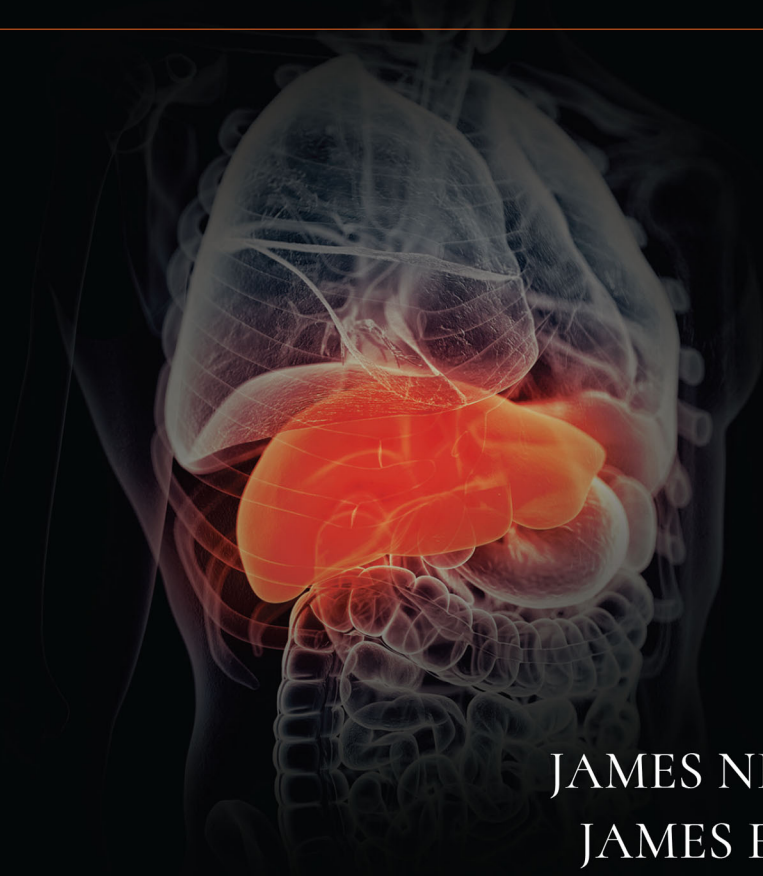


LIVER TRANSPLANTATION

CLINICAL ASSESSMENT AND MANAGEMENT



EDITED BY

JAMES NEUBERGER

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SECOND EDITION

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Liver Transplantation

Liver Transplantation

Clinical Assessment and Management

Second Edition

Edited by

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Foreword to the Second Edition

Without doubt, liver transplantation is one of the greatest success stories in medicine and I never cease to be amazed when I see in follow-up patients who I remember as having terminal illness, 20–30 years after transplantation, living happily in good health and on minimum immunosuppression.

Many more people are going to have this opportunity with the greater number of donor organs that advances in machine preservation are making possible. Donor livers that would not have been considered because of fatty change or ischemic damage can be restored with a period of preservation to a healthy functioning state. The move to an “opt-out” plan of deemed consent in England in May will also significantly increase the number of consents to donation, as has been proven by the experience in Wales. The scenario of patients suitable for transplant being on the waiting list for months and with a mortality of about 20% should become a matter of the past.

But there are important ongoing issues that need to be addressed, for instance the impairment of cognitive ability and educational attainment that has been demonstrated in children after transplantation for biliary atresia or autoimmune hepatitis, detracting from the otherwise remarkable survival figures. Also in the pediatric area are the difficulties that can occur in the transition period to adult life.

The biggest challenge, though, is the emergence of non-alcoholic fatty liver disease (NAFLD) taking over as the leading cause for liver transplantation, supplanting viral hepatitis cases now that there are effective drugs, particularly against hepatitis B and C. Cardiovascular and metabolic complications of obesity can add up to a considerable co-morbidity affecting NAFLD patients coming to transplantation, in both immediate and long-term outcomes. The long timeframe of NAFLD disease causes difficulties in assessing prognosis and need for transplantation. There can also be problems in the diagnosis of primary hepatocellular carcinoma (HCC) in patients who are likely to be obese. The steadily rising prevalence of HCC poses additional challenges to transplant programs with the burgeoning number of effective medical agents as well as ablative techniques used in conjunction with transplantation, making close collaboration between Hepatology and Oncology even more necessary.

