

TEXTBOOK OF ORGAN TRANSPLANTATION

EDITED BY ALLAN D. KIRK

STUART J. KNECHTLE, CHRISTIAN P. LARSEN
JOREN C. MADSEN, THOMAS C. PEARSON AND
STEVEN A. WEBBER



WILEY Blackwell

Textbook of Organ Transplantation

Textbook of Organ Transplantation

Editors

Allan D. Kirk, MD, PhD, FACS

Professor and Chairman, Department of Surgery
Duke University School of Medicine;
Surgeon-in-Chief for Duke University Health System
Duke University Medical Center
Durham, NC, USA

Stuart J. Knechtle, MD

Professor of Surgery
Emory University School of Medicine
Atlanta, GA, USA

Christian P. Larsen, MD, DPhil

Dean – Emory School of Medicine
Surgeon-in-Chief Emory Healthcare
Emory University
Atlanta, GA, USA

Joren C. Madsen, MD, DPhil

Professor of Surgery
W. Gerald and Patricia R. Austen
Distinguished Scholar in Cardiac Surgery
Massachusetts General Hospital
Boston, MA, USA

Thomas C. Pearson, MD

Emory Transplant Center
Emory University School of Medicine
Atlanta, GA, USA

Steven A. Webber, MBChB, MRCP

James C. Overall Professor and Chair, Department of Pediatrics
Monroe Carell Jr. Children's Hospital at Vanderbilt
Vanderbilt University School of Medicine
Nashville, TN, USA

WILEY Blackwell

This edition first published 2014 © 2014 by John Wiley and Sons, Ltd.

Wiley-Blackwell is an imprint of John Wiley & Sons, formed by the merger of Wiley's global Scientific, Technical and Medical business with Blackwell Publishing.

Registered office: John Wiley & Sons, Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial offices: 9600 Garsington Road, Oxford, OX4 2DQ, UK
The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK
111 River Street, Hoboken, NJ 07030-5774, USA

For details of our global editorial offices, for customer services and for information about how to apply for permission to reuse the copyright material in this book please see our website at www.wiley.com/wiley-blackwell

The right of the author to be identified as the author of this work has been asserted in accordance with the UK Copyright, Designs and Patents Act 1988.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, except as permitted by the UK Copyright, Designs and Patents Act 1988, without the prior permission of the publisher.

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are trade names, service marks, trademarks or registered trademarks of their respective owners. The publisher is not associated with any product or vendor mentioned in this book. It is sold on the understanding that the publisher is not engaged in rendering professional services. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

The contents of this work are intended to further general scientific research, understanding, and discussion only and are not intended and should not be relied upon as recommending or promoting a specific method, diagnosis, or treatment by health science practitioners for any particular patient. The publisher and the author make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of fitness for a particular purpose. In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of medicines, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each medicine, equipment, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. Readers should consult with a specialist where appropriate. The fact that an organization or Website is referred to in this work as a citation and/or a potential source of further information does not mean that the author or the publisher endorses the information the organization or Website may provide or recommendations it may make. Further, readers should be aware that Internet Websites listed in this work may have changed or disappeared between when this work was written and when it is read. No warranty may be created or extended by any promotional statements for this work. Neither the publisher nor the author shall be liable for any damages arising herefrom.

Library of Congress Cataloging-in-Publication Data

Textbook of organ transplantation / editors, Allan D. Kirk, Stuart J. Knechtle, Christian P. Larsen, Thomas C. Pearson, Joren C. Madsen, Steven A. Webber.

p. ; cm.

Includes bibliographical references and index.

ISBN 978-1-118-87014-3 (cloth)

I. Kirk, Allan, editor of compilation.

[DNLM: 1. Organ Transplantation. WO 660]

RD120.7

617.9'54-dc23

A catalogue record for this book is available from the British Library.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Cover image: courtesy of Michael Konomos

Cover design by Opta Design Ltd.

Set in 9/11 pt MinionPro-Regular by Toppan Best-set Premedia Limited

Contents

List of Contributors	xi		
Volume 1			
Section 1: History/Introduction			
Introduction			
<i>Allan D. Kirk</i>			
1 A Brief History of Clinical Organ Transplantation	5		
<i>Sir Roy Y. Calne</i>			
Section 2: Transplantation Biology			
Immunology			
2 An Overview of Physiologic Immunity	15		
<i>Hèth R. Turnquist, Giorgio Raimondi, Diana Metes, and Angus W. Thomson</i>			
3 Transplant Antigens: A Brief History of HLA	30		
<i>Paul I. Terasaki</i>			
4 Transplant Antigen Biology	36		
<i>Raja Rajalingam, Qiuheng Zhang, J. Michael Cecka, and Elaine F. Reed</i>			
5 Cellular Mechanisms of Adaptive Immunity	50		
<i>Maria-Luisa Alegre</i>			
6 Humoral Mechanisms of Adaptive Immunity	60		
<i>William M. Baldwin III and Robert L. Fairchild</i>			
7 Innate Immunity	68		
<i>Melissa Y. Yeung, Sacha A. De Serres, and Xian C. Li</i>			
8 Mechanisms of Immune Regulation	79		
<i>Kathryn J. Wood, Andrew Bushell, and Joanna Hester</i>			
9 The Spectrum of Alloimmunity, Heterologous Immunity, and Relevant Autoimmunity	87		
<i>Mandy L. Ford, Andrew B. Adams, and Christian P. Larsen</i>			
10 Fundamental Concepts Regarding Graft Injury and Regeneration: Tissue Injury, Tissue Quality, and Recipient Factors	99		
<i>Chatchai Kreepala, Konrad S. Famulski, and Philip F. Halloran</i>			
11 Mechanisms of Allograft Tolerance	119		
<i>Raul Badell and Allan D. Kirk</i>			
12 Xenoinmunity	134		
<i>Peter J. Cowan and Anthony J.F. d'Apice</i>			
Experimental Transplantation			
13 In Vitro Models of Alloreactivity	150		
<i>Charles A. Su, Anna Valujskikh, William M. Baldwin III, and Robert L. Fairchild</i>			
14 Small Animal Models of Transplantation	158		
<i>Lakshman Gunaratnam, Anthony M. Jevnikar, and Roslyn B. Mannon</i>			
15 Large Animal Models of Transplantation	185		
<i>Douglas J. Anderson, Benjamin M. Martin, Allan D. Kirk, and David H. Sachs</i>			
16 Advancing Transplantation In Silico: Studying Global Gene Expression Using Functional Genomics for Transplantation Research	208		
<i>Steven Head, Sunil M. Kurian, and Daniel R. Salomon</i>			
13 Mechanisms of Immune Modulation			
17 Current Pathways for Immune Manipulation	219		
<i>Jason R. Lees, Agnes M. Azimzadeh, Yaozhong Ding, Jiangnan Xu, and Jonathan S. Bromberg</i>			
18 Future Pathways for Immune Manipulation	239		
<i>Allison B. Webber and Flavio Vincenti</i>			
Section 3: Organ Procurement		251	
Organ Procurement and Allocation			
19 Administration of Organ Procurement and Allocation	253		
<i>Jennifer M. Porter, Lori E. Brigham, and Susan Gunderson</i>			
20 Deceased Donor Management	264		
<i>John Fung, Koji Hashimoto, Bijan Eghtesad, Daniel J. Lebovitz, and Melissa Watson</i>			
Techniques for Organ Procurement			
21 Techniques for Organ Procurement after Brain Death	277		
<i>Rupert Oberhuber, Timm Heinbokel, Zain Khalpey, Sayeed Malek, and Stefan G. Tullius</i>			
22 Techniques for Organ Procurement after Circulatory Death	288		
<i>Chandrasekar Santhanakrishnan and Anthony M. D'Alessandro</i>			
23 Techniques for Living Donor Kidney Procurement	293		
<i>Andrew B. Adams, Ashtar Chami, and Kenneth A. Newell</i>			
24 Techniques for Living Donor Liver Procurement	309		
<i>Koji Hashimoto, Cristiano Quintini, and Charles M. Miller</i>			
Organ Preservation and Resuscitation			
25 Abdominal Organ Preservation and Resuscitation	319		
<i>Henri G.D. Leuvenink and Rutger J. Ploeg</i>			
26 Thoracic Organ Preservation and Resuscitation	334		
<i>Jonathan C. Yeung, Marcelo Cypel, John M. Craig, and Shaf Keshavjee</i>			

27 Kidney Paired Donation Networks <i>Adam W. Bingaman and Cathi L. Murphey</i>	343	44 Intensive Care in Cardiac Failure <i>Josef Stehlik, Michael S. Kiernan, Deborah Budge, and Maryl R. Johnson</i>	503
Section 4: Pre-operative Management of Transplant Patients	351	45 Intensive Care in Pulmonary Failure <i>John Adam Reich and Richard Eliot Fagley</i>	520
Patient Selection and Indications for Organ Transplantation		Artificial Organs and Assist Devices	
28 Patient Selection and Indications for Kidney Transplantation <i>Jeremy Goodman and Robert S. Gaston</i>	353	46 Dialysis <i>Myriam Farah and John S. Gill</i>	530
29 Patient Selection and Indications for Liver Transplantation <i>Kimberly A. Brown and Marwan Kazimi</i>	364	47 The Artificial Liver, in vivo Tissue Engineering, and Organ Printing <i>Igor M. Sauer, Nathanael Raschzok, and Peter Neuhaus</i>	545
30 Patient Selection and Indications for Heart Transplantation <i>Andrew L. Smith and Daniel B. Sims</i>	377	48 Ventricular Assist Devices <i>O.H. Frazier and Steven M. Parnis</i>	554
31 Patient Selection and Indications for Lung Transplantation <i>Julia B. Becker and Edward R. Garrity Jr</i>	388	49 The Artificial Heart <i>Hannah Copeland, Jennifer Berumen, Richard G. Smith, and Jack G. Copeland</i>	563
32 Patient Selection and Indications for Pancreas and Islet Transplantation <i>Alexandra Turner and Nicole A. Turgeon</i>	404	50 Artificial Lungs <i>Claire A. Watkins and Bartley P. Griffith</i>	568
33 Patient Selection and Indications for Intestinal and Multivisceral Organ Transplantation <i>Douglas G. Farmer and Robert S. Venick</i>	412	51 The Artificial Pancreas <i>Desmond Barry Keenan and Garry M. Steil</i>	576
34 Role of Primary Care Provider in the Referral and Care of Abdominal Organ Transplant Patients <i>Peggy B. Hasley, Kristine S. Schonder, and Ron Shapiro</i>	416	52 Tissue and Organ Bioengineering <i>Tracy C. Grikscheit and Erik R. Barthel</i>	584
35 Role of Primary Care Provider in the Referral and Care of Thoracic Organ Transplant Patients <i>Remzi Bag, Arvind Bhimaraj, and Sireesha Garikipati</i>	428	Organ Acceptance and Risk Management Assessment	
The Histocompatibility Lab		53 Organ Assessment and Acceptance for Standard and Expanded Criteria Donors <i>Matthew Cooper and Stephen T. Bartlett</i>	594
36 Alloantibodies, Sensitization and Virtual Crossmatching <i>Howard M. Gebel and Robert A. Bray</i>	443	54 Organ Assessment and Acceptance for Donation after Circulatory Death Donors <i>Silke Niederhaus and Anthony M. D'Alessandro</i>	605
Waiting List Management		Section 5: Transplant Procedure and Surgical Technique	617
37 Waiting List Management for Kidney Transplantation <i>Phuong-Thu T. Pham, Phuong-Chi T. Pham, and Gabriel M. Danovitch</i>	452	55 Kidney Transplantation Procedure and Surgical Technique <i>Paul L. Tso and Thomas C. Pearson</i>	619
38 Waiting List Management for Liver Transplantation <i>John G. O'Grady</i>	462	56 Liver Transplantation Procedure and Surgical Technique <i>Joseph F. Magliocca, Steven I. Hanish, Eugenia K. Page, and Stuart J. Knechtle</i>	631
39 Waiting List Management for Heart Transplantation <i>Howard J. Eisen</i>	470	57 Living Donor Liver Transplantation Procedure and Surgical Technique <i>Sung-Gyu Lee, Deok-Bog Moon, and Jung-Man Namgoong</i>	639
40 Waiting List Management for Lung Transplantation <i>E. Clinton Lawrence and David C. Neujahr</i>	476	58 Heart Transplantation Procedure and Surgical Technique <i>John M. Craig, Soyoung Lee, Gus J. Vlahakes, and Joren C. Madsen</i>	657
41 Waiting List Management for Pancreas and Islet Transplantation <i>Jon S. Odorico</i>	482	59 Lung Transplantation Procedure and Surgical Technique <i>R. Duane Davis and Matt Hartwig</i>	667
42 Waiting List Management for Intestinal and Multivisceral Transplantation <i>Kareem M. Abu-Elmagd and Guilherme Costa</i>	489	60 Pancreas Transplantation Procedure and Surgical Technique <i>Dixon B. Kaufman, Jon Odorico, and Hans W. Sollinger</i>	674
Intensive Care in End Organ Failure			
43 Intensive Care in Hepatic Failure <i>Jenny E. Han and Ram M. Subramanian</i>	495		

