

## Book Reviews

### **Tamoxifen: Beyond the Antiestrogen**

Edited by J.A. Kellen

Birkhäuser Verlag: Basel

x+ 377 pages

ISBN 3-7643-3842-3. 1996

*Tamoxifen: Beyond the Antiestrogen* comprises of a collection of papers from notable experts that have worked for a number of years with the drug. Tamoxifen (ICI 46,474 Nolvadex) is a non-steroidal antiestrogen with demonstrated anti-fertility properties in mice and rats. It has been shown to have efficacy in the treatment of advanced breast cancer and has been evaluated as a preventive agent in women at the risk of breast cancer [Jordan (1993) *British Journal of Pharmacology* **110**, 507–517].

The book contains 17 well written and presented chapters. The excellent introductory chapter by Kellen is complemented with a review of the use of Tamoxifen in treatment of malignancies other than breast cancer. Rowlatt discusses 'neoplasia' in the second chapter—the reader is reminded that scientists are still dependent on clinical judgements which appear subjective in the absence of a verifying hypothesis. Other chapters "Interactions of Tamoxifen with lipid signal transduction cascades" (Cabot and Giuliano); "Carcinogenicity of Tamoxifen" (Sasco and Gendre)—an excellent account of randomised controlled clinical trials in the 1970–1980s which suggests the risk of endometrial cancer among women receiving Tamoxifen; "Mechanisms of resistance to antiestrogens and their implications for crossresistance" (Clarke and Lippman); "Tamoxifen and multidrug resistance

in cancer" (Kellen); "The effect of Tamoxifen on the immune response" (Baral, Nagy and Berczi); "Cellular effects of early exposure to Tamoxifen" (Iguchi and Ohta); "The covalent binding of Tamoxifen to proteins and DNA" (Kupfer); "Tamoxifen metabolism and oestrogen receptor function—implications for mechanisms of resistance in breast cancer" (Johnston and Dowsett); "Tamoxifen and the E-cadherin/catenin complex" (Bracke, Van Roy, Castronovo and Mareel); "Regulation of growth factor gene expression by Tamoxifen" (Murphy and Murphy); "Tamoxifen and drug metabolising enzymes" (Ahotupa); "Membrane antioxidant-mediated cardioprotective anti-carcinogenic actions of Tamoxifen" (Wiseman); "Antiestrogen regulation of *erbB2* expression in human breast cancer cells" (Wärri and Härkönen) and a concluding chapter by Kellen. As an add on to the involvement of Tamoxifen in oxidative reactions, this reviewer found that Tamoxifen reacts very rapidly with peroxy radicals—intermediate species in the process of lipid peroxidation, with a calculated rate constant of  $4.7 \times 10^7 \text{ M}^{-1}\text{s}^{-1}$  and its hydroxylated metabolite (discussed in Chapter 10 by Johnston and Dowsett) also reacts rapidly with peroxy radicals with a rate constant of  $5.3 \times 10^7 \text{ M}^{-1}\text{s}^{-1}$ .

In general the book gives an impressive account of the complex biopharmacy and pharmacology of Tamoxifen. The sense of accomplishment which elates the reader is borne out of the unique 'curtain raiser' and the 'final curtain' of quotes: "to single out causes, one must make loose assumptions"—Levy 1995, and, according

to Abraham Lincoln, "with high hope for the future, no prediction is ventured."

This is probably one of the better books on Tamoxifen in recent years.

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### **Free Radicals in Diagnostic Medicine**

#### **A systems approach to Laboratory Technology, clinical correlations and antioxidant therapy**

Edited by D. Armstrong

Plenum Press: New York. 1994. pp 464

I SBN 0-30644981-1

As a proceedings of an international symposium on "Free Radicals in Diagnostic Medicine", held in Buffalo, New York in 1993, this book addresses a subject come of age in laboratory medicine. The collection of papers from this symposium makes up volume 366 of the well known series 'Advances in Experimental Medicine and Biology'. The subjects covered are discussed by 57 scientists, mainly from North America, under four headings namely; pathophysiology and analysis, organ specific disorders, systemic involvement and therapeutic interventions. Finally, a large section with 23 contributors is devoted to poster presentations, covering diverse aspects of diagnostic medicine in man and animal models. The first section has an excellent introduction to lipid peroxides and their levels in disease processes by Professor Yagi and it would have been helpful if similar introductory chapters prefaced each major section.

For a camera-ready presentation the format is remarkably uniform and Professor Armstrong and the publishers are to be congratulated for making possible such a rapid publication. The topics covered are extremely important and timely yet such a book can, by definition, only serve to focus attention on a rapidly developing field.

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### **Nitric Oxide and Radicals in the Pulmonary Vasculature**

Editors: Weir, K; Archer, S. L. and Reeves, J. T.

Publisher: Futura Publishing Company, Inc.

