



# The AST Handbook of Transplant Infections

EDITED BY

**Deepali Kumar MD MSc FRCPC**

Transplant Infectious Diseases  
University of Alberta  
Edmonton  
Canada

**Atul Humar MD MSc FRCPC**

Transplant Infectious Diseases  
University of Alberta  
Edmonton  
Canada

## **Associate Editors**

Emily Blumberg MD  
Marian G. Michaels MD, MPH  
Kieren Marr MD

On behalf of The American Society of Transplantation  
Infectious Diseases Community of Practice

 **WILEY-BLACKWELL**

A John Wiley & Sons, Ltd., Publication



*This page intentionally left blank*

---

## **The AST Handbook of Transplant Infections**

## **Disclaimer**

This Document is provided for informational and general educational purposes only. This Document should not be used in place of professional medical advice and is not intended to be a substitute for consultation with or treatment by a medical professional. This Document is an educational tool designed only to enhance and support the treatment and education process. This Document should not be substituted for specific medical advice or instruction by a physician, nurse or pharmacist.

---

# The AST Handbook of Transplant Infections

EDITED BY

**Deepali Kumar MD MSc FRCPC**

Transplant Infectious Diseases  
University of Alberta  
Edmonton  
Canada

**Atul Humar MD MSc FRCPC**

Transplant Infections Diseases  
University of Alberta  
Edmonton  
Canada

## **Associate Editors**

Emily Blumberg MD  
Marian G. Michaels MD, MPH  
Kieren Marr MD

On behalf of The American Society of Transplantation  
Infectious Diseases Community of Practice

 **WILEY-BLACKWELL**

A John Wiley & Sons, Ltd., Publication



This edition first published 2011, © 2011 by Blackwell Publishing Ltd

Blackwell Publishing was acquired by John Wiley & Sons in February 2007. Blackwell's publishing program has been merged with Wiley's global Scientific, Technical and Medical business to form Wiley-Blackwell.

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](http://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 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. This publication is designed to provide accurate and authoritative information in regard to the subject matter covered. 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 physicians 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*

The AST handbook of transplant infections / edited by Deepali Kumar, Atul Humar ; associate editors, Emily Blumberg, Marian Michaels, Kieren Marr ; on behalf of the American Society of Transplantation Infectious Diseases Community of Practice.

p. ; cm.

Handbook of transplant infections

Includes bibliographical references and index.

ISBN 978-0-470-65827-7 (pbk. : alk. paper) 1. Communicable diseases—Handbooks, manuals, etc. 2. Transplantation of organs, tissues, etc.—Complications—Handbooks, manuals, etc. I. Kumar, Deepali. II. Humar, Atul. III. American Society of Transplantation. Infectious Diseases Community of Practice. IV. Title: Handbook of transplant infections.

[DNLM: 1. Transplants—adverse effects—Handbooks. 2. Bacterial Infections—therapy—Handbooks. 3. Mycoses—therapy—Handbooks. 4. Virus Diseases—therapy—Handbooks. WO 39]

RC112.A88 2011

616.9'8—dc22

2011002978

ISBN: 9780470658277

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

This book is published in the following electronic formats: ePDF 9781444397925; Wiley Online Library 9781444397949; ePub 9781444397932

Set in 9/12pt Meridien by MPS Limited, a Macmillan Company, Chennai, India

# Contents

List of Contributors, ix

Preface, xiii

Acknowledgements, xv

## **Part 1 General Issues and Infectious Syndromes, 1**

- 1** Timeline of Infections After Organ Transplant, 3  
*Christian van Delden*
- 2** Timeline of Infections After Hematopoietic Stem Cell Transplant, 4  
*Sarah P. Hammond & Francisco M. Marty*
- 3** Immune Reconstitution After Myeloablative Stem Cell Transplant, 5  
*Sarah P. Hammond & Francisco M. Marty*
- 4** Pre-transplant Infectious Disease Evaluation of the Organ Transplant Candidate, 6  
*Staci A. Fischer*
- 5** Pre-transplant Infectious Disease Evaluation of the Hematopoietic Stem Cell Transplant Candidate, 8  
*Staci A. Fischer*
- 6** Technical Complications after Organ Transplant and Associated Infections, 9  
*Abhinav Humar*
- 7** Evaluation and Initial Treatment of Infectious Complications Among Organ Transplant Recipients, 11  
*Kathleen Julian*
- 8** Management of Infections in Kidney Transplant Recipients, 20  
*Bartholomew Bono*
- 9** Management of Infections in Pancreas Transplant Recipients, 22  
*Bartholomew Bono*
- 10** Management of Infections in Liver Transplant Recipients, 23  
*Bartholomew Bono*
- 11** Management of Infections in Lung, Heart–Lung, and Heart Transplant Recipients, 25  
*Shahid Husain & S.M. Hosseini-Mogaddham*
- 12** Management of Infections in Intestinal Transplant Recipients, 29  
*Michael Green*