61 Islet Cell Transplantation Procedure and Surgical Technique <i>A.M. James Shapiro and Camillo Ricordi</i>	682	76 Clinical Transplantation Tolerance <i>Tatsuo Kawai, David H. Sachs, and A. Benedict Cosimi</i>	844
62 Intestinal Transplantation Procedure and Surgical Technique <i>Thomas Fishbein</i>	691	Clinical Recurrent Disease: Diagnosis and Management	
63 Multivisceral Transplantation Procedure and Surgical Technique <i>Lokesh Bathla and Alan Langnas</i>	697	77 Recurrent Disease after Kidney and Pancreas Transplantation <i>Lorna K. Henderson and Philip J. O'Connell</i>	855
64 Vascularized Composite Allograft Transplantation Procedure and Surgical Technique <i>Gerald Brandacher, Jaimie T. Shores, Chad R. Gordon, Damon S. Cooney, and W.P. Andrew Lee</i>	703	78 Recurrent Disease after Liver Transplantation <i>Samir Parekh and James R. Spivey</i>	869
Index		79 Recurrent Disease after Heart Transplantation <i>Jignesh K. Patel and Jon A. Kobashigawa</i>	883
		80 Recurrent Disease after Lung Transplantation <i>Todd L. Astor</i>	898
Volume 2		Histopathological Syndromes of Graft Rejection and Recurrent Disease	
Section 6: Post-transplant Management	715	81 Histopathological Syndromes of Kidney Allograft Rejection and Recurrent Disease <i>Alton Brad Farris, III and Michael H. Mengel</i>	910
Immunosuppressive Therapy		82 Histopathological Syndromes of Liver Allograft Rejection and Recurrent Disease <i>Anthony J. Demetris, Marta I. Minervini, Michael A. Nalesnik, Erin Rubin, Parmjeet Randhawa, and Eizaburo Sasatomi</i>	927
65 Induction Immunosuppressive Therapy <i>Ali H. Charafeddine and Allan D. Kirk</i>	717	83 Histopathological Syndromes of Heart Allograft Rejection and Recurrent Disease <i>E. Rene Rodriguez and Carmela D. Tan</i>	957
66 Maintenance Immunosuppressive Therapy <i>Karen L. Hardinger, Daniel C. Brennan, and Christina L.M. Klein</i>	732	84 Histopathological Syndromes of Lung Allograft Rejection and Recurrent Disease <i>Carol Farver and W. Dean Wallace</i>	981
67 Rescue Immunosuppressive Therapy <i>Mark D. Stegall and Patrick G. Dean</i>	754	85 Histopathological Syndromes of Pancreas and Islet Allograft Rejection and Recurrent Disease <i>Cinthia Beskow Drachenberg and John C. Papadimitriou</i>	989
68 Desensitization Protocols for Organ Transplantation <i>Carmen Lefaucheur and Denis Glotz</i>	763	86 Histopathological Syndromes of Intestinal Allograft Rejection and Recurrent Disease <i>Phillip Ruiz, Jennifer Garcia, Akin Tekin, Seigo Nishida, and Andreas Tzakis</i>	1011
Clinical Allograft Rejection Syndromes: Diagnosis and Management		87 Histopathological Syndromes of Vascularized Composite Allograft Rejection and Recurrent Disease <i>Alexandra P. Turner, Alton Brad Farris, III, Alessandrina M. Freitas, and Linda C. Cendales</i>	1023
69 Clinical Allograft Rejection Syndromes in Kidney Transplantation <i>Brian J. Nankivell</i>	773	Post-operative Monitoring	
70 Clinical Allograft Rejection Syndromes in Liver Transplantation <i>Matthew H. Levine and Sandy Feng</i>	789	88 Cardiovascular Disease and Preventive Healthcare after Organ Transplantation <i>Stephen Pastan and Divya Gupta</i>	1030
71 Clinical Allograft Rejection Syndromes in Heart Transplantation <i>Keyur B. Shah, Joren C. Madsen, and Mandeep R. Mehra</i>	802	89 Monitoring for HLA Antibody after Organ Transplantation <i>Robert A. Bray and Howard M. Gebel</i>	1059
72 Clinical Allograft Rejection Syndromes in Lung Transplantation <i>David C. Neujahr</i>	813	90 Biomarkers and Alloimmune Monitoring after Organ Transplantation <i>Oriol Bestard, Birgit Sawitzki, and Alberto Sánchez-Fueyo</i>	1065
73 Clinical Allograft Rejection Syndromes in Pancreas and Islet Transplantation <i>Parsia A. Vagefi and Peter G. Stock</i>	824	91 Protective Immune Competence after Organ Transplantation <i>Aneesh K. Mehta</i>	1079
74 Clinical Allograft Rejection Syndromes in Intestinal Transplantation <i>Andreas Tzakis, Gennaro Selvaggi, Akin Tekin, Jennifer Garcia, Ji Fan, and Phil Ruiz Jr</i>	830		
75 Clinical Allograft Rejection Syndromes in Vascularized Composite Allotransplantation <i>Stefan Schneeberger and Gerald Brandacher</i>	835		

Transplant Infectious Diseases

- 92** Donor-derived Infections after Organ Transplantation 1088
Marissa B. Wilck and Emily A. Blumberg
- 93** Perioperative Infections after Organ Transplantation 1105
Daniel Kaul and Michael Green
- 94** Late Infectious Disease after Organ Transplantation 1117
Jay A. Fishman and Robin K. Avery

Malignancy in Transplantation

- 95** General Malignancy after Organ Transplantation 1134
Oriol Bestard, Josep M. Cruzado, and Josep M. Grinyó
- 96** Post-Transplant Lymphoproliferative Disorders 1147
Michael Green and Steven A. Webber

Pregnancy and Contraception in Transplantation

- 97** Pregnancy and Contraception in Transplantation 1161
Serban Constantinescu, Veronica Gomez-Lobo, John M. Davison, Michael J. Moritz, and Vincent T. Armenti

The Transplant Pharmacopeia

- 98** Drugs Specifically Approved for Transplant Indications 1179
Winston A. Ally and Avinash Agarwal
- 99** Infectious Disease Prophylaxis after Organ Transplantation 1202
G. Marshall Lyon, III
- 100** Metabolic and Endocrine Management of the Organ Transplant Recipient 1213
Naim Issa, Scott A. Reule, and Aleksandra Kukla
- 101** Off-Label Use of Immunosuppressive Agents in Solid Organ Transplantation 1233
Jill C. Krisl, Rita R. Alloway, and E. Steve Woodle
- 102** Drug Interactions in Organ Transplantation 1242
William D. Simmons, Pamala A. Jacobson, and Karen L. Hardinger

Section 7: Long-term Transplant Outcomes 1257

- 103** Long-term Outcomes after Kidney Transplantation 1259
Sundus A. Lodhi and Neema Stephens
- 104** Long-term Outcomes after Liver Transplantation 1267
Heidi Yeh, Paulo Martins, and James F. Markmann
- 105** Long-term Outcomes after Heart Transplantation 1280
Michelle M. Kittleson and Jon A. Kobashigawa
- 106** Long-term Outcomes after Lung and Heart-Lung Transplantation 1288
Toshihiro Okamoto, David Wheeler, and Kenneth R. McCurry
- 107** Long-term Outcomes after Pancreas Transplantation 1300
Phillip Y. Wai and Hans W. Sollinger
- 108** Long-term Outcomes after Islet Transplantation 1314
A.M. James Shapiro and Camillo Ricordi
- 109** Long-term Outcomes after Intestinal and Multi-visceral Transplantation 1334
Jennifer Garcia, Gennaro Selvaggi, Akin Tekin, Phillip Ruiz, and Andreas Tzakis

- 110** Long-term Outcomes after Vascularized Composite Allograft Transplantation 1338
Alessandrina M. Freitas and Linda C. Cendales

Section 8: Pediatric Transplant 1353

- 111** An Introduction to Pediatric Organ Transplantation 1355
Steven A. Webber and Allan D. Kirk
- 112** Developmental Immunity: From Birth to Adult 1357
Simon Urschel and Lori J. West
- 113** Pediatric Kidney Transplantation 1370
William Harmon
- 114** Pediatric Liver Transplantation 1390
John C. Bucuvalas and Sandy Feng
- 115** Pediatric Heart Transplantation 1406
Steven A. Webber
- 116** Pediatric Lung Transplantation 1420
Albert Faro and Stuart C. Sweet
- 117** Pediatric Intestinal and Multivisceral Organ Transplantation 1430
Douglas G. Farmer

Special Pediatric Considerations

- 118** Growth and Development after Organ Transplantation 1435
Franz Schaefer
- 119** Cognitive Development and Functional Outcomes after Organ Transplantation 1443
Estella M. Alonso, Saeed Mohammad, and Lisa G. Sorensen
- 120** Nonadherence, Psychosocial Adaptation and Its Effects in Pediatric Transplantation 1453
Robert Ettenger and Margaret L. Stuber
- 121** Management of the Organ Transplant Recipient in the Transition from Pediatric to Adult Care 1475
Sandra Amaral and Lorraine E. Bell

Section 9: Transplant Administration 1489

- 122** Transplant Coordination 1491
Dianne LaPointe Rudow
- 123** Transplant Pharmacy Services 1497
Christin C. Rogers, Nicole A. Pilch, Eric M. Tichy, Lonnie D. Smith, David J. Taber, and Rita R. Alloway
- 124** Inpatient Transplant Unit Management 1509
Linda Ohler, Margaret Schaeffer, Kelly Carter, and Donna George
- 125** Transplant Clinic Management 1518
Elizabeth A. Kallenborn, Chris Shay-Downer, Kathy Schwab, and Shelley Zomak
- 126** Transplant Center Management and Leadership – A Case for Structured Intrapreneurship 1533
Luke Preczewski, Gwen McNatt, and Michael Abecassis

127	Transplant Quality Programs <i>Christian Morath, Peter Schemmer, and Martin G. Zeier</i>	1542	Section 11: Transplant Policy	1639
128	National and International Transplant Management and Oversight <i>Virginia A. McBride, Esther-Marie Carmichael, Linda Ohler, and Jeremy Chapman</i>	1549	Transplant Ethics	
	Transplant Education		136 Transplant Ethics for Clinicians	1641
129	Abdominal Solid Organ Transplantation Fellowship Training <i>Rachel C. Forbes and Mitchell L. Henry</i>	1562	137 The Ethics of Organ Allocation	1645
130	Medical Solid Organ Transplant Fellowship Training <i>Deirdre Sawinski and Roy D. Bloom</i>	1566	138 The Ethics of Living Donation	1654
131	Transplantation in General Medical Education <i>Rowena Delos Santos and Douglas J. Norman</i>	1572	139 Cultural Variations in Organ Transplantation	1662
	Section 10: Clinical Trials and Data Management		Economic and Societal Impact of Transplantation and Transplant Policy	
132	Building and Sustaining a Local Transplant Data Management Program <i>Regina Eady, Tim Morris, Marc J. Overcash, and Jeff Weaver</i>	1583	140 Federal and Private Insurance Coverage for Organ Transplantation	1673
133	National Transplant Data Registries and Population Studies <i>Allan B. Massie and Dorry L. Segev</i>	1598	141 Drug Development in Solid Organ Transplantation and the Approval Process for Transplant Immunosuppressants	1679
134	Clinical Research Methods and Analysis in Organ Transplantation <i>Jesse D. Schold and S. Joseph Kim</i>	1607	<i>Candace Wang, J. Mark Hexham, Alan Slade, Peter Heining, Ronald G. Van Valen, Guido Junge, and Marc I. Lorber</i>	
135	Comparative Effectiveness in Transplantation <i>Edward A. Meister and Bruce Kaplan</i>	1622	142 Organ Specific Benefits of Transplantation: Outcomes and Economics	1690
			<i>David A. Axelrod, Mark Schnitzler, and Richard Freeman</i>	
			143 National Healthcare Policy, Transplant-specific Statutes, and the Future of Organ Transplantation	1703
			<i>Keren Ladin, Rui Wang, and Douglas W. Hanto</i>	
			Index	

List of Contributors

Michael Abecassis, MD, MBA

J. Roscoe Miller Distinguished Professor
Department of Surgery and
Microbiology-Immunology
Chief, Division of Organ Transplantation
Founding Director, Comprehensive Transplant Center
Northwestern University Feinberg School of Medicine
Chicago, IL, USA

