Decline and Senescence: A Field for Basic Research

Topics in the Biology of Aging. A symposium, San Diego, California, November 1965, sponsored by the Salk Institute. PETER L. KROHN, Ed. Interscience (Wiley), New York, 1966. 191 pp., illus. $9.75.

Radiation and Ageing. Proceedings of a colloquium, Semmering, Austria, June 1966. PATRICIA J. LINDOP and G. A. SACHER, Eds. Taylor and Francis, London, 1966. 472 pp., illus. $6.50.

The subject of aging has emerged as a biological subdiscipline largely as a consequence of the energetic dedication of outstanding persons such as Fritz Verzar, Alex Comfort, Peter Medawar, Peter Krohn, George Sacher, Patricia Lindop, Howard Curtis, Marrott Sinex, Zh. A. Medvedev, James Birren, and the late Leo Szilard. Impetus was given to the attack on the basic problem about ten years ago by the Gatlinburg Conference on the Biology of Aging, under the leadership of a committee of the American Institute of Biological Sciences made up of Szilard, James Ebert, Bentley Glass, Henry Mahler, K. C. Atwood, and others. The two volumes here reviewed, containing the proceedings of two independent symposiums on aging, are therefore useful and timely, and provide—the first, particularly—a logical context for an appraisal of the progress made during this decade both in research and in gaining support for a continued, energetic effort.

The papers reflect remarkably well the major areas of progress, and the discussions following the papers reflect equally well the growing sophistication and the common language and concepts that have evolved during this decade. The clearest advances have been in the evaluation of genetic damage as a major source of senescence, a thesis which fascinated Szilard, and which resulted in the stimulating stochastic model he presented in the *Proceedings of the National Academy of Sciences* [**45**, 30 (1959)]. Significantly, the experimental testing of his and similar theories has been achieved largely under the sponsorship of the Atomic Energy Commission. Of particular note are the pioneering studies of Sacher, Lesher, and Brues, of Casarret, and of Curtis, in this country, and of Rothfels, Lindop, and Alexander in Great Britain. Studies reported in *Radiation and Ageing* do credit to the AEC sponsorship. The papers by Curtis, by Bucher and Swaffield, and by Fry, Tyler, and Lesher are particularly valuable. As J. Maynard Smith points out in a succinct paper in the Salk symposium volume, present evidence rules against a predominant role for somatic mutations in aging. Developmental biology as it impinges on aging is strongly represented in the Salk volume, particularly in the papers of Hayflick and of Puck, Waldren, and Tjio, which deal with the relation to senescence of the limited potential for division of cells in culture. The report on immunological tolerance and aging, notably studies by Walford, tangential to those of Blumenthal (of the VA) and of Makinodian (of the AEC), are related to the elegant series of studies carried out in England, and reported in this volume by Krohn, on transplantation of skin and ovary. Skin can apparently survive for at least six host lifetimes in serial transplantations among rodents; and ovaries undergo loss of viable eggs quite early in the life-span of female mice, although the loss in fertility is also ascribable to decreased hospitality of the aging uterine environment, even prior to cessation of ovulation. Evidence bearing on the thesis that age pigments are relics of lysosomes is presented by D. Brandes. This thesis, which has won easy acceptance despite some apparently contradictory evidence, is, in this reviewer's opinion, still in a conjectural status.

The keynotes of the Salk conference are set by the incisive analytical presentations of Maynard Smith and of Walford. Both implicitly and explicitly emphasize the pressing need, in the design of present and future research, for the critical testing of the various hypotheses of the cell-biological origins of aging. It is this keynote that relates this conference directly to the ideas that fired Szilard's imagination and hopes for research on aging as an emerging field. It is against these dicta that the successes and failures of the last decade should be measured.

Szilard believed the aging process was imminently susceptible of attack, and he succeeded in encouraging substantial basic effort; but in one crucial sense he failed, for despite his advocacy the NIH, with its vast potential for creative support of basic research on the problem, has been at best reluctant in its support and, at worst, an obstacle to progress. In a very real sense, those advances that have occurred during the last decade have taken place in spite of its discouraging lack of interest in the initiation of a vigorous effort to understand the fundamental phenomenon.

Aging is a biomedical problem that affects every human being. It is the root cause of most of the costs of medical care. Congress has repeatedly manifested strong interest in the subject, and if a mandate to the NIH to assume a leadership role in biological research on aging was necessary, it came from the White House Conference on Aging in 1960. Both the biological- and the medical-science members of the conference called unanimously, *inter alia*, for (i) the establishment of an Institute for Aging Research within the NIH, (ii) the reestablishment of a study section on aging within the Division of Research Grants of NIH, (iii) enlarged support for basic biological research on aging, and (iv) training programs to meet manpower demands.

Only with respect to the last of these has the NIH directorship responded. It has not established a separate institute. Gerontology has been assigned to the National Institute of Child Health and Human Development, where it is subsidiary to obstetrics, gynecology, and pediatrics. There is no study section on aging. Hence requests for grants are frequently considered by unsympathetic study-section committees with competitive interests, the approval rate is about half that accorded to other requests, and gerontology receives less than 10 percent of the grant funds distributed by NICHHD. In fact, NIH grants for studies of aging appear actually to have decreased since the White House conference (*1*).

