

NORMAL HUMAN AGING:
The Baltimore Longitudinal Study of Aging

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Dedication



Dr. W.W. Peter

This volume is dedicated to Dr. W.W. Peter (Fig. 1), whose foresight and enthusiasm played an important role in the recruitment of subjects for the Baltimore Longitudinal Study of Aging. Dr. Peter, a retired Medical Officer of the United States Public Health Service, provided the initial impetus that led to the recruitment of normal men residing in the community as subjects for their entire lifetimes in a study of aging. In 1958 very few people recognized the impact that the increasing number of elderly people in the population would have on our society. Only a few voices were raised to point out the need for research on aging. Dr. Peter's was one of them.

Perhaps because of his experience as a physician, Dr. Peter saw the need to study aging in individuals who were free from disabling diseases and were leading successful lives in the community. He "sold" this idea to his friends, neighbors, and colleagues and persuaded them to enroll as participants in a study that would involve repeated tests and examinations over their entire life spans. He represented participation in the study as a contribution to science and the future of mankind.

Dr. Peter soon realized that his own efforts were not likely to recruit enough subjects to answer many of the questions posed about aging. Hence he proposed to

participants already in the study that they join him in recruiting others among their colleagues and friends. Thanks to Dr. Peter's dedication, the system worked! The waiting list that was soon generated today provides new subjects for introduction into the study whenever vacancies occur.

Although Dr. Peter died suddenly on March 31, 1959, the recruitment system and the *esprit de corps* he helped to establish among the early participants have remained over the years. The study owes much to Dr. Peter and stands as a memorial to his vision. Many people—physicians, scientists, technicians, programmers, and secretaries—have contributed to the successful continuation of the study over the past 23 years. To mention all of them by name would require an additional volume of this book. To all of them, our sincere thanks.

Finally, acknowledgment must be made to the subjects themselves for their willingness to participate in procedures that were often demanding and tedious, and sometimes uncomfortable, in order to improve and extend knowledge about aging. Without their loyalty and dedication no study would have been possible.

Acknowledgments

The success and continuity of the Baltimore Longitudinal Study of Aging (BLSA) are due to the dedicated efforts of many people. First of all we must acknowledge the debt owed to the loyal subjects of the study, who faithfully met appointments and gave their maximum effort in performing tests of physiological and psychological functions. Our subjects accepted all kinds of tests as a challenge, even when some were boring and others uncomfortable. Without their loyalty and continued participation the study could not have endured for 23 years, and would not now look forward to a productive future.

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We are also indebted to the staff of the Gerontology Research Center (GRC), to the many physicians who conducted the detailed histories and physical examinations, to the scientists who designed the study, and to the technical staff who conducted tests and measurements.

We are especially indebted to the late Mr. Arthur H. Norris, who, from the inception of the study in 1958 until his untimely death in December 1980, provided major scientific input, consummate administrative acumen, and above all genuine personal support to the BLSA participants both during and between their visits.

Many people took part in the development of the collaboration between the National Institutes of Health (NIH) and the BCH, which resulted in the formation of the GRC on the grounds of the BCH. Dr. Henry Sebrell, Director of NIH, Dr. James Watt, Director of the National Heart Institute (NHI), and Dr. Robert Berliner, Scientific Director of NHI, played key roles over the years. Dr. T.J.S. Waxter, Director of Public Welfare, Baltimore City, Mr. Francis Davis, Chairman of the Welfare Board of Baltimore, Mr. P.J. McMillin, Superintendent of BCH, and Dr. John T. King, Chief of Medicine, BCH, were instrumental in the development of the GRC, which is essential to the BLSA.

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It is also important to acknowledge the role of the GRC itself in providing a stable and visible "home" for the BLSA, as well as resources that include housing facilities for subjects, laboratories, and a staff committed to the study of aging.

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Normal Human Aging:
The Baltimore Longitudinal Study of Aging

Note: References that appear in italics in the text identify longitudinal studies on the BLSA population. These studies are summarized in Chapter VI and, unless they are still in press, are reprinted in the Appendix.

Introduction

Since the inception of the Baltimore Longitudinal Study of Aging (BLSA) in 1958, its intent has been to trace the effects of aging in humans. It attempts to distinguish between the true effects of aging and those processes, including disease, socioeconomic disadvantage, and lack of educational opportunity, that may also appear or become more pronounced with time but are biologically irrelevant to the underlying mechanisms of human aging. It has sought to achieve this goal by making measurements on more than 1000 male volunteers¹ who at their entry into the study were aged 17 to 96 years and were living independently in the community. This report of its first 23 years of activity is an initial compilation of methods and findings pointing the way to further research and analysis that will enhance our understanding of the complex and highly individual processes of human aging.

