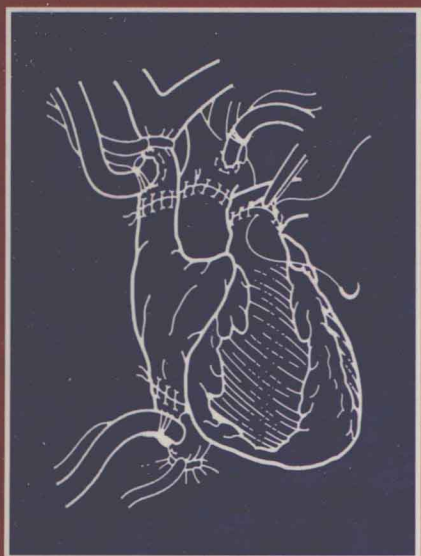


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心脏移植

HEART TRANSPLANTATION



- MEDICINE
- SURGERY
- IMMUNOLOGY
- RESEARCH

JAMES K. KIRKLIN

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HEART TRANSPLANTATION

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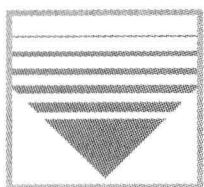
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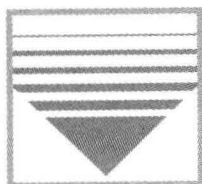
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Quality of Life After Heart Transplantation

Foreword



This is a book for the ages. It is comprehensive. It is beautifully written. It is the culmination of a most remarkable dedication to the science and art of heart transplantation by the authors. The completeness with which this subject is treated is reminiscent of bygone days when scribes would withdraw from the mundane world to create an oeuvre that would defy the passage of time.

Those of us who grew up with open heart surgery are well acquainted with the elder Kirklin, John W. His industry and attention to detail characterized a brilliant career that started in Minnesota at the Mayo Clinic and then to Birmingham, the University of Alabama. John's remarkable textbook on cardiac surgery must have been an inspiration for this book. The genetic link is indeed obvious, especially in regard to its intellectual peptides.

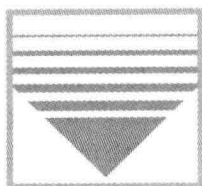
This book is authored, not edited. A few outstanding collaborators have joined the authors to provide specific information for some chapters. The book, therefore, exhibits a constancy not possible in edited textbooks. From the history of transplantation to the potential of xenografts, each chapter is a full treatise in itself.

Orthotopic transplantation of the heart in the laboratory is nearing the half century mark. Clinical application also is now very much grown up. The ancient adage that any cardiac surgical procedure successful in the dog is less difficult in the human proved to be quite correct. Societal changes resulting from the brain death definition of death opened the door for the extension of transplantation to include the heart and heart lungs. The influence of Sir Peter Medawar, who is truly the father of transplantation, is fully appreciated by the authors. Medawar was not only a brilliant basic scientist/ Nobel Laureate but also a great friend and even admirer of the clinician. He in fact trained several fortunate surgeons in his laboratories. Severely challenged physically he remained incredibly productive until his death in 1987. Finally, a word in praise of James Young is very much in order. With Starzl-like industry Jim Young and his surgical colleagues at the Cleveland Clinic have made that institution a destination for heart failure patients from all over the world.

Oscar Wilde once remarked after hearing a particularly erudite and witty statement, "I wish I had said that." To which the author of the epigram replied, "You will, Oscar, you will!" Well, I wish I had written a textbook like this of Kirklin, Young and McGiffin, but there is no way I ever could! You will join me in being delighted that the authors have gone to such great extremes to do so.

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Preface



This textbook is designed to provide comprehensive information about all aspects of cardiac transplantation, such that contained in one text is most of the relevant information which forms the basis for clinical and basic research in cardiac transplantation and for the comprehensive care of heart transplant patients prior to transplantation, during the transplant procedure, and for the remainder of their transplant lives. This book is intended for all persons with an interest in the subject of heart transplantation, including the most expert heart transplant physicians and surgeons; basic, clinical, and social scientists interested in this field; physicians, surgeons, and students in training; other medical professionals participating in the care of heart transplant patients; and non-medical persons who wish to use this as a resource for detailed information on all aspects of this complex field.