- 13** Antimicrobial Management of Patients with Fever and Neutropenia Following Hematopoietic Stem Cell Transplantation, 31  
*Upton D. Allen*

## **Part II Specific Pathogens, 33**

- 14** Cytomegalovirus, 35  
*Raymund R. Razonable & Atul Humar*
- 15** Epstein-Barr Virus and Post-transplant Lymphoproliferative Disorders, 42  
*Rebecca Madan & Betsy Herold*
- 16** Management of herpes simplex virus, 45  
*Marian G. Michaels*
- 17** Management of Varicella Zoster Virus, 47  
*Marian G. Michaels*
- 18** Prevention and Treatment of Human Herpesvirus 6, 7 and 8 Infections in Transplant Recipients, 49  
*Raymund R. Razonable*
- 19** BK Polyomavirus and Polyomavirus-associated Nephropathy, 51  
*Hans H. Hirsch*
- 20** Respiratory Viruses, 55  
*Oriol Manuel*
- 21** Human Papillomavirus, 59  
*Gail E. Reid*
- 22** Hepatitis B, 61  
*Karen E. Doucette*
- 23** Hepatitis C Management in Transplant Candidates and Recipients, 63  
*Karen E. Doucette*
- 24** Management Algorithm for Transplantation in Patients with Human Immunodeficiency Virus, 64  
*Shirish Huprikar*
- 25** Management of Selected Fungal Infections After Transplantation, 68  
*Michele I. Morris*
- 26** Treatment of *Nocardia* Infections, 73  
*Nina M. Clark*
- 27** Tuberculosis: Treatment and Prevention, 74  
*Nina M. Clark*
- 28** Treatment of Non-tuberculous *Mycobacterium* Infections, 77  
*Nina M. Clark*
- 29** *Pneumocystis jiroveci* Pneumonia: Prophylaxis and Therapy, 79  
*Nicolas J. Mueller*
- 30** Suggested Therapy of *Clostridium difficile* Colitis After Transplantation, 80  
*Aneesh K. Mehta*



- 31** Diagnosis and Treatment of Multidrug-Resistant Bacteria, 81  
*Emily A. Blumberg*
- 32** Management of Selected Parasitic Infections After Transplant, 84  
*Sanjay Mehta & Robert Huang*

### **Part III Donor Issues, 87**

- 33** Infectious Disease Evaluation of the Potential Organ Donor, 89  
*Staci A. Fischer*
- 34** Infectious Disease Evaluation of the Potential Hematopoietic Stem Cell Transplant Donor, 91  
*Staci A. Fischer*
- 35** Donor-derived Infections, 93  
*Michael G. Ison*
- 36** Estimates of Window Period Length for Serology and Nucleic Acid Testing, 97  
*Atul Humar*
- 37** Estimates of Residual Risk of HIV or HCV when using Selected Increased Risk Donor Categories, 98  
*Atul Humar*
- 38** Management of Recipients of Hepatitis B Core Antibody-Positive Donor Organ, 99  
*Karen E. Doucette*
- 39** Donor Tuberculosis Issues: Potential Scenarios and Management, 100  
*Camille N. Kotton & Michele I. Morris*

### **Part IV Prevention of Infections after Transplantation, 103**

- 40** Suggested Prophylaxis Regimens in Organ Transplant Recipients, 105  
*Nasia Safdar, Germana L.M. Silva & Jennifer Hsu*
- 41** Antimicrobial Prophylaxis Regimen for Allogeneic Hematopoietic Stem Cell Transplant Recipients, 107  
*Sherif Mossad*
- 42** Antimicrobial Prophylaxis Regimen for Autologous Hematopoietic Stem Cell Transplant Recipients, 109  
*Sherif Mossad*
- 43** Adult Vaccination Schedule After Solid Organ Transplant, 110  
*Marissa Wilck & Lindsey Baden*
- 44** Adult Vaccination Schedule After Allogeneic Stem Cell Transplant, 113  
*Lindsey Baden & Marissa Wilck*
- 45** Immunizations After Pediatric Solid Organ Transplant and Hematopoietic Stem Cell Transplant, 116  
*Tanvi Sharma & Lynne Lewis*
- 46** Recommendations for Travel-related Vaccinations and Medications for Transplant Travelers, 120  
*Camille N. Kotton*

