

Lung Transplantation

This book provides a detailed account of the principles and practice of contemporary lung transplantation. An accomplished and international team of contributing authors have combined their expertise to provide the latest scientific developments and clinical knowledge based on their extensive experience. The book covers pulmonary vascular and parenchymal lung disease that necessitate transplantation, together with all aspects of the multidisciplinary management of lung transplant patients. The volume concludes by looking at future developments in the treatment of advanced respiratory failure. This interdisciplinary approach makes the publication suitable for several subspecialties in addition to pulmonary medicine and lung transplantation surgery, including anaesthesia, immunology, pharmacology, infectious disease, haematology, radiology and clinical psychology. It will serve as a valuable source of reference and practical information for medical specialists in transplantation and all those working in thoracic organ transplant units.

Nicholas Banner is a consultant physician at the Royal Brompton and Harefield NHS Trust, Harefield Hospital, and also an honorary senior lecturer at Imperial College London. He is the senior transplant physician at Harefield and has extensive experience in the care of patients both before and after heart or lung transplantation. His research interests include the medical aspects of transplantation. He is a Fellow of the Royal College of Physicians, London and of the European Society of Cardiology.

Julia Polak is Professor of Endocrine Pathology at Imperial College London and Director of the Imperial College Tissue Engineering and Regenerative Medicine Centre. In 1995 Julia underwent a heart and lung transplant at Harefield because of severe primary pulmonary hypertension. After her transplant she was able to return to full time research and changed the focus of her work to address the twin problems of lung transplantation: the lack of donor organs and the risk of organ rejection. In collaboration with Professor Larry Hench, she now leads a team of researchers investigating tissue repair and regeneration. She is a member of the Council of the Academy of Medical Sciences, a founder governor of the Tissue Engineering Society International and European Editor of *Tissue Engineering*.

Magdi Yacoub is British Heart Foundation Professor of Cardiothoracic Surgery and the Director of Research for the Harefield Heart Science Centre and Harefield Research Foundation. He founded the heart and lung transplant programs at Harefield Hospital and was Clinical Director for Transplantation at the Royal Brompton and Harefield NHS Trust for many years. His research interests include clinical transplantation, pulmonary hypertension, the scientific basis of organ transplantation and alternative ways of treating cardiac and respiratory failure including gene therapy and cell transplantation. He is a Fellow of the American College of Cardiology and of the Royal Society.

Cambridge University Press
978-0-521-03677-1 - Lung Transplantation
Edited by Nicholas R. Banner, Julia M. Polak and Magdi H. Yacoub
Frontmatter
[More information](#)

Lung Transplantation

Edited by

Nicholas R. Banner

Royal Brompton and Harefield NHS Trust and
National Heart and Lung Institute, Imperial College London

Julia M. Polak

Imperial College London

and

Magdi H. Yacoub

Harefield Research Foundation and Imperial College London



Cambridge University Press
978-0-521-03677-1 - Lung Transplantation
Edited by Nicholas R. Banner, Julia M. Polak and Magdi H. Yacoub
Frontmatter
[More information](#)

CAMBRIDGE UNIVERSITY PRESS
Cambridge, New York, Melbourne, Madrid, Cape Town, Singapore, São Paulo

Cambridge University Press
The Edinburgh Building, Cambridge CB2 8RU, UK

Published in the United States of America by Cambridge University Press, New York

www.cambridge.org
Information on this title: www.cambridge.org/9780521651110

© Cambridge University Press 2003

This publication is in copyright. Subject to statutory exception and to the provisions of relevant collective licensing agreements, no reproduction of any part may take place without the written permission of Cambridge University Press.

