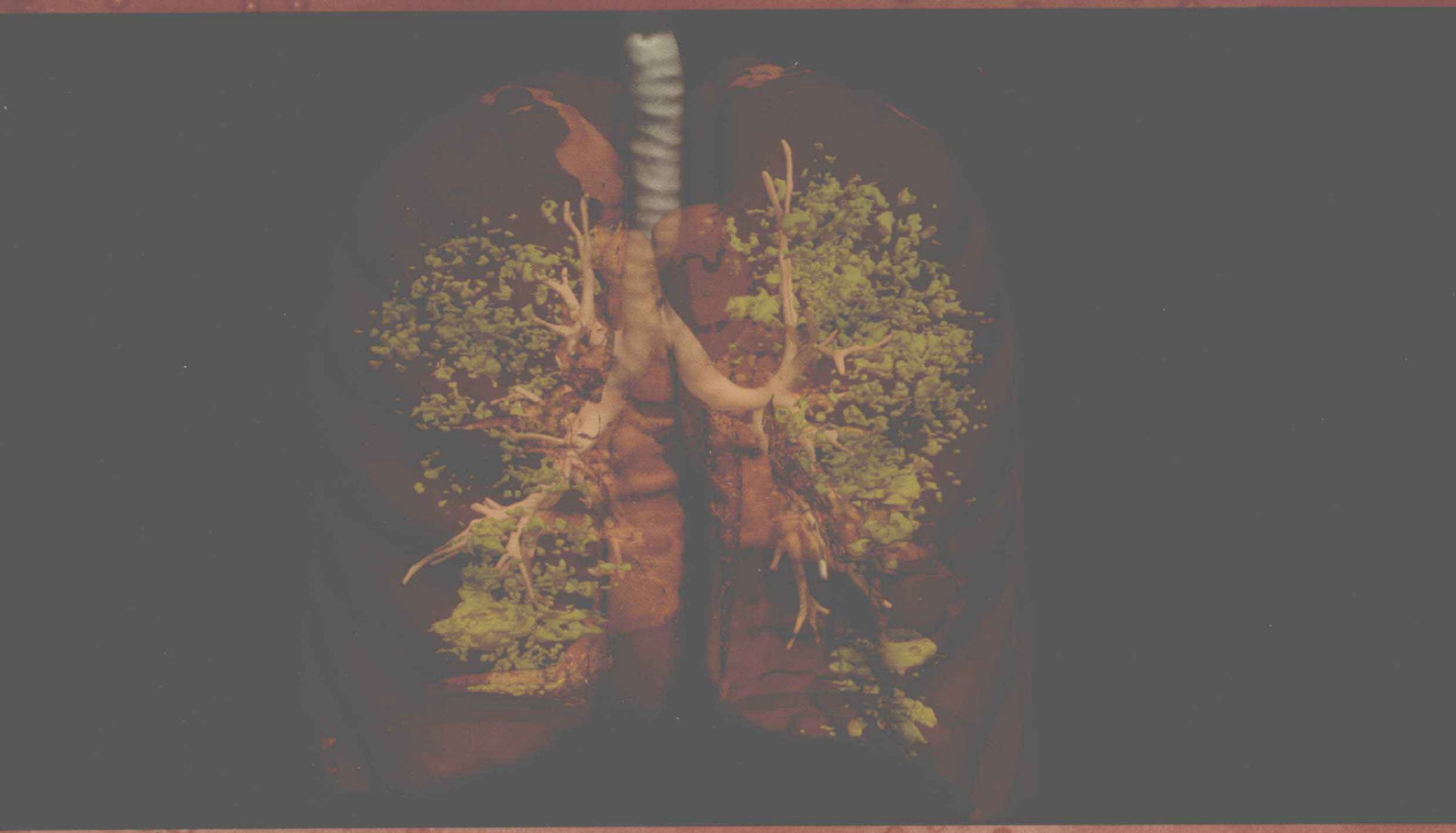
ASTHMA AND COPD

SECOND EDITION



Basic Mechanisms and Clinical Management

Edited by

Peter J. Barnes
Jeffrey M. Drazen
Stephen I. Rennard
Neil C. Thomson

AP

Asthma and COPD

Basic Mechanisms and Clinical Management

Second Edition

ELSEVIER

AMSTERDAM • BOSTON • HEIDELBERG • LONDON
NEW YORK • OXFORD • PARIS • SAN DIEGO
SAN FRANCISCO • SINGAPORE • SYDNEY • TOKYO