- 47** Safe Living Strategies for Transplant Patients, 123  
*Julia Garcia-Diaz & Shannon Bergeron*

**Part V Post-transplant Medications and Drug Interactions, 127**

- 48** Common Immunosuppressive Drugs, Mechanisms of Action, Side-effects, and Other Interactions, 129  
*Daniel Kaul*
- 49** Infectious Risks Associated with Anti-thymocyte Globulin (ATG, Thymoglobulin), 131  
*Steven D. Burdette*
- 50** Infectious Risks Associated with Alemtuzumab (Campath), 133  
*Steven D. Burdette*
- 51** Infectious Risks Associated with IL-2R Antagonist [Basiliximab (Simulect) and Daclizumab (Zenapax)], 135  
*Steven D. Burdette*
- 52** Infectious Risks Associated With Rituximab (Rituxan), 136  
*Steven D. Burdette*
- 53** Drug Interactions Between Antimicrobial Agents and Common Immunosuppressive Drugs Used in Transplantation, 137  
*Christian Garzoni*
- 54** Antiviral Agents for Adult Transplant Recipients, 140  
*Valentina Stosor*
- 55** Antifungal Agents in Adult Transplant Recipients, 146  
*Shmuel Shoham*
- 56** Antiviral Agents for Pediatric Transplant Recipients, 150  
*Lara Danziger-Isakov, Lizbeth Hansen & Elizabeth Neuner*
- 57** Antifungal Agents for Pediatric Transplant Recipients, 158  
*Lara Danziger-Isakov, Lizbeth Hansen & Elizabeth Neuner*

Index, 165

# List of Contributors

**Upton D. Allen MBBS, MSc, FAAP, FRCPC, FRCP (UK)**

Professor, Departments of Paediatrics and Health Policy Management and Evaluation  
University of Toronto  
Division Head, Infectious Diseases  
The Hospital for Sick Children  
Toronto, Canada

**Lindsey R. Baden MD**

Division of Infectious Disease  
Brigham and Women's Hospital  
Dana Farber Cancer Institute  
Boston, MA, USA

**Emily A. Blumberg MD**

Professor of Medicine  
Division of Infectious Diseases  
University of Pennsylvania School of Medicine  
Philadelphia, PA, USA

**Bartholomew Bono MD**

Program Director, Infectious Disease  
Albert Einstein Healthcare Network  
Philadelphia, PA, USA

**Steven D. Burdette MD, FIDSA**

Infectious Diseases Fellowship  
Director & Associate Professor of Medicine  
Infectious Disease Advisor to Miami Valley Hospital Transplant Program  
WSU Boonshoft School of Medicine  
Dayton, OH, USA

**Nina M. Clark MD**

Associate Professor  
Department of Internal Medicine  
University of Illinois at Chicago  
Chicago, IL, USA

**Lara Danziger-Isakov MD, MPH**

Staff, Center for Pediatric Infectious Diseases; Director for Pediatric Clinical Research  
The Children's Hospital at Cleveland Clinic  
Assistant Professor of Pediatrics  
Cleveland Clinic Lerner College of Medicine at CWRU  
Cleveland, OH, USA

**Karen Doucette MD, MSc (Epi), FRCPC**

Associate Professor, Division of Infectious Diseases  
Education Director, Transplant Infectious Diseases Fellowship  
University of Alberta  
Edmonton, AB, USA

**Staci A. Fischer MD, FACP, FIDSA**

Associate Professor of Medicine  
The Warren Alpert Medical School of Brown University  
Director, Transplant Infectious Diseases  
Rhode Island Hospital  
Providence, RI, USA

**Julia Garcia-Diaz MD, MS, FACP**

Department of Infectious Diseases  
Ochsner Clinic Foundation  
New Orleans, LA, USA

**Christian Garzoni MD**

University Clinic for Infectious Disease  
Bern University Hospital, Inselspital  
Bern, Switzerland

**Michael Green MD, MPH**

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

**Sarah P. Hammond MD**

Instructor of Medicine  
Harvard Medical School  
Division of Infectious Diseases  
Brigham and Women's Hospital  
Boston, MA, USA

