Primary Care of the Solid Organ Transplant Recipient

Christopher J. Wong
Editor

Springer

Primary Care of the Solid Organ Transplant Recipient

Christopher J. Wong
Editor

Primary Care of the Solid Organ Transplant Recipient

Springer

Editor
Christopher J. Wong
Department of Medicine
Division of General Internal Medicine
University of Washington
Seattle, WA
USA

ISBN 978-3-030-50628-5 ISBN 978-3-030-50629-2 (eBook)
https://doi.org/10.1007/978-3-030-50629-2

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

Dear colleagues,

Being a primary care provider is one of the most rewarding practices in the field of medicine. We take care of the young and the old, the sick and the well, and everything in between. We build and grow long-term relationships with patients and their families. We work with patients to improve what they can, yet are still there for them when we cannot fix or cure their illness. And we learn—from our patients as they undergo their own personal and healthcare journeys, from our colleagues who teach us and push us to improve, and from our own successes and mistakes.

I suspect that most primary care providers—known for their breadth of knowledge and experience—do not begin their careers with a goal of caring for solid organ transplant recipients. In fact, it can be quite daunting to try to understand what these patients have gone through and partner with them to maintain and improve their well-being. It may seem like something best left solely to specialty care.

This book was created with the idea that primary care providers can and should have a role in the care of solid organ transplant recipients. At the University of Washington we have a robust solid organ transplantation program, and as a result our primary care practices have the pleasure to care for many solid organ transplant recipients. I have found that caring for solid organ transplant recipients is highly rewarding: it requires a high level of the practice of medicine—we need to understand anatomy, physiology, drug side effects and interactions, immunosuppression, and also psychosocial aspects of care. There are ample opportunities to make a positive impact, including managing the many complications suitable to primary care, assessing urgent care needs, and being an important source of continuity.

For this first edition I have sought the expertise of primary care providers and specialists who work with adult solid organ transplant recipients—the goal is to provide a source of information that a primary care provider may find useful. As such, we have tried to balance having enough information to be useful without including excessively detailed transplant care that would not be managed by a primary care provider. I recognize that the practice of medicine, especially transplantation medicine, will continue to evolve—therefore, ongoing collaboration with the transplant specialists should be a routine part of care for this patient population.

I thank and acknowledge my patients and their families; the students, residents, and fellows who train here; the transplant specialists who are always willing to teach us on top of their direct patient care duties; my incredible general internal medicine colleagues; and most of all my own family for their support.

Seattle, WA, USA
April 2020

Christopher J. Wong, MD

Acknowledgments

I would like to acknowledge Sumaiya Sathar, student assistant, for help with obtaining references; the solid organ transplant recipients whom I have been privileged to help care for; my fellow general internists for their inspirational teaching and wisdom; and the transplant specialists at the University of Washington for their clinical expertise and energy in teaching generalists about the care of this special population.

Contents

Contributors

Melissa A. Bender, MD Department of Family Medicine, University of Washington School of Medicine, Seattle, WA, USA

Gabrielle N. Berger, MD Department of Medicine, Division of General Internal Medicine, University of Washington, Seattle, WA, USA

Lauren A. Beste, MD, MSc, FACP Department of Medicine, Division of General Internal Medicine, University of Washington, Seattle, WA, USA

Richard K. Cheng, MD, MSc Department of Medicine, Division of Cardiology, University of Washington Medical Center, Seattle, WA, USA

Eleanor Curtis, MD, MPVM Department of Trauma, Burns and General Surgery, University of California, Davis, Sacramento, CA, USA

Iris C. De Castro, MD Department of Medicine, Division of Nephrology, University of Washington, Seattle, WA, USA

Tyra Fainstad, MD Department of Medicine, Division of General Internal Medicine, University of Colorado, Denver, CO, USA

Anna Golob, MD Department of Medicine, Division of General Internal Medicine, University of Washington, Seattle, WA, USA

VA Puget Sound Healthcare System, Seattle, WA, USA

Deborah Greenberg, MD Division of General Internal Medicine, Department of Medicine, University of Washington, Seattle, WA, USA

Katherine G. Hicks, MD Department of Medicine, Division of General Internal Medicine, University of Washington School of Medicine, Seattle, WA, USA

Christopher Knight, MD Department of Medicine, Division of General Internal Medicine, University of Washington, Seattle, WA, USA

Anne M. Larson, MD, FACP, FAASLD, AGAF Hepatology & Liver Transplantation, Division of Gastroenterology, University of Washington, Seattle, WA, USA

Erika D. Lease, MD, FCCP Department of Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, University of Washington, Seattle, WA, USA

Andy Y. Lee, MD Department of Medicine, Division of Cardiology, University of Washington Medical Center, Seattle, WA, USA

Leah M. Marcotte, MD Division of General Internal Medicine, Department of Medicine, University of Washington, Seattle, WA, USA

Vidang P. Nguyen, MD Cedars-Sinai Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Kim O'Connor, MD Department of Medicine, Division of General Internal Medicine, University of Washington, Seattle, WA, USA

Genevieve L. Pagalilauan, MD Department of Medicine, Division of General Internal Medicine, University of Washington, Seattle, WA, USA

