**Executive Editor: Claude Lenfant** 

# Clinical Management of Chronic Obstructive Pulmonary Disease

Second Edition





edited by

Stephen I. Rennard Roberto Rodríguez-Roisin Gérard Huchon Nicolas Roche

> informa healthcare

# Clinical Management of Chronic Obstructive Pulmonary Disease

# **Second Edition**

# Edited by

# Stephen I. Rennard

University of Nebraska Medical Center Omaha, Nebraska, USA

# Roberto Rodríguez-Roisin

Hospital Clínic, Servei de Pneumologia Universitat de Barcelona Barcelona, Spain

# Gérard Huchon

Université Paris Descartes Hôpital de l'Hôtel-Dieu, Paris, France

# Nicolas Roche

Université Paris Descartes Hôpital de l'Hôtel-Dieu, Paris, France

# informa

healthcare

Informa Healthcare USA, Inc. 52 Vanderbilt Avenue New York, NY 10017

© 2008 by Informa Healthcare USA, Inc. Informa Healthcare is an Informa business

No claim to original U.S. Government works Printed in the United States of America on acid-free paper 10 9 8 7 6 5 4 3 2 1

International Standard Book Number-10: 0-8493-7587-8 (Hardcover)
International Standard Book Number-13: 978-0-8493-7587-3 (Hardcover)

This book contains information obtained from authentic and highly regarded sources. Reprinted material is quoted with permission, and sources are indicated. A wide variety of references are listed. Reasonable efforts have been made to publish reliable data and information, but the author and the publisher cannot assume responsibility for the validity of all materials or for the consequence of their use.

No part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, microfilming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, please access www.copyright.com (http://www.copyright.com/) or contact the Copyright Clearance Center, Inc. (CCC) 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. CCC is a not-for-profit organization that provides licenses and registration for a variety of users. For organizations that have been granted a photocopy license by the CCC, a separate system of payment has been arranged.

**Trademark Notice:** Product or corporate names may be trademarks or registered trademarks, and are used only for identification and explanation without intent to infringe.

## Library of Congress Cataloging-in-Publication Data

Clinical management of chronic obstructive pulmonary disease / edited by Stephen I. Rennard, Roberto Rodríguez-Roisin, Gérard Huchon, Nicolas Roche-2nd ed. p.; cm. - (Lung biology in health and disease; 222)

Rev. ed. of: Clinical management of chronic obstructive pulmonary disease. c2002. Includes bibliographical references and index.

ISBN-13: 978-0-8493-7587-3 (hardcover : alk. paper)

ISBN-10: 0-8493-7587-8 (hardcover: alk. paper) 1. Lungs—Diseases, Obstructive. I. Rennard, Stephen I., 1954-. II. Rodríguez-Roisin, Roberto. III. Huchon, Gérard. IV. Roche, Nicolas. V. Clinical management of chronic obstructive pulmonary disease. VI. Series.

[DNLM: 1. Pulmonary Disease, Chronic Obstructive-diagnosis. 2. Pulmonary Disease, Chronic Obstructive-therapy. 3. Respiratory Muscles-physiology. W1 LU62 v.222 2007 /

WF 600 C6413 2007]

RC776.O3C525 2007

616.2'4-dc22

2007026210

Visit the Informa Web site at www.informa.com

and the Informa Healthcare Web site at www.informahealthcare.com

# Clinical Management of Chronic Obstructive Pulmonary Disease

## LUNG BIOLOGY IN HEALTH AND DISEASE

### Executive Editor

### Claude Lenfant

Former Director, National Heart, Lung, and Blood Institute
National Institutes of Health
Bethesda, Maryland