Changes that take place during the early stages of life, which are almost entirely reflections of growth and development, are usually characterized by increases in size and in complexity of structure and function. By contrast, aging is manifest in a series of physiological and behavioral changes that occur after the attainment of maturity in all members of a species. Although aging changes proceed at a much slower rate than changes that occur with growth and development, and are often associated with decrements in performance, it cannot be assumed that aging is always characterized by impairment of function. In many people, for example, vocabulary continues to expand throughout life. Aging in adults is also characterized by great diversity; old organisms show a greater range of variation in many physiological and psychological indicators than any other adult age group. There are extraordinarily "young" 80-year-olds, along with extraordinarily "old" 40-year-olds.

Although the incidence of disease increases with age, aging and disease are not synonymous. Aging is a normal concomitant of the passage of time that takes place in everyone; disease occurs in only a part of the population. The changes by which aging is manifest, at all levels including the cellular, reduce an individual's adaptive capacities and the speed and excellence of his performance, and increase his susceptibility to disease and pathological processes. As a result, a traumatic event such as an accident or exposure to a disease, which may be of minor consequence to a young individual, may be of much greater consequence, even fatal, in the elderly. As adaptability and reserve capacities diminish, mortality rates increase. Although there are wide individual differences in the rate at which age changes take place, aging affects all members of a population, while specific diseases and accidents are selective.

Since many of the changes associated with aging reflect a reduction in adaptability and performance that may also characterize specific diseases, the effects of aging and disease are difficult to separate. One approach is to examine all subjects in great detail and to exclude from the analysis of age trends data from any subjects who show evidence of pathology or disease. Although this procedure may eliminate subjects with

¹Since January 1978, women have been systematically added to the BLSA. As of June 30, 1981, more than 300 had been examined and tested at least once, 150 two or more times. It is anticipated that the ultimate number of female BLSA participants will approach 700. Because of the short time over which observations have been made, no longitudinal data on aging in women will be reported in this volume. However, certain cross-sectionally derived data are reported in Chapter V.

gross pathology, there is no assurance that subjects with the early stages of a disease have been identified. The development of new diagnostic techniques more precise and sensitive than those previously available may reveal that some subjects, formerly judged normal, were in fact already in the early stages of a disease. It is thus impossible to be sure that only "healthy" subjects have been included; it can only be stated that individuals with pathology detectable by the best methods then available had been eliminated at that stage of data analysis.

The BLSA has attempted to measure age changes by making serial measurements on individual members of a group of community-residing adults. In order to minimize the effects of socioeconomic and educational factors on test results, subjects were recruited from a well-educated population with above-average income, which also had access to good medical care. Careful medical examination for specific conditions or diseases that might influence the "normality" of a particular performance has been employed to exclude "abnormal" data. As a result, age differences and age changes observed in this highly selected group of participants may be the best available index of "pure," i.e. optimal, aging.

Studies of growth and development, or of aging during the early part of life, have traditionally been conducted by the cross-sectional method, in which subjects of various ages are measured simultaneously. The effects of aging or growth were thus inferred from *differences* between average values found in groups of subjects of various ages. Only the longitudinal method, in which serial measurements are made on the same subjects as they age, can identify *age changes*.

This book is addressed to those who are interested in the objectively measurable changes that take place in adults as they grow older. The tests used to measure different aspects of aging, the functions they evaluate, and the methodology used are described. Neither the theory of longitudinal studies nor the mathematical and statistical issues inherent in longitudinal data analysis are discussed in detail, since other books and articles cover these issues (Jones, 1958; Birren and Renner, 1977; Schaie, 1977; Baltes, 1968; *Schlesselman, 1973a,b*;² Schulsinger et al., 1981). Although a description of past and existing longitudinal studies on adults is necessary to answer the primary question—"Why another longitudinal study?"—the book does not include an exhaustive review of all the longitudinal studies that have been conducted on children and adults. The literature review in Chapter II is limited to studies that illustrate the strengths and weaknesses of the longitudinal method and those that were conducted on normal community-residing adults—studies which may reasonably be compared with the BLSA.

The general design of the study, characteristics of the subjects, the tests used, data storage and retrieval, and methods of data analysis are described in Chapter III. Chapter IV describes in detail the testing procedures followed.

The results of published BLSA cross-sectional analyses are summarized in Chapter V. Those based on longitudinal examinations of selected variables (anthropometry, physiological performance, cognitive performance, and personality characteristics) are summarized in Chapter VI, and the articles themselves, except a few that are still in press, are reprinted in the Appendix, since they provide models that may be followed for the longitudinal analysis of other variables.