Cary H. Paine, MD Department of Medicine, Division of Nephrology, University of Washington, Seattle, WA, USA

Heidi Powell, MD Division of General Internal Medicine, Department of Medicine, University of Washington, Seattle, WA, USA

Lydia Sun, PharmD Department of Pharmacy, University of Washington Medical Center, Seattle, WA, USA

Christopher J. Wong, MD Division of General Internal Medicine, Department of Medicine, University of Washington, Seattle, WA, USA

Jennifer Wright, MD Department of Medicine, Division of General Internal Medicine, University of Washington, Seattle, WA, USA

Diana Zhong, MD Department of Medicine, Division of General Internal Medicine, University of Washington, Seattle, WA, USA

List of Abbreviations

AASLD	American Association for the Study of Liver Diseases
ACP	Advance care planning
ACR	Acute cellular rejection
AD	Advance directive
AIH	Autoimmune hepatitis
ARLD	Alcohol-related liver disease
AST	American Society of Transplantation (note can also refer to aspartate aminotransferase)
AUC	Area under the curve
AUDIT	Alcohol use disorders identification test
AZA	Azathioprine
BKVN	BK virus nephropathy
BMD	Bone mineral density
BMI	Body mass index
CAN	Chronic allograft nephropathy
CBT	Cognitive behavioral therapy
CDC	Centers for Disease Control
CMV	Cytomegalovirus
CNI	Calcineurin inhibitor
CPRA	Calculated panel reactive antibody
CsA	Cyclosporine
CT	Computed tomography
Cu-IUD	Copper-IUD
CVD	Cardiovascular disease
D/R	Donor/recipient (used to describe serologic status)
DAA	Direct-acting antiviral
DEXA	Dual-energy x-ray absorptiometry (also DXA)
DGF	Delayed graft function
DPOA-HC	Durable Power of Attorney for Healthcare
DSA	Donor-specific antibodies
DVT	Deep vein thrombosis

DXA	Dual-energy x-ray absorptiometry (also DEXA)
EBV	Epstein-Barr virus
ECG	Electrocardiogram
eGFR	Estimated glomerular filtration rate
EHR	Electronic health record
ERCP	Endoscopic retrograde cholangiopancreatography
ER	Emergency room
ESRD	End stage renal disease
EPTS	Estimated post transplant survival
F	Bioavailability
FSGS	Focal segmental glomerulosclerosis
GAD-7	General Anxiety Disorder -7
HAT	Hepatic artery thrombosis
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
IBW	Ideal body weight
ICU	Intensive care unit
IFTA	Interstitial fibrosis and tubular atrophy
IL	Interleukin
IPD	Invasive pneumococcal disease
IUD	Intrauterine device
KDIGO	Kidney Diseases Improving Global Outcomes
KDPI	Kidney donor profile index
LARC	Long-acting reversible contraception
LNG	Levonorgestrel
MBSR	Mindfulness-based stress reduction
MM	Malignant melanoma
MMF	Mycophenolate mofetil
MPA	Mycophenolic acid
MRCP	Magnetic resonance cholangiopancreatography
mTOR	Mammalian target of rapamycin
NAAT	Nucleic acid amplification test
NASH	Nonalcoholic steatohepatitis
NODAT	New onset diabetes after transplant (note also called post-transplant diabetes mellitus, PTDM)
NSAID	Non-steroidal anti-inflammatory drug
OPTN	Organ Procurement and Transplantation Network
OTC	Over the counter
PAK	Pancreas after kidney (transplant)
PBC	Primary biliary cholangitis
PCP	Primary care provider
PFT	Pulmonary function test

PHQ	Patient health questionnaire
POLST	Provider Orders for Life Sustaining Treatment (note similar abbreviations MOLST, POST, MOST, COLST, TPOPP)
PRA	Panel reactive antibody
PSC	Primary sclerosing cholangitis
PTA	Pancreas transplant alone
PTLD	Post-transplant lymphoproliferative disorder
PTSD	Post-traumatic stress disorder
rATG	Rabbit antithymocyte globulin
SCR	Subclinical rejection
SOT	Solid organ transplant
SOT recipient	Solid organ transplant recipient
SPK	Simultaneous pancreas-kidney (transplant)
SRTR	Scientific Registry of Transplant Recipients
$t_{1/2}$	Half-life
UPA	Ulipristal acetate
US MEC	United States Medical Eligibility Criteria

Chapter 1
Introduction

Christopher J. Wong

Why Primary Care?

Solid organ transplantation is a miracle of modern medicine. Transplant medicine has dramatically altered the natural history of end-organ failure—instead of death, there is life. While there are many potential complications, often solid organ transplant (SOT) recipients have excellent quality of life for their remaining years.

And yet, even after such a life-preserving intervention, there remains quite a bit of work to be done in order to maximize health and function of the transplanted organ and the well-being of the patient. While it may be convenient to believe that a solid organ transplant recipient's transplant center will provide all care that is needed, it is more likely that there will be at least some role for primary care. First, patients may live far from their transplant center and may need a local primary care provider for both urgent and chronic medical conditions. Second, patients often have a pre-existing relationship with their primary care provider prior to solid organ transplantation. Third, the number of surviving solid organ transplant recipients is increasing—transplant centers are not anticipated to have the resources to provide all care for this population.