Kareem M. Abu-Elmagd, MD, PhD, FACS

Professor of Surgery
Department of Surgery
Transplant Division
Intestinal Rehabilitation and Transplantation Center
University of Pittsburgh Medical Center
Pittsburgh, PA, USA

Andrew B. Adams, MD, PhD

Assistant Professor of Surgery
Emory Transplant Center
Emory University School of Medicine
Atlanta, GA, USA

Avinash Agarwal, MD, FACS

Assistant Professor of Surgery
Department of Surgery, University of Virginia
Charlottesville, VA, USA

Maria-Luisa Alegre, MD, PhD

Professor of Medicine
University of Chicago
Chicago, IL, USA

Rita R. Alloway, PharmD, FCCP

Research Professor of Medicine
Director, Transplant Clinical Research
Director, Transplant Pharmacy PGY 2 Residency and
Fellowship
University of Cincinnati
Cincinnati, OH, USA

Winston A. Ally, PharmD, BCPS

Pharmacy Clinical Coordinator
Solid Organ Transplantation
Director, PGY-2 Solid Organ Transplant Pharmacy
Residency
Department of Pharmacy Services
University of Virginia Health System
Charlottesville, VA;
Clinical Assistant Professor
Department of Pharmacotherapy and Outcomes
Science
Virginia Commonwealth University School of
Pharmacy
Richmond, VA, USA

Estella M. Alonso, MD

Professor of Pediatrics
Department of Pediatrics
Northwestern University Feinberg School of Medicine
Medical Director of Hepatology and Liver
Transplantation
Ann and Robert H. Lurie Children's Hospital of
Chicago
Chicago, IL, USA

Sandra Amaral, MD, MHS

Co-Director, Pediatric Kidney Transplant Program
Assistant Professor, University of Pennsylvania
The Children's Hospital of Philadelphia
Philadelphia, PA, USA

Douglas J. Anderson, MD

Senior Resident
Department of Surgery
Emory University School of Medicine
Atlanta, GA, USA

Vincent T. Armenti, MD, PhD

Principal Investigator
National Transplantation Pregnancy Registry (NTPR)
Gift of Life Institute
Philadelphia, PA;
Professor of Anatomy and Surgery
University of Central Florida College of Medicine
Orlando, FL, USA

Todd L. Astor, MD

Assistant Professor of Medicine, Harvard Medical
School
Medical Director, Lung and Heart-Lung Transplant
Program
Pulmonary and Critical Care Unit
Massachusetts General Hospital
Boston, MA, USA

Robin K. Avery, MD

Professor of Medicine
Johns Hopkins University School of Medicine
Infectious Disease Division
Johns Hopkins Hospital
Baltimore, MD, USA

David A. Axelrod, MD, MBA

Section Chief, Solid Organ Transplant Surgery
Dartmouth Hitchcock Medical Center
Lebanon, NH, USA

Agnes M. Azimzadeh, PhD

Assistant Professor of Surgery
University of Maryland School of Medicine
Baltimore, MD, USA

Raul Badell, MD

Chief Resident
Department of Surgery
Emory University School of Medicine
Atlanta, GA, USA

Remzi Bag, MD

McKelvey Scholar
The McKelvey Center for Lung Transplantation
Assistant Professor of Medicine, Pulmonary, Allergy
and Critical Care
Emory University School of Medicine
Atlanta, GA, USA

William M. Baldwin III, MD, PhD

Staff, Department of Immunology
Cleveland Clinic
Cleveland, OH, USA

Erik R. Barthel, MD, PhD

Resident in General Surgery
Harbor-UCLA Medical Center
UCLA David Geffen School of Medicine
Los Angeles, CA, USA

Stephen T. Bartlett, MD

Peter Angelos Distinguished Professor and Chairman
Department of Surgery
University of Maryland School of Medicine
Surgeon-in-Chief, University of Maryland Medical
System
Baltimore, MD, USA

Lokesh Bathla, MD

Transplant Surgeon
Methodist Specialty and Transplant Hospital
San Antonio, TX, USA

Julia B. Becker, MD

Fellow in Pulmonary and Critical Care Medicine
University of Chicago
Chicago, IL, USA

Lorraine E. Bell, MDCM, FRCPC

Associate Professor of Pediatrics, McGill University
Director, Pediatric Renal Transplant Programme
Director, Pediatric Transition to Adult Care
Montreal Children's Hospital-McGill University
Health Centre
Montreal, QC, Canada

Jennifer Berumen, MD

Chief Resident, General Surgery
UC San Diego
La Jolla, CA, USA

Oriol Bestard

Renal Transplant Unit
Nephrology Department
University Hospital of Bellvitge
University of Barcelona
Barcelona, Spain

Arvind Bhimaraj, MD, MPH, FACC

Assistant Professor of Medicine
Weill Cornell Medical College, NY;
Department of Cardiology
Methodist DeBakey Heart & Vascular Center
Houston Methodist Hospital
Houston, TX, USA

Adam W. Bingaman, MD, PhD

Director, Live Donor and Incompatible Kidney
Transplant Programs
Methodist Specialty and Transplant Hospital
San Antonio, TX, USA

Roy D. Bloom, MD

Professor of Medicine
Perelman School of Medicine
University of Pennsylvania
Medical Director
Penn Kidney Pancreas Transplant Program
Philadelphia, PA, USA

Emily A. Blumberg, MD

Professor of Medicine
Perelman School of Medicine
University of Pennsylvania
Philadelphia, PA, USA

J. Andrew Bradley, PhD, FRCS

Professor of Surgery
University of Cambridge
Cambridge, UK

Gerald Brandacher, MD

Associate Professor of Surgery (PAR)
Scientific Director
Reconstructive Transplantation Program
Department of Plastic and Reconstructive Surgery
Johns Hopkins University School of Medicine
Baltimore, MD, USA

Robert A. Bray, PhD

Professor of Pathology
Co-Director, Histocompatibility and Molecular
Immunogenetics Laboratory
Department of Pathology
Emory University Hospital
Atlanta, GA, USA

Daniel C. Brennan, MD

Professor of Medicine
Director, Transplant Nephrology
Washington University in St. Louis
School of Medicine
St. Louis, MO, USA

Lori E. Brigham, MBA

President and CEO
Washington Regional Transplant Community
Annandale, VA, USA

Jonathan S. Bromberg, MD, PhD

Professor of Surgery and Microbiology and
Immunology
University of Maryland School of Medicine
Baltimore, MD, USA

Kimberly A. Brown, MD

Chief, Gastroenterology and Hepatology
Henry Ford Hospital
Detroit, MI, USA

John C. Bucuvalas

Professor of Pediatrics
Associate Medical Director, Pediatric Liver Care
Center
Cincinnati Children's Hospital Medical Center
Cincinnati, OH, USA

Deborah Budge, MD

Associate Director
UTAH Cardiac Transplant Program
Intermountain Medical Center
Salt Lake City, UT, USA

Andrew Bushell, DPhil

Senior Scientist and University Research Lecturer
Transplantation Research Immunology Group
Nuffield Department of Surgical Sciences
John Radcliffe Hospital
Oxford, UK

Chris J. Callaghan, PhD, FRCS

Consultant Transplant and Vascular Access Surgeon
Guy's Hospital
London, UK

Sir Roy Y. Calne, FRCS

Emeritus Professor of Surgery
Cambridge University
Cambridge, UK;
Visiting Professor
National University of Singapore
Singapore

Esther-Marie Carmichael,

MT(ASCP), CLS, PHM, BSC
Quality Assurance Manager
Keck Hospital of USC, Transplant Institute
Los Angeles, CA, USA

Kelly Carter, MS, RN, NE-BC

Virginia Commonwealth University Health System
Medical College of Virginia Hospitals
Nurse Manager
Pauley Heart Center
Richmond, VA, USA

J. Michael Cecka, PhD

Emeritus Professor
Department of Pathology and Laboratory Medicine;
Director, Clinical Research
UCLA Immunogenetics Center
David Geffen School of Medicine
University of California, Los Angeles
Los Angeles, CA, USA

Linda C. Cendales, MD

Associate Professor of Surgery
Division of Plastic and Reconstructive Surgery and
Division of Transplantation (dual appointment)
Director, Vascularized Composite Allotransplantation
Duke University Medical Center
Durham, NC, USA

Ashtar Chami, MD

Assistant Professor of Medicine
Emory Transplant Center
Emory University School of Medicine
Atlanta, GA, USA

Jeremy Chapman, MD, FRCP

Director, Renal Medicine
Centre for Transplant and Renal Research
Westmead Millennium Institute
Sydney University
Westmead Hospital
Westmead, NSW, Australia

Ali H. Charafeddine, MD

General Surgery Resident
Montefiore Medical Centre
Albert Einstein College of Medicine
Bronx, New York, NY, USA

Serban Constantinescu, MD, PhD

Medical Director, Kidney Transplant Program
Associate Professor of Medicine
Temple University School of Medicine
Philadelphia, PA, USA

Damon S. Cooney, MD, PhD

Assistant Professor of Plastic Surgery
Department of Plastic and Reconstructive Surgery
Johns Hopkins University School of Medicine
Baltimore, MD, USA

Matthew Cooper, MD

Associate Professor of Surgery
Medstar Georgetown Transplant Institute
Georgetown University School of Medicine
Washington, DC, USA

Jack G. Copeland, MD

Professor of Cardiothoracic Surgery
Director of Cardiac Transplantation and Mechanical
Circulatory Support
UC San Diego
La Jolla, CA, USA

Hannah Copeland, MD

Chief Resident, General Surgery
UC San Diego
La Jolla, CA, USA

A. Benedict Cosimi, MD

Claude E. Welch Distinguished Professor of Surgery
Harvard Medical School
Chief Emeritus
Division of Transplantation
Massachusetts General Hospital
Boston, MA, USA

Guilherme Costa, MD, FACS

Assistant Professor of Surgery
Department of Surgery
University of Pittsburgh
Pittsburgh, PA, USA

Peter J. Cowan, PhD

Professor, Immunology Research Centre
St Vincent's Hospital Melbourne;
Department of Medicine
University of Melbourne
Melbourne, VIC, Australia

John M. Craig, MD

Clinical Assistant Professor of Surgery
University of Tennessee Health Science Center
Baptist Memorial Hospital
Memphis, TN, USA

Josep M. Cruzado

Renal Transplant Unit
Nephrology department.
University Hospital of Bellvitge
University of Barcelona
Barcelona, Spain

Marcelo Cypel, MD, MSc

Assistant Professor of Surgery
Toronto Lung Transplant Program
University Health Network
University of Toronto
Toronto, ON, Canada

Anthony M. D'Alessandro, MD

Professor of Surgery
Director of Liver Transplantation
University of Wisconsin School of Medicine and
Public Health
Madison, WI, USA

Gabriel M. Danovitch, MD

Professor of Medicine, Division of Nephrology
Medical Director, Kidney Transplant Program
Department of Medicine
David Geffen School of Medicine at UCLA
Los Angeles, CA, USA

Anthony J.F. d'Apice, MD, MBBS

Professor
Immunology Research Centre
St Vincent's Hospital Melbourne;
Department of Medicine
University of Melbourne
Melbourne, VIC, Australia

R. Duane Davis, MD, MBA

Director of Transplantation
Professor of Surgery
Duke University Medical School and Medical Center
Durham, NC, USA

John M. Davison, MD

Professor Emeritus and Consultant Obstetrician
Institute of Cellular Medicine
Newcastle University
Newcastle upon Tyne, UK

Rowena Delos Santos, MD

Assistant Professor of Medicine
Renal Division
Washington University in St. Louis
St. Louis, MO, USA

Sacha A. De Serres, MD, SM, FRCPC

Research Fellow, Brigham and Women's Hospital and
Harvard Medical School
Boston, MA;
Assistant Professor of Medicine
Universite Laval
Quebec, QC, Canada

Patrick G. Dean, MD

Assistant Professor of Surgery
Division of Transplant Surgery
Mayo Clinic
Rochester, MN, USA

Francis L. Delmonico, MD

President, The Transplantation Society;
World Health Organization
Advisory for Human Transplantation;
Professor of Surgery
Harvard Medical School
Massachusetts General Hospital
Transplant Center
Boston, MA;
Medical Director
New England Organ Bank
Waltham, MA, USA

Anthony J. Demetris, MD

Starzl Professor of Liver and Transplant Pathology
Director, Division of Liver and Transplant Pathology
Department of Pathology
University of Pittsburgh Medical Center
Pittsburgh, PA, USA

Yaozhong Ding, PhD

Associate Professor (retired)
Department of Surgery
University of Maryland School of Medicine
Baltimore, MD, USA

Cynthia B. Drachenberg, MD

Professor of Pathology
Director, Electron Microscopy Laboratory
University of Maryland School of Medicine
Baltimore, MD, USA

