due to IgA nephropathy received a cadaveric renal transplant (1, 1, 0 mismatch) in February 1995. The subsequent course was uneventful; she was maintained on prednisolone, azathioprine, and cyclosporin and was not receiving diuretics. In May 1996 serum creatinine was 145 μmol/l (normal 70–140 μmol/l). In June 1996 she was admitted with a 1-week history of malaise, and aching and swelling of the transplant. Two to three weeks earlier she had strained her neck, and had been prescribed DF118 for pain. On admission, creatinine was 658 μmol/l, haemoglobin 10.8 g/dl, white blood count 7.2×10^9/l, with a normal differential. Trough monospecific cyclosporin concentration was 140 ng/ml (therapeutic range 100–200 ng/ml). Urinalysis revealed both blood and protein. Cultures of blood and urine were sterile. Doppler ultrasound of the kidney showed normal appearances, no hydronephrosis, and a normal inter-lobar resistivity index of 0.6.

Biopsy of the transplant showed normal glomeruli and blood vessels with no evidence of intimal arteritis. There was marked interstitial oedema with a diffuse inflammatory infiltrate predominantly composed of eosinophils. There was widespread tubular epithelial flattening with vacuolation of the cytoplasm of the remaining tubular cells. There was only focal tubulitis, the majority of the tubules were devoid of inflammation. In the absence of a full-blown picture of rejection and in view of the presence of large numbers of eosinophils, the most likely cause of transplant dysfunction was considered to be an acute interstitial nephritis, probably drug-related.

The patient was treated with prednisolone 60 mg daily and serum creatinine improved to 211 μmol/l. Further questioning revealed that the prescribed analgesic had been ineffective and so she had purchased a proprietary brand of ibuprofen, which she had taken regularly up to the onset of symptoms.

Nonsteroidal anti-inflammatory drugs are well recognized as a cause of acute interstitial nephritis [1,2]. There are few previous reports [3] of acute allergic tubulointerstitial nephritis in renal transplant patients maintained on immunosuppressive therapy, which might be presumed to be protective. Concern has been expressed over the possible adverse effects of over-the-counter preparations, although the risks are recognized as being small [4,5]. This case highlights the need for a full and careful drug history in all cases, with attention being paid to the increasing number of drugs which have become available as over-the-counter preparations.

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Membranoproliferative glomerulonephritis associated pulmonary sarcoidosis

Sir,

Glomerulonephritis associated with sarcoidosis was first reported in 1951 when hyaline and fibrinoid changes were noted in the glomeruli of a patient with generalized sarcoidosis. Since that, numerous other histopathologic varieties of glomerulonephritis have been reported including membranous nephropathy, focal glomerulosclerosis and proliferative and membranoproliferative glomerulonephritis [1]. Hypercalcaemia, nephrolithiasis, nephrocalcinosis, granulomatous nephritis, interstitial nephritis without sarcoid granuloma, granulomatous arteritis, glomerulonephritis are seen in renal involvement of sarcoidosis. We reported membranoproliferative glomerulonephritis in a patient with pulmonary sarcoidosis. Prednisolon therapy caused resolution of nephrotic syndrome and pulmonary lesions.

A 37-year-old man was admitted to hospital for exertional dispne and oedema. Past history revealed headache, hypertension, and oedema. Physical examination disclosed blood pressure 190/100 mmHg, pretibial oedema, and ralles on the lungs. Abnormal laboratory findings were as follows: haematocrit 32.6%, haemoglobin 9.5 g/dl, white blood cells 11900/mm^3, total protein 8.4 g/dl, albumin 3.5 g/dl, cholesterol 249 mg/dl, HDL cholesterol 84 mg/dl, LDL cholesterol 142 mg/dl, serum Ca 9.9 mg/dl. Antinuclear antibody, rheumatoid factor, hepatitis markers for hepatitis A, B, and C were negative. PPD was negative. Daily proteinuria was 2.5 g. Chest X-ray film and CT scan of the chest showed mediastinal and bilateral hilar lymphadenopathy and an increase in density of the lung parenchyma. Respiratory function tests showed restrictive changes. Rectal and bone marrow biopsies and subcutaneous fat aspiration did not contain deposition of amyloidosis. Noncaseating granulomatous inflammation was found in bronchial mucosa obtained by fiberoptic bronchoscopy. Renal biopsy showed membranoproliferative glomerulonephritis (Figure 1). Deposition of amyloidosis was negative. T4 and T8 were 36% and 23.8%, respectively. NBT was 10%. Serum thyroid hormone levels were normal. Serum angiotensin converting enzyme (ACE) level was 10 U. The patient was treated with prednisolon 1 mg/kg/day, famotidin 20 mg/day, and amlodipin 5 mg/day.

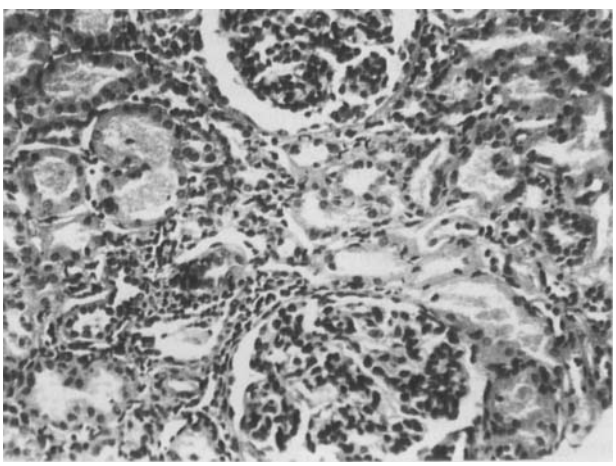


Fig. 1. Light microscopic examination (H & E × 375) showed: expansion of glomerular tuft, increment of cellularity and mesangial matrix, thickening basement membrane, infiltration of polymorphonuclear leucocytes (PMN) and mixed infiltration including PMN of the interstitium.

