GLOSSARY

EPSTEIN–BARR VIRUS
A herpes virus that causes disorders of lymphoid tissue

intervention was not feasible. The subjects were subsequently treated with rituximab, chemotherapy, or both at separate times. Complete responses were achieved in 13 (59%) of 22 patients who received rituximab, and in 13 (57%) of 23 patients who received chemotherapy. Patients in the rituximab group who were infected with the EPSTEIN–BARR VIRUS were significantly more likely to respond completely to treatment than those who were negative for the virus ($P = 0.014$). In the chemotherapy group, 52% of patients were hospitalized and 26% died as a result of treatment-related toxicities (mostly infections). No rituximab-treated patients died and only two were hospitalized because of therapy-associated toxicities.

Rituximab is therefore an effective and safe treatment for PTLD patients who fail to respond to immunosuppression reduction. Patients not responsive to reduction in immunosuppression or rituximab might benefit from chemotherapy. Prospective trials are needed to assess methods for minimizing chemotherapy-associated infection rates.

Rachael Williams

Original article Elstrom RL *et al.* (2006) Treatment of PTLD with rituximab or chemotherapy. *Am J Transplant* **6:** 569–576

Decreased heart-rate variation predicts poor prognosis in diabetic nephropathy

Cardiovascular autonomic neuropathy, a severe complication of diabetes, results from damage to autonomic nerve fibers leading to the heart. The earliest sign of this condition is a decrease in heart-rate variation (HRV) during deep breathing. Cardiovascular autonomic neuropathy is common in patients with diabetic nephropathy. Astrup *et al.* have investigated whether an abnormal HRV of ≤10 beats/min can be used to predict cardiovascular morbidity and mortality in patients with and without diabetic nephropathy.

This study included 197 patients with type 1 diabetes and diabetic nephropathy, and a control group of 191 age-matched and sex-matched patients with type 1 diabetes and normoalbuminuria. During a mean follow-up of 10.1 years, significantly more patients with nephropathy reached the combined primary endpoint of cardiovascular morbidity and mortality than did those with normoalbuminuria (40% vs 10%; $P < 0.0001$). In patients with diabetic nephropathy, abnormal HRV was significantly associated with development of cardiovascular disease or death even after adjustment for confounding factors (hazard ratio 6.4, 95% CI 1.5–26.3; $P = 0.010$). In normoalbuminuric patients, however, abnormal HRV was not a significant predictor of the primary endpoint.

The authors conclude that HRV could be used, along with other risk factors, to identify patients with diabetic nephropathy who are at risk of cardiovascular disease and death, thereby enabling early intervention.

Rebecca Ireland

Original article Astrup AS *et al.* (2006) Cardiac autonomic neuropathy predicts cardiovascular morbidity and mortality in type 1 diabetic patients with diabetic nephropathy. *Diabetes Care* **29:** 334–339

Patient factors explain variability in mycophenolic acid exposure

EBM

A standard dose of mycophenolate mofetil (MMF; 1 g twice daily) is administered to renal transplant recipients to prevent acute allograft rejection. MMF is a prodrug of mycophenolic acid (MPA); the exposure goal for MPA is 30–60 mg/l/h. MPA levels can vary greatly between renal transplant recipients and show large fluctuations within the same individual. If adequate exposure to MPA is to be ensured, doses of MMF might need to be tailored to individual patients. In a meta-analysis, van Hest *et al.* investigated the influence of various patient characteristics on levels of MPA.

Data were gathered retrospectively from 468 renal transplant patients who had participated in six trials; MMF doses were in the range 250–2,200 mg twice daily. Exposure to total MPA, determined by MPA clearance, was calculated from samples taken 1 day to >10 years following transplantation. Multivariate analysis indicated that total MPA exposure increased significantly with increasing renal function, albumin level and hemoglobin, and decreasing ciclosporin predose level ($P < 0.001$). These variables accounted for 38% of within-patient and 18% of between-patient variability in MPA exposure.

Changes in renal function and albumin level emerged as the most important factors affecting MPA clearance. Because the effect