Regina Eady

Research Data Informatics Analyst, Senior
Emory University
Atlanta, GA, USA

Bijan Eghtesad, MD

Professor of Surgery
Director, Fellowship Program
Hepato-Pancreato-Biliary/Liver Transplantation
Surgery
Cleveland Clinic
Cleveland, OH, USA

Howard J. Eisen, MD

Thomas J. Vischer Professor of Medicine
Chief, Division of Cardiology
Drexel University College of Medicine
Philadelphia, PA, USA

Robert Ettenger, MD

Professor of Pediatrics
Division of Nephrology
Department of Pediatrics
David Geffen School of Medicine at UCLA;
Director of Pediatric Renal Transplant Program
Director, Pediatric Nephrology Fellowship Program
Mattel Children's Hospital, UCLA
Los Angeles, CA, USA

Richard Eliot Fagley, MD

Anesthesiologist and Intensivist
Virginia Mason Medical Center
Seattle, WA, USA

Robert L. Fairchild, PhD

Staff, Department of Immunology
Cleveland Clinic
Cleveland, OH, USA

Konrad S. Famulski, PhD, DSc

Faculty Service Officer
Manager and Lead in Transcriptomics
Alberta Transplant Applied Genomics Centre
Department of Medicine
Division of Nephrology and Transplant Immunology
Edmonton, AB, Canada

Ji Fan, MD

Instructor of Clinical Surgery
University of Miami Miller School of Medicine
Miami Transplant Institute
Miami, FL, USA

Myriam Farah, MD, FRCPC

Clinical Assistant Professor
Division of Nephrology
University of British Columbia
Vancouver, BC, Canada

Douglas G. Farmer, MD

Professor of Surgery
Director, Intestinal Transplant Program
Surgical Director, Pediatric Liver Transplant Program
Dumont-UCLA Transplant Center
David Geffen School of Medicine at UCLA
Los Angeles, CA, USA

Albert Faro, MD

Associate Professor of Pediatrics
Division of Pediatric Allergy, Immunology and
Pulmonary Medicine
Washington University School of Medicine
St. Louis, MO, USA

Alton Brad Farris III, MD

Assistant Professor
Director, Laboratory of Nephropathology and Electron
Microscopy
Emory University
Atlanta, GA, USA

Carol Farver, MD, MS

Section Head, Surgical Pathology
Director, Pulmonary Pathology
Pathology and Laboratory Medicine Institute
Cleveland Clinic
Cleveland, OH, USA

Sandy Feng, MD, PhD

Professor of Surgery
Division of Transplant Surgery
University of California, San Francisco
San Francisco, CA, USA

Thomas Fishbein, MD

Executive Director, Georgetown Transplant Institute
Professor of Surgery
Georgetown University School of Medicine
Washington DC, USA

Jay A. Fishman, MD

Associate Director
MGH Transplantation Center;
Director, Transplant Infectious Disease &
Compromised Host Program
Massachusetts General Hospital;
Professor of Medicine
Harvard Medical School
Boston, MA, USA

Rachel C. Forbes, MD, MBA

Assistant Professor of Surgery
Division of Kidney and Pancreas Transplantation
Department of Surgery
Vanderbilt University
Nashville, TN, USA

Mandy L. Ford, PhD

Assistant Professor
Emory Transplant Center
Department of Surgery
Emory University
Atlanta, GA, USA

Richard N. Formica Jr, MD

Associate Professor of Medicine and Surgery
Director, Transplant Nephrology
Medical Director of Adult and Pediatric Kidney
Transplantation
Medical Director of Pancreas Transplantation
Yale University School of Medicine
New Haven, CT, USA

O.H. Frazier, MD

Chief, Transplant Services
Chief, Center for Cardiac Support
Director, Cullen Cardiovascular Research Laboratory
Texas Heart Institute
Houston, TX, USA

Richard Freeman, MD

Professor of Surgery
Dartmouth Hitchcock Medical Center
Lebanon, NH, USA

Alessandrina M. Freitas, MD, MPH

Resident in General Surgery
Department of Surgery
Emory University School of Medicine
Research Fellow
Vascularized Composite Allotransplantation
Emory Transplant Center
Atlanta, GA, USA

John Fung, MD, PhD

Professor of Surgery
Cleveland Clinic Lerner College of Medicine
Case Western Reserve University;
Chairman of Digestive Disease Institute
Cleveland Clinic
Cleveland, OH, USA

Jennifer Garcia, MD

Assistant Professor of Clinical Pediatrics
Division of Gastroenterology, Hepatology, and
Nutrition
University of Miami Miller School of Medicine
Miami Transplant Institute
Miami, FL, USA

Siresha Garikipati, MD

Fellow in Cardiology
University of Texas Medical Branch
Galveston, TX, USA

Edward R. Garrity Jr, MD, MBA

Professor of Medicine
Vice Chair for Clinical Operations
The University of Chicago Medical Center
Chicago, IL, USA

Robert S. Gaston, MD

Co-Director, Comprehensive Transplant Institute
Robert G. Luke Endowed Chair in Transplant
Nephrology
University of Alabama at Birmingham
Birmingham, AL, USA

Howard M. Gebel, PhD

Professor of Pathology
Co-Director, Histocompatibility and Molecular
Immunogenetics Laboratory
Department of Pathology
Emory University Hospital
Atlanta, GA, USA

Donna George, MS, RN, NEA-BC

Transplant Administrator & Nursing Director
The Hume-Lee Transplant Center
Virginia Commonwealth University Health System
Medical College of Virginia Hospitals
Richmond, VA, USA

John S. Gill, MD, MS, FRCP(C)

Associate Professor, Nephrology
Division of Nephrology
University of British Columbia
St. Paul's Hospital
Vancouver, BC, Canada

Alexandra K. Glazier, JD, MPH

Chair, UNOS Ethics Committee;
Vice-President and General Counsel
New England Organ Bank
Waltham, MA, USA

Denis Glotz

Department of Nephrology and Kidney
Transplantation and Research Unit INSERM U940
Hopital Saint Louis
Paris, France

Veronica Gomez-Lobo, MD

Director of Pediatric and Adolescent Obstetrics and
Gynecology
MedStar Washington Hospital Center and Children's
National Medical Center
Professor of Clinical Obstetrics and Gynecology
Department of Pediatrics, Georgetown University
Washington, DC, USA

Jeremy Goodman, MD, FACS

Assistant Professor of Surgery
Division of Transplant Surgery
University of Alabama at Birmingham
Birmingham, AL, USA

Chad R. Gordon, DO

Assistant Professor of Surgery
Department of Plastic and Reconstructive Surgery
Johns Hopkins University School of Medicine
Baltimore, MD, USA

Michael Green, MD, MPH

Professor of Pediatrics, Surgery and Clinical and
Translational Science
University of Pittsburgh School of Medicine
Division of Infectious Diseases
Children's Hospital of Pittsburgh
Pittsburgh, PA, USA

Bartley P. Griffith, MD

Thomas E. and Alice Marie Hales
Distinguished Professor in Transplantation
University of Maryland School of Medicine
Division of Cardiac Surgery
Baltimore, MD, USA

Tracy C. Grikscheit, MD, FACS

Assistant Professor of Surgery
Children's Hospital Los Angeles
Division of Pediatric Surgery
Keck University of Southern California School of
Medicine
Los Angeles, CA, USA

Josep M. Grinyó, MD

Chief of Nephrology
University Hospital of Bellvitge
University of Barcelona
Barcelona, Spain

Lakshman Gunaratnam

Assistant Professor of Medicine, Microbiology &
Immunology
University of Western Ontario
London, ON, Canada

Susan Gunderson, BSN, MHA

Chief Executive Officer
LifeSource
St. Paul, MN, USA

Divya Gupta, MD

Assistant Professor of Medicine
Division of Cardiology
Advanced Heart Failure and Transplant
Emory University School of Medicine
Atlanta, GA, USA

Philip F. Halloran, MD, PhD

Director
Alberta Transplant Applied Genomics Centre
University of Alberta
Edmonton, AB, Canada

Jenny E. Han

Assistant Professor, Division of Pulmonary and
Critical Care Medicine
Department of Medicine
Emory University School of Medicine
Atlanta, GA, USA

Steven I. Hanish, MD

Assistant Professor of Surgery
Emory University School of Medicine
Atlanta, GA, USA

Douglas W. Hanto, MD, PhD

Associate Dean for Continuing Medical Education
Continuing Medical Education Office
Professor of Surgery
Washington University School of Medicine in St. Louis
St. Louis, MO, USA

Karen L. Hardinger, PharmD, BCPS

Clinical Professor of Pharmacy Practice
University of Missouri – Kansas City
School of Pharmacy
Kansas City, MO, USA

William Harmon, MD

Professor of Pediatrics
Harvard Medical School;
Pediatric Nephrology
President, Physicians' Organization
Boston Children's Hospital
Boston, MA, USA

Matt Hartwig, MD

Assistant Professor of Surgery
Duke University
Durham, NC, USA

Koji Hashimoto, MD, PhD

Assistant Professor of Surgery
Cleveland Clinic Lerner College of Medicine
Case Western Reserve University;
Digestive Disease Institute
Cleveland Clinic
Cleveland, OH, USA

Peggy B. Hasley, MD, MHSc

Associate Professor of Internal Medicine
Associate Program Director for Ambulatory Medicine
Director, Generalist Track
University of Pittsburgh Medical Center
Pittsburgh, PA, USA

Steven Head, MS

Director
Microarray and Next Generation Sequencing Core
Laboratories
The Scripps Research Institute
La Jolla, CA, USA

Timm Heinbokel

Division of Transplant Surgery and Transplant Surgery
Research Laboratory
Brigham and Women's Hospital
Harvard Medical School, Boston, MA;
Institute of Medical Immunology
Charité – Universitätsmedizin Berlin
Berlin, Germany

Peter Heining, PhD

Senior Toxicologist
Novartis Pharmaceuticals Corporation
East Hanover, NJ, USA

Lorna K. Henderson, MBChB, MRCP, PhD

Transplant Fellow
National Pancreas Transplant Unit
University of Sydney at Westmead Hospital
Westmead, NSW, Australia

Mitchell L. Henry, MD

Professor of Surgery
Chief, Division of Transplantation
Department of Surgery
The Ohio State University
Columbus, OH, USA

Joanna Hester, PhD

Senior Scientist
Transplantation Research Immunology Group
Nuffield Department of Surgical Sciences
John Radcliffe Hospital
Oxford, UK

J. Mark Hexham, PhD, MSc

Clinical Research Director
Novartis Pharmaceuticals Corporation
East Hanover, NJ, USA

Naim Issa, MD

Assistant Professor of Medicine
Transplant Nephrologist
Division of Renal Diseases and Hypertension
Department of Medicine
University of Minnesota
Minneapolis, MN, USA

Pamala A. Jacobson, PharmD

Associate Professor
University of Minnesota, College of Pharmacy
Minneapolis, MN, USA

Anthony M. Jevnikar, MD, MSc

Professor of Medicine, Surgery, Microbiology &
Immunology
Co-Director Multi Organ Transplant Program
University of Western Ontario
London, ON, Canada

Maryl R. Johnson, MD

Professor of Medicine
Medical Director, Heart Failure and Transplantation
University of Wisconsin School of Medicine and
Public Health
Madison, WI, USA

Guido Junge, MD, MBA

Vice President and Global Therapeutic Area Head
Infectious Disease and Transplantation
Novartis Pharma AG
Basel, Switzerland

Elizabeth A. Kallenborn, MSN, RN, CCTC

Clinical Manager
Liver Transplant and Hepatology
Thomas E. Starzl Transplantation Institute
University of Pittsburgh Medical Center
Pittsburgh, PA, USA

Bruce Kaplan, MD

Professor of Medicine, Microbiology, Molecular
Genetics and Immunology
University of Kansas Medical Center
Kansas, MO, USA;
Adjunct Professor of Medicine
Alberta Applied Genomics and Transplant Center
University of Alberta, Canada

Dixon B. Kaufman, MD, PhD

Ray Owen Professor and Chair
Division of Transplantation
University of Wisconsin School of Medicine and
Public Health
Madison, WI, USA

Daniel Kaul, MD

Associate Professor of Medicine
Director, Transplant Infectious Diseases
Division of Infectious Disease
University of Michigan School of Medicine
Ann Arbor, MI, USA

Tatsuo Kawai, MD, PhD

Associate Professor of Surgery
Harvard Medical School
A. Benedict Cosimi Endowed Chair in Transplant
Surgery
Massachusetts General Hospital
Boston MA, USA

Marwan Kazimi, MD

Director
Multivisceral and Intestinal Transplantation Program
Division of Transplant Surgery
Transplant Institute
Henry Ford Hospital
Detroit, MI, USA