- 1. Immunologic and Infectious Reactions in the Lung, edited by C. H. Kirkpatrick and H. Y. Reynolds
- 2. The Biochemical Basis of Pulmonary Function, edited by R. G. Crystal
- 3. Bioengineering Aspects of the Lung, edited by J. B. West
- 4. Metabolic Functions of the Lung, edited by Y. S. Bakhle and J. R. Vane
- 5. Respiratory Defense Mechanisms (in two parts), edited by J. D. Brain, D. F. Proctor, and L. M. Reid
- 6. Development of the Lung, edited by W. A. Hodson
- 7. Lung Water and Solute Exchange, edited by N. C. Staub
- 8. Extrapulmonary Manifestations of Respiratory Disease, edited by E. D. Robin
- 9. Chronic Obstructive Pulmonary Disease, edited by T. L. Petty
- Pathogenesis and Therapy of Lung Cancer, edited by C. C. Harris
- Genetic Determinants of Pulmonary Disease, edited by S. D. Litwin
- 12. The Lung in the Transition Between Health and Disease, edited by P. T. Macklem and S. Permutt
- Evolution of Respiratory Processes: A Comparative Approach, edited by S. C. Wood and C. Lenfant
- 14. Pulmonary Vascular Diseases, edited by K. M. Moser
- Physiology and Pharmacology of the Airways, edited by J. A. Nadel
- Diagnostic Techniques in Pulmonary Disease (in two parts), edited by M. A. Sackner
- 17. Regulation of Breathing (in two parts), edited by T. F. Hornbein
- 18. Occupational Lung Diseases: Research Approaches and Methods, edited by H. Weill and M. Turner-Warwick
- 19. Immunopharmacology of the Lung, edited by H. H. Newball
- 20. Sarcoidosis and Other Granulomatous Diseases of the Lung, edited by B. L. Fanburg

- 21. Sleep and Breathing, edited by N. A. Saunders and C. E. Sullivan
- 22. Pneumocystis carinii Pneumonia: Pathogenesis, Diagnosis, and Treatment, edited by L. S. Young
- 23. Pulmonary Nuclear Medicine: Techniques in Diagnosis of Lung Disease, edited by H. L. Atkins
- 24. Acute Respiratory Failure, edited by W. M. Zapol and K. J. Falke
- 25. Gas Mixing and Distribution in the Lung, edited by L. A. Engel and M. Paiva
- 26. High-Frequency Ventilation in Intensive Care and During Surgery, edited by G. Carlon and W. S. Howland
- 27. Pulmonary Development: Transition from Intrauterine to Extrauterine Life, edited by G. H. Nelson
- 28. Chronic Obstructive Pulmonary Disease: Second Edition, edited by T. L. Petty
- 29. The Thorax (in two parts), edited by C. Roussos and P. T. Macklem
- 30. The Pleura in Health and Disease, edited by J. Chrétien, J. Bignon, and A. Hirsch
- 31. Drug Therapy for Asthma: Research and Clinical Practice, edited by J. W. Jenne and S. Murphy
- 32. Pulmonary Endothelium in Health and Disease, edited by U. S. Ryan
- 33. The Airways: Neural Control in Health and Disease, edited by M. A. Kaliner and P. J. Barnes
- 34. Pathophysiology and Treatment of Inhalation Injuries, edited by J. Loke
- 35. Respiratory Function of the Upper Airway, edited by O. P. Mathew and G. Sant'Ambrogio
- 36. Chronic Obstructive Pulmonary Disease: A Behavioral Perspective, edited by A. J. McSweenv and I. Grant
- 37. Biology of Lung Cancer: Diagnosis and Treatment, edited by S. T. Rosen, J. L. Mulshine, F. Cuttitta, and P. G. Abrams
- 38. Pulmonary Vascular Physiology and Pathophysiology, edited by E. K. Weir and J. T. Reeves
- 39. Comparative Pulmonary Physiology: Current Concepts, edited by S. C. Wood
- 40. Respiratory Physiology: An Analytical Approach, edited by H. K. Chang and M. Paiva
- 41. Lung Cell Biology, edited by D. Massaro
- 42. Heart-Lung Interactions in Health and Disease, edited by S. M. Scharf and S. S. Cassidy
- 43. Clinical Epidemiology of Chronic Obstructive Pulmonary Disease, edited by M. J. Hensley and N. A. Saunders
- 44. Surgical Pathology of Lung Neoplasms, edited by A. M. Marchevsky
- 45. The Lung in Rheumatic Diseases, edited by G. W. Cannon and G. A. Zimmerman