Academic Press is an imprint of Elsevier

Academic Press is an imprint of Elsevier

525 B Street, Suite 1900, San Diego, CA 92101-4495, USA
30 Corporate Drive, Suite 400, Burlington, MA 01803, USA
32 Jamestown Road, London, NW1 7BY, UK
Radarweg 29, PO Box 211, 1000 AE Amsterdam, The Netherlands

Second edition 2009

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

Library of Congress Cataloging-in-Publication Data
A catalog record for this book is available from the Library of Congress

ISBN: 978-0-12-374001-4

Printed and bound in USA

09 10 11 12 10 9 8 7 6 5 4 3 2 1

Preface to the 2nd Edition

In the 6 years since the publication of the first edition of *Asthma and COPD* there has been substantial progress in understanding the biological basis of both of these obstructive diseases. In contrast both our understanding of the physiological basis of these conditions and their treatment has improved very little. We firmly believe that the progress made in understanding the basic disease biology that has accrued since 2002 will lead, in the years to come to new and better treatments of these crippling obstructive airway diseases. As our knowledge advances, we now appreciate the areas of overlap and distinction between these two conditions which share many physiological similarities. Most of the chapters of this book highlight both the similarities and differences between these conditions.

In this era of widely available information on the internet it is reasonable to ask what value is served by a book of this type? The answer is simple. The editors have assembled the world's experts on these topics and commissioned them to write succinct reviews focusing on their particular area of expertise. For the student of the biology or treatment of these conditions, this compilation is an important resource of up-to-date information. For the researcher or clinician, the investigative or clinical problems that each of face on a daily basis are clearly illuminated by topic experts. We hope that you will find this summary of value to you in understanding these two highly variegated, closely similar but clearly distinct entities at the biological and clinical level.

Peter J. Barnes
Jeffery M. Drazen
Stephen I. Rennard
Neil C. Thomson

About the Editors

Peter J Barnes, DM, DSc, FRCP, FMedSci, FRS, is a Professor of Thoracic Medicine at the National Heart and Lung Institute, Head of Respiratory Medicine at Imperial College, and Honorary Consultant Physician at Royal Brompton Hospital, London. He qualified at Cambridge and Oxford Universities and was appointed to his present post in 1987. He has published over 1000 peer-review papers on asthma, COPD, and related topics and has edited over 40 books. He is also amongst the top 50 most highly cited researchers in the world and has been the most highly cited clinical scientist in the United Kingdom and the most highly cited respiratory researcher in the world over the last 20 years. He was elected a Fellow of the Royal Society in 2007, the first respiratory researcher for over 150 years. He is currently a Member of the Scientific Committee of the WHO/NIH global guidelines on asthma (GINA) and COPD (GOLD). He also serves on the Editorial Board of over 30 journals and is currently an Associate Editor of Chest and Respiratory Editor of PLoS Medicine. He has given several prestigious lectures, including the Amberson Lecture at the American Thoracic Society and the Sadoul Lecture at the European Respiratory Society.

Neil C Thomson, MD, FRCP, is a Professor of Respiratory Medicine at the University of Glasgow, Head of Respiratory Medicine within the Division of Immunology, Infection & Inflammation, and Honorary Consultant at Gartnavel General Hospital, Glasgow. He graduated from the University of Glasgow and undertook postgraduate training in Glasgow, London and McMaster University, Canada. He is a former Member of the Committee for Safety of Medicine and former Chair of the Scientific Committee of the British Lung Foundation. He has co-edited several textbooks on asthma and COPD and published over 150 peer-reviewed papers on asthma. His current research interests include corticosteroid insensitivity in smokers with asthma, biomarkers in asthma and COPD and assessment of novel treatments for asthma.

