Obesity has become increasingly prevalent, and the number of obese patients in need of liver transplant is expected to continue to increase. In addition, liver disease due to nonalcoholic fatty liver disease is expected to become the leading cause of liver transplantation in the near future. However, obesity remains a relative contraindication in liver transplant. New strategies in managing this patient population are clearly needed. To this end, the authors review the current literature on the efficacy of bariatric surgery in the setting of liver transplantation in obese patients.

Liver transplantation (LT) provides a good chance of cure for selected patients with hepatocellular carcinoma (HCC) and perihilar cholangiocarcinoma (pCCA). Patients with HCC on a waiting list for LT are at risk for tumor progression and dropout. Treatment of HCC with locoregional therapies may lessen dropout due to tumor progression. Strict selection and adherence to the LT criteria for patients with pCCA before and after neoadjuvant chemotherapy are critical for optimal outcome with LT. This article reviews the existing data for the various treatment strategies used for patients with HCC and pCCA awaiting LT.

The hemostatic environment in patients with cirrhosis is a delicate balance between prohemostatic and antihemostatic factors. There is a lack of effective laboratory measures of the hemostatic system in patients with cirrhosis. Many are predisposed to pulmonary embolus, deep vein thrombosis, and portal vein thrombosis in the pretransplantation setting. This pretransplantation hypercoagulable milieu seems to extend for at least several months post-transplantation. Patients with nonalcoholic fatty liver disease, inherited thrombophilia, portal hypertension in the absence of cirrhosis, and hepatocellular carcinoma often require individualized approach to anticoagulation. Early reports suggest a potential role for low-molecular-weight heparins and direct-acting anticoagulants.
The adoption of the model of end-stage liver disease (MELD) score as surrogate marker of liver disease severity has been the greatest change in liver allocation. Since its implementation, waiting time has lost significance. The MELD score calculation was later modified to reflect the contribution of hyponatremia in the estimation of mortality risk. However, the MELD score does not capture accurately the risk of mortality of patients with hepatocellular carcinoma (HCC). Therefore the arbitrary assignment of MELD points has been used for HCC patients. The current allocation system still prioritizes transplantation in HCC patients.

Mortality rates on the liver transplant waiting list are increasing. The shortage of organs has resulted in higher utilization of extended criteria donors (ECDs), with centers pushing the limits of what is acceptable for transplantation. Donor quality is more appropriately represented as a continuum of risk, and careful selection and matching of ECD grafts with recipients may lead to excellent outcomes. Although there is no precise definition for what constitutes an ECD liver, this review focuses on frequently cited characteristics, including donor age, steatosis, donation after cardiac death, and donors with increased risk of disease transmission.

Acute kidney injury (AKI) is common in patients with cirrhosis and ascites on the waiting list for liver transplant. Hepatorenal syndrome (HRS) is an important cause of AKI among cirrhotics. A dynamic definition of AKI in patients with cirrhosis has been introduced and changed the diagnosis criteria. Liver transplantation remains the better option but the medical management of HRS has changed. Terlipressin plus albumin is currently the gold standard. Surgery and liver or kidney support systems have been recommended. Clinical trials will assess the most appropriate approach for the treatment of HRS in light of the revised diagnostic criteria.

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in developing countries. Approximately 25% of patients with NAFLD develop nonalcoholic steatohepatitis (NASH). NASH-related cirrhosis is now a leading listing indication for liver transplantation in the United States. Although posttransplant survival for NASH-related cirrhosis is comparable with that of other liver diseases, many patients have features of metabolic syndrome, which can contribute to a recurrence of NAFLD or NASH. This article reviews the epidemiology,
pathophysiology, and treatment of de novo and recurrence of NASH after liver transplantation.

**Management of Immunosuppression in Liver Transplantation**

Renumathy Dhanasekaran

Liver transplantation outcomes have significantly improved over the past few decades owing largely to the introduction of effective immunosuppression medications. Further comprehension of the unique immune microenvironment of the liver has led to the development of newer molecular targeted therapeutics. Understanding the mechanism of action and adverse effect profiles of these medications is crucial for appropriate management of posttransplant patients. In this review, the author describes the immunologic response elicited by liver transplantation, chronicles the various immunosuppressant drug classes, discusses the evidence behind their use, and evaluates the management of special subpopulations of posttransplantation patients.

