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BOOK REVIEWS

Proteases, Protease Inhibitors and Protease – Derived Peptides
Edited by J.C. Cheronis and J.E. Repine
Birkhauser Verlag AG, Basle, Switzerland

This is a collection of nineteen papers representing a considerable sampling of the work presented at a symposium in Snowmass, Colorado, in mid-1992. The book begins with four overview papers which cover structure-function interrelationships, mechanisms for disrupting proteinase-antiproteinase balance in tissue, oxidants, metalloproteases and serine proteases in inflammation and synergistic interactions between elastases and oxygen radicals, the latter focusing on neutrophil-related mechanisms of lung injury in the adult respiratory distress syndrome and in hyperoxia. These papers set a useful and concise clinically-orientated tone for the following sections which represent state-of-the art reviews through 1991 (only 6 out of 133 references are 1992).

The next six papers cover a potpourri of clinical conditions in which neutrophil elastase inhibitors could prove to be useful, including acute inflammation, emphysema related to α-1 antitrypsin deficiency, and cystic fibrosis. These papers summarize some of the pharmacological strategies in designing and evaluating neutrophil elastase inhibitors, including those that are engineered to be resistant to oxidant-induced inactivation.

The third set of four papers considers proteases and protease-derived peptides in inflammation, focusing on factor XII activation, the kinin system, the role of bradykinin and microbial proteases and kinins in infection and sepsis, and the potential therapeutic applications of kinin antagonists in such human diseases as the systemic inflammatory response syndrome, asthma, pain, brain or spinal cord trauma and rhinitis.

The fourth and last set of five papers relates to the contribution of proteases to immunoregulation and cellular differentiation, including representations from such diverse areas as cytokine regulation of endothelial cell extracellular proteolysis, which focuses on the biological significance of TNFα-induced "endothelial cell activation" and the plasminogen activator proteolytic system of endothelial cells (a particularly concise and well-written unit), the biological spectrum of individual cysteine proteases utilizing in particular specific inhibitors of cathepsins L and B to define their participation in bone resorption and antigen processing, a useful review of the fast moving field of neuropeptide processing in pathophysiology, a review of studies on matrix metalloproteinases of transformed fibroblasts (which may have implications for pathological invasive processes including mestastasis) and a perfunctory but timely and relevant expanded abstract on selected interactions of endotoxin with arachidonic acid metabolic control pathways.

The theme of the book seems targeted at medical science practitioners who are indirectly or directly working in protease-related fields, and as such provides the PhD with a useful clinical perspective and the MD with a particularly useful basic perspective of current thinking regarding the biomedical applications of this important field. This small concise book does not pretend to be a authoritative state of

the art volume of the science of protease-antiproteases. It is, however, disappointing but understandable that a unit could not be included on the important and topical HIV-1 protease system . . . the book focuses on extracellular protease balance and not on intracellular proteolytic control mechanisms.

An inherent weakness in a collection of loosely-related expanded abstracts and papers like this one is its lack of cohesion (in fact no index is included and reference style is uneven). The question is whether laboratories and investigator-practitioners would buy this book for the sake of substituting for conference attendance or a broadening of individual perspectives. As there are important synergisms and parallelisms between the fields of protease/antiproteases and oxidants/antioxidants, including long anticipated therapeutic applicability of 1–2 decades of considerable scientific resource focus, those interested in oxidants should be aware of this book, and relevant laboratories and libraries ought to consider obtaining it.

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Cytotoxic Cells: Recognition, Effector Function, Generation and Methods
Edited by M.V. Sitkovsky and P.A. Henkart, Editors
Birkhäuser Publishing Co., Boston, 1993, 527 pages