Jeffrey M Drazen, MD, was born in St. Louis, Missouri. He graduated from Tufts University with a major in Physics, and from Harvard Medical School. He served his medical internship and residency at Peter Bent Brigham Hospital in Boston and was a Clinical Fellow and Research Fellow at Harvard Medical School and Harvard School of Public Health. Thereafter, he joined the Pulmonary Divisions of the Harvard hospitals and served for many years as Chief of the Combined Pulmonary Divisions at Beth Israel and Brigham and Women's Hospitals.

Currently, he is a Senior Physician at the Brigham and Women's Hospital, and the Distinguished Parker B. Francis Professor of Medicine at Harvard Medical School, as well as Professor of Physiology, Harvard School of Public Health, and adjunct Professor of Medicine at Boston University School of Medicine.

He has served on the NIH Respiratory and Applied Physiology Study Section, the NIH Pulmonary Disease Advisory Council, the NIH Lung Biology and Pathology Study Section, and the NHLBI Advisory Council.

Through his research, he defined the role of novel endogenous chemical agents in asthma. This led to four new licensed pharmaceuticals for asthma used in the treatment of millions of people worldwide. He has published nearly 500 papers and edited 6 books.

He has been a member of the Editorial Boards of many prestigious journals, including the *Journal of Applied Physiology*, *American Journal of Physiology*, *Pulmonary Pharmacology*, *Experimental Lung Research*, *Journal of Clinical Investigation*, *American Journal of Respiratory Cell and Molecular Biology*, and the *American Journal of Medicine*. In addition, he has been an associate editor of the *Journal of Clinical Investigation* and the *American Review of Respiratory Disease*.

In 2000, he assumed the post of Editor-in-Chief of the *New England Journal of Medicine*. During his tenure, the *journal* has published major papers advancing the science of medicine, including the first descriptions of SARS and papers modifying the treatment of cancer, heart disease, and lung disease. The journal, which has more than half a million readers every week, has the highest impact factor of any medical journal publishing original research.

Stephen I Rennard, MD, is Larson Professor of Medicine in the Pulmonary and Critical Care Medicine Section of the Department of Internal Medicine at the University of Nebraska Medical Center in Omaha, Nebraska, and courtesy Professor of the Department of Pathology and Microbiology and the Department of Genetics, Cell Biology and Anatomy. He received an AB with honors in Folklore and Mythology from Harvard University and an MD with honors from the Baylor College of Medicine, Houston, Texas. He completed internal medicine training at Barnes Hospital, Washington University, St. Louis, Missouri and trained in Pulmonary Diseases at the National Institutes of Health where he remained for seven years, conducting research in the cell biology of lung disease.

He joined the University of Nebraska in 1984 as Chief of Pulmonary and Critical Care, a position he retained until 1997. He was the Director of the Nebraska Office of Tobacco Control and Research from 1997 until 2008.

Dr. Rennard currently serves on the Board of Directors of the COPD Foundation and the Alpha-1 Foundation. He is a member of the American Thoracic Society Committee on Corporate Relations and the National Heart Lung Education Program Executive Committee. He is an external advisor to the Thomas Petty Aspen Lung Conference and the University of California-Davis Pulmonary Training Grant.

Dr. Rennard is active in several professional societies and has previously served on the Board of Directors for the American Thoracic Society, the Council of the American Lung Association and was a Governor for the American College of Chest Physicians. He served on the American Board of Internal Medicine, Pulmonary Section and was a member of the expert panel which prepared the global GOLD guidelines for COPD for the WHO/NHLBI. He has served on several task force committees, including the ATS/ERS task force that prepared the ATS/ERS joint COPD Standards.

Professor Rennard maintains an active program of clinical investigation in COPD and smoking cessation and a program of basic research in the mechanisms of lung tissue repair and remodeling, including the role of stem cells in disease pathogenesis and repair.