The three authors of this textbook bring a wealth of personal experience to this effort, with a combined experience in heart transplantation exceeding 50 man-years. Two of the three authors (JKK and DCM) are heart transplant surgeons and one (JBY) is a heart failure specialist and transplant cardiologist. The two heart transplant surgeons (JKK and DCM) have, between them, personally performed over one thousand thoracic transplant operations (heart, heart/lung, and lung transplantation), a vast experience encompassing all aspects of heart transplantation from neonates to adults. These authors also have an extensive personal experience with mechanical circulatory support devices and alternative surgical procedures for advanced heart failure. The other author (JBY) has a huge experience in all medical aspects of heart failure and heart transplantation at two institutions, currently directing medical care for this complex group of patients in one of the highest volume heart transplant centers (Cleveland Clinic) in the United States. All three authors have held or currently hold director positions in cardiac transplantation and/or heart failure programs. As further evidence of their combined expertise, one author (JKK) is currently Editor of the *Journal of Heart and Lung Transplantation* and another (JBY) is the current President of the International Society for Heart and Lung Transplantation. These comments are intended only to indicate the level of experience and expertise brought to bear on this subject by the three authors and the depth of coverage that the reader should expect.

The decision to produce an *authored text* rather than an edited one deserves special comment. It is the authors' belief that most edited textbooks suffer

to some degree from variability in commitment, depth of coverage, and overlapping content of individual chapters written by separate contributing authors. In contrast, the three authors, working together to provide a finished product reflective of their combined views, expertise, and experience, wrote the final versions of all chapters in this textbook. We hope this approach provides a comprehensive yet cohesive resource on the current state of heart transplantation. We are indebted to a small group of collaborators who are recognized experts in their field and agreed to provide specific and sometimes comprehensive information about particular aspects of certain chapters. However, the final writing of every chapter was the responsibility of the three authors.

Of necessity, many of the experiences and views of the authors reflect the practices of cardiac transplantation at the authors' home institutions; namely, the Cleveland Clinic and the University of Alabama at Birmingham. However, the entire field of cardiac transplantation has been researched for this text, and we have made intense efforts to include special viewpoints of other institutions through some of our collaborators, through our many interactions with other experts in the field, and through their writings.

Several comments about the organization of the book should be helpful to the reader. The 24 chapters of the textbook encompass all major areas of heart transplantation. The first section, *Background of Heart Transplantation*, includes chapters on history, immunology, and clinical research methodology. The second section includes five chapters relevant to *The Patient Before Transplantation*, including the clinical and physiologic basis of heart failure, medical and nontransplant surgical heart failure therapies, the selection of patients for transplantation, special aspects of pretransplant immunologic evaluation, and mechanical support as a bridge to transplantation. The third section, *The Transplanted Heart*, includes three chapters which cover organ donation and the donor heart, the heart transplant operations, and physiology of the transplanted heart. The fourth section, *Management of the Transplant Patient*, includes four chapters dealing with early postoperative management of the transplant recipient, immunosuppressive drugs and other modalities, detailed information on all aspects of cardiac allograft rejection, and a comprehensive discussion of infectious complications after heart transplantation. The fifth section includes four chapters which focus on *Long-Term Outcome After Heart Transplantation*, including extensive analyses of short- and long-term survival, the vexing problem of chronic rejection (allograft coronary artery disease), numerous other long-term complications, and an extensive discussion of quality of life after heart transplantation. The final section includes five chapters which discuss *Special Situations in Heart Transplantation*, including detailed coverage of pediatric heart transplantation, the experience and results of heart/lung and other transplants combining hearts with other organs, cardiac retransplantation, the basic foundations and current expectations of xenotransplantation, and allocation of resources in the field of heart transplantation.

Each chapter outline includes the primary (bolded in box form) and secondary headings within the chapter. When necessary for clarity, secondary headings

within the text also are subdivided by tertiary (bolded heading in italics) and quaternary (non-bolded, freehanging) headings. Key words are bolded for easy reference. An important additional feature of the book is the liberal use of "boxes" to designate more technical information which may be of interest to some readers but can be omitted without interrupting the natural flow of the text. When a phrase within the text is followed by the notation (see Box), this alerts the reader that this phrase will be the title of more detailed information contained in a subsequent box. The reference list for each chapter is organized alphabetically to facilitate the identification of specific references. All 24 chapters were updated with current references during the final year of the project (2000) prior to the forwarding of chapters to the publisher.

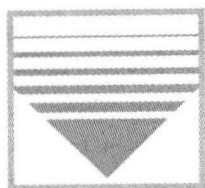
One of the major drawbacks in writing a comprehensive textbook about such a rapidly evolving field as heart transplantation is the risk that major portions of the book are already outdated within a short time after publication. While acknowledging that risk, it is our hope that this book will convey the essential aspects of the state of heart transplantation today, and that it will provide the reader with a sound foundation which will facilitate the acquisition and interpretation of future information about this fascinating and life-extending therapy for advanced heart failure.