First published 2003
This digitally printed version 2007

A catalogue record for this publication is available from the British Library

ISBN 978-0-521-65111-0 hardback
ISBN 978-0-521-03677-1 paperback

Every effort has been made in preparing this book to provide accurate and up-to-date information which is in accord with accepted standards and practice at the time of publication. Nevertheless, the authors, editors and publisher can make no warranties that the information contained herein is totally free from error, not least because clinical standards are constantly changing through research and regulation. The authors, editors and publisher therefore disclaim all liability for direct or consequential damages resulting from the use of material contained in this book. Readers are strongly advised to pay careful attention to information provided by the manufacturer of any drugs or equipment that they plan to use.

Cambridge University Press has no responsibility for the persistence or accuracy of URLs for external or third-party Internet websites referred to in this publication, and does not guarantee that any content on such websites is, or will remain, accurate or appropriate.

Cambridge University Press

978-0-521-03677-1 - Lung Transplantation

Edited by Nicholas R. Banner, Julia M. Polak and Magdi H. Yacoub

Frontmatter

[More information](#)

To Ursula and Mary

N. R. B.

To Daniel

J. M. P.

To Marianne

M. H. Y.

Contents

List of contributors	ix
Preface	xv

Part I Pulmonary disease

1 Primary pulmonary hypertension: pathophysiology and therapy Stuart Rich	3
2 Genetics of pulmonary hypertension Richard C. Trembath and Rachel Harrison	11
3 Pathology of pulmonary hypertension Anne E. Bishop and Julia M. Polak	19
4 Pulmonary hypertension and the right ventricle Norbert F. Voelkel, Rubin M. Tuder, Carlyne Cool, Mark Geraci, Robert Quaife and Michael Bristow	29
5 Emphysema Gordon L. Snider	39
6 Alpha-1-antitrypsin deficiency Duncan C. S. Hutchison	54
7 Bronchiectasis Mary T. Keogan	61
8 Cystic fibrosis Margaret E. Hodson	71

9	Diffuse lung disease R. M. du Bois	85	20	Infectious complications Keith McNeil, Juliet Foweraker and Tim Wreghitt	250
10	Explant pathology Susan Stewart	96	21	Cytomegalovirus infection Nicholas R. Banner	261
Part II Lung transplantation			22	Imaging R. Jane Chambers	274
11	Overview Magdi H. Yacoub and Emma J. Birks	113	23	Transplant pathology Margaret M. Burke	294
12	Patient selection and indications for lung transplantation Janet R. Maurer	120	24	Haematology David Cummins	326
13	Single and bilateral lung transplantation John Dark	132	25	Psychology Claire N. Hallas and Jo Wray	337
14	Combined heart and lung transplantation Rosemary Radley-Smith, Asghar Khaghani and Nicholas R. Banner	141	26	The current status of lung transplantation Allan R. Glanville	353
15	Anaesthesia and intensive care Michael J. Boscoe and Shane J. George	158	Part III Future directions		
16	Medical management Paul A. Corris	176	27	Tissue engineering Larry L. Hench, Julian R. Jones, Rubia F. S. Lenza and Wander L. V. Vasconcelos	367
17	Immunological mechanisms of graft injury Marlene L. Rose and Ian V. Hutchinson	185	28	Xenotransplantation Agnes M. Azimzadeh, Carsten Schroeder and Richard N. Pierson III	374
18	Pharmacological immunosuppression Nicholas R. Banner and Haifa Lyster	205	29	The artificial lung Brack G. Hattler and William J. Federspiel	386
19	Chronic lung allograft dysfunction Marshall I. Hertz	243	Index		
					399

Contributors

Agnes M. Azimzadeh

Research Assistant
Department of Cardiothoracic Surgery
Vanderbilt University Medical Center
2986 The Vanderbilt Clinic
Nashville
TN 37323-5734
USA

Present address

Assistant Professor of Surgery
University of Maryland
Cardiac Surgery N4W94
22 South Greene St.
Baltimore MD 21201-1595
USA
aazimadeh@smail.umaryland.edu