Armonk, NY

Publication date: 1996

The pulmonary vasculature is clearly an important setting for oxidant mediated damage, due to its intimate contact with the air we breathe, and because airway inflammation has been demonstrated as a pathological end point in a number of pulmonary diseases. This book, weighing in at over 500 pages long, has a feast of information on NO $\cdot$ . If this is what you are interested in, then you only need to look at the latter half, as the early part of the book deals with the response of the vasculature to the imposition of oxidative stress. In this respect, the title is really a misnomer, as much of this work relates to H $_2$ O $_2$ . One of the strengths of the book however is that it describes how radicals and oxidants react within the biological setting. It introduces and discusses new and novel concepts in radical and oxidant pathophysiology and protection, and perhaps, most importantly of all, places free radical/oxidant mechanisms into the context of the broader biological response.

An overview, presented in the first chapter by Sylvester addresses oxidative stress in the vasculature and importantly, introduces a concept that is carried through subsequent chapters, that free radical species may have beneficial actions in certain contexts, eg. NO $\cdot$  in the maintenance of vascular tone. Background information on the types of radicals produced in the biological setting, and protective antioxidant mechanisms are presented in two chapters by Halliwell *et al.* and Koppenol. Thereafter, the book is particularly strong in two areas: First, in those chapters addressing the role of oxidants and free radicals as integrated components of the biological response: protein and lipid oxidation in pulmonary ischemia reperfu-

sion injury (Fisher and Al-Mehdi); oxidant involvement in oedema formation in the ischemic and reperfused lung (Heffner and Fracia); the potential of oxidants to act as vascular oxygen sensors (Wolin); and the role of NO<sup>•</sup> in vascular cell proliferation, vascular tone, and inflammatory processes (Scott-Burden; Dinh-Xuan *et al.*, and Wong *et al.*, respectively). Second, in addressing the early cellular responses of the vascular endothelium to changes in cellular and extra-cellular redox. Stimulation of specific signal transduction pathways, proto-oncogenes and other transcription factors, and how these may influence adaptive and pathologic cellular responses. With respect to NO<sup>•</sup>, the final two chapters which discuss this radical as a therapeutic agent in congenital heart disease and pulmonary hypertension of the new-born are particularly interesting. These later discussions show how thinking about free radicals has evolved from the concept that they are purely injurious species to an appreciation of their involvement in normal cellular and organ homeostasis, and hence as potential targets for therapeutic intervention.

Each chapter within this book is self contained, giving a brief review of the area covered (publications cited up to and including 1995) and the authors contribution to the field. However, as a consequence of this format, considerable repetition of background information occurs throughout the book, especially with regard to NO<sup>•</sup>. Although this repetition is frustrating and the overall ordering of the chapters sometimes bizarre, the book is a worthwhile source of reference of contemporary knowledge in this field. It will be of interest not only to workers studying NO<sup>•</sup> or the pulmonary vasculature, but to a much broader readership interested in the role of free radicals and oxidants in the whole organism.

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### **Handbook of Antioxidants**

Cadenas E. Packer L (eds)

Marcel Dekker Inc: New York. 1996. pp 602

ISBN 082479298-X

The purpose of this book is to serve as an authoritative treatise on the chemical, biological and clinical aspects of antioxidant molecules, and in the process to develop a valuable book series. Ten low molecular mass antioxidant molecules are discussed by 41 authors, often working in multidisciplinary collaborative international teams. The topics covered are; vitamin E, ascorbic acid, coenzyme Q, uric acid, carotenoids, vitamin A, flavonoids and other polyphenols, herbal antioxidants, melatonin, aminoindoles, and  $\alpha$ -lipoic acid. The reader is soon aware that this is an in-depth and quality treatise with an enormous amount of unique information distilled into a single volume. The presentation is clear and pleasing with bold headings and many well thought out figures and tables. References are given in full at the end of each chapter, further increasing the usefulness of the book to specialised researchers and students alike. A book with such an authoritative and intellectual content surely deserves a more attractive and eye-catching cover, not the exceptionally dull one given it. The book fulfils all the objectives it set out to cover and comes highly recommended to all those working on aspects of free radicals and antioxidant protection.

John M. C. Gutteridge

### **Transgenic Organisms: Biological and Social Implications**

Edited by J Tomuik, K Wöhrmann and A Senter  
Birkhäuser Verlag, Basel, 1996

The use of transgenic animal technology is becoming almost a standard technique in biomolecular research, and the use of transgenic animals

has led to fascinating insights into the metabolic role of antioxidant defence enzymes and nitric oxide synthases, to name but two of the topics of interest to readers of this journal. The present volume summarizes the proceedings of a meeting in 1995 to examine developments in, and the implications of, transgenic organisms. Topics reviewed include inactivation of transgenes in plants, e.g. by methylation, transposable elements, food from genetically modified organisms, horizontal gene transfer between bacteria in their natural environments and its relationship to the risk of release of

genetically-altered organisms, the problems of using transgenic crop plants, the use of baculoviruses, monitoring genetically-modified organisms and the status of the Human Genome Project. The volume contains a great deal of useful information, with a particular focus on safety issues, and I am pleased to have it on my shelf. My only criticism is the superficial index.

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