

Book Review

New Developments in the Therapy of Allergic Disorders and Asthma

(International Academy for Biomedical and Drug Research Vol. 6)

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Published 1993 Karger, Basel

VI + 136 pages

ISBN 3 8055 5748 5 SFr.160.00, DM192.00 (FRG),

\$128.00 (USA only)

The context of this book is clearly of current interest; more than 10% of the population will, at some time in their lives, seek help from a doctor in connection with an allergic disorder or asthma. Despite the introduction of potent new drugs such as corticosteroids and adrenergic β_2 -agonists, the morbidity and mortality from asthma has increased. Safe and effective treatment of atopic disease remains a major challenge for pharmaceutical and medical research.

This book describes some of the lines of research which are being explored to define the underlying pathology, and biological properties which subserve safe and effective treatment. It is an account of the proceedings at a workshop, and provides a mainly European view of research. Books of this type are valuable if they provide a synthesis of shortcomings of existing therapies, evaluation of methods for advancing knowledge on the disease, and identify new drugs appearing on the horizon. This is achieved in respect of some classes of drugs but not others. On the one hand, there is only passing mention of compounds such as β_2 -agonists, xanthine derivatives and chromoglycate and its newer derivatives which are the mainstay of present therapy and will provide ideas for some improved drugs. On the other hand, histamine H_1 antagonists, leukotriene antagonists and adhesion molecule modifiers, are dealt with at length.

The first five chapters deal with aspects of the underlying pathology; chapter 1 provides a concise and informative account of the discovery of antihistamines, and the recognition and characterization of different types of histamine receptors.

The first generation of antihistaminics were compounds made as anticholinergics and sympatholytics, and have been a rich source of pharmacologically active compounds. The idea is developed that the newer generation of H_1 antagonists with low CNS penetration may also have anti-allergic activity. Compounds of this type have a clinical role in seasonal asthma but their use in other, more serious types of asthma has still to be established. Caution is expressed that the use of some new H_1 antagonists to stabilize mast cells, or inhibit eosinophil accumulation may result in adverse events at the higher doses being proposed.

The chapters on immunological aspects of asthma describe the immunobiology of T-lymphocytes and the role of lymphokines. Attention is drawn to the distinction between cell-

mediated and IgE-mediated mechanisms, and the light this sheds on the clinical use of corticosteroids and agents such as cyclosporin A. Some of the chapters summarize the role of different types of white cell in aspects of the disease such as bronchial hyper-responsiveness, and the role of adhesion molecules (CD54) expressed on bronchial epithelial cells. Agents which modify the expression of adhesion molecules and the sequelae of leucocyte-derived inflammatory mediators may point to new classes of drugs (and explain the mode of action of some already in use). The mechanisms whereby ethanol induces severe changes in bronchomotor tone are reviewed, and there is a classical, pharmacological analysis of the effect of its metabolic products on receptors and enzymes.

The chapters on clinical aspects of the disease and the choice of antihistamines are uneven in content, and in the main, reflect clinical priorities in Northern Europe. Apart from a reminder of some aspects of clinical management it is difficult to see the justification for inclusion of standard guidelines for the diagnosis of atopic dermatitis. Perhaps a chapter reviewing more widely the gaps in the therapeutic armamentarium as seen from the clinic, would better complement the chapters on new agents and methods of treatment.

The chapters describing the involvement of leukotrienes in the pathological process, and their inhibitors as drugs of the future, are good summaries of the state of the art and illustrate the methods of testing.

Atopic dermatitis is dealt with in the context of aeroallergens and contact dermatitis. A discussion of immune markers such as CD23, whose expression is increased in eczema, is missing. The index does not help here; it does not contain a reference to CD23 or to Langerhan cells whose important role is referred to in this chapter and elsewhere in the book. In the table dealing with therapeutic management, present and newer treatments are listed but not critically discussed. A perspective on the efficacy (and shortcomings) of standard and newer treatments would provide a useful platform in a book dealing with "new development". There is no reference to the successful treatment of steroid-resistant atopic eczema by cyclosporin A and specific phytomedicines. Although their mode of action is not as yet understood, the activity of phytomedicines is on a par with that of immune suppressants and their toxicity considerably less. Products of this type could provide leads for development of new drugs.

The final chapters concerning new targets and current issues deal only with the H_1 antagonists and the characterization and regulation of adhesion molecule expression in the allergic response. A similar depth of treatment on the growing points referred to in other chapters would have been welcome, as would an introductory chapter setting out the scope of the book. Nevertheless, there are excellent chapters in this book and it will be of interest to pharmacologists and others in the pharmaceutical industry.

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