- 46. Diagnostic Imaging of the Lung, edited by C. E. Putman
- 47. Models of Lung Disease: Microscopy and Structural Methods, edited by J. Gil
- 48. Electron Microscopy of the Lung, edited by D. E. Schraufnagel
- 49. Asthma: Its Pathology and Treatment, edited by M. A. Kaliner, P. J. Barnes, and C. G. A. Persson
- 50. Acute Respiratory Failure: Second Edition, edited by W. M. Zapol and F. Lemaire
- 51. Lung Disease in the Tropics, edited by O. P. Sharma
- 52. Exercise: Pulmonary Physiology and Pathophysiology, edited by B. J. Whipp and K. Wasserman
- 53. Developmental Neurobiology of Breathing, edited by G. G. Haddad and J. P. Farber
- 54. Mediators of Pulmonary Inflammation, edited by M. A. Bray and W. H. Anderson
- 55. The Airway Epithelium, edited by S. G. Farmer and D. Hay
- 56. Physiological Adaptations in Vertebrates: Respiration, Circulation, and Metabolism, edited by S. C. Wood, R. E. Weber, A. R. Hargens, and R. W. Millard
- 57. The Bronchial Circulation, edited by J. Butler
- 58. Lung Cancer Differentiation: Implications for Diagnosis and Treatment, edited by S. D. Bernal and P. J. Hesketh
- 59. Pulmonary Complications of Systemic Disease, edited by J. F. Murray
- 60. Lung Vascular Injury: Molecular and Cellular Response, edited by A. Johnson and T. J. Ferro
- 61. Cytokines of the Lung, edited by J. Kelley
- 62. The Mast Cell in Health and Disease, edited by M. A. Kaliner and D. D. Metcalfe
- 63. Pulmonary Disease in the Elderly Patient, edited by D. A. Mahler
- 64. Cystic Fibrosis, edited by P. B. Davis
- Signal Transduction in Lung Cells, edited by J. S. Brody,
   D. M. Center, and V. A. Tkachuk
- 66. Tuberculosis: A Comprehensive International Approach, edited by L. B. Reichman and E. S. Hershfield
- 67. Pharmacology of the Respiratory Tract: Experimental and Clinical Research, edited by K. F. Chung and P. J. Barnes
- 68. Prevention of Respiratory Diseases, edited by A. Hirsch, M. Goldberg, J.-P. Martin, and R. Masse
- 69. Pneumocystis carinii Pneumonia: Second Edition, edited by P. D. Walzer
- 70. Fluid and Solute Transport in the Airspaces of the Lungs, edited by R. M. Effros and H. K. Chang
- 71. Sleep and Breathing: Second Edition, edited by N. A. Saunders and C. E. Sullivan
- 72. Airway Secretion: Physiological Bases for the Control of Mucous Hypersecretion, edited by T. Takishima and S. Shimura