Drs. Sitkovsky and Henkart state in the Preface of the book that their "motivation for putting together this book was the need for a single source reference that could be used as an introduction to cell-mediated cytotoxicity for newcomers to this field". Apparently, this is the first book on cell-mediated cytotoxicity that covers such a broad spectrum of research interests. As someone who has only a peripheral interest in this area, I found this book to be very helpful in quickly familiarizing me with the most recent developments in this area. The book is divided into 10 major sections and contains a total of 60 chapters. I found section I (Introduction and Overview; Chapters 1–3) particularly helpful to understanding some of the more detailed chapters appearing later in the book. Sections II (Target Cell Recognition; Chapters 4–9), III (Generation of Cytotoxic Cells; Chapters 10–13), IV (Molecular Mechanisms of Cellular Cytotoxicity; Chapters 14–21), V (Granule Proteases; Chapters 22–27) and VI (Alternative Mechanisms of Cytolysis; Chapters 28–30) represent approximately half the total length of the book. Sections VII (Biochemical and Immunological Manipulations of Cytotoxic Cells; Chapters 31 and 32) and VIII (Functions of Cytotoxic Cells in Vivo; Chapters 33–41) present chapters describing the various functions of cytotoxic cells in vivo and how they may be pharmacologically manipulated. Section IX (Macrophage-Mediated Cytotoxicity; Chapter 42) describes the mechanisms by which macrophages injure target cells (tumor cells and viral particles) whereas Section X (Methods; Chapters 43–60) provide an extensive summary of the pertinent methods used in the area of cytotoxic cells. The editors have done an outstanding job in assembling a large number of internationally-recognized authors who contributed concise and well-written chapters. The only criticism I have was the relative lack of emphasis on macrophage-mediated cytotoxicity. The inclusion of an entire section on methods used in this area of research was particularly attractive and a major strength of the book. Overall, I thought the authors did an excellent job in

achieving their objective of providing an inclusive text and reference for the novice interested in cell-mediated cytotoxicity and would whole-heartedly recommend this book.

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The Handbook of Immunopharmacology
Series Editor Clive Page
Immunopharmacology of the Heart
Edited by Michael J. Curtis
Academic Press: London, 1993, ca £40.00
ISBN 0-12-200245-8 xii + 146 pages

"A consideration of a variety of cardiac diseases for which drugs may play a therapeutic role by virtue of their effects on aspects of the immune system" is the stated object of this volume.

The book is presented in 10 chapters, each written to a very high standard. Ferrari *et al.* present in Chapter 1 an overview of the diseases of the heart with particular emphasis on those due to immunological injury (acute rheumatic fever, myocarditis, pericarditis, vasculitis and acquired immunodeficiency syndrome).

Chapters 2 through to 10 cover, in some depth, methods for evaluating cardiac function (Pugsley and Walker), immunopharmacology of the coronary vascular endothelium (Lefer), the role of macrophages and the modification of LDL in the pathogenesis of atherosclerosis (Darley-Usmar and Hassall), the role of leukocytes in ischaemic heart disease (Entman *et al.*), complement activation in cardiac disease (Rossen), prevention of sudden cardiac death by immunopharmacological intervention (Curtis), inflammatory mediators and the stunned myocardium (Gross), immunotherapy and reperfusion injury in the heart (Yamazaki *et al.*), and immunopharmacology of heart transplantation (Nyulassy *et al.*).

A useful glossary is included, making the book accessible to the "young at hearts". Immunopharmacology of the Heart is a useful contribution which will dovetail nicely with the forthcoming volume "Immunopharmacology of Free Radical Species" in the same series and should be viewed as a valuable addition to the libraries of researchers in this field.

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Vitamin E: Its Usefulness in Health and in Curing Diseases
Edited by Makoto Mino, Haruo Nakamura, Anthony T. Diplock and Herbert J. Kayden
Japan Scientific Societies Press: 1993, ¥13000
ISBN 4-7622-6727-9 xiv + 368 pages

It is difficult to open a biomedical joumal without seeing some mention of the involvement of vitamin E in a physiological process. In his introductory overview,

Professor A.T. Diplock points out that "the elucidation of the biological consequences of uncontrolled proliferation of free radical-initiated or mediated reactions as been a major pre-occupation of research scientists from many different disciplines, and the central role of vitamin E as a free radical scavenger among membrane polyunsaturated fatty acids has led to an upsurge in interest in vitamin E." Vitamin E: Its Usefulness in Health and in Curing Diseases emanates from an international Symposium on Vitamin E organized to commemorate the 70th anniversary of the work of Drs. Evans and Bishop and the 50th anniversary of the founding of Eisai Co, Japan. The book is presented in seven sections. The sections respectively examine (in some detail), chemistry, biochemistry, physiology, deficiency and nutrition, environment, pharmacology and clinical aspects, of vitamin E.