Nicholas R. Banner

Consultant in Cardiology and Transplant Medicine
Royal Brompton and Harefield NHS Trust
Harefield Hospital
Harefield
Middlesex
UB9 6JH
UK
n.banner@rbh.nthames.nhs.uk

Emma J. Birks

Specialist Registrar in Cardiology
Harefield Research Foundation
Harefield Hospital
Harefield
Middlesex
UBP 6JH
UK
ebirks@ic.ac.uk

x **Contributors**

Anne E. Bishop

Senior Lecturer
 Tissue Engineering and Regenerative Medicine Centre
 Imperial College Faculty of Medicine
 Chelsea and Westminster Hospital
 369 Fulham Road
 London
 SW10 9NH
 a.e.bishop@ic.ac.uk

Michael J. Boscoe

Consultant Anaesthetist
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 m.boscoe@rbh.nthames.nhs.uk or boscoemj@aol.com

Michael Bristow

Professor of Medicine
 Division of Cardiology
 University of Colorado Health Sciences Center
 University of Colorado
 Health Science Center
 4200 East 9th Avenue #C310
 Denver
 CO 80220-3706
 USA

Margaret M. Burke

Consultant Histopathologist
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 m.burke@rbh.nthames.nhs.uk

R. Jane Chambers

Consultant Radiologist
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 jane.chambers@rbh.nthames.nhs.uk

Carlyne Cool

Assistant Professor
 Department of Pathology
 University of Colorado Health Sciences Center
 University of Colorado
 Health Science Center
 4200 East 9th Avenue #C310
 Denver
 CO 80220-3706
 USA

Paul A. Corris

Professor of Thoracic Medicine
 The Freeman Hospital
 High Heaton
 Newcastle upon Tyne
 NE7 7DN
 UK
 paul.corris@ncl.ac.uk

David Cummins

Consultant Haematologist
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 d.cummins@rbh.nthames.nhs.uk

John Dark

Professor of Cardiothoracic Surgery
 Regional Cardiothoracic Centre
 The Freeman Hospital
 Newcastle upon Tyne
 NE7 7DN
 UK
 j.h.dark@ncl.ac.uk

R. M. du Bois

Professor of Respiratory Medicine
 Royal Brompton Hospital
 Sydney Street
 London
 SW3 6NP
 UK
 r.dubois@rbh.nthames.nhs.uk

William J. Federspiel

Department of Chemical Engineering, Departments of
 Surgery and Bioengineering
 McGowan Institute of Regenerative Medicine
 University of Pittsburgh
 Pittsburgh PA 15219
 USA
 federspielwj@msx.upmc.edu

Juliet Foweraker

Consultant Microbiologist
 Microbiology Laboratory
 Papworth Hospital
 Papworth Everard
 Cambridgeshire
 CB3 8RE
 UK
 juliet.foweraker@papworth-tr.anglox.nhs.uk

Shane J. George

Consultant in Anaesthesia and Intensive Care
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 s.george@rbh.nthames.nhs.uk

Mark Geraci

Associate Professor
 Division of Pulmonary Sciences and Critical Care
 Medicine
 University of Colorado Health Sciences Center
 University of Colorado
 Health Science Center
 4200 East 9th Avenue #C310
 Denver
 CO 80220-3706
 USA

Allan R. Glanville

Associate Professor of Medicine
 St Vincent's Hospital
 Xavier 4
 Victoria Street
 Darlinghurst
 Sydney
 NSW 2010
 Australia
 aglanville@stvincents.com.au

Claire N. Hallas

Health Psychologist
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 c.hallas@rbh.nthames.nhs.uk

Rachel Harrison

Research Fellow
 Division of Medical Genetics
 Adrian Building
 University of Leicester
 University Road
 Leicester
 LE1 7RH
 reh17@le.ac.uk

Brack G. Hattler

Professor of Surgery
 Artificial Lung Program
 University of Pittsburgh
 200 Lothrop Street
 C-700
 Pittsburgh
 PA 15213
 USA
 Hattlerbg@msx.upmc.edu