- 73. Sarcoidosis and Other Granulomatous Disorders, edited by D. G. James
- 74. Epidemiology of Lung Cancer, edited by J. M. Samet
- 75. Pulmonary Embolism, edited by M. Morpurgo
- 76. Sports and Exercise Medicine, edited by S. C. Wood and R. C. Roach
- 77. Endotoxin and the Lungs, edited by K. L. Brigham
- 78. The Mesothelial Cell and Mesothelioma, edited by M.-C. Jaurand and J. Bignon
- 79. Regulation of Breathing: Second Edition, edited by J. A. Dempsey and A. I. Pack
- 80. Pulmonary Fibrosis, edited by S. Hin. Phan and R. S. Thrall
- 81. Long-Term Oxygen Therapy: Scientific Basis and Clinical Application, edited by W. J. O'Donohue, Jr.
- 82. Ventral Brainstem Mechanisms and Control of Respiration and Blood Pressure, edited by C. O. Trouth, R. M. Millis, H. F. Kiwull-Schöne, and M. E. Schläfke
- 83. A History of Breathing Physiology, edited by D. F. Proctor
- 84. Surfactant Therapy for Lung Disease, edited by B. Robertson and H. W. Taeusch
- 85. The Thorax: Second Edition, Revised and Expanded (in three parts), edited by C. Roussos
- 86. Severe Asthma: Pathogenesis and Clinical Management, edited by S. J. Szefler and D. Y. M. Leung
- 87. Mycobacterium avium—Complex Infection: Progress in Research and Treatment, edited by J. A. Korvick and C. A. Benson
- 88. Alpha 1-Antitrypsin Deficiency: Biology Pathogenesis Clinical Manifestations Therapy, edited by R. G. Crystal
- 89. Adhesion Molecules and the Lung, edited by P. A. Ward and J. C. Fantone
- 90. Respiratory Sensation, edited by L. Adams and A. Guz
- 91. Pulmonary Rehabilitation, edited by A. P. Fishman
- 92. Acute Respiratory Failure in Chronic Obstructive Pulmonary Disease, edited by J.-P. Derenne, W. A. Whitelaw, and T. Similowski
- 93. Environmental Impact on the Airways: From Injury to Repair, edited by J. Chrétien and D. Dusser
- 94. Inhalation Aerosols: Physical and Biological Basis for Therapy, edited by A. J. Hickey
- 95. Tissue Oxygen Deprivation: From Molecular to Integrated Function, edited by G. G. Haddad and G. Lister
- 96. The Genetics of Asthma, edited by S. B. Liggett and D. A. Meyers
- 97. Inhaled Glucocorticoids in Asthma: Mechanisms and Clinical Actions, edited by R. P. Schleimer, W. W. Busse, and P. M. O'Byrne
- 98. Nitric Oxide and the Lung, edited by W. M. Zapol and K. D. Bloch

- 99. Primary Pulmonary Hypertension, edited by L. J. Rubin and S. Rich
- 100. Lung Growth and Development, edited by J. A. McDonald
- 101. Parasitic Lung Diseases, edited by A. A. F. Mahmoud
- 102. Lung Macrophages and Dendritic Cells in Health and Disease, edited by M. F. Lipscomb and S. W. Russell
- 103. Pulmonary and Cardiac Imaging, edited by C. Chiles and C. E. Putman
- 104. Gene Therapy for Diseases of the Lung, edited by K. L. Brigham
- 105. Oxygen, Gene Expression, and Cellular Function, edited by L. Biadasz Clerch and D. J. Massaro
- 106. Beta<sub>2</sub>-Agonists in Asthma Treatment, edited by R. Pauwels and P. M. O'Byrne
- 107. Inhalation Delivery of Therapeutic Peptides and Proteins, edited by A. L. Adjei and P. K. Gupta
- 108. Asthma in the Elderly, edited by R. A. Barbee and J. W. Bloom
- 109. Treatment of the Hospitalized Cystic Fibrosis Patient, edited by D. M. Orenstein and R. C. Stern
- 110. Asthma and Immunological Diseases in Pregnancy and Early Infancy, edited by M. Schatz, R. S. Zeiger, and H. N. Claman
- 111. Dyspnea, edited by D. A. Mahler
- 112. Proinflammatory and Antiinflammatory Peptides, edited by S. I. Said
- 113. Self-Management of Asthma, edited by H. Kotses and A. Harver
- 114. Eicosanoids, Aspirin, and Asthma, edited by A. Szczeklik, R. J. Gryglewski, and J. R. Vane
- 115. Fatal Asthma, edited by A. L. Sheffer
- 116. Pulmonary Edema, edited by M. A. Matthay and D. H. Ingbar
- 117. Inflammatory Mechanisms in Asthma, edited by S. T. Holgate and W. W. Busse
- 118. Physiological Basis of Ventilatory Support, edited by J. J. Marini and A. S. Slutsky
- 119. Human Immunodeficiency Virus and the Lung, edited by M. J. Rosen and J. M. Beck
- 120. Five-Lipoxygenase Products in Asthma, edited by J. M. Drazen, S.-E. Dahlén, and T. H. Lee
- 121. Complexity in Structure and Function of the Lung, edited by M. P. Hlastala and H. T. Robertson
- 122. Biology of Lung Cancer, edited by M. A. Kane and P. A. Bunn, Jr.
- 123. Rhinitis: Mechanisms and Management, edited by R. M. Naclerio, S. R. Durham, and N. Mygind
- 124. Lung Tumors: Fundamental Biology and Clinical Management, edited by C. Brambilla and E. Brambilla
- 125. Interleukin-5: From Molecule to Drug Target for Asthma, edited by C. J. Sanderson
- 126. Pediatric Asthma, edited by S. Murphy and H. W. Kelly