Desmond Barry Keenan, PhD, MBA

Research Director and Technical Fellow
Closed Loop Development
Medtronic Diabetes
Northridge, CA, USA

Shaf Keshavjee, MD, MSc, FRCS, FACS

Surgeon-in-Chief, University Health Network
Professor, Division of Thoracic Surgery
Director, Toronto Lung Transplant Program
University of Toronto
Toronto, ON, Canada

Zain Khalpey, MD, PhD, MRCS(Eng)

Surgical Director of Heart Transplant and Mechanical Circulatory Support
Distinguished Tony Marnell Chair in Cardiothoracic Surgery
Surgical Director of Regenerative Medicine
Associate Professor of Surgery
Physiological Sciences & Biomedical Engineering
University of Arizona
Tucson, AZ, USA

Michael S. Kiernan, MD, MS

Assistant Professor of Medicine
Medical Director, Ventricular Assist Device Program
Tufts University School of Medicine
Boston, MA, USA

S. Joseph Kim

Division of Nephrology
Toronto General Hospital;
University Health Network and the Institute for Health Policy, Management and Evaluation
Faculty of Medicine
University of Toronto
Toronto, ON, Canada

Allan D. Kirk, MD, PhD, FACS

Professor and Chairman, Department of Surgery
Duke University School of Medicine;
Surgeon-in-Chief for Duke University Health System
Duke University Medical Center
Durham, NC, USA

Michelle M. Kittleson, MD, PhD

Assistant Clinical Professor of Medicine, UCLA
Director, Heart Failure Research
Director, Post-Graduate Education in Heart Failure and Transplantation
Cedars-Sinai Heart Institute
Los Angeles, CA, USA

Andrew Klein, MD, MBA, FACS

Director, Comprehensive Transplant Center
Esther and Mark Schulman Chair of Surgery and Transplant Medicine
Professor and Vice Chair
Department of Surgery
Cedars-Sinai Medical Center
Los Angeles, CA, USA

Christina L.M. Klein, MD

Assistant Professor of Medicine
Medical Director, Pancreas Transplant
Director, High Risk Kidney Transplant
Washington University in St. Louis
St. Louis, MO, USA

Stuart J. Knechtle, MD

Professor of Surgery
Emory University School of Medicine
Atlanta, GA, USA

Jon A. Kobashigawa, MD

DSL/Thomas D. Gordon Chair in Heart Transplantation Medicine
Director, Advanced Heart Disease Section
Director, Heart Transplant Program
Cedars-Sinai Heart Institute
Los Angeles, CA, USA

Chatchai Kreepala, MD

Clinical and Research Fellow
Alberta Transplant Applied Genomics Centre
Department of Medicine
Division of Nephrology and Transplant Immunology
University of Alberta
Edmonton, AB, Canada

Jill C. Krisl, PharmD

Transplant Pharmacy Fellow
Department of Surgery
Division of Transplantation
University of Cincinnati
Academic Health Center
Cincinnati, OH, USA

Aleksandra Kukla, MD

Assistant Professor of Medicine
Transplant Nephrologist;
Medical Director of Pancreas Transplant Program
Division of Renal Diseases and Hypertension
Department of Medicine
University of Minnesota
Minneapolis, MN, USA

Sunil M. Kurian, PhD

Staff Scientist
Laboratory of Functional Genomics
Department of Molecular and Experimental Medicine
The Scripps Research Institute
La Jolla, CA, USA

Keren Ladin, PhD, MSc

Director
Research on Ethics, Aging, and Community Health
Tufts University;
Assistant Professor
Department of Occupational Therapy
Tufts University
Medford, MA;
Department of Public Health and Community Medicine
Tufts University School of Medicine
Boston, MA, USA

Alan Langnas

Chief, Section of Transplant Surgery
University of Nebraska Medical Center
Omaha, NE, USA

Dianne LaPointe Rudow, ANP-BC, DNP, CCTC

Associate Professor
Department of Health Evidence and Policy
Director, Zweig Family Center for Living Donation
Medical Director of Liver and Kidney Donor Program
Recanati/Miller Transplant Institute
The Mount Sinai Medical Center
New York, NY, USA

Christian P. Larsen, MD, DPhil

Dean – Emory School of Medicine
Surgeon-in-Chief Emory Healthcare
Emory University
Atlanta, GA, USA

E. Clinton Lawrence, MD

Director, Andrew J. McKelvey Lung Transplant Center
Emory Transplant Center
Emory University Hospital;
Augustus J. McKelvey Professor of Lung Transplantation Medicine
Emory University School of Medicine
Department of Medicine
Division of Pulmonary, Allergy and Critical Care Medicine
Emory University
Atlanta, GA, USA

Daniel J. Lebovitz, MD

Associate Director, Critical Care
Akron Children's Hospital
Akron, OH;
Director, PICU
MetroHealth Medical Center
Cleveland OH;
Medical Director
Lifebank
Cleveland, OH, USA

Sung-Gyu Lee

Professor of Surgery
Hepato-Biliary Surgery and Liver Transplantation
Department of Surgery
Asan Medical Center
University of Ulsan College of Medicine
Seoul, Korea

W.P. Andrew Lee, MD

The Milton T Edgerton, MD, Professor and Chairman
Department of Plastic and Reconstructive Surgery
Johns Hopkins University School of Medicine
Baltimore, MD, USA

Soyoung Lee, MD

Research Fellow
Massachusetts General Hospital
Boston, MA, USA

Jason R. Lees, PhD

Assistant Professor
Department of Microbiology and Immunology
Uniformed Services of Health Sciences
Bethesda, MD, USA

Carmen Lefaucheur

Department of Nephrology and Kidney Transplantation and Research Unit INSERM U940
Hopital Saint Louis
Paris, France

Henri G.D. Leuvenink, PhD

Associate Professor
Principle Investigator, Experimental Transplantation
Surgical Research Laboratory
Department of Surgery
University Medical Center Groningen
Groningen, The Netherlands

Matthew H. Levine, MD, PhD

Assistant Professor of Surgery
Division of Transplant Surgery
Perelman School of Medicine
University of Pennsylvania
Philadelphia, PA, USA

Xian C. Li, MD, PhD, ASCI

Director
Immunobiology & Transplantation Research
Houston Methodist Hospital
Texas Medical Center
Houston, Texas

Sundus A. Lodhi, MD,

Assistant Professor
Transplant Nephrology
Emory University
Atlanta, GA, USA

Marc I. Lorber, MD

Sr. Vice President and Chief Medical Officer
XenoLung Clinical Development
Lung Biotechnology, Inc
United Therapeutics Corporation
Silver Spring, MD, USA

Richard S. Luskin, MPA

President and CEO
New England Organ Bank
Waltham, MA, USA

G. Marshall Lyon, MD, MMSc

Associate Professor of Medicine
Director of Transplant Infectious Disease
Emory University School of Medicine
Atlanta, GA, USA

Joren C. Madsen, MD, DPhil

Professor of Surgery
W. Gerald and Patricia R. Austen
Distinguished Scholar in Cardiac Surgery
Massachusetts General Hospital
Boston, MA, USA

Joseph F. Magliocca, MD

Assistant Professor of Surgery
Emory University School of Medicine
Atlanta, GA, USA

Sayed Malek, MD

Clinical Director, Division of Transplant Surgery
Brigham and Women's Hospital
Harvard Medical School
Boston, MA, USA

Roslyn B. Mannon, MD

Professor of Medicine and Surgery
University of Alabama at Birmingham
Birmingham, AL, USA

James F. Markmann, MD, PhD

Professor of Surgery
Harvard Medical School;
Chief, Division of Transplantation
Massachusetts General Hospital
Boston, MA, USA

Benjamin M. Martin, MD

Senior Resident, Department of Surgery
Emory University School of Medicine
Atlanta, GA, USA

Paulo Martins, MD, PhD

Instructor, Harvard Medical School
Clinical Fellow, Massachusetts General Hospital
Boston, MA, USA

Allan B. Massie, PhD

Department of Surgery
Johns Hopkins School of Medicine
Baltimore, MD, USA

Virginia A. McBride, RN, MPH

President
AMVAT Consulting
Grand Junction, CO, USA

Kenneth R. McCurry, MD

Staff Surgeon
CCF
Cleveland Clinic
Cleveland, OH, USA

Gwen McNatt, MS, RN, CNN, FNP-BC

Director, Operations
Kovler Organ Transplantation Center and Infectious
Disease
Northwestern Memorial Hospital
Chicago, IL, USA

Mandeep R. Mehra, MD

Brigham and Women's Hospital
Harvard Medical School
Boston, MA, USA

Aneesh K. Mehta, MD

Assistant Professor of Medicine
Assistant Director of Transplant Infectious Diseases
Emory University School of Medicine
Atlanta, GA, USA

Edward A. Meister, PhD

College of Medicine
Division of Nephrology
University of Arizona
Tucson, AZ, USA

Michael H. Mengel, MD

Associate Professor
University of Alberta
Edmonton, AB, Canada

Diana Metes, MD

Associate Professor of Surgery and Immunology
Starzl Transplantation Institute
Department of Surgery and Department of
Immunology
University of Pittsburgh School of Medicine
Pittsburgh, PA, USA

Charles M. Miller, MD

Professor of Surgery
Cleveland Clinic Lerner College of Medicine
Case Western Reserve University;
Director, Liver Transplant Program
Digestive Disease Institute
Cleveland Clinic
Cleveland, OH, USA

Marta I. Minervini, MD

Assistant Professor of Pathology
Department of Pathology
University of Pittsburgh Medical Center
Pittsburgh, PA, USA

Saeed Mohammad, MD, MS

Assistant Professor
Department of Pediatrics
Northwestern University Feinberg School of Medicine
Ann and Robert H. Lurie Children's Hospital of
Chicago
Chicago, IL, USA

Deok-Bog Moon

Professor of Surgery
Hepato-Biliary Surgery and Liver Transplantation
Department of Surgery
Asan Medical Center
University of Ulsan College of Medicine
Seoul, Korea

Christian Morath, MD

Department of Medicine
Division of Nephrology and Hypertension
University of Heidelberg
Heidelberg, Germany

Michael J. Moritz, MD

Chief, Transplant Services
Lehigh Valley Health Network
Allentown, PA;
Professor of Surgery
University of South Florida
Morsani College of Medicine
Tampa, FL, USA

Tim Morris

Director, Research Informatics
Research and Woodruff Health Sciences IT
Emory University
Atlanta, GA, USA

Cathi L. Murphey, PhD

Director, Histocompatibility and Immunogenetics
Laboratory
Southwest Immunodiagnostics, Inc.
San Antonio, TX, USA

Michael A. Nalesnik, MD

Professor of Pathology
Department of Pathology
University of Pittsburgh Medical Center
Pittsburgh, PA, USA

Jung-Man Namgoong

Clinical Instructor of Surgery
Hepato-Biliary Surgery and Liver Transplantation
Department of Surgery
Asan Medical Center
University of Ulsan College of Medicine
Seoul, Korea

Brian J. Nankivell, MD, PhD, FRACP

Transplant Physician
Department of Renal Medicine
Westmead Hospital
Sydney, NSW, Australia

Peter Neuhaus, MD, PhD

Chairman of General, Visceral, and Transplantation
Surgery
Experimental Surgery and Regenerative Medicine
Charité – Campus Virchow, Universitätsmedizin Berlin
Berlin, Germany

David C. Neujahr, MD

Medical Director
Andrew McKelvey Adult Lung Transplant Program
Emory University Transplant Center
Assistant Professor of Medicine, Pulmonary, Allergy
and Critical Care
Emory University School of Medicine
Atlanta, GA, USA

Kenneth A. Newell, MD, PhD

Professor of Surgery
Emory Transplant Center
Emory University School of Medicine
Atlanta, GA, USA

Silke Niederhaus, MD

Assistant Professor of Surgery
University of Maryland Medical System
Division of Transplantation
Baltimore, MD, USA

Seigo Nishida, MD

Department of Surgery, Division of Transplantation
University of Miami
Miami, FL, USA

Douglas J. Norman, MD

Professor of Medicine
Director, Transplant Medicine
Director, Laboratory of Immunogenetics and
Transplantation
Oregon Health & Science University
Portland, OR, USA

Rupert Oberhuber, MD

Division of Transplant Surgery and Transplant Surgery
Research Laboratory
Brigham and Women's Hospital
Harvard Medical School
Boston, MA;
Department of Visceral, Transplant and Thoracic
Surgery
Medical University of Innsbruck
Innsbruck, Austria

**Philip J. O'Connell, MBBS, PhD,
FRACP**

Professor and Director of Transplantation
University of Sydney at Westmead Hospital
Sydney, NSW, Australia

Jon S. Odorico, MD, FACS

Professor of Surgery
Director, Pancreas Transplantation
Co-director, Islet Transplantation
University of Wisconsin School of Medicine and
Public Health
Madison, WI, USA