There are many notable chapters contributed by eminent scientists that makes choosing a favourite chapter a redundant exercise. Nevertheless, Miyashita and Nishibata consider nutritional supplements and athletic performance with special reference to vitamin E. During exercise oxygen uptake and utilization are higher than in normal conditions and increased free radical levels have been observed in exercise-exhausted animals. Antioxidant supplementation in sports merits urgent attention. It is against this quest that the reviewer welcomes the present chapter.

Igarashi considers the nutritional requirement and oral safety of vitamin E and comments on three influential factors: requirement of vitamin E as RRR-α-tocopherol in humans, dietary factors such as quantity and quality of dietary oils and fats consumed, and environmental factors such as pollution, smoking and xenobiotics in the diet.

Esterbauer *et al.* present an overview on vitamin E and atherosclerosis, Massay and Burton consider vitamin E and ischemia-reperfusion injury in the heart, and Yoshikana *et al.* consider gastric ulcer and vitamin E.

The editors are commended for their efforts in putting the varied chapters into a coherent text. The inadequacy of the index is my only complaint.

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Nutritional Toxicology
Edited by: F.N. Kotsonis, M. Mackey and J.J. Hjelle
Raven Press: New York. Price $170
ISBN 0-7817-0121-X, 1994, *xii* + 319 pages

Nutritional Toxicology is the latest addition to the Target Organ Toxicology Series. It addresses one of the most important areas of biomedical research and consumer awareness. The book is presented in 14 well-written and presented chapters: the role of nutrients in detoxification mechanisms (Netter); antioxidant nutrients and protection from free radicals (Bonorden and Pariza); impact of aging on detoxification mechanisms (Meydani); the role of fat, calories and fibre in disease (Kritchevsky); ethanol toxicity and nutritional status (Seitz and Suter); allergic reactions and food intolerances (Lemke and Taylor); nutrient-drug interactions (Thomas and Tschanz); food irradiation (Ellas); biotechnology-derived and novel foods: safety approaches and regulations (Younes, Speijers and van der Heijden); estimation of food chemical intake (Rees and Tennant); threshold of regulation: a unifying concept in food safety

assessment (Flamm, Kotsonis and Hjelle); postmarketing surveillance in the food industry: the aspartame case study (Butchko and Kotsonis); health claims regulation: impact on food development (Mackey, Hill and Gund) and mechanistic considerations in the regulation and classification of chemical carcinogens (McClain).

The safety of dietary components and the complex interactions between the diet and the body's response to xenobiotics is of current interest. It is generally accepted that evaluation of the role of free radicals in disease pathology would provide a logical basis for the therapeutic use of antioxidants. Such practice may be visualised given the complexity of the mechanisms of tissue injury, as:

(1) administration of antioxidants that occur naturally (e.g. β-carotene, α-tocopherol and ascorbic acid),
(2) administration of synthetic antioxidants or chelating agents that might suppress iron ion-dependent free radical reaction and
(3) the use of drugs developed to protect against other mechanisms of tissue injury that might have additional physiological action because they have antioxidant properties.

Against this background, it is noteworthy that Bonorden and Pariza suggested caution on the use of non-nutritive dietary antioxidants until they are fully evaluated, a notion that is continually advocated (ref. 1–2). Seitz and Suter argues that "the best strategy to avoid any nutritional deficiencies in heavy drinkers is reduction of excessive ethanol consumption". The chapter on the impact of health claims regulations addresses, in particular, designer foods, functional foods and nutraceuticals and argues that "for manufacturers to have an incentive to pursue the development of the products, there must be a legal mechanism to describe their health benefit in labelling. Food components must retain their food attributes to qualify for a health claim. If otherwise, such components may be viewed as drugs". In developing the new food concepts (NFC), the manufacturer has to consider if the NFC is "(1) a food or food ingredient and not a drug, (2) safe and (3) is effective for the claimed benefit".

In the main, *Nutritional Toxicology* contains a wealth of information and is highly recommended.

References

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