Thus it is quite likely that primary care providers will play an important role in the care of solid organ transplant recipients. The balance of what aspects of care are performed by which provider should be a continued conversation between the transplant specialist and primary care provider. The transplant specialist typically will maintain immunosuppression and continue to assess function of the transplanted organ. Some transplant centers will follow patients closely even if the patients are doing well, while others may see patients yearly with the bulk of the patients' care returned to primary care and local specialists. For example, a liver

C. J. Wong (✉)
Department of Medicine, Division of General Internal Medicine,
University of Washington, Seattle, WA, USA
e-mail: cjwong@uw.edu

C. J. Wong (ed.), *Primary Care of the Solid Organ Transplant Recipient*,
https://doi.org/10.1007/978-3-030-50629-2_1

transplant recipient may return yearly to the liver transplant clinic, and be followed by a primary care provider and a local gastroenterologist in between those yearly visits, unless there are complications that would require a return evaluation sooner. Sometimes the transition back to primary care after the initial postoperative period is colloquially called “graduating.”

Primary Care Roles in the Care of Solid Organ Transplant Recipients

While there will always be a vital role for the transplant specialist, primary care providers nevertheless are front-line in managing other illnesses that may arise in solid organ transplant recipients. Primary care providers who care for solid organ transplant recipients must be ever-vigilant in identifying and treating other complications and comorbidities.

- Is a solid organ transplant recipient’s diarrhea from his or her mycophenolate, or is there a new cause of diarrhea, and if so, is it infectious or non-infectious?
- In a solid organ transplant recipient presenting with cough and shortness of breath, are these symptoms a sign of organ failure or an opportunistic infection, or just a viral upper respiratory infection?
- What medications should a solid organ transplant recipient be expected to be taking, and what side effects are likely?
- Will medication therapy for other conditions interfere with the patient’s transplant drugs?
- When should the transplant specialist be consulted?

These questions can pose clinical challenges but are nevertheless important to the patient and rewarding to the provider. Caring for solid organ transplant recipients requires all the tools of a clinician to synthesize the presentation and determine the best evaluation and treatment.

In addition to new symptoms, primary care providers are front-line for delivering preventive health and care of chronic conditions to their patients. The primary care provider has an important role in making sure recommended screenings take place, modify screening as indicated, and be alert for metabolic complications and manage them appropriately. Questions might include:

- Should the recommended vaccination schedule be altered?
- How is cancer screening different in a solid organ transplant recipient?
- What metabolic problems, such as diabetes and osteoporosis, should be screened for?
- How should common conditions be managed differently in a solid organ transplant recipient?

How to Use This Book

This book is written with primary care providers in mind, as they try to sort out whether new symptoms and syndromes might represent a transplant-related complication, or, instead, fall into the category of routine primary care; as they navigate recommended preventive health and metabolic complications; and as they learn about complications specific to the transplanted organ. Many patients become experts in their own health, having taken quite a journey to make it through organ failure, transplant approval, and then successful organ transplantation. Primary care providers will take this journey with their patients and learn from the experience as well.

In this book, we hope to provide guidance for primary care providers in the rich and rewarding care of adult solid organ transplant recipients.

Chapter 2 covers a general overview of solid organ transplantation, including review of the pre-transplant course and taking a basic medical history of the patient after transplantation.

Chapter 3 addresses the basics of common anti-rejection medications used in solid organ transplantation and their common side effects. The authors discuss drug interactions for medications commonly used in the primary care setting.

Chapters 4, 5, 6, and 7 provide overviews of the care of kidney and kidney-pancreas, liver, heart, and lung transplant recipients. (Note that this book does not address combined heart-lung or small intestine transplantation.)

Chapter 8 is a review of infections in the solid organ transplant recipient. It includes discussion of select respiratory, gastrointestinal, urinary tract, central nervous system, and skin and soft tissue infections.

Chapter 9 provides a general approach to a set of common syndromes, including shortness of breath and cough, diarrhea, urinary tract symptoms, and skin lesions.

Chapter 10 addresses the important topic of cancer, a life-limiting complication in the immunosuppressed population.

Chapter 11 is an overview of metabolic complications including diabetes, hypertension, hyperlipidemia, gout, and osteoporosis, all of which are common in the solid organ transplant population.

Chapter 12 provides an overview of preventive health, highlighting similarities and differences between recommendations for solid organ transplant recipients compared to the general population.

Chapter 13 addresses palliative care, as solid organ transplant recipients may have important symptoms that impact quality of life, and discusses end-of-life issues.

This book does not need to be read cover-to-cover. The chapters specific to a transplanted organ will provide useful knowledge for primary care providers should they be involved in the care of patients with these transplanted organs. All providers may find useful the general overview chapter and the chapters on medications and complications. Those who see patients for urgent symptoms may find the chapters

discussing common syndromes to be helpful, as well as the individual organ chapters as needed.