- 127. Viral Infections of the Respiratory Tract, edited by R. Dolin and P. F. Wright
- 128. Air Pollutants and the Respiratory Tract, edited by D. L. Swift and W. M. Foster
- 129. Gastroesophageal Reflux Disease and Airway Disease, edited by M. R. Stein
- 130. Exercise-Induced Asthma, edited by E. R. McFadden, Jr.
- 131. LAM and Other Diseases Characterized by Smooth Muscle Proliferation, edited by J. Moss
- 132. The Lung at Depth, edited by C. E. G. Lundgren and J. N. Miller
- 133. Regulation of Sleep and Circadian Rhythms, edited by F. W. Turek and P. C. Zee
- 134. Anticholinergic Agents in the Upper and Lower Airways, edited by S. L. Spector
- 135. Control of Breathing in Health and Disease, edited by M. D. Altose and Y. Kawakami
- 136. Immunotherapy in Asthma, edited by J. Bousquet and H. Yssel
- 137. Chronic Lung Disease in Early Infancy, edited by R. D. Bland and J. J. Coalson
- 138. Asthma's Impact on Society: The Social and Economic Burden, edited by K. B. Weiss, A. S. Buist, and S. D. Sullivan
- 139. New and Exploratory Therapeutic Agents for Asthma, edited by M. Yeadon and Z. Diamant
- 140. Multimodality Treatment of Lung Cancer, edited by A. T. Skarin
- 141. Cytokines in Pulmonary Disease: Infection and Inflammation, edited by S. Nelson and T. R. Martin
- 142. Diagnostic Pulmonary Pathology, edited by P. T. Cagle
- 143. Particle-Lung Interactions, edited by P. Gehr and J. Heyder
- 144. Tuberculosis: A Comprehensive International Approach, Second Edition, Revised and Expanded, edited by L. B. Reichman and E. S. Hershfield
- 145. Combination Therapy for Asthma and Chronic Obstructive Pulmonary Disease, edited by R. J. Martin and M. Kraft
- 146. Sleep Apnea: Implications in Cardiovascular and Cerebrovascular Disease, edited by T. D. Bradley and J. S. Floras
- 147. Sleep and Breathing in Children: A Developmental Approach, edited by G. M. Loughlin, J. L. Carroll, and C. L. Marcus
- 148. Pulmonary and Peripheral Gas Exchange in Health and Disease, edited by J. Roca, R. Rodriguez-Roisin, and P. D. Wagner
- 149. Lung Surfactants: Basic Science and Clinical Applications, R. H. Notter
- 150. Nosocomial Pneumonia, edited by W. R. Jarvis
- 151. Fetal Origins of Cardiovascular and Lung Disease, edited by David J. P. Barker