List of Contributors

Ian M. Adcock (31)
National Heart and Lung Institute, Imperial College School of Medicine, London, UK

Alvar Agusti (44)
Hospital University Son Dureta, Servi Pneumologia, Palma de Majorca, Spain
Fundacion Caubet-CIMERA
CIBER Enfermedades Respiratorias

Jennifer A. Alison (38)
Discipline of Physiotherapy, Faculty of Health Sciences, University of Sydney, Lidcombe, NSW, Australia

Yassine Amrani (18)
Department of Infection, Immunity and Inflammation, University of Leicester, UK

Sandra D. Anderson (38)
Department of Respiratory Medicine, Royal Prince Alfred Hospital, Camperdown, NSW, Australia

Kjetil Ask (29)
Centre for Gene Therapeutics, Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada

Jon Ayres (39)
Department of Environmental and Occupational Medicine, Liberty Safe Work Research Centre, University of Aberdeen, Aberdeen, UK

Joan Albert Barberà (20)
Servei de Pneumologia, Hospital Clinic, IDIBAPS, Universitat de Barcelona, Barcelona, Spain

Peter J. Barnes (32, 33, 34, 40, 49, 50, 51, 52, 61)
National Heart and Lung Institute (NHLI), Clinical Studies Unit, Imperial College, London, UK

Bianca Beghè (41)
Department of Respiratory Diseases, University of Modena and Reggio Emilia, Modena, Italy

Richard C. Boucher (16)
Department of Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Andrew Briggs (62)
Section of Public Health and Health Policy, University of Glasgow, Glasgow, Scotland, UK

Guy G. Brusselle (10)
Department of Pulmonary Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands

A. Sonia Buist (1)
Division of Pulmonary and Critical Care Medicine, Oregon Health Sciences University, Portland, OR, USA

Kimberlie Burns (16)
Department of Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Andrew Bush (65)
Department of Respiratory Pediatrics, Imperial College of Science, Technology and Medicine, Royal Brompton Hospital and National Heart and Lung Institute, London, UK

Carlos A. Camargo Jr. (64)
Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Gaetano Caramori (31)
National Heart and Lung Institute, Imperial College School of Medicine, London, UK

George H. Caughey (9)
Cardiovascular Research Institute and Department of Medicine, University of California at San Francisco, USA

Bartolome R. Celli (54)
Division of Pulmonary and Critical care, Caritas -St. Elizabeth's Medical Center, Tufts University, Boston, MA, USA

Michael A. Chandler (47)
University of Nebraska Medical Center, Omaha, NE, USA

Richard N. Channick (56)
Division of Pulmonary and Critical Care Medicine, University of California, San Diego School of Medicine, La Jolla, CA, USA

Moira Chan-Yeung (36)
Department of Medicine, Respiratory Division, University of British Columbia, Vancouver, BC, Canada

Kian Fan Chung (27, 52)
National Heart and Lung Institute (NHLI), Imperial College, London, UK

Donald W. Cockcroft (35)
Division of Respirology, Critical Care and Sleep Medicine, Department of Medicine, University of Sasketchewan, Royal University Hospital, Saskatoon, Saskatchewan, Canada

Lorenzo Corbetta (41)
Department of Respiratory Diseases, University of Firenze, Firenze, Italy

Christopher J. Corrigan (55)
Department of Asthma, Allergy and Respiratory Science, Guy's Hospital, London, UK

MRC and Asthma UK Centre in Allergic Mechanisms of Asthma King's College London, UK

Manuel G. Cosio (13)
Meakins-Christie Laboratories and the Respiratory Division, Department of Medicine, McGill University, Montreal, Quebec, Canada

Harvey O. Coxson (43)
Department of Radiology, James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, University of British Columbia, Vancouver, BC, Canada

Adnan Custovic (46)
University of Manchester, Manchester, UK

Marc Decramer (58)
Respiratory Rehabilitation and Respiratory Division, University Hospital, Leuven, Belgium

Faculty of Kinesiology and Rehabilitation Sciences, Department of Rehabilitation Sciences, Katholieke Universiteit Leuven, Leuven, Belgium