**Lizbeth Hansen**

Cleveland Clinic  
Lerner College of Medicine at CWRU  
Cleveland, OH, USA

**Betsy Herold MD**

Professor, Department of Pediatrics (Infectious Diseases)  
Professor, Department of Microbiology & Immunology  
Professor, Department of Obstetrics & Gynecology and Women's Health  
Albert Einstein College of Medicine  
New York  
NY, USA

**Hans H. Hirsch MD, MSc, FMH (Inf Diseases), FMH (Internal Medicine), FAMH (Medical Microbiology)**

Acting Director, Institute for Medical Microbiology  
Department of Biomedicine  
University of Basel, and  
Attending Physician,  
Division of Infectious Diseases & Hospital Epidemiology  
University Hospital Basel  
Basel, Switzerland

**S.M. Hosseini-Mogaddham**

Urology and Nephrology Research Center (UNRC)  
Shahid Beheshti University  
Tehran, Iran

**Jennifer Hsu MD**

Division of Infectious Diseases  
Department of Medicine  
University of Wisconsin School of  
Medicine and Public Health  
Madison, WI, USA

**Robert Huang MD**

Department of Medicine  
Division of Infectious Diseases  
University of California at San Diego  
La Jolla, CA, USA

**Abhinav Humar MD**

Professor, Department of Surgery  
Clinical Director, Starzl Transplant  
Institute  
University of Pittsburgh  
Pittsburgh, PA, USA

**Shirish Huprikar MD**

Director, Transplant Infectious Diseases  
Program  
Associate Professor, Department of  
Medicine  
Mount Sinai School of Medicine  
New York, NY, USA

**Shahid Husain MD, MS**

Assistant Professor of Medicine  
Director, Transplant Infectious  
Diseases  
Division of Infectious Diseases and  
Multi-organ Transplantation  
University Health Network/University  
of Toronto  
Toronto, Canada

**Michael G. Ison MD MS**

Assistant Professor, Divisions of  
Infectious Diseases and Organ  
Transplantation  
Northwestern University Feinberg  
School of Medicine  
Medical Director, Transplant &  
Immunocompromised Host  
Infectious Diseases Service  
Northwestern University  
Comprehensive Transplant Center  
Chicago, IL, USA

**Kathleen Julian MD**

Assistant Professor of Medicine  
Division of Infectious Diseases  
Penn State Hershey Medical Center  
Hershey, PA, USA

**Daniel Kaul MD**

Director, Transplant ID Service  
Division of Infectious Disease  
University of Michigan Medical School  
Ann Arbor, MI USA

**Camille Nelson Kotton MD**

Clinical Director, Transplant and  
Immunocompromised Host Infectious  
Diseases  
Infectious Diseases Division  
Massachusetts General Hospital and  
Assistant Professor  
Harvard Medical School  
Harvard University  
Boston, MA, USA

**Lynne Lewis RN, MS, CPHP**

Coordinator, Division of Pediatric  
Infectious Diseases  
Section on Immunocompromised Hosts  
Children's Hospital Boston  
Boston, MA, USA

**Rebecca P. Madan MD, MSc**

Assistant Professor  
Division of Pediatric Infectious Diseases  
Albert Einstein College of Medicine  
New York, NY, USA

**Oriol Manuel MD**

Infectious Diseases Service and  
Transplantation Center  
University Hospital Center (CHUV) and  
University of Lausanne  
Lausanne, Switzerland

**Francisco M. Marty MD**

Division of Infectious Disease  
Brigham and Women's Hospital  
Boston, MA, USA

**Sanjay R. Mehta MD, DTM&H**

Assistant Clinical Professor of Medicine  
Division of Infectious Diseases  
University of California  
San Diego, CA, USA

**Aneesh K. Mehta MD**

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

**Marian G. Michaels MD, MPH**

Professor of Pediatrics and Surgery  
University of Pittsburgh School of  
Medicine  
Children's Hospital of Pittsburgh of  
UPMC  
Division of Pediatric Infectious  
Diseases  
Pittsburgh, PA, USA

**Michele I. Morris MD, FACP,  
FIDSA**

Clinical Chief, Division of Infectious  
Diseases  
Director, Immunocompromised Host  
Section  
Associate Professor of Clinical Medicine  
University of Miami Miller School of  
Medicine  
Miami, FL, USA

**Sherif Beniamen Mossad MD,  
FACP, FIDSA**

Staff Department of Infectious Diseases  
Section Head of Transplant Infectious  
Diseases  
Medicine Institute and Transplant  
Center  
Associate Professor of Medicine  
CCLCM of CWRU Cleveland  
OH, USA