John G. O'Grady, MD, FRCPI

Professor of Hepatology
Institute of Liver Studies
King's College Hospital
London, UK

Linda Ohler, MSN, RN, CCTC, FAAN

Quality and Compliance Manager
Georgetown Transplant Institute
Georgetown University Hospital
Washington, DC, USA

Toshihiro Okamoto, MD, PhD

Department of Thoracic and Cardiovascular Surgery,
Heart and Vascular Institute
Cleveland Clinic
Cleveland, OH, USA

Marc J. Overcash

Deputy Chief Information Officer
Assistant Dean, Information Technology
Emory University School of Medicine
Atlanta, GA, USA

Eugenia K. Page, MD

Surgical Resident
Emory University School of Medicine
Atlanta, GA, USA

John C. Papadimitriou, MD, PhD

Professor of Pathology
Director, Surgical Pathology
University of Maryland School of Medicine
Baltimore, MD, USA

Samir Parekh, MD

Assistant Professor of Medicine
Transplant Hepatology Fellowship Director
Emory University School of Medicine
The Emory Transplant Center
Atlanta, GA, USA

Steven M. Parnis, BS

Assistant Director, Center for Technology
Development
Texas Heart Institute
Houston, TX, USA

Stephen Pastan, MD

Medical Director, Kidney and Pancreas Transplant
Program
Emory Transplant Center
Associate Professor of Medicine
Emory University School of Medicine
Atlanta, GA, USA

Jignesh K. Patel, MD, PhD

Medical Director, Heart Transplant Program
Cedars-Sinai Heart Institute
Los Angeles, CA, USA

Thomas C. Pearson, MD, DPhil

Livingston Professor of Surgery
Emory University School of Medicine;
Executive Director
Director, Kidney Transplant Program
Emory Transplant Center
Atlanta, GA, USA

Alice Peng, MD

Associate Professor of Medicine
Medical Director
Pancreas Transplantation Program
Cedars-Sinai Medical Center
Los Angeles, CA, USA

Phuong-Chi T. Pham, MD

Professor of Medicine
David Geffen School of Medicine at UCLA
Olive View-UCLA-Medical Center
Chief, Division of Nephrology and Hypertension
Director, UCLA-OVMC Nephrology Training Program
Sylmar, CA, USA

Phuong-Thu T. Pham, MD

Professor of Medicine
David Geffen School of Medicine at UCLA
Department of Medicine, Nephrology Division
Director, Outpatient Services
Kidney Transplant Program
Los Angeles, CA, USA

Nicole A. Pilch, PharmD, MSCR, BCPS

Residency Program Director, PGY-2 Transplant
Residency Program
Clinical Specialist, Solid Organ Transplantation
Clinical Assistant Professor, Department of Pharmacy
and Clinical Sciences
South Carolina College of Pharmacy – MUSC Campus
Medical University of South Carolina
Department of Pharmacy Services
Charleston, SC, USA

Rutger J. Ploeg, MD, PhD, FRCS

Professor of Transplant Biology
University of Oxford;
Professor of Transplant Surgery
University of Groningen;
Honorary Consultant Transplant Surgeon
OUH NHS Trust
Nuffield Department of Surgical Sciences
Oxford, UK

Jennifer M. Porter, Esq

Partner, Gurne Porter, PLLC
Washington, DC, USA

Luke Preczewski

Administrative Director
Comprehensive Transplant Center
Northwestern University Feinberg School of Medicine
Chicago, IL, USA

Timothy L. Pruett, MD

John S. Najarian Clinical Chair
Professor of Surgery and Internal Medicine
University of Minnesota
Minneapolis, MN, USA

Cristiano Quintini, MD

Assistant Professor of Surgery
Cleveland Clinic Lerner College of Medicine
Case Western Reserve University
Liver Transplant Program
Digestive Disease Institute
Cleveland Clinic
Cleveland, OH, USA

Giorgio Raimondi, PhD

Department of Plastic and Reconstructive Surgery
Johns Hopkins School of Medicine
Baltimore, MD, USA

Raja Rajalingam, PhD

Professor of Clinical Surgery
Director of Immunogenetics and Transplantation
Laboratory
University of California, San Francisco
San Francisco, CA, USA

Parmjeet Randhawa, MD

Professor of Pathology
Department of Pathology
University of Pittsburgh Medical Center
Pittsburgh, PA, USA

Nathanael Raschzok, MD

General, Visceral, and Transplantation Surgery
Experimental Surgery and Regenerative Medicine
Universitätsmedizin Berlin
Berlin, Germany

Elaine F. Reed, PhD

Professor
Department of Pathology and Laboratory Medicine;
Director, UCLA Immunogenetics Center
David Geffen School of Medicine
University of California, Los Angeles
Los Angeles, CA, USA

John Adam Reich, MD

Instructor of Anesthesiology
Tufts University
Staff Anesthesiologist
Director, Post Anesthesia Care Unit
Tufts Medical Center
Boston, MA, USA

Scott A. Reule, MD

Nephrology Fellow
Division of Renal Diseases and Hypertension
Department of Medicine
University of Minnesota
Minneapolis, MN, USA

Camillo Ricordi, MD

Stacy Joy Goodman Professor of Surgery
Director, Cell Transplant Center and Diabetes
Research Institute
University of Miami
Miami, FL, USA

E. Rene Rodriguez, MD

Professor of Pathology
Director, Cardiovascular Pathology
Director, Autopsy Pathology
Department of Anatomic Pathology/L25
The Cleveland Clinic
Cleveland, OH, USA

Christin C. Rogers, PharmD, FCCP, BCPS

Clinical Pharmacy Coordinator – Solid Organ
Transplant
Beth Israel Deaconess Medical Center
Boston, MA, USA

Erin Rubin, MD

Associate Professor of Pathology
Department of Pathology
University of Pittsburgh Medical Center
Pittsburgh, PA, USA

Phillip Ruiz Jr, MD, PhD

Professor of Pathology and Surgery
Medical Director, Transplant Laboratories
University of Miami Miller School of Medicine
Miami, FL, USA

David H. Sachs, MD

Scientific Director, Transplantation Biology Research
Center
Massachusetts General Hospital;
Paul S Russel/Warner-Lambert Professor of Surgery
Harvard Medical School
Boston, MA, USA

Daniel R. Salomon, MD

Professor, Department of Molecular and Experimental
Medicine
Program Medical Director, Scripps Center for Organ
Transplantation
The Scripps Research Institute
La Jolla, CA, USA

Alberto Sánchez-Fueyo, MD, PhD

Institute of Liver Studies
School of Medicine
King's College London
Denmark Hill
London, UK

Chandrasekar Santhanakrishnan, MD

Assistant Professor of Clinical Surgery
Division of Transplant Surgery
Department of Surgery
University of California Davis Medical Center
Sacramento, CA, USA

Eizaburo Sasatomi, MD, PhD

Assistant Professor of Pathology
Department of Pathology
University of Pittsburgh Medical Center
Pittsburgh, PA, USA

Igor M. Sauer, MD

Chairman of Research
General, Visceral, and Transplantation Surgery
Experimental Surgery and Regenerative Medicine
Charité – Campus Virchow, Universitätsmedizin Berlin
Berlin, Germany

Deirdre Sawinski, MD

Assistant Professor of Medicine
Department of Medicine
University of Pennsylvania Perelman School of
Medicine
Philadelphia, PA, USA

Birgit Sawitzki

Institute of Medical Immunology
Charite University Medicine
Berlin, Germany

Franz Schaefer, MD

Professor of Pediatrics
Center for Pediatrics and Adolescent Medicine
University of Heidelberg
Heidelberg, Germany

Margaret Schaeffer, MS, MSHA, RN

Virginia Commonwealth University Health System
Medical College of Virginia Hospitals
Nurse Manager
Hume-Lee Transplant Center
Richmond, VA, USA

Peter Schemmer, MD, MBA

Department of Surgery
Division of Visceral and Transplantation Surgery
University of Heidelberg
Heidelberg, Germany

Stefan Schneeberger, MD

Department of Visceral, Transplant and Thoracic
Surgery
Innsbruck Medical University
Innsbruck, Austria;
Department of Plastic and Reconstructive Surgery
Johns Hopkins University School of Medicine
Baltimore, MD, USA

Jesse D. Schold, PhD

Associate Staff
Department of Quantitative Health Sciences
Cleveland Clinic
Cleveland, OH, USA

Kristine S. Schonder, PharmD

Assistant Professor
Pharmacy and Therapeutics
Clinical Pharmacist, Transplant
University of Pittsburgh School of Pharmacy
Thomas E. Starzl Transplantation Institute
Pittsburgh, PA, USA

Kathy Schwab, RN, BSN, CCTC

Compliance Coordinator
Mayo Clinic
Rochester, MN, USA

Dorry L. Segev, MD, PhD

Associate Vice Chair of Research
Associate Professor of Surgery
Associate Professor of Epidemiology
Johns Hopkins University
Baltimore, MD, USA

Gennaro Selvaggi, MD

Associate Professor of Clinical Surgery
University of Miami Miller School of Medicine
Miami Transplant Institute
Miami, FL, USA

Keyur B. Shah, MD

Virginia Commonwealth University;
Medical College of Virginia Hospital
Richmond, VA, USA

A.M. James Shapiro, MD, PhD, FRCS(Eng), FRCS(C), MSM, DSc, FRS(Canada)

Canada Research Chair in Transplantation Surgery and
Regenerative Medicine
Director, Clinical Islet Transplant Program
University of Alberta
Edmonton, AB, Canada

Ron Shapiro, MD

Professor of Surgery
Robert J. Corry Chair in Transplantation Surgery
University of Pittsburgh Medical Center
Thomas E. Starzl Transplantation Institute
Pittsburgh, PA, USA

Chris Shay-Downer, RN, BSN, CCTC

Transplant & Cardiac Program Director
BioScrip, Inc.
Elmsford, NY, USA

Jaimie T. Shores

Assistant Professor of Plastic Surgery
Department of Plastic and Reconstructive Surgery
Johns Hopkins University School of Medicine
Baltimore, MD, USA

William D. Simmons, RPh

US Medical
Novartis Pharmaceuticals Corporation
Madison, WI, USA

Daniel B. Sims, MD

Assistant Professor
Montefiore Medical Center
Albert Einstein College of Medicine
Bronx, NY, USA

Alan Slade, PharmD

Translational Medicine Director, Transplantation
Novartis Pharmaceuticals Corporation
East Hanover, NJ, USA

Richard G. Smith, MSEE

Director, Marshall Foundation Artificial Heart
Laboratory
University Medical Center
Tucson, AZ, USA

Andrew L. Smith, MD

Professor of Medicine
Medical Director, Heart Failure and Transplantation
Division of Cardiology
Emory University School of Medicine
Atlanta, GA, USA

Lonnie D. Smith, PharmD

Manager, Department of Solid Organ Transplant
Director, PGY-2 Pharmacy Residency – Transplant
University of Utah Hospitals and Clinics
Salt Lake City, UT, USA

Mark Schnitzler, PhD

Professor
St. Louis University School of Medicine
St. Louis, MO, USA

Hans W. Sollinger, MD, PhD

Folkert Belzer Professor
Division of Transplantation
University of Wisconsin School of Medicine and
Public Health
Madison, WI, USA

Lisa G. Sorensen, PhD

Assistant Professor of Clinical Psychiatry and
Behavioral Sciences
Northwestern University Feinberg School of Medicine;
Ann and Robert H. Lurie Children's Hospital of
Chicago
Chicago, IL, USA

James R. Spivey, MD

Associate Professor of Medicine and Surgery
Director of Hepatology
Medical Director, Liver Transplantation
Emory University School of Medicine
The Emory Transplant Center
Atlanta, GA, USA

Mark D. Stegall

Professor of Surgery and Immunology
Mayo Clinic
Rochester, MN, USA

Josef Stehlik, MD, MPH

Associate Professor of Medicine
University of Utah School of Medicine
Salt Lake City, UT, USA

Garry M. Steil, PhD

Research Scientist, Division of Medicine Critical Care
Boston Children's Hospital;
Assistant Professor of Pediatrics
Harvard Medical School
Boston, MA, USA

Neema Stephens, MD

Assistant Professor
Transplant Nephrology
University of Texas – San Antonio
San Antonio, TX, USA

Peter G. Stock, MD, PhD

Division of Transplant Surgery
University of California, San Francisco
San Francisco, CA, USA

Margaret L. Stuber, MD

Assistant Dean of Student Affairs for Career
Development and Well-Being
Vice Chair for Education in Psychiatry
Daniel X. Freedman Professor, Psychiatry and
Biobehavioral Sciences
David Geffen School of Medicine at UCLA
Los Angeles, CA, USA