²References that appear in italics in the text indicate longitudinal studies on the BLSA population. These studies are summarized in Chapter VI and, unless they are still in press, are reprinted in the Appendix.

The primary focus of the BLSA is the scientific characterization of aging in individuals over the entire adult life span. Unlike many other studies whose chief purpose was to identify factors that increase the probability of the development of specific diseases, principally cardiovascular, the BLSA has from its inception emphasized healthy aging; it thus includes a much broader spectrum of both physiological and psychological tests than other studies. In studies of aging it is particularly important to rule out the possibility that occult disease is the source of the observed differences. At the same time, no subject in whom disease was discovered during the study was excluded or dropped, although observations made on such individuals were excluded from analyses for pure age effects. As a result, the progressive effects of such conditions as diabetes and cardiovascular disease on specific physiological functions can be described.

The BLSA was extraordinarily fortunate in its early recruitment and retention of a highly homogeneous group of well-educated and dedicated volunteer participants who were willing to commit themselves to visit the Gerontology Research Center (GRC) at regular intervals for an indefinite period, perhaps for the remainder of their lives. Without the initiative and assistance of Dr. W.W. Peter in their recruitment, and without the continued commitment of the participants (see "Dedication," "Acknowledgments," and Chapter III), the essential stability of the sample population could not have been maintained. Because of their dedication, the study was able to collect reliable historical and background data, to compare measurements of responses to standardized stimuli under basal conditions with previous measurements, and to include more tests across a broader spectrum of research areas, as well as to characterize its subjects in much greater detail, than most other studies. Their loyalty has also made it possible to introduce many tests that not only are time-consuming but often involve some degree of personal discomfort.

Few studies have been pursued over periods long enough, and with enough repeated measurements, to permit true longitudinal analysis of changes in a variable in a single individual as he ages. The BLSA is unique in providing as many as 21 sequential measurements on the same subject, from which linear regressions on age and standard errors of estimate have been calculated for some functions. As of June 30, 1981, five or more data points were available for some measurements on 667 subjects.

The BLSA is unique both in the frequency of visits and in the time devoted to each. A visit of 2½ days, which includes two nights at the GRC, makes possible measurement under basal conditions of many physiological functions, such as blood pressure, heart rate, and oxygen consumption, as well as such time-consuming tests as studies of glucose and insulin homeostasis, hypothalamic-pituitary-gonadal function, and 24-hour renal-clearance rates. Measurements made both under basal conditions and during stress are necessary to identify more subtle changes in function and to detect occult disease. This is particularly true of the cardiovascular system; clinically occult coronary artery disease, which is present in a substantial proportion of elderly subjects, can be detected only through the imposition of stress on the heart. The length and frequency of visits have made possible a large number of measurements for many participants, with a consequent increase in the statistical reliability of mean values and regression coefficients.

The BLSA is also unique in the potential it offers of future study in its present and projected population. Participants recruited in their early adult years are still actively committed to the study, while new subjects are introduced in order to maintain the

population and to make possible analyses that will help identify "period"³ and birth-cohort effects. Although it is clear from the BLSA experience to date that both cross-sectional and longitudinal analyses are required for studies of aging, neither method by itself identifies exclusively the effects of aging. In cross-sectional analysis, age differences between groups of subjects are confounded with birth-cohort differences, i.e., effects due to events that occur at different ages in the lives of persons born at different times. Some of these events, such as economic depressions, war, or shifts in social policy, may have far-reaching effects that vary with the subject's age and situation at the time the events occurred. Longitudinal analysis confounds changes due to aging with those that result from "period" or secular influences, which affect whole populations. The attempt to differentiate among the three effects is strengthened by the addition of "cross-sequential" and "time-sequential" analyses described in Chapter I. Although in many areas of investigation this sort of analysis remains to be done, the data bases necessary for its accomplishment are now becoming available.

The BLSA has already achieved some of the goals set for the study. It has contributed to knowledge about aging in normal persons and has shown that age changes can be estimated for some variables in individual subjects. It has highlighted, and suggested approaches to, some of the problems inherent in the analysis of both cross-sectional and longitudinal data for age changes.

A number of critical questions remain for the future, among them the interrelations among age changes in different organ systems, the time courses of different diseases, and the effects of critical life events. In the coming years the study on women will mature, and insight should be gained into the remarkable but still unexplained difference between the sexes in disease development and longevity.

³See Chapter I for definitions of terms.