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**New Onset Diabetes Mellitus After Solid Organ  
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Gerald S. Lipshutz, and Alan H. Wilkinson

This article presents an overview of the literature on the current diagnostic criteria for new onset diabetes mellitus after transplantation (NODAT) and discusses suggested risk factors for the development of NODAT, its potential pathogenic mechanisms, and its impact on post-transplant outcomes after solid organ transplantation. Suggested guidelines for early identification and management of NODAT are also discussed.

**Immunosuppressive Agents: Effects on Glucose  
and Lipid Metabolism** 891  
Savitha Subramanian and Dace L. Trence

Immunosuppressive therapies are critical elements in successful organ transplantation. Although immunosuppressant drugs are essential in preventing graft rejection and graft maintenance after transplantation, their use is complicated by adverse effects, many being detrimental to graft and even patient long-term survival. Commonly used agents are associated with dysregulated glucose metabolism and dyslipidemia. This article focuses on the effects of immunosuppressive agents on glucose and lipid metabolism. Adrenal effects of these drugs, where known, also are discussed.

**Comprehensive Management of Post-Transplant Diabetes Mellitus: From Intensive Care to Home Care**

907

Philip A. Goldberg

Post-transplant diabetes mellitus (PTDM) is a common complication of solid organ and hematopoietic transplantation. This clinically oriented review article briefly summarizes the pathophysiology of PTDM, then presents a comprehensive clinical approach to diagnosis and therapy. Topics include the key clinical aspects of PTDM screening, diagnosis, and management during all phases following transplantation from the intensive care unit, to the inpatient ward, to the outpatient arena.

**Calcium and Bone Metabolism Pre- and Post-Kidney Transplantation**

923

Neveen A.T. Hamdy

Chronic kidney disease (CKD) is associated with significant disturbances in bone and mineral metabolism, the manifestations of which are heterogeneous in their expression and clinical impact. Over the last 2 decades, advances in the management of CKD and improved outcomes of kidney transplantation have led to the emergence of post-transplantation bone disease as a serious cause of morbidity in long-term survivors. The management of post-kidney transplantation bone disease represents a difficult challenge because of its complex pathophysiology and the paucity of clinical data on effective therapies. The optimal management of disturbances of bone and mineral metabolism before kidney transplantation forms the cornerstone of their successful management after transplantation. Therapeutic strategies to effectively and safely decrease skeletal morbidity after kidney transplantation are not yet clearly established.

**Post-Transplantation Osteoporosis**

937

Emily Stein, Peter Ebeling, and Elizabeth Shane

Osteoporosis is prevalent in transplant recipients and is related to pre- and post-transplantation factors. Low bone density and fractures may antedate transplantation, related to traditional risk factors for osteoporosis, effects of chronic illness, and end-stage organ failure and its therapy, on the skeleton. Bone loss after transplantation is related to adverse effects of immunosuppressive drugs (glucocorticoids and calcineurin inhibitors) on bone remodeling. Newer immunosuppressive medications may permit lower doses of glucocorticoids and may be associated with decreased bone loss and fractures. Bisphosphonates are currently the most effective agents for the prevention and treatment of post-transplantation osteoporosis.

## **Cardiac Allograft Vasculopathy and Insulin Resistance—Hope for New Therapeutic Targets**

965

Luciano Potena and Hannah A. Valantine

Cardiac allograft vasculopathy (CAV) is a major cause of death in patients surviving more than 1 year after heart transplantation. An important cluster of CAV risk factors occurs as a consequence of insulin resistance and manifests as part of the metabolic syndrome. This article summarizes the pathologic features of CAV and reviews the contribution of the major components of insulin resistance in CAV development and progression. It focuses on the few studies that have analyzed the impact of the individual metabolic abnormalities and inflammation and on therapeutic strategies to minimize the clinical manifestation of insulin resistance after heart transplantation.

## **Endocrine Complications of Hematopoietic Stem Cell Transplantation**

983

Wassim Chemaitilly and Charles A. Sklar

Advances in hematopoietic stem cell transplantation (HSCT) have resulted in broader indications for this therapeutic modality in both malignant diseases and nonmalignant conditions. This article focuses on the late endocrine abnormalities that are most commonly observed following successful HSCT, with a special emphasis on pediatric HSCT recipients, for whom long-term follow-up data are increasingly available.