Dawn L. DeMeo (2)
Channing Laboratory, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Jeffrey M. Drazen (24, 33)
Department of Medicine, Pulmonary Division, Birgham and Women's Hospital, Boston, MA, USA

Harvard Medical School, Editorial Office New England Journal of Medicine, Boston, MA, USA

Leonardo M. Fabbri (41)
Department of Respiratory Diseases, University of Modena and Reggio Emilia, Modena, Italy

Jack Gauldie (29)
Centre for Gene Therapeutics, Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada

Maurice Godfrey (22)
Center for Human Molecular Genetics, Munroe Meyer Institute, University of Nebraska Medical Center, Omaha, NE, USA

Stefano Guerra (3)
Arizona Respiratory Center and Mel and Enid Zuckerman College of Public Health, University of Arizona, Tucson, AZ, USA

Ian P. Hall (48)
Division of Therapeutics and Molecular Medicine, University Hospital of Nottingham, Nottingham, UK

Trevor T. Hansel (49)
National Heart and Lung Institute (NHLI), Clinical Studies Unit, Imperial College, London, UK

James C. Hogg (6)
UBC McDonald Research Laboratories, St. Paul's Hospital, University of British Columbia, Vancouver, BC, Canada

Stephen T. Holgate (7)
School of Medicine, University of Southampton, Southampton, UK

Gabor Horvath (19)
Department of Pulmonology, Semmelweiss University, Budapest, Hungary

Charles G. Irvin (5)
Department of Medicine and Physiology, University of Vermont College of Medicine, Burlington, VT, USA

Kazuhiro Ito (30)
Section of Airway Disease, National Heart and Lung Institute, Imperial College, London, UK

Wim Janssens (58)
Respiratory Rehabilitation and Respiratory Division, University Hospital, Leuven, Belgium

Sebastian L. Johnston (37)
Department of Respiratory Medicine, National Heart and Lung Institute, Imperial College London, London, UK

Susan Kennedy (36)
School of Environmental Health, University of British Columbia, Vancouver, BC, Canada

Sergei A. Kharitonov (30, 42)
Section of Airway Disease, National Heart and Lung Institute, Imperial College, London, UK

Darryl A. Knight (15)
Department of Pharmacology and Therapeutics, University of British Columbia, Vancouver, BC, Canada

Martin Kolb (29)
Centre for Gene Therapeutics, Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada

Onn Min Kon (49)
National Heart and Lung Institute (NHLI), Clinical Studies Unit, Imperial College, London, UK

Samuel L. Krachman (57)
Section of Pulmonary and Critical Care Medicine, Temple University School of Medicine, Philadelphia, PA, USA

Vera P. Krymskaya (18)
Pulmonary, Allergy and Critical Care Division, Airways Biology Initiative, University of Pennsylvania, Philadelphia, PA, USA

Bart N. Lambrecht (10)
Department of Respiratory Medicine, University Hospital Ghent, Belgium

Department of Pulmonary Medicine, Erasmus University, Rotterdam, The Netherlands

Geoffrey J. Laurent (15)
UCLMS, Center for Respiratory Research, University St/Rayne Institute, London, UK

Bruce D. Levy (24)
Department of Medicine, Pulmonary Division, Brigham and Women's Hospital, Boston, MA, USA

Fabrizio Luppi (41)
Department of Respiratory Diseases, University of Modena and Reggio Emilia, Modena, Italy

Jean-Luc Malo (36)
Department of Chest Medicine, Sacré-Coeur Hospital, Montreal, Canada

James G. Martin (13)
Meakins-Christie Laboratories and the Respiratory Division, Department of Medicine, McGill University, Montreal, Quebec, Canada

Fernando D. Martinez (3)
Arizona Respiratory Center and Mel and Enid Zuckerman College of Public Health, University of Arizona, Tucson, AZ, USA

Simon D. Message (37)
Department of Respiratory Medicine, National Heart and Lung Institute, Imperial College London, London, UK