For this edition, we focus on heart, lung, liver, kidney, and pancreas transplants, and are not covering pediatric solid organ transplantation, small intestine, skin, and other organ transplants.

The goal of this book is to provide a framework and a starting point—as with any such clinical guidance, individualizing care based on the patient's unique circumstances is critical, and one must consult with the patient's specialty providers when the need arises. The care of solid organ transplant recipients is rewarding but requires background knowledge and clinical acumen—it is hoped that this book proves useful in furthering this care.

Chapter 2
Overview of Solid Organ Transplantation for Primary Care Providers

Diana Zhong and Christopher J. Wong

Introduction

Solid organ transplantation is increasing in prevalence. With each passing year, it becomes more likely that primary care providers will encounter patients who are recipients of a solid organ transplant.

In the United States, the number of solid organ transplantations has risen steadily over the past 20 years (Fig. 2.1), with 36,529 solid organ transplants performed in 2018 [1]. The greatest increases have been in liver and kidney transplants (Fig. 2.2). As the actuarial survival has also increased over this period of time, so too has the overall prevalence of living solid organ transplant recipients. It is estimated that as of 2017, there were approximately 220,000 kidney transplant recipients [2], 84,000 liver transplant recipients [3], 32,000 heart transplant recipients [4], and 14,000 lung transplant recipients [5] living in the United States. In total, the number of living solid organ transplant recipients could populate an entire mid-size US city.

Internationally, the World Health Organization estimated that a total of 135,860 solid organ transplants were performed in 2016—a number that has been increasing annually based on provisional data, including in the United States [6]. The majority of solid organ transplants worldwide occur in high-income countries, but transplantation is spreading to an increasing number of countries [7].

The demographics of organ transplantation continue to change. Age is no longer a contraindication to transplantation at many transplant centers; although practices vary by country and region, some countries are moving away from age-based criteria [8, 9]. Indeed, 21% of transplants in the United States in 2018 were received by recipients aged 65 and over [1]. Donor demographics are also changing: there is now expanded use of potentially higher risk, or "extended criteria" donors to help

D. Zhong · C. J. Wong (✉)
Department of Medicine, Division of General Internal Medicine, University of Washington, Seattle, WA, USA
e-mail: zhongd@uw.edu; cjwong@uw.edu

C. J. Wong (ed.), *Primary Care of the Solid Organ Transplant Recipient*,
https://doi.org/10.1007/978-3-030-50629-2_2

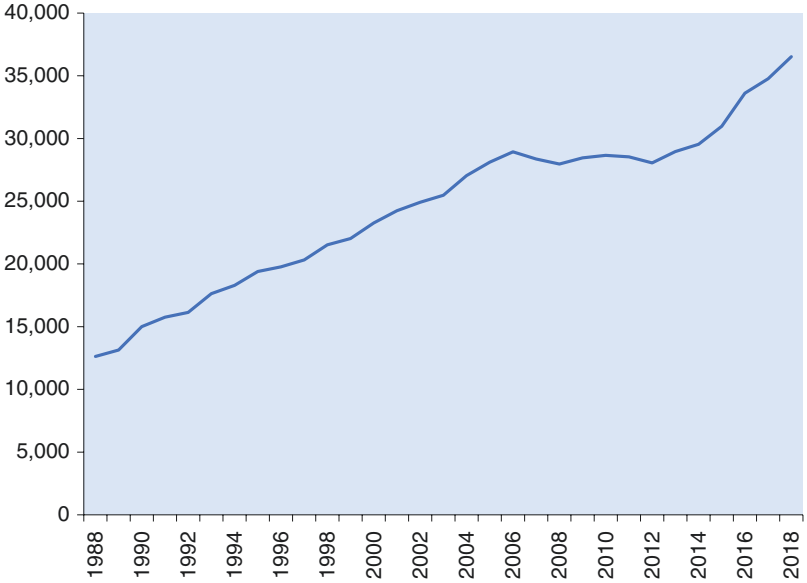

Fig. 2.1 Number of solid organ transplant recipients per year in the United States, 1988–2018. (Based on OPTN data from 2019, from https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/. Accessed April 22, 2019)

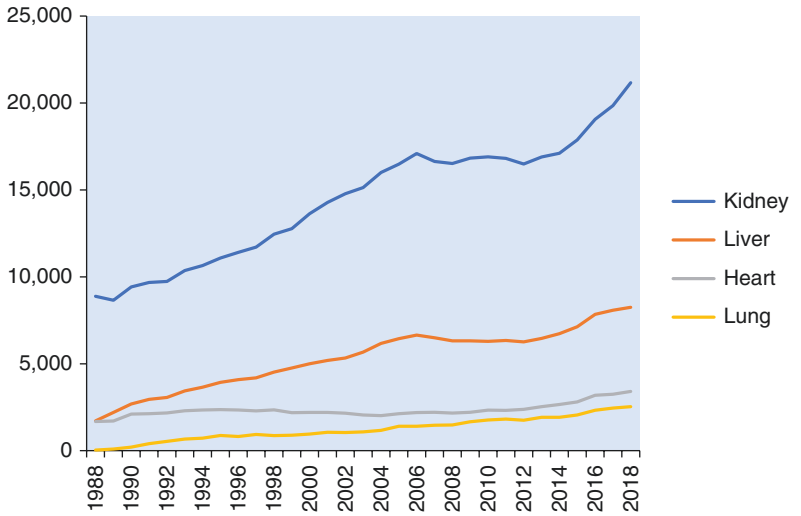

Fig. 2.2 Solid organ transplantation in the United States, by Organ, 1988–2018. *Kidney-pancreas, pancreas, heart-lung, and intestine transplantation data not shown. (Based on OPTN data from 2019, from https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/. Accessed April 22, 2019)