Finally, the unmet need for transplantation in instances of severe liver failure consequent on decompensated cirrhosis or on acute alcohol hepatitis will need to be addressed, and here there have been reports of successful transplantation even at the stage of multiorgan failure. Even at 50 years since transplantation got underway, there are unsolved issues to be solved and new challenges – in other words, much to do, but with continuing great outcomes for the patients.

Professor Roger Williams, CBE

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(Roger Williams sadly died on 25 July 2020; see <https://bts.org.uk/passing-of-prof-roger-williams/>)

Foreword to the First Edition

Liver transplantation in humans has come a very long way in a short period of time. My first studies of liver transplantation in animals began in 1958 when I showed that such a procedure was technically possible. I identified three key challenges: the need to preserve the liver between retrieval and implantation, the need to preserve the recipient in hemodynamic stability, and the need to prevent rejection.

The first human liver transplant was performed in 1963 and identified a number of issues that needed resolution, so the program was put on hold, but restarted with the first successful transplant in 1967. The program, initially in Denver and subsequently in Pittsburgh, grew rapidly and was followed by the successful program in Cambridge, UK, in 1968, led by Sir Roy Calne and Roger Williams. Those early pioneering days were exciting but stressful, physically and emotionally. Outcomes improved slowly but surely. In 1983, the procedure came of age when liver transplantation was recognized by the NIH as an effective treatment. Other programs developed around the world and liver transplantation is now routine, with many recipients surviving 20 and more years with an excellent quality of life.

The progression from a high-risk and resource-intensive procedure, where blood use of less than 100 units was considered a success and outcomes were measured in 1-year survival, to a low-risk, routine, and usually blood-free procedure has been achieved as a result of the dedication, hard work, enthusiasm, imagination, and sheer persistence of a large number of people: surgeons, physicians, scientists, intensivists, microbiologists, and many others have all made huge contributions to the success of the procedure. The contribution of both donors and recipients must also be acknowledged for, without their support, these advances could never have occurred.

Yet many challenges remain. Despite advances in medical care, the need for liver transplantation is increasing and the availability of donor livers inadequate. Liver preservation is still a concern: new perfusion fluids and machine perfusion may mitigate some of the problems. While immunosuppression has improved enormously, with the introduction initially of ciclosporin and tacrolimus and, more recently, mycophenolate, sirolimus, and biologic agents, most recipients require long-term treatment, with its associated side effects; tolerance remains an elusive goal. Selection and allocation policies are attracting, quite appropriately, public scrutiny. Regulation is increasing: indeed, it is doubtful whether liver transplantation could have developed as quickly as it did under the current risk-averse climate.

Liver transplantation is expanding and outcomes are better than ever, so more clinicians will be touched by the procedure, whether for referral or for follow-up. It is hoped that this volume will provide a useful and practical guide to the successful management of these patients.

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Preface

Welcome to the second edition of *Liver Transplantation*. Since the first edition, there have been many changes in the management of patients with liver disease, both before and after transplantation, and this new edition reflects this.

As with the first edition, the aim of the volume is to provide a concise, practical, and authoritative guide for junior medical staff and other health professionals working in liver transplant units, for healthcare professionals looking after those patients with liver disease who are or may become liver transplant candidates, and for patients following liver transplantation.

We have expanded both the number and the reach of authors, with a consequent increase in chapters. We have sought to represent the breadth of liver transplant medicine across Europe and North America, while recognizing also the role of liver transplantation in the rest of the world. We appreciate that this means some duplication and occasional divergence of views. We have intentionally retained these so that each chapter is entire in and of itself and the reader understands where there is uncertainty.

