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Book Reviews

Metals and Oxidative Damage in Neurological Disorders
Editor J.R. Connor
Plenum Press, New York and London, 1997

This attractively-presented book, with a cover photograph showing astrocytes loaded with fluorescent dyes, aims "to bring together scientists and clinicians interested in oxidative injury in the nervous system". However the focus of the book is narrower, in that most chapters deal with the relationship of metals to neurodegeneration, and even then the focus is on the consequences of excessive amounts, or maldistribution, of essential metals (zinc, copper, and especially iron) rather than the effects of xenobiotic metals such as lead. Nevertheless, the book has excellent chapters on iron, copper, manganese and zinc, and on the role of metals in Alzheimer's disease. Overall, iron receives the most attention, but it is still remarkable how little we know about the biochemistry of brain iron in humans, and the mechanisms by which iron maldistribution occurs in the neurodegenerative diseases. The same is true for copper – the concept of a "low molecular mass non-caeruloplasmin plasma copper pool" was disproven by Gutteridge in the 1980s, but it still appears in the literature. I particularly enjoyed the chapter by Smith *et al.* on the mechanisms by which metals cross the blood–brain barrier.

Other useful chapters review the roles of ascorbate and vitamin E in the brain, nitric oxide synthesis and toxicity, the role of mtDNA damage in Alzheimer's disease and neurodegeneration generally, LAMMA analysis as applied to Parkinson's disease, mutations in CuZnSOD in ALS, and tardive dyskinesia. In the latter chapter, most of the literature cited was pre-1990, perhaps indicative of the general lack of current interest in the role that free radicals might play in this condition. The last chapter of the book might well have served as a useful introduction.

Overall, this book is a helpful compilation that I am pleased to have on my bookshelf. It serves to underline how much more research is needed in this important area.

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Radical-Mediated Protein Oxidation. From Chemistry to Medicine
M.J. Davies and R.T. Dean
Oxford University Press, 1997

This is an excellent and long-overdue book. For too long proteins have been the Cinderella of the free radical field, given passing mention in reviews which usually focus on lipid peroxidation and oxidative DNA damage. This is not due to a lack of chemical knowledge: our understanding

of the chemistry of free radical attack on amino acids and proteins is probably better than it is for DNA, as the authors so ably illustrate in Chapter 2. I enjoyed the historical perspective, in particular the appropriate attention paid to the seminal work of Dakin, in Chapter 1. Chapter 3 reviews what is known about the fate of oxidatively-damaged proteins in cells and takes an appropriately critical view of the widely-stated simplification that "oxidized proteins are degraded at an accelerated rate by the proteasome system". Indeed, this chapter underlines how little we know about how cells handle oxidized proteins, and illustrates the flaws in some of the methods that have been used to study this.

Measurement of protein oxidation is now becoming more fashionable, probably because of the availability of the carbonyl assay. The authors critically review the shortcomings of the assay, suggesting that it probably over-estimates oxidative protein damage *in vivo*. One hopes that the carbonyl assay will not cause as much confusion as did the plasma and tissue TBA tests. The authors also identify specific end-products of protein oxidation that might be valuable biomarkers, although the question of their presence in, and absorption from, the diet (e.g. from cooked foods) needs to be considered.

The role of protein oxidation in cell physiology/pathology is discussed in Chapters 4 and 5, which really boil down to almost nothing, i.e. there is no clear-cut case where protein oxidation has been *proved* to be the primary insult caused by oxidative stress. Indeed, this will be difficult to demonstrate. The authors briefly mention ion channels, but I would like to have seen more attention given to K^+ channels, and to proteins regulating intracellular "free" Ca^{2+} levels. The discussion of abnormal proteins in lipofuscin on page 219 could have been expanded to include the specific protein abnormalities identified in the various NCL diseases.

Just to prove that I did read the book thoroughly, here are a few minor quibbles. Tables 4.1 and 5.1 overlap extensively. The authors missed one artefact relating to nitrotyrosine measurement – *never* expose biological material containing NO_2^- (as most diseased samples do, because $NO^\bullet$ production is upregulated) to low pH. Artefactual generation of tyrosine-nitrating HNO_2-derived species during sample processing at low pH has very probably contributed to some of the high levels of 3-nitrotyrosine reported in the literature. Pages 217/218 do not mention that binding of certain metal ions, e.g. Ni^{2+}, to nuclear proteins can render these metals more active in Fenton-type chemistry. Page 232 misses the point about metals in atherosclerotic lesions: it is not surprising that homogenized tissue contains released metals, but this is not an appropriate control for lesion material. The section on apoptosis misses the obvious point that caspase activity is probably redox-sensitive.

Nevertheless, these are all minor points of debate. What is important is that this excellent book should be widely read by everyone in the free radical field. I recommend it highly.

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