In NIH's intramural program on aging—the Gerontology Research Center at Baltimore City Hospital—N. W. Shock and his medically oriented group have made valuable contributions with descriptive studies of human aging. The center is being enlarged and will contribute substantially to knowledge of the physiology of aging, especially in the painstaking and methodical description of various functional parameters. It is in basic biology, particularly the systematic testing of hypotheses concerning the origins of aging—the kind of theoretical work for which a separate institute would be highly suited—that NIH support has not been forthcoming. The director of NIH, James A. Shannon, has expressed this view of the matter: "Our job is to make the means available for qualified investigators to undertake worthy research. Nobody, I hope, wants NIH to lead investigators by the hand into

certain fields. Nobody, I hope, wants a federal prescription of research undertakings. I can only say that if investigators and institutions are uninterested in gerontology, there is little we can do. NIH can only go as far as Congress and the scientific community permit" (*Geriatrics*, Sept. 1965, p. 77A). The statement stands in marked contrast to the recommendations made by the scientific community at the White House Conference and are a source of discouragement to those who are deeply committed to work in this challenging field. This reviewer would suggest that the following program could bring some semblance of order into the present disorder:

1) The appointment of a 10- to 15-man biological research advisory committee to outline the various promising avenues for basic studies of the mechanisms of aging. It can readily be demonstrated that the number of scientists who are qualified to serve on such a committee by virtue of interest in the problem as well as by professional standing is more than adequate.

2) Establishment of a study section within the NIH (or the NSF) to stimulate effective attack on the topics thus outlined, thereby encouraging relevant grant applications and the growth of appropriate training programs.

3) Expansion of the human physiology and psychology program of the Gerontology Research Center in Baltimore and transfer of its basic-biology component to a suitable academic environment.

4) Creation of a National Institute for Aging Research, either in NIH or in another suitable governmental agency.

If these or analogous steps are undertaken promptly, one may expect that within the next decade there will be the kind of progress that Szilard knew to be possible in the last decade; and in 1977 a book review such as this would be an undiluted discussion of solid achievements.

BERNARD L. STREHLER
Aging Research Laboratory,
Veterans Administration Hospital,
Baltimore, Maryland

Notes

1. In 1955, grants for research on aging totaled less than $1 million (*U.S. Public Health Serv. Publ.* No. 799, p. iii); in 1961, the total—for 245 grants—was $5.7 million, or, if studies secondarily related to aging are included, $16.2 million (*U.S. Public Health Serv. Publ.* No. 841, p. iii); in 1966, there were 64 grants totaling $4.6 million (NICHHD, *Program Statistics Branch Rept.*, 26 Oct. 1966, and *U.S. Senate Report, 90th Congr.*, No. 169, p. 69, 12 April 1967).

Augmentor of the Human Eye

The Evolution of the Microscope. S. BRADBURY. Pergamon, New York, 1967. 367 pp., illus. $12.50.

This book contains a fascinating, well-illustrated, and very readable description of the development of the microscope from its first beginnings around 1610. Soon after the Galilean and Keplerian telescopes had been invented it was observed that they could be converted into microscopes by moving the eyepiece far enough from the objective to permit focusing on a near object. However, the poor definition of early compound microscopes led many experimenters, including Leeuwenhoek, to prefer homemade simple magnifiers, which were often of extremely high power.

The historian of the microscope is fortunate that the early developments were well documented. Numerous diagrams and engravings of early equipment are reproduced in this book, and many photographs of early microscopes, one dating back to 1678, are shown.

The essential parts of a microscope system, namely, a light source, condenser, object holder, objective, and eyepiece, with coarse and fine focusing adjustment, were understood and embodied in microscopes described by Hooke and others as early as 1665. Great improvements were made during the next hundred years, and indeed some microscopes made as early as 1780 bear a strong resemblance to present-day instruments in their general external appearance. The microscope, unique among scientific instruments, early became a thing of beauty, and at one time was considered a suitable plaything for a king.

Bradbury has not overlooked the development of the optical parts of the microscope. Achromatic objective lenses were made by Chevalier and others as early as 1808, although these were designed by empirical methods. The theory of the objective was firmly established by the work of J. J. Lister in 1830. Water-immersion objectives for biological studies date from 1867, and Abbe developed his "homogeneous immersion" principle in 1878. Much praise is given to the designers who brought microscope optics almost to their present state of perfection around the end of the last century.

This book is packed with interesting facts about early microscopes. The author obviously loves his subject and thoroughly understands the purpose of everything he describes. His numerous verbatim quotations from early writers are interesting and serve to illuminate the story he tells. The author appears to have had the good fortune of being able to examine many of the ancient instruments which are still in existence in European museums, so that his descriptions are first-hand and critical.

The electron microscope is dealt with fully, and other modern developments such as ultraviolet, phase, and interference microscopy are briefly discussed. There is no mention of zoom, metallographic, or petrographic microscopes, or of flat-field microscope objectives. I detected no obvious errors other than the spelling of some proper names, Zernike and Greenough in particular. The brief index is scarcely adequate for the mass of valuable information contained in this excellent book.

RUDOLF KINGSLAKE
Eastman Kodak Company,
Rochester, New York

On Chemical Kinetics

Gas Phase Reaction Rate Theory. HAROLD S. JOHNSTON. Ronald, New York, 1966. 372 pp., illus. $10.

This well-written monograph is a useful addition to a field with a seeming surfeit of texts. As the title suggests, its scope is too restricted to make it a suitable substitute for Frost and Pearson or Laidler as the required text in the typical senior-first-year-graduate course in chemical kinetics, although it does have short, introductory chapters on quantum mechanics, potential functions, and statistical mechanics that students would find interesting. What this book sets out to do, and does do very effectively, is to highlight the similarities in inexactness and incompleteness between applied "collision theory" and "absolute rate theory." It then builds a case for espousing neither point of view to the exclusion of the other. In reality few practitioners of either theory are so partisan that they do not adapt to their own noble designs features of the "opposing" theory that they find especially suitable, but Johnston's slightly contentious thumping for a superposition of the two theories is useful in stirring the blood of the usually torpid reader. For instance, on page 323 Johnston points out that for bimolecular reactions with activation energy one can consider three sets of