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At the sixth week of the treatment the patient was well and oedema free. Proteinuria was <0.5 g/day. Prednisolon dose was decreased to 20 mg/day. After 4 months, proteinuria disappeared, renal function was again normal, serum proteins and lipid levels were normal. In the second thorasic CT scan, parahilar lymphadenopathies and interstitial changes were regressed. At that time serum ACE value was 6.5 IU. With prednisolon (5 mg/day) and amlodipin he was normotensive, oedema free, with normal renal function and negative proteinuria at the 30th month. Respiratory function was not further impaired.

Pulmonary sarcoidosis is a chronic granulomatous disease of unknown aetiology. Interleukines and T cell growth factors are released from T lymphocytes found in pulmonary inflammation [2]. It is known that interleukins may play a role in the pathogenesis of nephrotic syndrome [3]. Regression of systemic findings and especially proteinuria in patients treated with corticosteroids could be due to the anti-inflammatory effects of steroids. In some reports corticosteroid therapy did not affect membranous glomerulonephritis associated with sarcoidosis [1,4]. But our case responded to steroid therapy for renal and extrarenal findings. Also, the serum ACE concentration decreased with corticosteroid therapy, and respiratory findings improved. Glomerulopathy with normal complement levels as in our case may occur in patients with sarcoidosis. Some tissue factors can lead to glomerular injury and corticosteroids can be used effectively in the treatment of glomerulopathy associated with sarcoidosis.

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Recombinant erythropoietin improves cognitive function in chronic haemodialysis patients

Sir,

It is well known that recombinant erythropoietin (rHuEpo) therapy reliably corrects anaemia and recent attention has been focused on an associated improvement of other factors, such as exercise capacity and well-being, which previously restricted the rehabilitation of dialysis patients.

We investigated cognitive function (memory and attention) [2,3] by performing a series of psychometric tests on 14 dialysis patients treated with rHuEpo and 14 matched control patients [4]. Patients with a history of head injury, epilepsy, stroke, or cerebral lesion, as well as those with malignant disease, sepsis, or poorly controlled hypertension were not included in the study. All haemodialysis patients were in stable condition for a minimum of 6 months. Fourteen patients with severe anaemia were selected for treatment with rHuEpo and another group of anaemia patients, matching the treatment group for age, duration of dialysis, education and DFO/desferrioxamine test served as controls (Table 1).

The patients in group 1 were treated with Eprex Alfa epoetin (Janssen Cilag) at an initial dose of 50 U/kg thrice weekly. No patient received psychotropic or antidepressant therapy during the study. Tests of cognitive ability were performed over a 90-min period immediately before a dialysis session. Memory was evaluated by the Baumler test [2] and by the ability to memorize 10 words [2]. Attention was assessed using the Labyrinth test according to Chapuis [2], the Symbol digit test [2], Fave Labyrinths [2] and Interweaving Lines according to Platonov [2]. At the time of each psychometric assessment, the patients were also scored for their degree of hypochondria, depression and anxiety using the MMPI/Minnesota Multiphasic Personality Inventory scale [1,3]. The ability of the patients to cope with the tasks assigned to them was assessed. Based on the results of the attention and memory evaluations, we scaled the patients according to the predicted degree of deficit in their cognitive process; ranging from normal to very severe deficiency (normal <84%, mild 68–83%, moderate 51–67%, considerable 34–50%, severe 18–33%, very severe 0–17%).

The average haemoglobin values of group one increased from 6.4 ± 0.5 to 12.1 ± 1.7 g/dl following rHuEpo treatment, while no change in average haemoglobin level was observed for group 2. At baseline, mild (degree II) and moderate deficits (degree III) in cognitive function were observed. Twelve months following the initiation of therapy, there was improvement in the results of the memory and attention tests in group 1. Memory improved by $23.2 \pm 6.3\%$ using the Baumler test ($P < 0.001$) and by $21.1 \pm 6.9\%$ as assessed by the 10 word memorization exercise ($P < 0.001$). The patients in group 1 scored higher on the tests evaluating attention: Labyrinth test according to Chapuis, Symbol–Digit test, Five Labyrinths test and Interweaving Lines according to Platonov.

Our results are consistent with recent reports on improved cognitive function in chronic haemodialysis patients treated with rHuEpo. The beneficial effects of rHuEpo on cognitive function suggest that anaemia is a reversible contributor to cerebral dysfunction previously thought to be secondary to uraemia.

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Table 1. Study groups expressed as median or mean ± SD

	Group 1 rHuEpo $n=14$	Group 2 Controls $n=14$
Male/Female	8/6	7/7
Age (years)	47 (19–64)	40 (18–62)
Duration of haemodialysis (months)	42 (12–70)	59 (8–110)
Education	High school University	High school University
DFO-test	Negative	Negative

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