

# Pathology of Solid Organ Transplantation

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1st Edition. 2010. Buch. xii, 405 S. Hardcover  
ISBN 978 3 540 79342 7  
Format (B x L): 19,3 x 26 cm

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## Preface

Solid organ transplantation is now the treatment of choice for end-stage kidney, heart, liver, pancreas, and lung diseases and increasingly so for intestinal disease. Experimental transplantation in animals provided the impetus for transplantation in humans, first with the kidney [1–3]. A brief account of successful human “experiments” in the time frame of the last 50 years is given in the Table 1 below. These successes were preceded by multiple failures or short-lived grafts. It is through the combined efforts of many researchers, surgeons, and the development of successful immunosuppressive drugs that graft survival and patient outcomes improved [4, 5]. More than a dozen Nobel prizes since 1901 were awarded to those who worked on the fundamentals of transplantation [6]. Currently, the search for agents that perfect induction of tolerance is intensified and transplant services and organ sharing continue to improve [7]. In this remarkable journey of pioneer surgeons, transplant immunologists, and chemists, pathologists were instrumental in recognizing allograft rejection, and more recently, defining the criteria that distinguish acute from chronic rejection, rejection from drug toxicity, and recurrent from de novo disease. Pathology has also been in the forefront of the endeavor of new therapies participating in the evaluation of the effects of drugs on tissue, thus maintaining clear and ethical views in the search for better treatments. Pathologic interpretation of the transplanted organs in humans was first described for the kidney in the 1960s by Gustav Dammin at Harvard and Kendrick Porter at St. Mary’s Hospital in London [8, 9]. It soon became the most reliable tool to distinguish rejection from other complications of transplantation such as drug toxicity, recurrent/de novo disease, and infection. Transplantation pathology is now an indispensable guide to prompt therapy. As the field of transplantation advances, so is transplant pathology. New criteria for donors and the effectiveness of alternative immunosuppression drugs are better understood by histopathologic study of the tissue immune response in the graft, short- and long-term. Innovative approaches of immune tolerance, such as mixed allogeneic chimerism, monoclonal antibodies, and fusion proteins and stem cells for immune modulation, may in the next decade become a reality, therefore changing the pathology of grafted organs [10–12]. Finally, new molecular mechanisms to explain early dysfunction or late graft loss may eventually become diagnostic tools.

This book aims to present a thorough account of the pathology of solid organ transplantation in the dawn of the twenty-first century. The book is organized in a detailed practical diagnostic approach which we hope the reader will find didactic and clear. Molecular studies are discussed when relevant to diagnosis. Introductory chapters are written by our clinical colleagues who describe the immune response from their perspective on treatment and management issues. A chapter on xenotransplantation and

**Table 1** Human transplantation: a brief account

1902	Alexis Carrel	Technique to join blood vessels
1943	Willem J. Kolf	First artificial kidney
1944	Peter Medawar	Rejection is an immune-related phenomenon
1954	Joseph Murray	First kidney transplant in identical twins
1958	Georges Mathé	First bone marrow transplantation
1960	Renè Kuss	First living related ABO compatible kidney transplant
1966	William D. Key Richard Lillehei	First kidney/pancreas transplant
1967	Christian Barnard	First heart transplant
1967	Thomas Starzl	First liver transplant
1983 1986	Joel Cooper The Southeast Organ Procurement foundation (SEOPF) is formed	First successful lung transplant Scientific organization for transplant professionals Predecessor of the “United Network for Organ Sharing “UNOS”
1981	Bruce Reitz Norman Shumway	First heart–lung transplant
1983	Santoz Ltd. (Basel)	Cyclosporine A was FDA approved
1984	NOTA	National Organ Transplant Act establishes national system of matching donors to recipients UNOS separates from SEOPF
1986	Alexander Patterson	First bilateral lung transplant
1987	Pittsburgh surgeons team	First successful intestinal transplant
1982	William C. DeVries	First artificial heart transplant
1989	Fujisawa	Tacrolimus was introduced
1991	Ray V. Rajotte	Islet transplantation with insulin independence
1997	Antonio Secchi	Islet transplantation with insulin independence
1998	Jean Michel Dubernard	First hand transplant
2005	Duvauchelle, Dubernard	First face transplantation
2007	Transplant Growth and Management Collaborative Group	Assessment of nationwide transplant center capacity

organogenesis is a forecast for possible solutions in organ transplantation and one that will, if successful, may change the field and patient care.

We would like to thank with gratitude all our colleagues who contributed their invaluable time and experience. We hope that the book will be useful to our colleagues, also in countries around the world, where transplantation is becoming increasingly more available and frequently the only organ replacement modality within financial reach.

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