the precipitation (saturation point) of the diluting elements. Thus, taking samples from the upper part of the U24h (unshaken sample) may give wrong values for the degree of Upr and Ccr. In CKD patients, the quantification of Upr excretion is the most important test for the initial diagnosis and follow-up of patients with glomerulopathies. The response to immunosuppressive drugs or to other therapeutic interventions is defined by the degree of Upr reduction in patients with nephrotic and non-nephrotic types of Upr. An estimation of the degree of Upr which is based on BS samples falsely leads to the assumption that a partial remission is evident, whereas the real degree of Upr is actually higher. On the other hand, the value of Ccr guides the nephrologist to adjust the patient’s protein intake, and avoid potentially nephrotoxic drugs or interfering with sodium and potassium homeostasis.

In conclusion, it seems that the procedure of U24h sampling can influence the estimation of renal dysfunction based on Ccr and the degree of Upr. For that reason, correct U24h collection and sampling examination after shaking are the necessary procedures for the correct initial estimation of renal dysfunction.

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A case of post-allogeneic haematopoietic stem cell transplantation membranous nephropathy

Sir,

We read with special interest the paper by Terrier et al. [1], regarding the occurrence of membranous nephropathy (MN) after allogeneic haematopoietic stem cell transplantation (HSCT). The authors described five patients who presented with membranous nephropathy, with history and active manifestations of chronic graft-vs-host disease (GVHD) at MN diagnosis, suggesting that chronic GVHD might contribute to the development of MN after allogeneic HSCT. We have, however, encountered a patient who showed nephrotic syndrome due to MN after allogeneic HSCT without any history or manifestations of GVHD.

A 38-year-old Japanese man with acute myeloid leukaemia (AML, M4 with eosinophilia) in second remission underwent an allogeneic HSCT from an HLA-identical donor. Total body irradiation and cyclophosphamide were used as conditioning therapy, a short-time methotrexate and cyclosporine (CsA) as GVHD prophylaxis. As he did not show any evidence of acute or chronic GVHD, CsA was tapered and withdrawn after 10 months. Several months later, hypoalbuminaemia developed, and marked proteinuria was found at 20 months after HSCT; he was thus referred to our department. On admission he presented with nephrotic syndrome, with daily protein excretion of 13.1 g, serum albumin of 2.4 g/dl and reduced renal function (serum creatinine, 0.79 mg/dl and glomerular filtration rate, 44.5 ml/min). He had never presented any clinical or laboratory manifestations of chronic GVHD (e.g. skin lesions, gastrointestinal manifestations or liver function abnormalities), nor signs of recurrence of leukaemia. Serological studies including complements, anti-nuclear antibodies and hepatitis B/C, yielded negative/normal results. A perepuetaneous renal biopsy revealed normocellular glomeruli with mild capillary wall thickening and marked renal tubular atrophy with interstitial fibrosis. Immunofluorescent study revealed granular immune deposition for IgG on the capillary wall, but no deposition of IgA, IgM, C3 C4 or Clq. Electron microscopy showed small and discreet electron-dense subepithelial deposits without basement membrane reaction, indicating early stage MN. As we suspected, his renal interstitial lesions might be evoked by CsA nephrotoxicity, we initiated corticosteroid therapy (prednisolone, 40 mg/day).

As described by Terrier et al. [1], several reviews of the literature reveal a close temporal relationship between the development of MN shortly after cessation of immunosuppressants and the diagnosis/presentation of chronic GVHD in allogeneic HSCT patients [1–5]. Further, there are few reports describing MN patients without acute or chronic GVHD after allogeneic HSCT, indicating that MN is thought to be a renal manifestation of GVHD. As his nephrotic syndrome developed after the cessation of CsA, MN is thought to be the only manifestation of chronic GVHD. Our patient is, however, characterized by the presentation of MN without any history or manifestations of GVHD; thus, there is a possibility that de novo MN might have occurred in our case. Our case merits presentation because further accumulation of clinical studies including case reports is necessary, to confirm whether MN is a real manifestation of GVHD after allogeneic HSCT or merely a coincidence.

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**Everolimus-associated interstitial pneumonitis in a patient with a heart transplant**

Sir,

Pneumonitis is a severe complication of different immunosuppressive treatment regimens; in particular, cases of sirolimus-associated pneumonitis have been reported so far [1–3]. Here, we report for the first time a patient who developed pneumonitis as a result of an everolimus-based immunosuppressive treatment regimen.

A 71-year-old man was admitted to the hospital because of severe diarrhoea, intermittent fever and generalized malaise. Nineteen years previously, he underwent a heart transplantation and was therefore on immunosuppressive treatment with everolimus (1.75 mg twice daily), mycophenolate mofetil (500 mg twice daily) and prednisone (7.5 mg/day). Despite a target serum level of about 8–10 µg/l, the 24 h everolimus trough level was markedly increased (22.6 µg/l). Laboratory indicators of systemic inflammatory reaction were elevated at this time (C-reactive protein 271 mg/l, pro-calcitonin 7.5 mg/l). After institution of empiric intravenous antibiotic treatment (ceftriaxone, metronidazole), clinical symptoms of gastrointestinal tract infection disappeared rapidly. However, low-grade fever remained and slowly developing respiratory symptoms came to the focus of our attention. The patient was tachypnoeic at rest and had fine bilateral basal crackles on auscultation. Peripheral oxygen saturation was found to be low and even fell under exertion to 85%, blood gases showed partial respiratory insufficiency (pO2 61 mmHg, pCO2 32.7 mmHg). Acute endocarditis was excluded by echocardiography. CRP was still elevated (148 mg/l), blood cultures taken before empiric antibiotic therapy were negative for bacterial and fungal pathogens and, despite changing the antibiotic therapy to piperacillin/tazobactam, the fever increased to 40 °C (see clinical course—Figure 1). The chest X-ray did not reveal pulmonary infiltrations, but in the high-resolution computed tomography of the chest bipulmonal ‘air trapping’

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**Fig. 1.** The clinical course, serum CRP concentrations and serum trough levels of everolimus in relation to treatment. The bronchoscopy was performed on day 9.