We are very grateful to the authors who have written and revised their contributions during the height of the Covid-19 pandemic. We are grateful to those at Wiley-Blackwell, especially Jennifer Seward, Pri Gibbons, Bhavya Boopathi and Sally Osborn, for their help and patience and, most importantly, to our partners and children who have been patient with us during the preparation of this second edition.

Finally, we would like to acknowledge the work of Professor Roger Williams, who died in July 2020 and who contributed so much to hepatology worldwide; he was one of the first to recognize the importance of liver transplantation and helped ensure that it rapidly transitioned from an experimental, high-risk procedure to a routine operation that has benefited so many people. We are delighted and honored to include his Foreword to this second edition.

James Neuberger
James Ferguson
Philip N. Newsome
Michael Ronan Lucey

Abbreviations

6MWD/6MWT	6-minute walk distance/time
AA	amino acids
AASLD	American Association for the Study of Liver Diseases
ABC	adenosine triphosphate-binding cassette
ABOi LT	ABO-incompatible liver transplant
ABP	arterial blood pressure
ACE	angiotensin-converting enzyme
ACLF	acute-on-chronic liver failure
ACP	advance care planning
ACR	albumin creatinine ratio/acute cellular rejection
AD	acute decompensation
ADH	antidiuretic hormone
ADL	activity of daily living
ADV	adefovir
AH	alcoholic hepatitis
AICD	activation-induced cell death
AIH	autoimmune hepatitis
AILD	autoimmune liver disease
AKI	acute kidney injury
ALD	alcohol-related liver disease
ALDLT	adult living donor liver transplantation
ALF	acute liver failure
ALP	alkaline phosphatase
ALPPS	associating liver partition and portal vein ligation for staged hepatectomy
ALT	alanine aminotransferase
AMA	American Medical Association/antimitochondrial antibody
AMR	antibody-mediated rejection
ANA	antinuclear antibody
APA	American Psychiatric Association
APAP	N-acetyl-para-aminophenol (acetaminophen)
APC	antigen-presenting cell

APOLT	auxiliary partial orthoptic liver transplantation
aPTT	activated partial thromboplastin time
ARB	angiotensin II receptor blocker
ASCVD	atherosclerotic cardiovascular disease
ASMA	anti-smooth muscle antibody
AST	aspartate transaminase
AT	anaerobic threshold
ATG	anti-thymocyte globulin
ATP	adenosine triphosphate
AUC	area under the curve
AUD	alcohol use disorder
AUDIT	Alcohol Use Disorder Identification Test
AZA	azathioprine
BCAA	branched chain amino acid
BCC	basal cell carcinoma
BCG	Bacille Calmette–Guerin
Bcl6	B-cell lymphoma 6
BCLC	Barcelona Clinic Liver Cancer
BD	twice daily
BEC	biliary epithelial cell
BIA	bioelectric impedance analysis
BMD	bone mineral density
BMI	body mass index
BP	blood pressure
BSEP	bile salt export pump
CA	cancer antigen/carbohydrate antigen
CAD	coronary artery disease
CAM	cell adhesion molecule
CANONIC	CLIF Acute-oN-ChrONic LIver Failure in Cirrhosis
CBC	complete blood count
CBD	common bile duct
CBT	cognitive behavioral therapy
CCA	cholangiocarcinoma
CCM	cirrhotic cardiomyopathy
CCR	CC chemokine receptor
cccDNA	covalently closed circular DNA
CDC	complement detection cytotoxicity
CDR	crude death rate
CHA	common hepatic artery
CHOP	cyclophosphamide, doxorubicin, vincristine, and prednisone
CI	confidence interval
CIA	common iliac artery
CIT	cold ischemia time
CKD	chronic kidney disease
CKD-EPI	CKD-Epidemiology Collaboration
CLEVER-1	common lymphatic endothelial and vascular endothelial receptor-1
CLIF-SOFA	Chronic Liver Failure-Sequential Organ Failure Assessment

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