Charles A. Su, BS

Graduate Student
Department of Immunology
Cleveland Clinic
Cleveland, OH, USA

Ram M. Subramanian

Assistant Professor of Medicine and Surgery
Emory University School of Medicine
Atlanta, GA, USA

Stuart C. Sweet, MD, PhD

W. McKim Marriott Professor of Pediatrics
Division of Pediatric Allergy, Immunology and
Pulmonary Medicine
Washington University School of Medicine
St. Louis, MO, USA

David J. Taber, PharmD, BCPS

Assistant Professor
Division of Transplant Surgery
Department of Surgery
Medical University of South Carolina
Charleston, SC, USA

Carmela D. Tan, MD

Assistant Professor
Department of Anatomic Pathology
The Cleveland Clinic
Cleveland, OH, USA

Akin Tekin, MD

Assistant Professor of Clinical Surgery
University of Miami Miller School of Medicine
Miami Transplant Institute
Miami, FL, USA

Paul I. Terasaki, PhD

Professor Emeritus
University of California, Los Angeles;
Terasaki Foundation
Los Angeles, CA, USA

Angus W. Thomson, PhD, DSc

Distinguished Professor of Surgery and Immunology
Starzl Transplantation Institute;
Department of Surgery and Department of
Immunology
University of Pittsburgh School of Medicine
Pittsburgh, PA, USA

Eric M. Tichy, PharmD, FCCP, BCPS

Clinical Pharmacy Specialist
Solid Organ Transplant
Director, PGY-2 Residency – Transplant
Yale-New Haven Hospital
Department of Pharmacy
New Haven, CT, USA

Paul L. Tso, MD

Associate Professor of Surgery
Emory University School of Medicine
Atlanta, GA, USA

Stefan G. Tullius, MD, PhD, FACS

Professor of Surgery, Harvard Medical School
Chief, Division of Transplant Surgery & Director,
Transplant Surgery Research Laboratory,
Brigham and Women's Hospital
Boston, MA, USA

Nicole A. Turgeon, MD, FACS

Assistant Professor of Surgery
Emory University Hospital
Atlanta, GA, USA

Alexandra P. Turner, MD

Abdominal Transplant Fellow
Emory Transplant Center
Department of Surgery
Emory University School of Medicine
Atlanta, GA, USA

Heth R. Turnquist, PhD

Assistant Professor of Surgery and Immunology
Starzl Transplantation Institute
Department of Surgery and Department of
Immunology
University of Pittsburgh School of Medicine
Pittsburgh, PA, USA

Andreas Tzakis, MD, PhD, Dhc

Director of Liver and Kidney Transplant
Cleveland Clinic Florida
Weston, FL, USA

Simon Urschel, MD

Assistant Professor of Pediatrics and Immunology
Department of Pediatrics
Alberta Transplant Institute
University of Alberta
Edmonton, AB, Canada

Parsia A. Vagefi, MD

Division of Transplant Surgery
Massachusetts General Hospital;
Harvard Medical School
Boston, MA, USA

Anna Valujskikh, PhD

Associate Staff, Department of Immunology
Cleveland Clinic
Cleveland, OH, USA

Ronald G. Van Valen

Sr. Global Program
Regulatory Director/Transplantation
Novartis Pharmaceuticals
East Hanover, NJ, USA

Robert S. Venick, MD

Assistant Professor of Pediatrics
David Geffen School of Medicine at UCLA
Los Angeles, CA, USA

Flavio Vincenti, MD

Professor of Clinical Medicine
University of California
San Francisco, CA, USA

Gus J. Vlahakes, MD

Professor of Surgery
Massachusetts General Hospital
Boston, MA, USA

Philip Y. Wai, MD

Assistant Professor of Surgery
Division of Intra-abdominal Transplantation
Department of Surgery
Loyola University Medical Center
Maywood, IL, USA

W. Dean Wallace, MD

Associate Professor
Chief, Pulmonary Pathology
Department of Pathology and Laboratory Medicine
David Geffen School of Medicine at UCLA
Los Angeles, CA, USA

Candace Wang, MD

Novartis Pharmaceuticals Corporation
East Hanover, NJ, USA

Rui Wang

The Transplant Institute and Center for Transplant
Outcomes and Quality Improvement
Beth Israel Deaconess Medical Center;
Harvard Medical School
Boston, MA, USA

Claire A. Watkins, MD, MS

Resident Physician in Cardiothoracic Surgery
University of Maryland School of Medicine
Division of Cardiac Surgery
Baltimore, MD, USA

Melissa Watson, MD

Clinical Fellow
Abdominal Multiorgan Transplantation Surgery
Cleveland Clinic
Cleveland, OH, USA

Jeff Weaver, MBA

Director, Data Solutions
Research and Woodruff Health Sciences IT
Emory University
Atlanta, GA, USA

Steven A. Webber, MBChB, MRCP

James C. Overall Professor and Chair
Department of Pediatrics
Vanderbilt University School of Medicine
Nashville, TN, USA

Allison B. Webber, MD

Assistant Clinical Professor of Medicine
University of California
San Francisco, CA, USA

Lori J. West, MD, DPhil, FRCPC

Professor of Pediatrics, Surgery and Immunology
Department of Pediatrics
Alberta Transplant Institute
University of Alberta
Edmonton, AB, Canada

David Wheeler, RRT

Anesthesia Institute
Cleveland Clinic
Cleveland, OH, USA

Marissa B. Wilck, MBChB

Assistant Professor
Department of Medicine
University of Pennsylvania
Philadelphia, PA, USA

Kathryn J. Wood, DPhil

Professor of Immunology
Transplantation Research Immunology Group
Nuffield Department of Surgical Sciences
John Radcliffe Hospital
Oxford, UK

E. Steve Woodle, MD, FACS

William A. Altemeier Chair in Surgery
Professor of Surgery
Director, Division of Transplantation
Director, Isreal Penn International Transplant Tumor
Registry
University of Cincinnati
Cincinnati, OH, USA

Jiangnan Xu, MD

Associate Professor
Capital Medical University
Beijing, China

Heidi Yeh, MD

Surgical Director
Pediatric Transplantation;
Instructor, Harvard Medical School
Assistant in Surgery, Massachusetts General Hospital
Boston, MA, USA

Jonathan C. Yeung, MD, PhD

Fellow in Thoracic Surgery
Toronto Lung Transplant Program
University Health Network
University of Toronto
Toronto, ON, Canada

Melissa Y. Yeung, MD, FRCPC

Instructor in Medicine
Transplantation Research Center
Brigham and Women's Hospital and Harvard Medical
School
Boston, MA, USA

Martin G. Zeier, MD, FASN

Head, Division of Nephrology
Heidelberg University Hospital
Heidelberg, Germany

Qiheng Zhang, PhD

Assistant Professor
Department of Pathology and Laboratory Medicine;
Associate Director
UCLA Immunogenetics Center
David Geffen School of Medicine,
University of California, Los Angeles
Los Angeles, CA, USA

Shelley Zomak, RN MS CCTC

Unit Director, Cardiothoracic Transplant
University of Pittsburgh Medical Center
Pittsburgh, PA, USA

SECTION 1

History/Introduction

Introduction

Allan D. Kirk

Duke University Medical Center, Durham, NC, USA

To understand organ transplantation is to understand all of modern medicine, and to practice organ transplantation is to comprehend the fundamental challenges of advanced healthcare delivery in general.

Although these introductory statements are biased by a lifetime of study and admiration of this field, they are not wholly derived of hyperbole. Indeed, when considered objectively, there are few serious students of medicine that would argue the principles they espouse.

Consider the most fundamental diagnosis of medicine: alive or dead. The objective determination of death has been conceived in large part in pursuit of ethical grounds for organ donation; the concepts of brain death are unarguably intertwined with clinical organ donation, and the transplant clinician must understand this most critical of states as much as anyone in any field. Similarly, beyond knowing what constitutes a living individual, the transplant professional is continuously defining where the individual resides by objectively demonstrating that most of *what* we are exists as parts in support of *who* we are. From a utilitarian standpoint, the vast majority of a person is replaceable! This concept is experienced in transplantation as a matter of fact, and the transplant professional's proximity to it provides a unique vantage point relative to other specialties. At a more granular level, the transplant (a term used to avoid distinguishing between scientists, surgeons, non-surgeons, and the numerous combinations thereof ubiquitous in the field of transplantation) uses biological definitions of individuality, namely molecular histocompatibility, as a daily tool of the trade. This fundamental biological characteristic has arisen through the study of transplantation and is as central to transplantation as brain death is to organ donation. From these high level examples, it is clear that the practicing transplant more regularly deals in rather heady biological concepts than many other professions. That same characteristic applies to the most difficult of ethical concepts, as transplanters, more than any other specialists, must grapple daily with very practical applications of beneficence, justice, and utility.

Beyond the high-level concepts discussed above, the delivery of transplantation has emerged in such a way as to solidify its location in the core of the day-to-day details of medical practice. The nature of transplantation has always been to treat those with end stage illness, and while the etiology of the disease in question may be organ system specific, the consequences of any organ disease requiring transplantation become systemic in end stage. As such, transplanters have always had to treat the entire patient simply as a matter of practicality. The patient in fulminant hepatic failure not

infrequently has critical brain, cardiopulmonary and renal dysfunction, as well. While these resolve when the underlying liver failure is reversed (in a way so dramatic as to have been unimaginable before the advent of liver transplantation), the transplant must understand these systems exceptionally well just to get the patient to the operation; he or she cannot be overly focused on an organ of choice. Similarly, given the complexity of post-transplant immunomodulatory management, the transplant's need to maintain a role in primary care and rehabilitation eclipses that of most subspecialties. As the need to stay involved for immune management has combined with improving life spans of transplant recipients, the understanding of long-term health maintenance required of the transplant far exceeds that required of any other subspecialist. The transplant surgeon knows far more about medical management of diabetes and hypertension than the general surgeon, and the transplant physician understands surgical complications and wound healing much better than their non-transplant counterparts. Additionally, patients with transplants get the same diseases as patients without transplants, and thus, any illness arising in a transplant recipient will (or at least should) involve a transplant at some level. A reciprocal effect of the growth and success of transplantation has impelled transplantation to be a core aspect of almost all subspecialties. One cannot consider himself or herself a fully trained cardiologist, endocrinologist, gastroenterologist, intensivist, hepatologist, nephrologist, pediatrician, pulmonologist, or surgeon without at least rudimentary knowledge of transplantation.

Transplant pharmacology similarly has driven pharmacology in general. The concept of therapeutic immune suppression derives from transplant applications and the first clinically approved monoclonal antibody (muromonab) and engineered biologic (daclizumab) were introduced in transplantation. As transplant pharmacology is with rare exception, poly-pharmacy, the role of the clinical pharmacist has been a long-standing feature of transplant care delivery, a model that many other areas have since adopted.

The means by which transplantation has been practiced is turning out to be prophetic for healthcare's ongoing evolution. Transplantation has always been a multidisciplinary craft, as evidenced by the inclusive nature of the depiction of the first successful transplant (see Figure 1.5, Chapter 1). From the start of the field, surgeon and non-surgeon physicians, nurses, allied health professionals, and basic scientists have mingled with a symbiotic fluidity that has typically exceeded that in other fields of medicine. Transplantation has not *become* a team sport, it *always has been* a team

sport, and as such has stood as a tested example of the way forward for healthcare delivery. At a higher hierarchical level, transplantation has long ago adopted means of healthcare delivery that are just now emerging as vogue: elements of accountable care networks, capitated payment plans, pay for performance agreements, public/private partnerships, and rationing algorithms have been in place for transplantation for decades, and again, other fields of medicine can look to transplantation as a source for data on how these health services models are likely to perform.

In a similar vein, transplantation has led the way in terms of keeping track of outcomes on a local and national level, using these data to provide objective means of charting the future. The limited availability of donors and the life-or-death nature of the diseases treated, no doubt, have stimulated the desire to measure and improve the field. While other fields may have differences in the degree of these basic restraints (scarcity and severity) at some level they are applicable, and the model of transplant clinical databases has much to teach other areas of medicine. Transplantation has been aggressive in reporting its complications, and this has led to fundamental revelations in the biology of cancer, infectious diseases, metabolic syndrome, and numerous conditions. Basic physiology has also derived incalculably from the natural experiment of organ replacement.

With all this said, the breadth and depth of content implied by a textbook aiming to cover organ transplantation as a whole might be considered daunting. However, it is no more so than the challenges routinely faced in our field: replacing one person's heart with that of another, operating within the Venn diagrams of allo- and protective immunity, ethically allocating scarce donor organs, paying for it all . . .

