New Developments in Antirheumatic Therapy
New Developments in Antirheumatic Therapy

Edited by

KD Rainsford
Department of Biomedical Sciences
McMaster University Faculty of Health Sciences
Hamilton, Ontario
Canada

GP Velo
Institute of Pharmacology
University of Verona
Italy

KLUWER ACADEMIC PUBLISHERS
DORDRECHT / BOSTON / LONDON
## Contents

Preface vi  
List of Contributors vii  
1 Recent developments in antirheumatic therapy  
   *P Nash and BL Hazleman*  
   1  
2 Osteoarthritis: a metabolic disorder  
   *CW Denko*  
   29  
3 Concepts of mode of action and toxicity of anti-inflammatory drugs. A basis for safer and more selective therapy, and for future drug developments  
   *KD Rainsford*  
   37  
4 Animal models of arthritic disease: influence of novel, compared with classical, antirheumatic agents  
   *IM Hunneyball, MEJ Billingham and KD Rainsford*  
   93  
5 Novel eicosanoid inhibitors  
   *LA Marshall and J Chang*  
   133  
6 New steroidal anti-inflammatory drugs  
   *HJ Lee, AS Heiman and IB Taraporewala*  
   153  
7 Oxyradicals, inflammation and drugs acting on oxyradical production  
   *DV Parke, AM Symons and AL Parke*  
   187  
8 Gold(I) thiolates: slow-acting anti-arthritic drugs  
   *DR Haynes and MW Whitehouse*  
   207  
9 Do platelet activating factor antagonists have a potential role in the therapy of rheumatoid arthritis?  
   *CP Page and AJ Coyle*  
   235  
10 Interleukin 1: past, present, future  
   *MC Powanda and ED Moyer*  
   255  
11 The T cell as a therapeutic target  
   *IG Otterness and ML Bliven*  
   277  
12 Superoxide dismutase modifications for anti-inflammatory therapy  
   *FM Veronese, A Conforti and GP Velo*  
   305  
Index 315
At present we may be at the cross-roads in the therapeutic approaches we have for the treatment of the 100 or more rheumatic conditions. This is because we now recognise that although some advances have been made with the development of a large range of non-steroidal and steroidal drugs during the past two decades or so, we now recognise that many, if not all, of these have rather limited effects on many of the disease processes which underlie the manifestations of the various rheumatic states. Advances in molecular biology in the past 5–10 years have enabled these tools to be applied extensively for developing further our understanding of the rheumatic disease processes. In some cases these molecular tools (e.g., γ-interferon, interleukin-2, T-cell antibodies) have been directly employed as therapies themselves. While the outcome from trials with such agents in rheumatoid arthritis in particular has not been as would have been hoped, these results as with cyclosporin A and low-dose methotrexate in the therapy of rheumatoid arthritis have given us important indications for the approach employing what are generally described as “immunomodulators” to control this disease. But this may not be the same type of approach which is desirable for all types of rheumatic conditions. Indeed, even the way which the present range of drugs and other therapies are applied may not be the most effective and safe means of treating different types of arthritic conditions.

Thus, it was considered that the time is appropriate to review what we understand about the current range of therapies; what basic developments are occurring in the search for the newer, more specific and more effective agents; and what progress has been made in the understanding of the disease processes which can give clues or leads for future therapeutic approaches. While it may be considered that the coverage of some areas may be limited because of the size limitations necessary for such a book, it should be pointed out that further consideration is being given in some newly emerging approaches in the fields of, for example, neuro-inflammation, the broader range of cytokines other than interleukin-1, and the non-articular rheumatic conditions in companion volumes which are currently in preparation.

Special thanks are given to the valued efforts of the contributors, Dr Peter Clarke (Publishing Director, Kluwer Academic Publishers) and Mrs Veronica Rainsford-Koechli for her help in proof-reading the manuscripts.

K D Rainsford
Hamilton, Ontario, Canada
February 1989
List of Contributors

M.E.J. BILLINGHAM
Lilly Research Centre
Eli Lilly and Co.
Windlesham, Surrey GU20 6PH
UK

M.L. BLIVEN
Department of Immunology and Infectious Diseases
Pfizer Central Research
Groton, CT 06340
USA

J. CHANG
Immunopharmacology Subdivision
Wyeth-Ayerst Research Inc.
CN 8000
Princeton, NY 08543-8000
USA

A. CONFORTI
Istituto di Farmacologia
Università di Verona
Policlinico Borgo Roma
37134 Verona
Italy

A.J. COYLE
Department of Pharmacology
King's College
University of London
Chelsea Campus, Manresa Road
London SW3
UK

C.W. DENKO
Departments of Rheumatology and Medicine
Case Western Reserve University
Cleveland, OH 44106
USA

D.R. HAYNES
Department of Pathology
University of Adelaide
GPO Box 498
South Australia 5001
Australia

B.L. HAZLEMAN
Rheumatology Research Unit
Addenbrooke's Hospital
Hills Road
Cambridge CB2 2QQ
UK

A.S. HEIMAN
Center for Anti-inflammatory Research
College of Pharmacy
Florida A&M University
Tallahassee, FL 32307
USA

I.M. HUNNEYBALL
The Boots Company plc
Nottingham NG2 3AA
UK

H.J. LEE
Center for Anti-inflammatory Research
College of Pharmacy
Florida A&M University
Tallahassee, FL 32307
USA

L.A. MARSHALL
Immunopharmacology Subdivision
Wyeth-Ayerst Research Inc.
CN 8000
Princeton, NY 08543-8000
USA

E.D. MOYER
KabiVitrum Inc
1311 Harbor Bay Parkway
Alameda, CA94501
USA