- 152. Long-Term Mechanical Ventilation, edited by N. S. Hill
- 153. Environmental Asthma, edited by R. K. Bush
- 154. Asthma and Respiratory Infections, edited by D. P. Skoner
- 155. Airway Remodeling, edited by P. H. Howarth, J. W. Wilson, J. Bousquet, S. Rak, and R. A. Pauwels
- 156. Genetic Models in Cardiorespiratory Biology, edited by G. G. Haddad and T. Xu
- 157. Respiratory-Circulatory Interactions in Health and Disease, edited by S. M. Scharf, M. R. Pinsky, and S. Magder
- 158. Ventilator Management Strategies for Critical Care, edited by N. S. Hill and M. M. Levy
- 159. Severe Asthma: Pathogenesis and Clinical Management, Second Edition, Revised and Expanded, edited by S. J. Szefler and D. Y. M. Leung
- 160. Gravity and the Lung: Lessons from Microgravity, edited by G. K. Prisk, M. Paiva, and J. B. West
- 161. High Altitude: An Exploration of Human Adaptation, *edited by T. F. Hornbein and R. B. Schoene*
- 162. Drug Delivery to the Lung, edited by H. Bisgaard, C. O'Callaghan, and G. C. Smaldone
- 163. Inhaled Steroids in Asthma: Optimizing Effects in the Airways, edited by R. P. Schleimer, P. M. O'Byrne, S. J. Szefler, and R. Brattsand
- 164. IgE and Anti-IgE Therapy in Asthma and Allergic Disease, edited by R. B. Fick, Jr., and P. M. Jardieu
- 165. Clinical Management of Chronic Obstructive Pulmonary Disease, edited by T. Similowski, W. A. Whitelaw, and J.-P. Derenne
- 166. Sleep Apnea: Pathogenesis, Diagnosis, and Treatment, edited by A. I. Pack
- 167. Biotherapeutic Approaches to Asthma, edited by J. Agosti and A. L. Sheffer
- 168. Proteoglycans in Lung Disease, edited by H. G. Garg, P. J. Roughley, and C. A. Hales
- 169. Gene Therapy in Lung Disease, edited by S. M. Albelda
- 170. Disease Markers in Exhaled Breath, edited by N. Marczin, S. A. Kharitonov, M. H. Yacoub, and P. J. Barnes
- 171. Sleep-Related Breathing Disorders: Experimental Models and Therapeutic Potential, edited by D. W. Carley and M. Radulovacki
- 172. Chemokines in the Lung, edited by R. M. Strieter, S. L. Kunkel, and T. J. Standiford
- 173. Respiratory Control and Disorders in the Newborn, edited by O. P. Mathew
- 174. The Immunological Basis of Asthma, edited by B. N. Lambrecht, H. C. Hoogsteden, and Z. Diamant
- 175. Oxygen Sensing: Responses and Adaptation to Hypoxia, edited by S. Lahiri, G. L. Semenza, and N. R. Prabhakar

- 176. Non-Neoplastic Advanced Lung Disease, edited by J. R. Maurer
- 177. Therapeutic Targets in Airway Inflammation, edited by N. T. Eissa and D. P. Huston
- 178. Respiratory Infections in Allergy and Asthma, edited by S. L. Johnston and N. G. Papadopoulos
- 179. Acute Respiratory Distress Syndrome, edited by M. A. Matthay
- 180. Venous Thromboembolism, edited by J. E. Dalen
- 181. Upper and Lower Respiratory Disease, edited by J. Corren, A. Togias, and J. Bousquet
- 182. Pharmacotherapy in Chronic Obstructive Pulmonary Disease, edited by B. R. Celli
- 183. Acute Exacerbations of Chronic Obstructive Pulmonary Disease, edited by N. M. Siafakas, N. R. Anthonisen, and D. Georgopoulos
- 184. Lung Volume Reduction Surgery for Emphysema, edited by H. E. Fessler, J. J. Reilly, Jr., and D. J. Sugarbaker
- 185. Idiopathic Pulmonary Fibrosis, edited by J. P. Lynch III
- 186. Pleural Disease, edited by D. Bouros
- 187. Oxygen/Nitrogen Radicals: Lung Injury and Disease, edited by V. Vallyathan, V. Castranova, and X. Shi
- 188. Therapy for Mucus-Clearance Disorders, edited by B. K. Rubin and C. P. van der Schans
- 189. Interventional Pulmonary Medicine, edited by J. F. Beamis, Jr., P. N. Mathur, and A. C. Mehta
- 190. Lung Development and Regeneration, edited by D. J. Massaro, G. Massaro, and P. Chambon
- 191. Long-Term Intervention in Chronic Obstructive Pulmonary Disease, edited by R. Pauwels, D. S. Postma, and S. T. Weiss
- 192. Sleep Deprivation: Basic Science, Physiology, and Behavior, edited by Clete A. Kushida
- 193. Sleep Deprivation: Clinical Issues, Pharmacology, and Sleep Loss Effects, edited by Clete A. Kushida
- 194. Pneumocystis Pneumonia: Third Edition, Revised and Expanded, edited by P. D. Walzer and M. Cushion
- 195. Asthma Prevention, edited by William W. Busse and Robert F. Lemanske, Jr.
- 196. Lung Injury: Mechanisms, Pathophysiology, and Therapy, edited by Robert H. Notter, Jacob Finkelstein, and Bruce Holm
- 197. Ion Channels in the Pulmonary Vasculature, edited by Jason X.-J. Yuan
- 198. Chronic Obstuctive Pulmonary Disease: Cellular and Molecular Mechanisms, edited by Peter J. Barnes
- 199. Pediatric Nasal and Sinus Disorders, edited by Tania Sih and Peter A. R. Clement
- 200. Functional Lung Imaging, edited by David Lipson and Edwin van Beek
- 201. Lung Surfactant Function and Disorder, edited by Kaushik Nag