reduce the number of patients on the transplant waiting lists. Extended criteria vary, but may include older age donors as well as the presence of potentially treatable viruses such as hepatitis C [10]. Terminology varies, and some transplant specialists recommend using the least stigmatizing terms to classify donor organs so that providers are not dissuaded from recommending suitable donations.

There are many implications for primary care. First, the volume of solid organ transplant recipients will likely lead to more primary, urgent, and emergent medical care taking place outside of a transplant center. For example, there are an estimated 244 kidney transplant centers in the United States [11]. These centers would have to deliver primary care to all 220,000 living kidney transplant recipients while also evaluating the pre-transplant population; it is preferable that patients could continue routine care with their own primary care providers. Second, patients often live far from their transplant center, making it more imperative to have effective local care. In the United Kingdom, the median distance to the transplant center for liver transplant recipients was 67 km [12]. A study of patients in the United States' Veterans Affairs healthcare system found that distance from the transplant center was inversely correlated with being waitlisted for transplantation—notably in that same study, the vast majority of pre-liver transplant candidates were over 100 miles from a transplant center [13]. In another study of patients in the United States listed for liver transplant, 28% lived over 100 miles from the transplant center [14]. While it is conceivable that some solid organ transplant recipients may move closer to a transplant center after transplantation, this percentage is likely to be small. Third, lessening age requirements and improved overall survival are resulting in an increasingly older population of solid organ transplant recipients. The general practitioner, experienced in the comorbidities of aging, is well-suited to provide care for these patients.

Pre-Transplant Evaluation

Overview

While this book focuses on the primary care of patients after receiving a solid organ transplant, knowledge of the pre-transplant process is useful in their ongoing treatment.

The pre-transplant process begins when a patient with end-stage organ failure is referred to a transplant specialist. This referral may arise from primary care, a specialist, or during an acute-care hospitalization. Pre-transplant testing can take place in a variety of settings, including outpatient clinics (not necessarily only in the transplant center) and inpatient hospital stays.

The transplant team typically includes a medical and surgical team (for example, a transplant hepatologist and a transplant surgeon, in the case of end-stage liver disease), as well as a social worker and other staff to assess social support and

psychological health. Other specialists may be involved, such as an infectious disease specialist, psychiatrist, dietician, cardiologist, or pulmonologist, depending on the patient's needs and comorbidities. Testing generally includes laboratory studies, assessment of cardiac tolerance for surgery (other than for heart transplant), and cancer screening. Treatment often includes vaccinations and medication adjustments for medical optimization.

From there, a transplant committee evaluates a patient's candidacy for transplantation. The evaluation will include many factors, including the need for transplant, medical comorbidities, results of medical testing, suitability for major surgery, psychiatric evaluation, and other psychosocial considerations. If a patient is accepted as a candidate for transplantation, the patient is most commonly placed on a waiting list.

The transplant workup, evaluation, and candidate selection process vary depending on the transplant center, organ(s) affected, the patient's underlying disease, the urgency of transplantation, and many other individual patient factors. The information provided here is not intended to be comprehensive; rather, it will hopefully provide the primary care provider an overview of what the solid organ transplant recipient who presents to the outpatient clinic may have experienced prior to transplantation.

The pre-transplant evaluation is summarized in Table 2.1.

History and Exam

The initial pre-transplant medical evaluation will include a detailed history and physical exam. Active or chronic medical conditions are treated or optimized prior to transplantation. Severe medical conditions may be contraindications to transplantation, including untreatable significant dysfunction of another major organ system

Table 2.1 Pre-transplant evaluation

History and exam
Laboratory testing
Functional status
Nutrition and body mass index
Bone density
Cardiopulmonary assessment
Dental evaluation
Family planning (if applicable)
Infection screening
Immunizations
Cancer screening
Surgical evaluation
Psychosocial evaluation

(unless combined organ transplantation can be performed), uncorrected atherosclerotic disease with end-organ ischemia or coronary disease not amenable to revascularization, and other severe and uncorrectable diseases that may lead to a significantly shortened life expectancy [15, 16].

Laboratory Testing

Typical laboratory testing is shown in Table 2.2. In addition to routine testing, patients are evaluated for their risk of prior sensitization, including whether they have a history of blood or platelet transfusions, pregnancies, abortions, or previous transplants [15]. Patients are screened prior to transplant to help identify and treat active infections pre-transplant, to recognize infectious risks including latent infections, and to help prevent and manage post-transplant infections [17] (see "*Infections*" below).