## **Pancreatic Islet Cell Transplant for Treatment of Diabetes**

999

Paolo Fiorina and Antonio Secchi

Islet cell transplantation recently has emerged as one the most promising therapeutic approaches to improving glycometabolic control in type 1 diabetic patients, and, in many cases, to obtaining insulin independence. Islet cell transplantation requires a relatively short hospital stay and has the advantage of being a relatively noninvasive procedure. The rate of insulin independence 1 year after islet cell transplantation has improved significantly in recent years (60% at 1 year after transplantation compared to the 15% in the past years). Data from a recent international trial confirmed that islet cell transplantation potentially can be a cure for type 1 diabetes. Recent data indicate that insulin independence after islet cell transplantation is associated with an improvement in glucose metabolism and quality of life and with a reduction in hypoglycemic episodes. Islet cell transplantation is still in its initial stages, and many obstacles still need to be overcome. Once clinical islet transplantation has been established, this treatment could be offered to diabetic patients long before the onset of diabetic complications or to patients with life-threatening hypoglycemic unawareness and brittle diabetes.

**Pancreas-Kidney and Pancreas Transplantation  
for the Treatment of Diabetes Mellitus**

1015

Gerald S. Lipshutz and Alan H. Wilkinson

Kidney transplantation is the treatment of choice for end-stage diabetic nephropathy, but the ultimate treatment today for type 1 diabetes mellitus is the whole vascularized pancreas transplant. Although its use is increasing, pancreas transplantation remains an uncommonly used therapeutic option that normalizes glucose levels and results in stabilization or improvement in secondary complications far better than any other strategy available for treatment of type 1 diabetes. These documented benefits of a simultaneous kidney and pancreas transplant are the basis for its acceptance as an appropriate therapy for patients who have type 1 diabetes mellitus and end-stage renal disease.

**Preemptive Kidney Transplantation in Patients  
with Diabetes Mellitus**

1039

Rajani Dinavahi and Enver Akalin

Kidney transplantation is the most preferred treatment for end-stage renal disease because it improves not only the patient's survival compared with dialysis, but also the quality of life. Preemptive transplantation is transplantation performed prior to the initiation of renal dialysis. Recent observational studies have shown increased patient and graft survival with preemptive transplantation, compared to patients receiving transplantation after the initiation of dialysis. Preemptive simultaneous pancreas and kidney transplantation in type 1 diabetic recipients has also been shown to improve patient survival. These results indicate the importance of early referral of patients who have chronic kidney disease to nephrologists and transplant centers.

**Interferon Alpha Treatment and Thyroid Dysfunction**

1051

Yaron Tomer, Jason T. Blackard, and Nagako Akeno

Interferon alpha (IFN $\alpha$ ) is the cornerstone therapeutic agent for chronic hepatitis C virus (HCV) infection. Prospective studies have shown that up to 15% of HCV patients receiving IFN $\alpha$  develop clinical thyroid disease, and up to 40% become thyroid antibody positive. In some cases IFN-induced thyroiditis (IIT) may result in discontinuation of interferon therapy; thus, IIT represents a major clinical problem for hepatitis C patients receiving IFN $\alpha$  therapy. Recently, the mechanisms leading to the development of IIT have begun to be unraveled. It is now clear that HCV itself plays a role in the disease. Moreover, recent data suggest the IFN $\alpha$  precipitates thyroiditis by both immune modulatory mechanisms and direct thyroid toxic effects. Genetic factors also play a major role in the etiology of IIT. IIT can manifest both as clinical autoimmune thyroiditis (ie, Hashimoto's thyroiditis and Graves' disease) and as nonautoimmune thyroiditis (ie, destructive thyroiditis). Early detection and therapy of these conditions are important to avoid

complications of thyroid disease such as cardiac arrhythmias. This article reviews the epidemiology and clinical manifestations of IIT and the mechanisms causing IIT, focusing on the role of HCV.

**Use of Insulin Sensitizers in NASH**

**1067**

Mouen Khashab and Naga Chalasani

This article briefly discusses nonalcoholic fatty liver disease (NAFLD) and its association with the metabolic syndrome, its pathogenesis and natural history. It then presents a detailed discussion on the efficacy and safety of different insulin sensitizers in patients who have NASH.

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