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BOOK REVIEWS

The Biology of Life Span—A Quantitative Approach, **by Leonid A. Gavrilov and Natalia S. Gavrilova, Harwood Academic Publishers, New York, 1991, ISBN 3-7186-4983-7, 385 pp., $120.00 (case).**

I YAWNED when I first saw this book. "Another theoretical treatise, with little practical value," I assumed. However, not knowing to whom I should send this book for review, I read it myself and was pleasantly surprised. The aim of the book is to investigate the question of whether organisms have a limited life span. In addition to an insightful analysis of the subject, the authors have also done a monumental service to other investigators in the field by compiling what certainly must be the most comprehensive bibliography on the subject ever published.

Chapter 1 introduces life span as a field of inquiry that involves a multitude of disciplines: gerontology; demography, ecology, genetics, radiobiology, toxicology, oncology, and zoology. The authors start right off by explaining why it is necessary to study life span at all. They believe it is a means of discovering ways to extend the human life span! To this end, the authors refer to a Soviet government-sponsored program which aims to experimentally develop new approaches to life span extension and test these therapies on human beings. The problem with much of the research in this field is that life span scientists in each of the above-mentioned disciplines tend to overlook advances made by their colleagues in other fields. Theoretical approaches have diverged, and works used and authors cited in their respective papers turn out to be almost totally nonintersecting. Furthermore, most scientists have stopped publishing the complete life tables they obtain. Since quantitative observation with subsequent mathematical analysis of the resulting measurements is of prime importance to the biology of life span, such demographic data are critical. Consequently, one important aspect of this book is the massive bibliography of worldwide demographic data which the authors have compiled, thereby assisting others to continue research in this area. The authors challenge the well-accepted premise that maximum life spans for any species (including humans) have been decisively determined, and they cite a great deal of conflicting data and opinions from eminent researchers around the world that appear to confirm their premise.

In chapter 2, the authors discuss the various causes for lifespan variability, including population heterogeneity, environmental variations, and the stochastic (kinetic) nature of the survival process. They painstakingly examine a plethora of mind-numbing formulae for predicting the lifespan distribution, to determine which is the most accurate model. Despite the numerous formulae that have been developed using modern computers and mathematical modeling techniques, the authors contend that the force of mortality is best representated by Sacher's classic formula, and the life span distribution law is best represented by the original Gompertz–Makeham law.

In chapter 3, the authors focus specifically on the human life span curve. They demonstrate that the shape of the human survival curve is indistinguishable from that of lower organisms. They also discuss the futility of the orthodox approach to life span extension by the treatment of individual diseases. They review several large-scale interventionist approaches to various diseases that resulted in a reduction in deaths due to the particular disease studied, but which were always accompanied by increases in deaths due to other causes, resulting in no increase in overall survival. They point out that it is essential to identify and treat the mechanisms of the aging process itself in order to delay it and extend maximum life span. An example of such an approach is the neuroendocrine theory of aging, as promulgated by Professor Vladimir Dilman, which demonstrates the existence of unitary mechanisms in the origin of aging and the diseases of aging, and which provides the basis for a new, integrated theory of medicine and treatment of disease based on solid scientific foundations.

Although the concept of a species-specific life span is now nearly universally accepted in the gerontological literature, the authors claim that it is a premise based on "soft" data and has become established through a long period of "mutual citation." To support their argument, the authors include a three-page table of citations regarding human life span length from a number of eminent authorities, with estimates ranging from 60–200 years—none of which include confidence intervals. The authors conclude from this morass of "studies" that estimates made regarding length of life are unsuitable for scientific research. One solution that has been proposed for this dilemma is to simply record the longest-lived well-documented case (which, according to the Guinness Book of Records, is currently 120 years and 237 days). However, the authors point out that this analysis smacks of sporting records, not science, and is always subject to being broken. They propose that the "compensation effect of mortality" be used to determine species-specific life spans, and using this technique, they demonstrate that the human life span is 95 ± 2 years.