Table 2.2 Typical pre-transplant laboratory tests

Routine tests [15, 18, 19]
Complete blood count
Kidney function and electrolytes
Liver function tests
Coagulation studies
Urinalysis and urine culture
Pregnancy test (if applicable)
Urine drug screen
Compatibility tests [15]
ABO-Rh blood type
Human leukocyte antigen (HLA) type
Panel reactive antibody assay (PRA)
Crossmatching
Infectious disease tests [17]
Human immunodeficiency virus (HIV): HIV antibody/antigen screening
Cytomegalovirus (CMV): CMV IgG
Hepatitis B virus (HBV): HBV surface antigen (HBsAg), HBV core antibody (HBcAb-IgM and IgG, or total core antibody), HBV surface antibody (HBsAb)
Hepatitis C virus (HCV): HCV antibody
HCV nucleic acid amplification testing (NAAT)
Epstein-Barr virus (EBV): EBV antibody (EBV viral capsid antigen IgG, IgM)
Toxoplasma gondii: *Toxoplasma* IgG antibody
Syphilis: available tests may vary by institution
Tuberculosis: Purified protein derivative (PPD) *or* Interferon gamma release assay (IGRA)
Additional testing if indicated by exposures and risk factors

Table 2.3 Pre-transplant cardiopulmonary screening tests

Most patients [21]:
Chest radiography (X-ray)
Electrocardiogram (ECG)
Depending on age and comorbidities, many patients will undergo further evaluation [21]:
Transthoracic echocardiogram (TTE)
Cardiac stress testing
Coronary angiography (if abnormal stress testing or echocardiogram)
Other testing considered may include [20]:
Cardiopulmonary exercise testing (CPET)
6-minute walk test (6MWT)
Noninvasive coronary CT angiography (CCTA)
Coronary artery calcium (CAC) score
Right heart catheterization
Some patients may have additional pulmonary evaluation with [18]:
Pulmonary function tests (PFTs)
Chest computed tomography (CT) scanning

Cardiopulmonary Screening

Screening is performed to evaluate for many cardiopulmonary conditions, including coronary artery disease, cardiomyopathy and heart failure, pulmonary hypertension, cardiac arrhythmias, valvular heart disease, and congenital heart disease [20]. Testing may vary by center, organ to be transplanted, and a patient's individual clinical features. Examples of cardiopulmonary testing are shown in Table 2.3.

Functional Status, Nutrition, and Bone Density

Poor functional status with limited rehabilitation potential may be a contraindication to transplantation. A patient's frailty can be assessed by whether they need assistance with activities of daily living (ADL), the sit-to-stand test, as well as whether they have unintentional weight loss and low physical activity [22]. Older age is increasingly not a contraindication by itself but is considered in the context of a patient's functional status and comorbidities [23].

Obesity can be a contraindication to transplantation. Patients are usually considered poor candidates for transplantation if they have a body mass index (BMI) $\geq$ 35 kg/m^2 for lung transplant candidacy and BMI $\geq$ 40 kg/m^2 for liver transplant candidacy. Conversely, malnourished patients are usually considered poor candidates as well [16, 18].

Most patients will have bone densitometry measured with dual-energy X-ray absorptiometry (DEXA). As patients will take chronic glucocorticoids

post-transplantation, having baseline data is helpful for follow-up testing and management [18].

Dental Evaluation

A dental evaluation is performed to evaluate for dental abscesses, dental caries, buried roots, and gum disease. Dental problems can be a source of post-transplant infection. Dental procedures are performed prior to transplantation whenever possible [18].

Family Planning

Pregnancy in the first 12 months following transplantation is associated with both an increased risk of preterm delivery as well as graft dysfunction or rejection. It is therefore recommended to avoid pregnancy in the first year after transplantation [24]. A patient's family planning goals should be addressed prior to transplantation, including contraception. Intrauterine devices (IUD) are a preferred and effective method of contraception that will avoid interactions with medications—if placed prior to transplantation, identifying the type of IUD and date of implantation is needed for future management.

Organ-Specific Testing

Further organ-specific testing is performed in conjunction with specialist consultation. While all such testing is not necessary to review, especially if no longer relevant (e.g., the organ is removed), some tests may be helpful for future management. For example, a patient with end-stage liver disease will likely have had esophagogastroduodenoscopy (EGD) performed to evaluate for esophageal varices—having the results of these evaluations may be useful for comparison if a repeat EGD is needed. Sometimes the workup for organ failure may uncover other syndromes that should be followed. For example, a monoclonal gammopathy may be identified during workup for chronic kidney disease; even if it was not the underlying etiology for the patient's kidney disease, it will still need to be followed post-transplantation. Finally, the explanted organ pathology may sometimes be useful. For example, a heart transplant recipient may have had negative biopsies, but on explant the finding of non-caseating granulomas may suggest sarcoidosis, a condition which could arise in other organs after transplantation.