Larry L. Hench

Professor of Materials
 Centre for Tissue Regeneration and Repair
 Imperial College of Science Technology and Medicine
 Prince Consort Road
 London
 SW7 2BP
 UK
 l.hench@ic.ac.uk

Marshall I. Hertz

Professor of Pulmonary/Critical Care Medicine
 Pulmonary Medicine/Lung Transplant Program
 University of Minnesota
 420 Delaware Street SE
 276 Mayo Mail Room
 Minneapolis
 MN 55455
 USA
 hertz001@umn.edu

Margaret Hodson

Professor of Respiratory Medicine
 Department of Cystic Fibrosis
 Royal Brompton Hospital
 Sydney Street
 London
 SW3 6NP
 UK
 s.hockley@ic.ac.uk

Duncan C. S. Hutchison

Consultant in Respiratory Medicine
 King's College Hospital
 Denmark Hill
 London
 SE5 9RS
 UK
 dhutchison@arlingtonave.demon.co.uk

Ian V. Hutchinson

Professor of Immunology
 Manchester University
 Oxford Road
 Manchester
 M13 9PL
 UK
 ian.hutchinson@man.ac.uk

Julian R. Jones

Research Associate
 Department of Materials
 Imperial College of Science Technology and Medicine
 Prince Consort Road
 London
 SW7 2BP
 UK

Mary T. Keogan

Consultant Immunologist
 Papworth Hospital
 Papworth Everard
 Cambridge
 CB3 8RE
 UK
Present address
 Consultant Immunologist
 Beaumont Hospital
 Department of Immunology
 Beaumont Road
 Dublin 9
 Ireland
 mary.keogan@beaumont.ie

A. Khaghani

Clinical Director of Transplantation
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 a.khaghani@rbh.nthames.nhs.uk

Rubia F. S. Lenza

Research Associate
 Federal University of Minas Gerais
 Department of Metallurgical and Materials Engineering
 Rua Espirito Santo, 35–200 Andar
 30160–030 Belo Horizonte
 MG
 Brazil

Haifa Lyster

Transplant Pharmacist
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 h.lyster@rbh.nthames.nhs.uk

Janet R. Maurer

Medical Director
 LIFESOURCE Transplant Network
 CIGNA HealthCare
 900 Cottage Grove Road
 Bloomfield
 CT
 USA
 Janet.Maurer@CIGNA.com

Keith McNeil

Consultant Physician
 Papworth Hospital
 Papworth Everard
 Cambridge
 CB3 8RE
 UK
Present address
 Department of Thoracic Medicine
 Prince Charles Hospital
 Rode Road
 Chermside
 Brisbane
 Queensland 4032
 Australia
 keith_mcneil@health.qld.gov.au

Richard N. Pierson III

Associate Professor of Surgery
 Department of Cardiothoracic Surgery
 Vanderbilt University Medical Centre
 2986 The Vanderbilt Clinic
 Nashville
 TN 37232-5734
 USA

Present address

Associate Professor of Surgery
 University of Maryland
 Cardiac Surgery N4 W94
 22 South Greene St.
 Baltimore
 MD 21201-1595
 USA
 rpierson@smail.umaryland.edu

Julia M. Polak

Professor of Endocrine Pathology
 Tissue Engineering and Regenerative
 Medicine Centre
 Imperial College Faculty of Medicine
 Chelsea and Westminster Hospital
 369 Fulham Road
 London
 SW10 9NH
 UK
 julia.polak@ic.ac.uk or s.lock@ic.ac.uk

Robert Quaife

Assistant Professor
 Division of Cardiology
 University of Colorado Health Sciences Center
 University of Colorado
 Health Science Center
 4200 East 9th Avenue #C310
 Denver
 CO 80220-3706
 USA