**Nicolas J. Mueller MD**

Senior Attending Physician  
Division of Infectious Diseases and  
Hospital Epidemiology  
University Hospital Zurich  
Zurich, Switzerland

**Elizabeth A. Neuner PharmD,  
BCPS**

Infectious Diseases Clinical Specialist  
Department of Pharmacy  
Cleveland Clinic  
Cleveland, OH, USA

**Raymund R. Razonable MD**

Associate Professor of Medicine  
Director, Transplant Infectious  
Diseases  
Associate Chair for Faculty  
Development and Diversity  
Division of Infectious Diseases  
College of Medicine  
Mayo Clinic Rochester, MN, USA

**Gail Elizabeth Reid MD, BA**

Assistant Professor of Medicine  
Division of Infectious Diseases  
Department of Medicine  
University of Illinois  
Chicago Medical Center  
Chicago, IL, USA

**Nasia Safdar MD, PhD**

Hospital Epidemiologist  
UWHC Section of Infectious  
Diseases  
Department of Medicine and Infection  
Control  
University of Wisconsin-Madison  
School of Medicine and Public  
Health  
and Wm S Middleton VA Center  
Madison, WI, USA

**Tanvi Sharma MD**

Instructor in Pediatrics, Assistant in  
Medicine  
Division of Pediatric Infectious Diseases  
Children's Hospital Boston and Harvard  
Medical School  
Boston, MA, USA

**Shmuel Shoham MD, FACP**

Scientific Director, MedStar Clinical  
Research Center and  
Director, Transplant Infectious Diseases  
Washington Hospital Center  
Washington, DC, USA

**Germana L.M. Silva MD**

Resident, Medical College of Wisconsin  
Department of Anesthesiology  
Milwaukee, WI, USA

**Valentina Stosor MD**

Associate Professor  
Division of Infectious Diseases  
Chicago, IL, USA

**Christian van Delden MD**

Head, Immunocompromised Host  
Program  
Service of Infectious Diseases  
Department of Medical Specialties  
University Hospital  
Geneva, Switzerland

**Marissa B. Wilck MD**

Division of Infectious Disease  
Brigham and Women's Hospital  
Dana Farber Cancer Institute  
Boston, MA, USA

*This page intentionally left blank*

# Preface

Transplantation is a complex, multidisciplinary specialty. Modern immunosuppressive therapy has improved patient and graft outcome. However, this places transplant patients at risk for a variety of infectious complications. Advances in transplant infectious diseases such as molecular diagnostics and novel therapeutics, coupled with the changing epidemiology of infectious agents, have greatly increased the complexity surrounding appropriate prevention and management of infections in these patients.

This is the first edition of the *AST Handbook of Transplant Infections*. It offers practical guidance on both common and unusual issues encountered in both solid organ and hematopoietic stem cell transplant patients. The handbook offers a practical approach to specific clinical syndromes after transplantation, as well as diagnosis, prevention and therapy of specific infections. We also address scenarios related to the prevention of donor-derived infections, common drug interactions, and

other issues specifically related to the transplant patient.

The book does not go through comprehensive dosing or spectrum of activity of commonly used antimicrobials. It is assumed that the reader has some general knowledge of antimicrobials, their overall spectrum of coverage and dose adjustments in renal failure.

The handbook will be updated regularly. This book is endorsed by the American Society of Transplantation (AST). We acknowledge the members of the AST Infectious Diseases Community of Practice, whose members conceived the idea, and wrote and reviewed the chapters. In addition, we thank the members of the AST Pharmacy Community of Practice for reviewing selected sections.

We hope that you will find the handbook useful in your daily clinical practice.

Deepali Kumar & Atul Humar  
Edmonton

*This page intentionally left blank*



# Acknowledgements

We would like to gratefully acknowledge the following individuals who contributed as reviewers to the 2011 edition of the handbook:

Emily Blumberg, Barrett R. Crowther, Lara Danziger-Isakov, Steven Gabardi, Shirish Huprikar, Michael Ison, Sarah Jones, Zakiyah Kadry, Tsing Yi Koh-Pham, Camille Kotton, Oriol Manuel,

Kieren Marr, Marian Michaels, Raymund Razonable, Christin Rogers, Nina Singh, Eric M. Tichy, and Nicole A. Weimert.

We would also like to thank the AST Pharmacy Community of Practice for their review of the handbook.

*This page intentionally left blank*