Lynne A. Murray (15)
Manager of Pharmocology Promedior, Inc.
Malvern, PA, USA

Paul M. O'Byrne (23)
Firestone Institute for Respiratory Health, St. Joseph's Healthcare and Department of Medicine, McMaster University, Hamilton, ON, Canada

Reynold A. Panettieri Jr. (18)
Pulmonary, Allergy and Critical Care Division, Airways Biology Initiative, University of Pennsylvania, Philadelphia, PA, USA

Martyn R. Partridge (68)
The Faculty of Medicine, Imperial College, London, UK

Rodolfo M. Pascual (63)
Section on Pulmonary, Critical Care, Allergy and Immunologic Diseases, Department of Internal Medicine, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC, USA

Ian D. Pavord (42)
Department of Respiratory Medicine and Thoracic Surgery, Institute for Lung Health, Glenfield Hospital, Leicester, UK

James E. Pease (26)
Leukocyte Biology Section, National Heart and Lung Institute, Imperial College London, London, UK

Stephen P. Peters (63)
Section on Pulmonary, Critical Care, Allergy and Immunologic Diseases, Department of Internal Medicine, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC, USA

Michael I. Polkey (59)
Royal Brompton Hospital and National Heart and Lung Institute, London, UK

Dirkje S. Postma (4)
Department of Pulmonology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Irfan Rahman (25)
Department of Environmental Medicine, Lung Biology and Disease Program, University of Rochester Medical Center, Rochester, NY, USA

Scott H. Randell (16)
Departments of Cell and Molecular Physiology and Medicine, The University of North Carolina at Chapel Hill, NC, USA

Stephen I. Rennard (34, 47, 66)
Pulmonary and Critical Care Medicine, University of Nebraska Medical Center, Omaha, NE, USA

Roberto Rodríguez-Roisin (20)
Servei de Pneumologia, Hospital Clinic, IDIBAPS, Universitat de Barcelona, Barcelona, Spain

Duncan F. Rogers (17)
Section of Airway Disease, National Heart and Lung Institute, Imperial College, London, UK

Brian H. Rowe (64)
Department of Emergency Medicine, University of Alberta, and Capital Health, Edmonton, AB, Canada

Lewis J. Rubin (56)
Division of Pulmonary and Critical Care Medicine, University of California, San Diego School of Medicine, La Jolla, CA, USA

Elizabeth Sapey (14)
Department of Medicine, Birmingham University, Birmingham, UK

Sanjay Sethi (53)
Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, University of Buffalo, State University of New York, and Veterans Affairs Western New York Health Care System, Buffalo, New York, USA

Pallav L. Shah (59)
Royal Brompton Hospital and National Heart and Lung Institute, London, UK

Steven D. Shapiro (8, 28)
Department of Medicine, University of Pittsburgh, Pittsburgh, PA, USA

Dean Sheppard (21)
Department of Medicine and Lung Biology Center, University of California, San Francisco, CA, USA

Stephanie A. Shore (8)
Molecular and Integrative Physiological Sciences Program, Harvard School of Public Health, Boston, MA, USA

Edwin K. Silverman (4)
Channing Laboratory and Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Dagmar Simon (12)
Department of Dermatology, Inselspital, University of Bern, Bern, Switzerland

Hans-Uwe Simon (12)
Department of Pharmacology, University of Bern, Bern, Switzerland

Michael W. Sims (18)
Pulmonary, Allergy and Critical Care Division, Airways Biology Initiative, University of Pennsylvania, Philadelphia, PA, USA

Don D. Sin (45)
The James Hogg iCAPTURE Center for Cardiovascular and Pulmonary Research, St. Paul's Hospital, Vancouver, BC, Canada

Helen Starkie (62)
Section of Public Health and Health Policy, University of Glasgow, Glasgow, Scotland, UK

Robert A. Stockley (14)
Lung Investigation Unit, University Hospital Birmingham, NHS Foundation Trust, Edgbaston, Birmingham, UK

Andrew J. Tan (49)
National Heart and Lung Institute (NHLI), Clinical Studies Unit, Imperial College, London, UK