James K. Kirklin

James B. Young

David C. McGiffin

Acknowledgments



A comprehensive work of this type requires the help of numerous colleagues to “make it happen.” Through the six years of research and writing (and several earlier years of dreaming), countless individuals have contributed their time, knowledge, and energy to this process. We are particularly indebted to the *collaborators*, all of whom provided special expertise in specific areas. Without their input, the final product would have been far less than it is. However, two of our collaborators made special ongoing contributions; Dr. Jim George and Dr. David Naftel, our close colleagues in heart transplantation research at UAB. They provided the bulk of information on Chapter 2 (JFG) and Chapter 3 (DCN), spending countless hours interacting with the authors to produce these chapters which are comprehensive with respect to research and immunology, yet designed to be readable and easily digested. A special tribute also goes to Ms. Peggy Holmes, the Publications Manager for JKK, who throughout the years of this project single-handedly provided the clerical support for the final chapter manuscripts, was a colleague and confidant for many difficult decisions during the process, and committed a major portion of her life to this effort.

At the University of Alabama at Birmingham, our medical and surgical colleagues in heart failure and transplantation, including Dr. Robert C. Bourge, Dr. Barry K. Rayburn, Dr. Raymond L. Benza, Dr. Brian A. Foley, Dr. Mark F. Aaron, Dr. William L. Holman, and Dr. George L. Zorn, Jr. provided the intellectual and patient-care environment in the management of patients with advanced heart failure and heart transplantation from which we have gained much of our experience and viewpoints. Dr. Arnold G. Diethelm provided the leadership in overall transplantation and Dr. Albert D. Pacifico the leadership in Cardiothoracic Surgery which fostered a successful heart transplant program. Other colleagues provided valuable assistance in reviewing specific chapters, including Dr. John Stevenson Bynon, Jr., Director of Liver Transplantation, Dr. William Lell, formerly Director of Cardiac Anesthesia, and Dr. Craig Hoesley, Division of Infectious Disease. Our knowledge and techniques of organ procurement were aided in a major way by the individuals providing leadership in the Alabama Organ Bank, including Dr. Arnold G. Diethelm, Dr. Mark H. Deierhoi, Mr. Michael G. Phillips, and Mr. Charles Patrick along with all of their colleagues.

At the Cleveland Clinic Foundation, we are equally indebted to our medical and surgical colleagues. The heart failure and cardiac transplant medicine section includes Drs. Corinne Bott-Silverman, Gary Francis, Donald Ham-

mer, Robert Hobbs, Karen James, Suzanne Lutton, Roger Mills, Gustavo Rincon, Randall Starling, David Taylor, and Mohamed Yamani. Drs. Michael Banbury, Patrick McCarthy, Nicholas Smedira, and Jose Navia provide superb surgical services. The huge volume of patients cared for by this team and the outstanding clinical results are a testimonial to the collective expertise, which contributed immeasurably to the attitudes and therapeutic strategies expressed in this book.