Rosemary Radley-Smith

Consultant Paediatric Cardiologist
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 j.henning@rbh.nthames.nhs.uk

Stuart Rich

Professor of Medicine and Director
 Center for Pulmonary Heart Disease
 Rush Presbyterian St Luke's Medical Center
 1725 West Harrison Street
 Suite 020
 Chicago
 IL 60612
 USA
 PPH@rush.edu

Marlene Rose

Professor of Immunology
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 marlene.rose@ic.ac.uk

Carsten Schroeder

Research Fellow
 Department of Cardiothoracic Surgery
 Vanderbilt University Medical Center
 2986 The Vanderbilt Clinic
 Nashville
 TN 37232-5734
 USA

Present address

University of Maryland
 Cardiac Surgery
 22 South Greene St.
 Baltimore
 MD 21201-1595
 cshroeder@smail.umaryland.edu

Gordon L. Snider

Professor of Medicine
 Boston University School of Medicine
 VA Boston Healthcare System (111RmB9-74)
 150 South Huntington Avenue
 Boston
 MA 02130
 USA
 Gordon.Snider@med.va.gov

Susan Stewart

Consultant Histopathologist
 Department of Histopathology
 Papworth Hospital
 Papworth Everard
 Cambridge
 CB3 8RE
 UK
 susan.stewart@papworth-tr.anglox.nhs.uk

Richard C. Trembath

Professor of Medical Genetics
 Division of Medical Genetics
 Departments of Medicine and Genetics
 Adrian Building
 University of Leicester
 University Road
 Leicester
 LE1 7RH
 UK
 rtrembath@hgmp.mrc.ac.uk

Rubin M. Tuder

Associate Professor of Pathology and Director of
 Cardiopulmonary Pathology
 Department of Pathology
 Johns Hopkins Medical School
 Ross Research Building, Room 519B
 Baltimore
 Maryland 21205
 USA

Wander L. V. Vasconcelos

Professor
 Federal University of Minas Gerais
 Department of Metallurgical and Materials Engineering
 Rua Espirito Santo, 35–200 Andar
 30160–030 Belo Horizonte
 MG
 Brazil

Norbert F. Voelkel

Professor of Emphysema Research and Director of the
 Pulmonary Hypertension Center
 Pulmonary Sciences and Critical Care Medicine
 University of Colorado
 Health Sciences Centre
 4200 East 9th Avenue
 Box C272
 Denver
 Colorado 80262
 USA
 norbert.voelkel@uchsc.edu

Jo Wray

Health Psychologist
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 j.wray@rbh.ivthames.nhs.uk

Tim Wreghitt

Consultant Virologist and Director
 Addenbrookes Hospital
 Clinical Microbiology and Public Health Laboratory
 Box 236 Hills Road
 Cambridge
 CB2 2QW
 UK
 tim.wreghitt@msexc.addenbrookes.anglox.nhs.uk

Magdi H. Yacoub

Professor and Director of the Harefield
 Research Foundation
 Heart Science Centre
 Harefield Hospital
 Harefield
 Middlesex
 UB9 6JH
 UK
 m.yacoub@ic.ac.uk

Preface

Organ transplantation has been one of the major medical achievements of the twentieth century. Transplants have saved the lives of countless patients with failure of one, or more, of their vital organs and have returned most to a happy and productive existence. The lung proved to be one of the most difficult organs to transplant and clinically successful lung transplantation was first achieved two decades after the first renal allografts were performed. The results of lung transplantation have steadily improved and the procedure is now accepted as a standard therapy for patients with advanced parenchymal or vascular pulmonary disease. This success has produced a growing population of lung transplant recipients but has also highlighted the problems and limitations of lung transplantation that now represent challenges for the twenty-first century.