Vaccines and Pre-transplant Prophylaxis

In most cases, the transplant team will attempt to make sure patients are as up to date as possible on vaccines *prior* to transplant [25]. Both inactivated and live-attenuated vaccines can be given to patients pre-transplant (unless otherwise contraindicated), but live vaccines are contraindicated post-transplant due to risk of disseminated infection. Additionally, vaccines have variable immunogenicity after transplant due to immunosuppression and thus may be less effective. Therefore, the pre-transplant window is a crucial time for most vaccines to be administered, ideally earlier in a patient's disease course as immunogenicity can also decline due to the relative immunocompromise from organ failure. It is recommended that live vaccines be administered by ≥4 weeks prior to immunosuppression, and that inactivated vaccines be administered ≥2 weeks prior to immunosuppression [24, 26]. All vaccines that are appropriate for age, exposure history, and immune status should be administered prior to transplantation according to the Centers for Disease Control (CDC) guidelines. In addition to the usual vaccine schedule, there are further recommendations for patients awaiting solid organ transplantation, which include hepatitis A, herpes zoster, and pneumococcal vaccination, as shown in Table 2.4 [25]. If a patient is unable to receive vaccinations prior to transplantation, an infectious disease specialist will typically assist with post-transplant vaccination decisions. (For post-transplant guidelines, see Chap. 12).

Less common vaccines that may have been given prior to transplant include meningococcus, Bacille Galmette-Guerin (BCG), smallpox, anthrax, rabies, yellow

Table 2.4 Typical vaccination recommendations prior to solid organ transplantation[a]

Vaccine	Type	Evaluate for serologic response?	Notes
Influenza inactivated (IIV)	Inactivated	No	High-dose formulation often used
Influenza live-attenuated (LAIV)	Live-attenuated	No	Intranasal vaccine*
Hepatitis B	Inactivated	Yes	Various formulations (2-dose, 3-dose, or 4-dose series)
Hepatitis A	Inactivated	Sometimes	Sometimes given in combined formulation with Hepatitis B vaccine
Tetanus	Inactivated	No	
Pertussis (Tdap)	Inactivated	No	If no tetanus booster in the past 10 years, administer Tdap. At least one dose of acellular pertussis should be given in adulthood, especially women of child-bearing age and individuals in contact with infants.
Inactivated Polio	Inactivated	No	
H. influenzae type B	Inactivated	Yes	

Table 2.4 (continued)

Vaccine	Type	Evaluate for serologic response?	Notes
S. pneumoniae	Inactivated	No	There are two inactivated vaccines, PCV13 (Prevnar 13®) and PPSV23 (Pneumovax 23®). See CDC guidelines for details, as timing and dosing vary based on indication. Most solid organ transplant recipients should have received at last PPSV23 prior to transplant, as it is indicated for patients with chronic lung disease, chronic liver disease, and chronic heart disease. Some patients will have also received PCV13 as it is indicated for patients with chronic renal failure, or if they were immunosuppressed pre-transplant for other medical conditions [27]. PCV13 should be completed 8 weeks prior to PPSV23 [24]
Human papilloma virus (HPV)	Inactivated	No	Indicated for age 9–45 years
Measles, mumps, rubella (MMR)	Live-attenuated	Yes	
Varicella (VAR or Varivax®)	Live-attenuated	Yes	Given if not immune
Herpes zoster (recombinant zoster vaccine, RZV or Shringrix®)	Inactivated	No	Recommended for patients ≥50 years old. This is generally the preferred form of zoster vaccination due to its higher efficacy as compared with the live-attenuated vaccine, and because it is inactivated it will not delay transplantation
Herpes zoster (live zoster vaccine, LZV or Zostavax®)	Live-attenuated	No	Two doses should be administered ≥3 months apart, while considering that live vaccines should be given ≥4 weeks prior to transplant [24]

[a]Recommendations change and should be reassessed periodically. All live vaccines are only administered if the patient is not already severely immunocompromised
*The intranasal, live-attenuated influenza vaccine is not recommended for adults age 50 and over; guidelines for this vaccine have changed periodically

fever, Japanese encephalitis, typhoid, and cholera, depending on a patient's exposures and travel [25].

Infections

Transplant candidates are assessed for past infections and a detailed exposure history (travel, residence, occupation, lifestyle, animal, and environmental) [17]. In addition to the routine laboratory testing shown in Table 2.2, further testing may be performed for patients with certain exposures or from endemic areas, including

assessment for *Strongyloides*, *Trypanosma cruzi*, and *Coccidioides* species [17, 28]. A rigorous separate screening process is used for potential organ donors.

HIV infection does not preclude receiving transplantation, though HIV should be well-controlled prior to pursuing transplantation [29]. Patients with hepatitis B and chronic hepatitis C can still be considered for transplantation but are evaluated for liver cirrhosis and considered for antiviral treatment prior to transplant [16, 23].

Viral serologies such as CMV and EBV testing can be used to guide donor selection and to stratify risk. Transplant recipients who are CMV seronegative are at higher risk for CMV infection if the donor is CMV seropositive; similarly, recipients who are EBV seronegative are at higher risk for EBV infection and post-transplant lymphoproliferative disorder (PTLD) if the donor is EBV seropositive. These cases require additional post-transplant monitoring and prevention strategies (see Chaps. 8 and 10) [17].