In chapter 5, life span data are used to analyze the validity of a number of theories of aging, including genetic programming, wear and tear, and the authors' own *reliability theory of life span.* They believe that the data best support the wear-and-tear theory and that this theory has been prematurely discarded by many scientists. Several categories of life span extension experiments are discussed, particularly as to their relation with the above-mentioned theories of aging. Finally, the authors extensively review the history and significance of cell division studies to human aging, concluding that "it is unclear how the results obtained from cell culture research are related to life span" (p. 224).

Chapter 6 is a discussion of mathematical models of life span. The authors discuss the dubious nature of many of the models, pointing out that "the uncritical use of modern statistical techniques and computers has, in a number of cases, created a thick biometric fog which hides the superiousness of the published conclusions" (p. 234). After a lengthy analysis of a number of published papers in prestigious journals, referring to them as "mathematical hocus pocus," the authors conclude with the statement that "the only purpose of this discussion has been to forwarn the reader to adopt a critical attitude towards mathematical models of life span, no matter where they might be published" (p. 240).

In their conclusion, the authors propose that scientists around the world join forces with them in a targeted attack on understanding the mechanisms of the aging process, with the ultimate goal of extending the human maximum life span.

As previously mentioned, one appendix contains references from the most reliably obtained lifespan data for many different species. A second appendix lists citations for biomarkers in humans and other species. The book includes over 600 references—many

of which are from the Soviet literature. Finally, it is extensively indexed. Clearly, this is a very interesting, provocative, and thought-provoking book, which asks and raises as many critical questions as it attempts to answer. In addition to being a scholarly analysis of the subject, with numerous references and extensive appendices, the book is also of practical value, encouraging gerontologists to answer the call of the authors in their international project to extend the human life span.

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Liver and Aging—1990, Proceedings of the Fourth Tokyo Symposium on Liver and Aging, 15–17 August 1990, **Kinichi Kitani (Ed.), Excerpta Medica, New York, 1991, ISBN 0-444-81388-8, 364 pp.**

THE PROCEEDINGS of the Fourth Tokyo Symposium on Liver and Aging, as with the previous three symposia and the associated volumes, is a tribute to the perseverance and efforts of Dr. Kenichi Kitani, the editor and primary organizer of this series since its inception. While the topic may seem narrowly focused to some, this perception is misleading since many researchers who lack an intrinsic interest in hepatology currently employ the liver or hepatocytes as a model in their aging studies. Although EURAGE and the Falk Foundation have sponsored occasional symposia on this or broader related topics, the Tokyo Symposium is the primary forum for this growing subdisciplinary arena. *Proceedings* provides a comprehensive review of the current status of aging research on the liver within a single volume and consists of concise, camera-ready reports reflecting the content of the symposium presentations, as well as the subsequent discussions. The major topics are liver drug metabolism/toxicity and alterations in hepatic proteins during aging, although several other areas such as hepatobiliary function, membranes, and aging mechanisms are represented.

The effect (or lack thereof) of age, gender, and diet on liver Phase I and II drug metabolism are documented in rodents, nonhuman primates, and humans. Fujita *et al.* extend their studies on the age-associated "feminization" of the male liver microsomal monooxygenase system and implicate shifts in the relative distribution of gender-specific cytochromes P-450. In collaborative in vivo and in vitro studies using monkeys and humans, investigators from the United Kingdom, United States, Australia, and Belgium provide the first definitive evidence that changes intrinsic to liver monooxygenases do not contribute significantly to the well-documented age-related deficits in hepatic drug clearance. The data suggests that (a) this decline, as well as the "femininization" of the male liver monooxygenase system, may be restricted to the male rat model and (b) concomitant declines in liver volume and blood flow may account for reduced hepatic drug clearance in the elderly.

Laura Rikans and colleagues implicate shifts in the expression of specific cytochromes P-450 (Phase I), coupled with a decline in glutathione-dependent homestasis (Phase II), in the variations in susceptibility to drug-induced hepatotoxicities. However, Carrillo *et al.* suggest that aging per se may have a minimal effect on the activities of the glutathione-S-transferases, critical enzymes in the Phase II pathways.