- 202. Pharmacology and Pathophysiology of the Control of Breathing, edited by Denham S. Ward, Albert Dahan and Luc J. Teppema
- 203. Molecular Imaging of the Lungs, edited by Daniel Schuster and Timothy Blackwell
- 204. Air Pollutants and the Respiratory Tract: Second Edition, edited by W. Michael Foster and Daniel L. Costa
- 205. Acute and Chronic Cough, edited by Anthony E. Redington and Alvn H. Morice
- 206. Severe Pneumonia, edited by Michael S. Niederman
- 207. Monitoring Asthma, edited by Peter G. Gibson
- 208. Dyspnea: Mechanisms, Measurement, and Management, Second Edition, edited by Donald A. Mahler and Denis E. O'Donnell
- 209. Childhood Asthma, edited by Stanley J. Szefler and Søren Pedersen
- 210. Sarcoidosis, edited by Robert Baughman
- 211. Tropical Lung Disease, Second Edition, edited by Om Sharma
- 212. Pharmacotherapy of Asthma, edited by James T. Li
- 213. Practical Pulmonary and Critical Care Medicine: Respiratory Failure, edited by Zab Mosenifar and Guy W. Soo Hoo
- 214. Practical Pulmonary and Critical Care Medicine: Disease Management, edited by Zab Mosenifar and Guy W. Soo Hoo
- 215. Ventilator-Induced Lung Injury, edited by Didier Dreyfuss,
  Georges Saumon, and Rolf D. Hubmayr
- 216. Bronchial Vascular Remodeling In Asthma and COPD,
- edited by Aili Lazaar
  217. Lung and Heart-Lung Transplantation, edited by
- Joseph P. Lynch III and David J. Ross 218. Genetics of Asthma and Chronic Obstructive Pulmonary
- Disease, edited by Dirkje S. Postma and Scott T. Weiss
  219. Reichman and Hershfield's Tuberculosis: A Comprehensive,
- International Approach, Third Edition (in two parts), edited by Mario C. Raviglione
- 220. Narcolepsy and Hypersomnia, edited by Claudio Bassetti, Michel Billiard, and Emmanuel Mignot
- 221. Inhalation Aerosols: Physical and Biological Basis for Therapy, Second Edition, edited by Anthony J. Hickey
- 222. Clinical Management of Chronic Obstructive Pulmonary Disease, Second Edition, edited by Stephen I. Rennard, Roberto Rodriguez-Roisin, Gérard Huchon, and Nicolas Roche

The opinions expressed in these volumes do not necessarily represent the views of the National Institutes of Health.

We are pleased to dedicate this second edition of Clinical Management of Chronic Obstructive Pulmonary Disease to four major contributors to the advancement of COPD research and care:

Mitchell Friedman, Romain Pauwels, Paul Vermeire, and Maurizio Vignola.

