changes with age are measured in more than 600 community volunteers who periodically visit the Gerontology Research Center. This test measures arm and shoulder strength.

Conclusion

Repeatedly, we hear that Americans value things, including people, according to their productive capacity. The elderly—as a group—are thus viewed as burdens. Yet, they can and do contribute much, given the chance. To increase their opportunities for more meaningful later years, research on aging has shifted from its exclusive disease orientation toward a more comprehensive investigation of the normal physiological changes with age, the behavioral constitution of the aged, and the social, cultural, and economic environment in which the elderly live. This is the direction that present and future research on aging must take so that the increasing numbers of aged people, realizing their full capacities, will be valued and respected by any standard.