Currently, the potential long-term benefits of lung transplantation are reduced by the frequent occurrence of bronchiolitis obliterans, which leads to progressive dysfunction of the pulmonary allograft and eventually to respiratory failure. Our understanding of the pathogenesis of this condition remains limited but there is some hope that newer approaches to pharmacological immunosuppression, including the use of drugs with antiproliferative properties, together with more effective prophylaxis against infection may reduce the impact of this condition. The burden of long-term pharmacological immunosuppression (infection and malignancy), as well as side effects of individual immunosuppressive drugs, are other important problems faced by transplant recipients. Progress has been made in this area through the more effective use of drug combinations to minimize the side effects of individual agents, the introduction of agents with better side effect profiles, and prophylaxis against some specific complications, such as infection with *Pneumocystis* or cytomegalovirus and against corticosteroid-related osteoporosis. In the longer term, however, it is to be hoped that

Cambridge University Press

978-0-521-03677-1 - Lung Transplantation

Edited by Nicholas R. Banner, Julia M. Polak and Magdi H. Yacoub

Frontmatter

[More information](#)

our growing understanding of transplant immunology will provide methods of producing immunosuppression that are specific for the allograft without the need for continuing drug therapy.

The number of lung transplant operations that can be performed is now limited by availability of donor lungs that are suitable for transplantation; there is an urgent need for effective alternative medical and surgical treatments for the conditions that currently require transplantation. Recently, significant progress has been made both in our understanding of the pathogenesis of pulmonary hypertension and in its medical treatment. It is to be hoped that scientific progress in other areas of pulmonary disease will lead to new therapeutic approaches for these conditions as well. Nevertheless, there is likely to be a continuing need for 'pulmonary replacement' therapy for the foreseeable future. New approaches such as the development of an artificial lung to bridge patients to transplantation may lead to technology that will become a long-term alternative to transplantation. In the future, growth of replacement organs using the techniques of molecular and developmental biology together with tissue engineering may provide alternative sources of lungs for transplantation. The use of genetically modified xenotransplants may provide another route to this goal if the concerns about safety can be addressed adequately.

Lung transplantation is a complex endeavour that requires the cooperation of physicians, surgeons and scientists working in many different fields. The care and assessment of the patient before surgery can have a profound effect on the outcome of transplantation and a successful programme must integrate all stages and aspects of the patient's care. In this book, we have gathered contributions from specialists working in many of the fields that contribute to a lung transplant programme; they have produced a comprehensive account of contemporary lung transplantation. The first section addresses specific as-

pects of the medical conditions that commonly necessitate transplantation; this highlights some recent advances and issues that are of particular importance from the transplant perspective. The second section provides a detailed and systematic account of the various aspects of transplantation. The final section looks at some of the directions that 'pulmonary replacement' therapy may take in the future.

The contributors come from Europe, North America and Australia and they have provided a 'state of the art' description of this rapidly developing field. Evidence to determine the optimum practice in some aspects of lung transplantation is lacking or equivocal. Consequently, there are significant variations in clinical practice between institutions; whenever possible, these have been highlighted by individual authors or by differing perspectives between authors. We believe that this book will be of value to those working in all aspects of lung transplantation as well as to pulmonary specialists and family physicians who either refer patients as potential candidates for transplantation or who cooperate with a transplant centre in providing long-term care for transplant recipients.

We offer our heartfelt thanks to the friends and colleagues who have contributed to this book. In addition we would like to acknowledge Peter Silver, Athena Horsten, Sandi Irvine and Lucille Murby at Cambridge University Press for their excellent support and guidance throughout the project. We thank Joan Green and Sandra Lock for their help with the management of the manuscripts and the authors as well as of the editors! Finally, we must thank our families who have supported and encouraged us throughout this project and in our many other professional endeavours.

Nicholas R. Banner
Julia M. Polak
Magdi H. Yacoub

Harefield and London

Editorial note

For consistency, the recommended international nonproprietary names of drugs have been used. These some times differ from those that have been used in many countries e.g. ciclosporin is used here rather than cyclosporin or cyclosporine.