Thus, this textbook has been created with the opening sweeping statements at its heart. It is not meant to cover everything to its maximal depth (there are texts dedicated exclusively to each of most of the topics covered in this text), but rather is designed to provide a reasonable introduction to most of what transplanter's do. It is arranged with topics presented in an order that a clinician might encounter them. Basic concepts are presented first, moving from requisite historical and general scientific concepts to transplant-specific biology and the fundamental principles of alloimmunity and immune modulation. Beginning, as do all transplants, with donor considerations, the clinical sections of the text then proceed through pre-operative, operative, and post-operative topics. Each of these sections contain chapters specific to the major organ systems presented in order of clinical volume: kidney, liver, heart, lung, pancreas and islet, intestinal and multivisceral, and in selected areas, vascularized composite transplantation. Within the pre-operative section, specific chapters related to the complex management of critically ill patients with end stage organ disease are presented, including intensive care and artificial life support devices. A technique for each major operation is presented in the operative section, acknowledging that there are numerous ways to do everything. The goal is to provide the fundamental starting point for the surgeon, and a reasonable idea of the scope of a procedure for the non-surgeon. The postoperative section includes organ specific post-transplant management, including acute and chronic management issues, as well as substantial attention to immune management and its consequences, particularly infectious and malignant complications. Rejection, being a central diagnosis

driving much of a patient's post-operative care, is presented in two ways: from its organ-specific histopathological definition, and from an organ-specific clinical management vantage. The postoperative section ends with current accountings of long-term outcomes for each transplanted organ type.

We have chosen to provide a specific section dedicated to pediatric transplantation. While much of the biology and conduct mirrors that of adult transplantation, there are numerous areas, particularly related to indications, technical nuances and complications that clearly are unique to children. Indeed, the pediatrician will find the pediatric section to be a very satisfactory primer for transplantation in children in and of itself, complete with its own introductory comments.

As discussed above, the infrastructure and organizational requirements, ethical principles, and administrative guidelines for transplantation are exceptional examples of similar issues now facing the healthcare community at large. As such, the Textbook closes with sections dealing with these issues, both to provide the student of transplantation with transplant-specific knowledge of "how things get done", and to provide the general student of an example of how they might be done in other fields.

The overall goal of this textbook is to bring together a reasonable representation of modern transplantation in all its complexity into a single place. It is anticipated that there are several settings in which such a reference work will be useful. For the graduate or medical student, resident, or allied health trainee, this will serve as a centralized touchstone to help them orient their thoughts and prepare for rotations in transplantation. For non-transplant professions whose practice involves the care of patients awaiting or following a transplant, such as cardiologists, endocrinologists, gastroenterologists, hepatologists, nephrologists and pulmonologists, this will provide sufficient information to help in following patients and understanding when referral is prudent. Indeed, there are two chapters specifically directed toward the concerns of the community physician. For the established transplanter, the knowledge here will be useful when considering aspects of transplantation not typically encountered: for example information about heart transplantation for a kidney transplanter; clinical information for the basic scientist (or vice versa); or background information about a topic to aid in the interpretation of an article in the primary literature. Finally, for the transplant unit or hospital administrator, the content herein will provide substantial subject matter information helpful in organizing and staffing transplant cost centers, and understanding the contribution margins and risks derived from clinical transplant practices.

This first edition has emerged slowly, hindered somewhat by the substantial inertia of its scope. At some point, completeness has given way to practicality, and it is hoped that this same property will aid in its continuation—it is not, and may never be, "done". As the Textbook will be published in an electronic format, it will allow for continuous updates, and it is planned that approximately 10% of the content will be updated annually, making this a perpetually current resource. It will not replace the primary literature, but will be a constant source of information on which to base readings from the primary literature. Future enhancements linking the Textbook directly to the primary literature, particularly journals published by Wiley-Blackwell, are underway, and should provide a new paradigm for textbook utility.

A Brief History of Clinical Organ Transplantation

Sir Roy Y. Calne

Professor Emeritus, Cambridge University, Cambridge, UK

Introduction

Transplantation is one of the most visible and influential medical accomplishments of the twentieth century. Arising from technical advances and insights of the early twentieth century, the concept that transplantation was technically feasible gave rise to earnest investigations into its physiological barriers by a small number of visionary investigators driven by recognized clinical problems. From their descriptions of the genetic and immunological basis for graft rejection and the pioneering work of the first transplant surgeons, the clinical practice of transplantation rapidly became interwoven into the fabric of clinical care, not only from a practical standpoint but also as an example of the immense possibilities and challenges inherent in advanced medical practice. Multiple concepts now taken for granted in modern medical practice, such as immunosuppression, monoclonal antibody use, and indeed the concept of death as a definable state, have their origins in transplantation. Numerous modern ethical quandaries also trace their roots to problems introduced by transplantation.

The history of transplantation has been the subject of numerous books, and while its in-depth treatment is not practical in this text, it is important to make evident the major contributions that brought the field to where it stands currently: a prime example of the power of science and medicine combined for a common good. This chapter will provide the reader with a reasonable orientation to the history of the field, referring to more definitive works when necessary and to other chapters in this text. In doing so it will serve as an important introduction to the subject of organ transplantation in general. Throughout this textbook, more specific historical references will be introduced in individual chapters.

The concept of transplant surgery

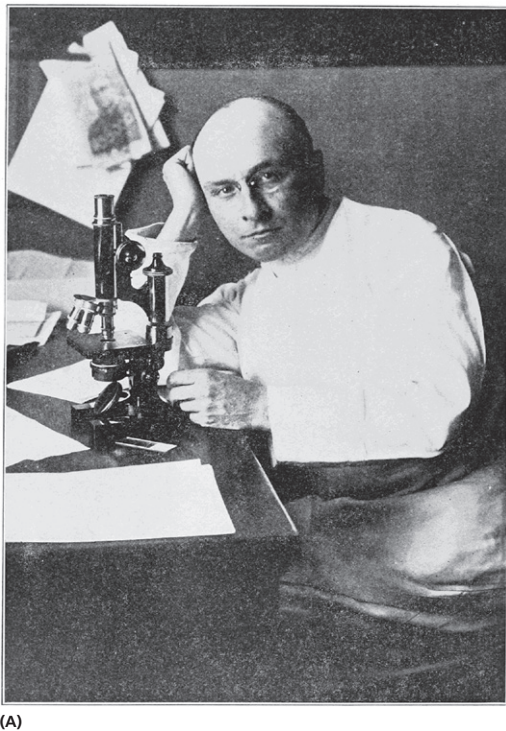
The idea of organ transplantation is a surgical concept based on an understanding of anatomy and the physiological requirements of an organ to stay viable and fulfil its biological role. Its origins relate to intuitive concepts of like replacing like that date back hundreds of years, including the oft cited Catholic miracle of Cosmos and Damian. However, its serious pursuit arose independently from work conducted in a number of European countries in the early twentieth century, the products of which led to the kidney as the chief candidate for speculations on organ transplantation. Kidney failure was a relatively common fatal condition, the physiological role of the kidney was understood and the kidneys were well defined anatomically. Importantly, it was recognized that one well-

functioning organ was sufficient to maintain an individual in good health for a normal lifespan. The kidney's essential anatomical connections, namely a single artery and vein and a urinary drainage vessel, were apparently sufficient for it to perform its physiological role. Nerves, lymphatic and fascial connections, although important, did not seem to be essential. At the beginning of the twentieth century, Alexis Carrel (Figure 1.1) devised a method of joining blood vessels together surgically [1], a technique that became the subject of his 1912 Nobel Prize in Physiology or Medicine. Carrel himself used this technique to show that a kidney could be removed and transplanted and would function after restoration of the arterial in-flow and venous out-flow, provided these surgical procedures were undertaken expeditiously, since a prolonged period without a blood circulation led to irreversible damage from ischaemia.

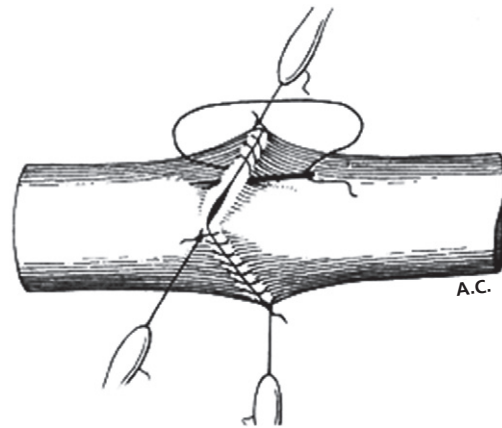
In cats and dogs Carrel and Guthrie proved the technical feasibility of the operation and also observed that moving a kidney from an animal to another site in the same animal could result in long-term survival of the kidney and the animal after removal of the opposite kidney [2]. However, transplanting a kidney from one individual to another, after a short period of satisfactory kidney function, was soon doomed to failure. Carrel recorded this observation, but at that time there was no explanation for the fairly rapid failure of what are now called renal allografts [3]. Priority for the transplantation of a kidney in a human patient has been claimed and disputed by a number of surgeons and their historians. Transplants to the brachial or femoral vessels of human kidneys or animal kidneys to humans were described. The early claims and a critical discussion of these unsuccessful experiments can be found in Dr. Francis Moore's book *Transplant* [4]. None of them functioned for a long period of time and with hindsight the procedures were premature in relation to the knowledge that was gradually accumulating from Carrel and Guthrie's experiments.

Transplant biology

In the 1940s and 50s, Morten Simonsen in Denmark and William Dempster in London independently described experiments similar in nature to those of Carrel and Guthrie and long-term, life-sustaining function of autografts was confirmed. However, experimental allografts were shown to fail universally and a second kidney transplanted from the same donor to the same recipient was destroyed almost instantaneously. These observations were the culmination of many years of painstaking research by Simonsen and Dempster, who also reported on the use of cortisone in renal



(A)



(B)

Figure 1.1. (A) Alexis Carrel, widely considered the father of surgical transplantation for his development of (B) the techniques for vascular anastomoses, an accomplishment recognized by the 1912 Nobel Prize in Physiology or Medicine.

allograft recipients. Both workers described histological changes that occurred in renal allografts. The renal cortex became infiltrated with neutrophils, eosinophils, macrophages, lymphocytes and pyronin-positive plasma cells, and these inflammatory changes were accompanied by necrosis of nephrons. Both Simonsen and Dempster felt that it was likely that the cells originated from the grafted organ and were in fact a graft-against-host reaction [5,6]. Subsequently, using a newly developed isotope labelling technique it was shown by Porter and Calne that most of the infiltrated cells came from the recipient [7].

At the time that these experiments were being performed by Simonsen and Dempster in canine renal allografts, Peter Medawar (Figure 1.2) and his colleagues had studied the biology of rejection of skin grafts in rabbits and mice. The first set of grafts became infiltrated with leukocytes after a few days, the graft becoming necrotic after 7–10 days. A second set of grafts from the same donor were usually destroyed immediately and never achieved a capillary circulation. They were called ‘white grafts’. The immune nature of skin graft rejection was proved beyond doubt by Medawar’s group [8], and from their experiments it seemed likely that kidney grafts between identical twins would behave like skin grafts between identical twins and, provided the surgery was satisfactory, would be accepted without any immune reaction. From this scientifically established basis reciprocal skin grafting should differentiate identical from non-identical cattle twins, and Medawar and his colleagues were confident that this would be straightforward. However, they were astonished, and presumably initially disappointed, when the non-identical cattle twins accepted skin grafts in the same way that grafts were accepted between identical cattle twins [9]. They became aware of studies of non-identical cattle twins by Ray Owen who had observed that non-identical cattle twins frequently had blood

groups of more than one type, circulating in apparently healthy animals [10]. This would be equivalent to a human having some red cells Group A and some Group B, which was known not to occur because of natural antibodies. Owen described the unusual status of their red cells blood groups as ‘chimeric’ from the fanciful resemblance to the mythical ancient Greek animal with organs derived from different species (Figure 1.3).

Medawar and his colleagues, Billingham and Brent, then set about performing a series of carefully controlled experiments between inbred strains of mice. The individuals of each strain after many sibling matings would be regarded as identical or ‘isologous’ individuals, so skin grafts were accepted between members of each inbred strain. However, grafts from a given strain transplanted into individuals of a different strain would be rejected, by what was later called the ‘allograft’ reaction.

Based on these observations in the cattle twins, Medawar’s group found that injecting cells from one inbred strain into the foetus of another strain, although a formidable technical achievement, resulted in some survivors, which were then rendered ‘tolerant’ to grafts from the strain that donated the tissue (Figure 1.2B) [11]. They later found that this tolerance could also be reproduced with neonatal animals, where the technical challenges were still grave but less demanding than in the foetus. This discovery of ‘specific immunological tolerance’ was awarded the Nobel Prize in Medicine or Physiology and was a fundamental advance in immunology and also raised the practical question of whether the plasticity of the developing foetal immunological system could be reproduced in an adult, at least temporarily while a graft was performed, although it would be important that normal immunity would later be restored. Another factor of importance observed by Medawar’s group was that if lymphocytes were included in the donor inoculum they