Neil C. Thomson (32, 40, 60)
Department of Respiratory Medicine, Division of Immunology, Infection and Inflammation, University of Glasgow, Glasgow, UK,

Omar Tliba (18)
Pulmonary, Allergy and Critical Care Division, Airways Biology Initiative, University of Pennsylvania, Philadelphia, PA, USA

Martin J. Tobin (57)
Loyola University of Chicago, Stritch School of Medicine and Hines Veterans Administration Hospital, Maywood, IL, USA

Galen B. Toews (11)
Division of Pulmonary and Critical Care Medicine, University of Michigan Health System, Ann Arbor, MI, USA

Thierry Troosters (58)
Respiratory Rehabilitation and Respiratory Division, University Hospital, Leuven, Belgium

Faculty of Kinesiology and Rehabilitation Sciences, Department of Rehabilitation Sciences, Katholieke Universiteit Leuven, Leuven, Belgium

Adam Wanner (19)
Division of Pulmonary and Critical Care Medicine, University of Miami Miller School of Medicine, Miami, FL, USA

Jadwiga A. Wedzicha (67)
Department of Respiratory Medicine, University College of London, London, UK

Scott T. Weiss (2)
Channing Laboratory, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Timothy J. Williams (26)
Leukocyte Biology Section, National Heart and Lung Institute, Imperial College London, London, UK

Ashley Woodcock (46)
University of Manchester, Manchester, UK

Olivia Wu (62)
Section of Public Health and Health Policy, University of Glasgow, Glasgow, Scotland, UK

Zhou Xing (29)
Centre for Gene Therapeutics, Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada

Contents

PART VIII: THERAPIES FOR ASTHMA AND COPD

PART IX: CLINICAL MANAGEMENT OF ASTHMA AND COPD

PART 1

Definitions, Epidemiology, and Genetics of Asthma and COPD

1 CHAPTER

Definitions

A. Sonia Buist

Division of Pulmonary and Critical Care Medicine, Oregon Health and Sciences University, Portland, OR, USA

Definitions of diseases evolve over time as our understanding of them changes. For example, until recently, the presence or absence of *reversibility* was considered to be the key distinction between asthma and chronic obstructive pulmonary disease (COPD) – with reversible airflow obstruction the hallmark of asthma, and irreversible airflow obstruction the hallmark of COPD. Better understanding of both diseases has brought new definitions that acknowledge the overlap and highlight the similarities and differences between them. The important change in our understanding is the recognition that chronic inflammation underlies both diseases. The nature of the inflammation differs, however, as does the response to anti-inflammatory medications, as described in detail in later chapters. This chapter draws heavily on the latest information on asthma and COPD that is included in the guidelines on the diagnosis and management of these diseases from two widely respected global initiatives, the Global Initiative for Asthma (GINA) [1] and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [2], as updated in 2006.

DEFINITIONS

Asthma

Most of the definitions for asthma have emphasized the characteristics of fluctuations over time in bronchoconstriction and the reversible nature of the disease [1, 3]. As the pathophysiological basis of asthma became clearer, definitions began to include a statement about the pathological characteristics. The 2006 revision of the GINA Guidelines [1] proposes an operational description of asthma as:

> *a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.*

This is very similar to the definition proposed by the National Asthma Education and Prevention Program in their 1997 guidelines [3]. Both definitions imply that asthma is one disorder, rather than multiple complex disorders and syndromes – a notion that is receiving increasing attention [4, 5].

COPD

Until quite recently, definitions of COPD used to include the terms "chronic bronchitis" and "emphysema". The GOLD Guidelines, first published in 2002 [6], and revised in 2006 [2], the American Thoracic Society/European Respiratory Society (ATS–ERS) Guidelines published in 2004 [7], and the NICE Guidelines [8, 9] published in 2004 deliberately omitted these terms and used just the umbrella term COPD. The main reason for this is that the use of many different terms for COPD has led to confusion on the part of health-care providers and the public. This in turn has stood in the way of COPD becoming widely recognized.