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Book Review

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Aging and Age-Related Disorders, edited by S. Bondy and K. Maiese, New York, Springer, 2010, ISBN 978-1-60761-602-3

The first point to make about this otherwise well-edited monograph is that the title, "Aging and Age-Related Disorders", could be misleading to those who did not realize that this is one of a series of publications on "Oxidative Stress in Applied Basic Research and Clinical Practice". (The volume number is not given in this book, but the reader is directed to http://www.springer.com/series/8145 for other titles.) Accordingly, all 22 chapters take, as their point of departure, a focus upon the roles of oxidative stress in aging and in various diseases of aging—more specifically, diseases that predominately impact either the cardiovascular or nervous systems. A few other diseases get some attention. For example, diabetes is discussed in many chapters and cataractogenesis is briefly mentioned in the very helpful and basic introductory chapter by Ufuk Çakatay, a member of the Faculty of Medicine of Istanbul University. A particularly nice feature of the volume is that one gets "to meet" colleagues from around the world with whom one may have had very little opportunity to know. Although US authors dominate, 11 other nations are represented, including 7 contributions from Japan, 7 from Canada, 6 from Spain, and 5 from Taiwan.

Because of my own growing interest in the role of epigenetic drift in the pathogenesis of aging phenotypes, I read the very last chapter first: "An Epigenetic Model for the Susceptibility to Oxidative Damage in the Aging and Alzheimer's Disease", by Nasser H. Zawia and Fernando Cardizo-Pelaez (University of Rhode Island). Motivated by their own research and those of others on a possible link between early developmental exposure to lead and late life Alzheimer's disease, they propose an interesting molecular model on the dual interactive roles of oxidized guanines and methylated cytosines at CpG islands within promoters, leading to age-related alterations in transcription and epigenetic drifts with important phenotypic consequences. This chapter is also notable because, although it confines itself to neurodegeneration, it provides a one sentence summarization of the state of this entire field of research: "It is still unresolved if increased oxidative damage to DNA plays a role in the neurodegenerative process or is just an epiphenomenon of the neurodegenerative process." It could turn out to be one or the other or both. Should it prove to be largely an epiphenomenon, this should not argue against the importance of developing rational interventions. Like many complex disorders, the pathogenesis of dementias of the Alzheimer type (DAT) can perhaps best be envisioned as a series of sequential pathogenetic nodes, each of which is worthy of attack.

One such DAT node, presumably downstream from neuritic plaques, is microglial-mediated inflammation. The chapter by Predrag Ljubuncic, Einat Gochman, and Abraham Z. Reznick on "Nitrosative Stress in Aging-Its Importance and Biological Implications in NF-κB Signaling", one of the early basic science chapters, is therefore quite significant and very well done. The senior author, from Haifa, is finally, someone I DO know from international meetings over the years. "Inflamm-aging" is specifically mentioned in the text, in keeping with the mounting degree of attention it is getting. Inflammation, however, seems to be embracing an ever widening spectrum of events. In the old days, when I taught introductory pathology to medical students, it was simply defined as "rubor, tumor,

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calor, dolor and loss of function". For acute inflammation, we expected to see lots of neutrophiles; for chronic inflammation, there were lots of lymphocytes. Nowadays, however, elevation of NFκB expression in unexpected places such as adipose tissue, plus a few macrophages, seem to suffice!

Another important basic science contribution is the review, by Edward H. Sharman (University of California at Irvine), of the seven mammalian members of the sirtuin family. Sirtuins, named after the yeast Sir2 gene (silent mating-type information regulation 2) are thought to usually act as deacetylases. They are among the many enzymes that can post-translatiptonally alter the structure of histones and thus modulate gene expression. This story can be linked to the one on NFκB, as sirtuins can suppress excessive inflammation, perhaps among the reasons they may be important in the maintenance of healthspan, if not lifespan, in mammals. Sharman briefly addresses the roles of sirtuins in a variety of age-relate diseases, including DAT, but does not come to any strong conclusions. The chapter could also have had a connection to the chapter on the epigenetics of neurodegenerative disorders discussed at the beginning of this review. Unfortunately, although this book was published in 2010, the review of the literature misses many published that year, including a high profile Cell paper from the laboratory of Leonard Guarente (G. Donmez et al., Cell 142: 494, 2010). Using a mouse model of Alzheimer's disease, those authors came to the conclusion that Sirt1 activation could be a viable modality of intervention.

Those of us interested in neurodegenerative diseases of aging can only ignore the vasculature at our peril. The seven chapters on this subject are almost entirely devoted to ideas about oxidative stress. There is thus a fair amount of overlap, but such overlap can be useful.

This reviewer apologizes to the many authors and co-authors whose contributions, because of space constraints, could not be commented upon. They are nonetheless all appreciated by me and most certainly would have been appreciated by the late Mark A. Smith, the former Editor-in-Chief of the *Journal of Alzheimer's Disease*.