Many of the analyses presented in this textbook were based on two large multi-institutional databases, the Cardiac Transplant Research Database (CTRD) and the Pediatric Heart Transplant Study (PHTS), for which UAB was the data analysis center. We are greatly indebted to the member institutions of both databases for their generous participation, long hours of data collection, and their profound intellectual contributions to the many presentations and publications based on these analyses. In the CTRD, we acknowledge the generous participation of the following institutions: Abbott Northwestern Hospital, Albuquerque Presbyterian Hospital, Hahnemann University Hospital, Bowman Gray School of Medicine, Brigham and Women's Hospital, Cleveland Clinic Foundation, Columbia Presbyterian, Downstate Heart Transplant Center, Emory University, University of Florida, Shands Hospital, Henry Ford Hospital, Hershey Medical Center, Indiana University Hospital, Johns Hopkins Hospital, Loyola University Medical Center, St. Luke's Hospital, Medical College of Virginia, Massachusetts General Hospital, Methodist Hospital of Indiana, St. Mary's Hospital, Mayo Clinic, Northwestern University, Ochsner Clinic Transplant Program, Ohio State University, Cardiology, Rush Presbyterian-St. Luke's Medical Center, Medical University of South Carolina, Charleston, Sharp Memorial, St. Joseph's Hospital, St. Luke's Episcopal Hospital, Sentara Norfolk Hospital, St. Louis University, Tampa General Hospital, Baylor College of Medicine/The Methodist Hospital, Temple University School of Medicine, Tulane University, University of Alabama at Birmingham, University Hospitals of Cleveland, University of California, LA, University of Cincinnati Medical Center, University of Louisville, Jewish Hospital, University of Iowa, University of Michigan Medical Center, University of Minnesota, University of Utah Health Sciences Center, University of Texas SW Medical Center, University of Washington Medical Center, Hunter Holmes McGuire VA Medical Center, Vanderbilt University, Washington University Medical Center, and Yale University School of Medicine. In the PHTS, we acknowledge the generous participation of the following institutions: Arkansas Children's Hospital, Albuquerque Presbyterian Hospital, Cleveland Clinic Foundation, Children's Hospital Medical Center, Cardinal Glennon Children's Hospital, Children's Hospital of Michigan, Children's Hospital of Pittsburgh, Children's Memorial Hospital, University of Texas SW Medical School/Children's Medical Center, Children's National Medical Center, Children's Hospital of Philadelphia, Columbia University-Babies Hospital, University of Florida/Shands Hospital. The Hospital for Sick Children, Indiana University Medical Center, Loma Linda University Medical Center, Loyola University Medical Center, Mayo Clinic, Medical College of Virginia, Minneapolis Heart Institute, Mount Sinai Medical Center, Oregon Health Sciences University, Ohio

State University Medical Center, Primary Children's Medical Center, Rainbow Babies and Children's Hospital, Rush Children's Heart Center, St. Louis Children's Hospital, St. Francis Medical Center, Stanford University Medical Center, Texas Children's Hospital, University of Alabama at Birmingham, University of California at Los Angeles, University of Colorado/The Children's Hospital-Denver, University of Michigan Transplant, University of South Florida/All Children's Hospital, Vanderbilt University Medical Center, Children's Hospital of the King's Children/Eastern Virginia Medical School, Children's Hospital, and Engleston Children's Hospital.

Most of the surgical illustrations were provided by Sam and Amy Collins, who spent many hours working with the authors to create accurate depictions of the transplant operations.

A book of this size requires tremendous support in the generation of text, tables, and graphics. At UAB this invaluable service was provided by Ms. Jane Owenby, Ms. Apryl Crosswy, Ms. Mary Lynn Clark, Mr. Robert Brown, and Mr. Todd Weiss; and at Cleveland Clinic by Ms. Lisa Paciorek.

Throughout this process, we had the incredibly good fortune to deal with two outstanding publishing companies, and their editors, namely, Allan Ross at Churchill Livingstone and Richard Lampert at W. B. Saunders. Their encouragement, sage advice, and at times intense stimulation was pivotal in moving the project forward.

It is almost unbelievable to calculate the literally thousands of man-hours put in by the authors on this project. With this time commitment, in the midst of busy professional careers in cardiac surgery, heart failure, and transplantation, the toll on the authors' families was excessive. Yet, they remained loving, tolerant, and for the most part cheerful supporters of this undertaking, although at times renamed the book with certain expletives. We would, therefore, like to lovingly acknowledge the support of our spouses, Terry Kirklin, Claire Young, Alison McGiffin, and George Holmes (husband of Peggy Holmes); and our children, Kimberly and Adam Kirklin, Brad Vernon, Ben and Peter McGiffin, and Joseph, James, Rebecca, and Christine Young.

A special tribute must also be paid to Dr. John W. Kirklin, who provided continuous moral support to the project, and whose legendary textbook, *Cardiac Surgery*, was the inspiration for this effort.

Finally, with deep humility, we would like to acknowledge the unselfish and continuous efforts of the United Network of Organ Sharing in their efforts to make transplantation possible, and to the International Society for Heart and Lung Transplantation, whose commitment to scientific advancements in thoracic transplantation provided the forum for much of the information contained in this text.

James K. Kirklin
James B. Young
David C. McGiffin

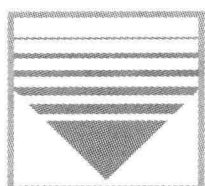
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THE PUBLISHER

This book is dedicated to the physicians, surgeons, and researchers who have committed their lives to the quest for successful transplantation of the human heart; to the patients who have gained and lost their lives in pursuit of or after receiving the gift of transplantation; to the organ donors and their families who have provided that gift; and to our families, who have provided unconditional love, tolerance, and support throughout this project.

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