**Liver Transplantation in Alpha-1 Antitrypsin Deficiency**

Virginia C. Clark

Alpha-1 antitrypsin (AAT) deficiency is a common inherited metabolic disorder caused by a point mutation in the SERPIN1A gene. A small portion of homozygous PI*ZZ individuals develop severe liver disease that requires liver transplantation. Posttransplant survival is excellent. The largest burden of advanced liver disease lies within the adult population rather than children. Evaluation of lung function in adults before transplant is essential because of the underlying risk for chronic obstructive pulmonary disease. Post–liver transplantation lung function should also be monitored for decline. Although uncommon, cases of simultaneous lung and liver transplant for AAT deficiency have been reported.

**Predictors of Cardiovascular Events After Liver Transplantation**

Juan F. Gallegos-Orozco and Michael R. Charlton

Indications for liver transplant have been extended, and older and sicker patients are undergoing transplantation. Infectious, malignant, and cardiovascular diseases account for the most posttransplant deaths. Cirrhotic patients can develop heart disease through systemic diseases affecting the heart and the liver, cirrhosis-specific heart disease, or common cardiovascular. No single factor can predict posttransplant cardiovascular complications. Patients with history of cardiovascular disease, and specific abnormalities on echocardiography, electrocardiography, or serum markers of heart disease seem to be at increased risk of complications. Pretransplant cardiovascular evaluation is essential to detecting these risk factors so their effects can be mitigated through appropriate intervention.

**Autoimmune Hepatitis in the Liver Transplant Graft**

Eliza W. Beal, Sylvester M. Black, and Anthony Michaels

Recurrent autoimmune hepatitis (AIH) and de novo AIH are 2 important causes of late graft failure after liver transplantation (LT). Recurrent AIH
occurs in patients who undergo LT for AIH. De novo AIH occurs in patients who are transplanted for etiologies other than AIH. Although typically treated with standard treatment for AIH, including corticosteroids and azathioprine, both recurrent and de novo AIH may progress to end-stage liver disease requiring retransplantation.

Cholestatic Liver Diseases After Liver Transplant

Nathalie A. Pena Polanco, Cynthia Levy, and Eric F. Martin

Primary sclerosing cholangitis (PSC) and primary biliary cholangitis (PBC) are the most common cholestatic liver diseases (CLD) in adults. Liver transplant (LT) is desirable for those who progress to end-stage liver disease. CLD have become an uncommon indication for LT. PSC and PBC accounted for 7.1% of all adult LT in 2015. CLD have the best post-LT outcomes compared with other indications for LT. Disease recurrence of PSC and PBC after LT is reported in up to 37% and 43% of LT recipients, respectively. Although recurrent PBC does not affect post-LT outcomes, recurrent PSC is associated with worse post-LT survival.

The New Era of Hepatitis C: Therapy in Liver Transplant Recipients

Ester Coelho Little and Marina Berenguer

Hepatitis C virus (HCV) is the leading cause of end-stage liver disease in both Europe and the United States and is the most common reason for liver transplant. In the absence of antiviral therapy, recurrent infection is the norm with subsequent graft hepatitis and impaired survival. Whether it may be better to postpone therapy in patients in whom higher risk of failure and toxicity is coupled with lower chance of liver function improvement likely depends on several factors, including waiting time, center allocation policy, presence of hepatocellular carcinoma and local prevalence of anti-HCV-positive donors.

Liver Retransplantation: How Much Is Too Much?

Jennifer Berumen and Alan Hemming

Hepatic retransplantation has been surgically challenging since the beginning of liver transplant. Outcomes have improved over time, but patient survival with retransplant continues to be significantly worse than that of primary transplant. Many studies have focused on factors to predict outcomes. Models have been developed to help predict risk, but the decision for retransplant must be a multidisciplinary transplant team decision. The question of “when is too much?” can be guided by recipient and donor factors but is an ethical decision that must be made by the liver transplant team.