Each was deeply appreciated and all will be missed.

# Introduction

In 1978, one year after the initiation of this series of monographs, *Lung Biology in Health and Disease* presented a volume (#9) titled *Chronic Obstructive Pulmonary Disease*, edited by Dr. Thomas L. Petty. In the following three decades we have witnessed extraordinary successes in the fight against COPD—as it is globally called today.

Since the publication of the first volume on COPD, the series published no less than fifteen volumes on many aspects or topics about this disease. In addition, many other monographs were published which, in part, covered topics relevant to the understanding of COPD or to its treatment regimens, albeit palliative. The rationale behind so many volumes was simply to follow and report the very productive avenues for both fundamental and clinical research which were being pursued in the United States and abroad with the support of the respective governments and of the pharmaceutical industry. The many outcomes of this research have been augmenting our understanding of COPD at a very fast pace, and patients have started to receive very positive and significant benefits from this research. Of course, it was, and still is recognized, that these benefits are temporary and that no cure is in sight. But, yet, so much can be of help to these patients. As per the slogan for World COPD Day, these patients are "Breathless, not Helpless."

Thus, it was inevitable that one of the volumes on COPD in this series would eventually focus on the *Clinical Management of Chronic Obstructive Lung Disease*. It appeared in 2002 and was edited by Thomas Similowski, William A. Whitelaw, and Jean-Philippe Derenne. But since, progress has marched on, actually at a faster pace, and it became evident that more research outcomes could be explained and comprehensively translated into a "practical" source that could help and enhance

vi Introduction

clinical practice. This is what led to this new volume, now titled *Clinical Management of Chronic Obstructive Pulmonary Disease*. This volume, edited by Stephen I. Rennard, Roberto Rodríguez-Roisin, Gérard Huchon, and Nicolas Roche, is more than just a second edition, it is a new phase in the journey of COPD. It is a tool to provide even better care to the patients.

COPD research today is a very global goal, simply because the disease has no frontiers and it affects all peoples and nations. The editors are well aware of this situation and, in response, they called on contributors of many nations so that all advances from can be presented to the readership.

As the Executive Editor of the series of monographs Lung Biology in Health and Disease, I am very proud to introduce this volume to our readers, and am very thankful to the editors and the contributors that they gave us the opportunity to include this volume in the series.

Claude Lenfant, MD Gaithersburg, Maryland, U.S.A.

# **Foreword**

The first edition of Clinical Management of Chronic Obstructive Pulmonary Disease, the 165th volume of the Lung Biology in Health and Disease series edited by Claude Lenfant, was published during the spring of 2002. The first letters to putative authors had been sent out by the editors, Jean-Philippe Derenne, William Whitelaw, and myself, early in 1998. The Global Initiative for Obstructive Lung Disease (GOLD) had been launched in 1997, and the first version of the Global Initiative for Obstructive Lung Disease guidelines was issued during the fall of 2001. In a way, the first edition of this book therefore marked the end of an era, during which COPD was the preoccupation of a minority of clinicians and researchers. In that era, the disease was considered in a rather nihilistic manner, and although pathophysiological studies had disentangled many of its mechanisms, few therapeutic approaches had been the object of "serious" studies (none of which would currently meet publication standards). Among other things, full realization of the inflammatory nature of the disease was lacking, as well as clear awareness of its systemic impact.

In a very few years, the COPD landscape has changed dramatically. The disease has become the focus of much attention. As underlined in the editors' preface, this enormous amount of attention has led to a better understanding of the epidemiology and burden of the disease, has permitted the dissection of the mechanisms of dyspnea, the main COPD—related symptom, and, beyond that, of the determinants of exercise limitation. It has made us realize that COPD is a global disease and not a mere set of lung and bronchi lesions, has provided us with a more complete image of what exacerbations are and represent from a prognostic point of view, and has led to the rationalization of available treatments and to the conception of new ones, among them practical tools soon to come from genetic research. Very clearly, there is still a long