Colonization, Latent Infection, Chronic or Recurrent Infection, and Active Infection

Identification of infection risks can affect transplant candidacy and post-transplant treatment:

- *Colonization*: Microbial colonization can increase the risk of infection after transplantation. For example, a patient with cystic fibrosis awaiting lung transplantation may be colonized with multi-drug resistant strains of bacteria such as *Pseudomonas*, *Staphylococcus aureus, Stenotrophomonas*, and *Burkholderia*, as well as fungi such as *Aspergillus*. Patients are carefully evaluated to exclude active infection. Colonization with certain multi-drug resistant organisms or virulent organisms such as *Burkholderia* is associated with poor outcomes after transplantation and may be weighed as a consideration against transplantation [16]. Knowledge of this colonizing flora can aid in development of an individualized peri-transplant and post-transplant prophylactic antimicrobial regimen.
- *Latent infection*: Risk of recurrent infection is assessed and mitigated prior to transplantation. For example, a pre-transplantation history of active disease or seropositivity for coccidioidomycosis may warrant lifelong azole prophylaxis. In contrast, other endemic mycoses such as histoplasmosis are not routinely checked and do not directly alter management, but should be considered when evaluating a patient presenting with illness post-transplantation [17]. Patients with latent tuberculosis infection (LTBI) are ideally treated prior to transplantation [30].
- *Chronic or recurrent infections*: These infections generally require definitive treatment prior to transplantation. For example, patients with a history of severe and/or recurrent infection with *Clostridioides difficile* may receive secondary prevention with fecal microbiota transplant (FMT) or bezlotoxumab [31].
- *Active or uncontrolled infections*: These infections require treatment and often delay transplantation until the infection resolves or is controlled [17].

Cancer Screening

Pre-transplant evaluation requires age-appropriate cancer screening to be up to date. Patients with an active malignancy or recent history of malignancy will not be offered transplantation, as transplantation may not improve survival. Furthermore, immunosuppression increases the risk of malignancy post-transplant [32]. If a patient's cancer has been treated and the patient has been disease-free for a certain period of time, they may often be evaluated for transplantation [16, 19]. All patients should remain up to date on gender and age-appropriate cancer screening, which may include colonoscopy, mammogram, Papanicolaou (Pap) smear, skin examination, and additional screening if indicated for the patient's medical history (e.g., hepatocellular carcinoma screening for patients who have hepatitis B infection) [15].

Surgical Evaluation

A patient's surgical candidacy is a major component of the transplant evaluation, and factors in medical comorbidities as well as the patient's functional and nutritional status, as discussed above.

There are specific additional surgical considerations related to a patient's individual anatomy and history of prior surgeries and prior thromboses. Further workup such as CT scans or vascular studies may be warranted. Furthermore, depending on the organ site, there can be discussion of donor options (deceased, living, extended criteria donors). Specific comorbidities that confer especially high operative risk, such as portopulmonary hypertension in a patient with cirrhosis, will warrant evaluation with anesthesia and consultation with specialists [18]. A full discussion of the surgical evaluation is beyond the scope of this book.

Psychosocial Evaluation

The process of transplantation is fraught with difficult decisions and ethical dilemmas. Organs are a scarce resource. Although transplantation may be life-saving, patients are also encumbered by a lifelong need for medications, follow-up appointments, and management of care. Due to the immense post-transplant burden, the screening process for transplant candidacy encompasses many psychosocial factors, including having adequate social support, financial resources, and sufficient health literacy to be able to manage care. Unfortunately, these factors are often reflective of socioeconomic disparities [33].

Patients will be evaluated by a transplant social worker and often a transplant psychiatrist. There is not a universal evaluation metric, though several scoring scales exist [34, 35].

Patients will typically be evaluated for [34]:

- Treatment adherence and health behaviors
- Mental health history
- Substance use history
- Cognitive status and capacity to give informed consent
- Knowledge and understanding of their current illness
- Knowledge and understanding of current treatment options
- Coping abilities
- Social support
- Social history

Financial Evaluation

Depending on the country's health care system, the patient's insurance and the transplant center, financial approval may need to be secured at the beginning of the process to begin the transplant workup. In the United States, insurance coverage will be considered in terms of the costs of transplantation and post-transplantation care (including medication coverage), and the transplant center will typically have staff to assist with financial planning.

Psychiatric Evaluation

Patients with psychiatric disorders are required to have their diseases well-controlled prior to transplantation [16, 18]. Patients who are already taking psychotropic medications may need to have medications stopped or dose-reduced once transplant immunosuppression is introduced. For example, patients with bipolar disorder are often switched off of lithium to avoid postoperative metabolic shifts or renal insufficiency that could lead to medication toxicity. Such decisions should be made in conjunction with a transplant psychiatrist and a transplant pharmacist [36].

Depression and anxiety are common post-transplantation, either de novo or recurrent—knowing the patient's pre-transplant psychiatric history can be helpful with management after transplantation. Post-transplant patients have an increased risk of suicide and should be assessed regularly for mood disorders [37] (see Chap. 12).

Medication Adherence

Medication adherence is an important aspect of the psychosocial assessment. It is considered a contraindication to transplantation if a patient has current or a repeated history of medication non-adherence. Although a patient who has received a solid