haemodialysis. In fact, plasma AM levels were significantly increased after a haemodialysis session.

Although the exact mechanism of elevation of plasma AM concentrations in patients with ESRD on haemodialysis is not clear. These observations suggest that elevation of plasma AM in patients with ESRD may be in response to the conditions elicited by ESRD such as hypercalcaemia and/or hypertension [10]. Moreover, the increase of plasma AM concentrations after the single haemodialysis session may be caused by activation of monocytes/neutrophils by the biocompatible cuprophane membrane or from injured vascular endothelial cells throughout the body. Further studies are needed to establish the exact origin of the circulating AM in patients on haemodialysis.

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Atheroembolic disease associated with the use of low-molecular-weight heparin during haemodialysis

Sir,
Systemic anticoagulation is a well known risk factor for atheroembolic disease in atheromatous patients. To our knowledge, cholesterol crystal embolization has never been described as a consequence of the use of low-molecular-weight heparin during haemodialysis.

A 72-year-old man with a past history of hypertension and diabetes mellitus was admitted to our unit in January 1997 because of acute renal failure following an arteriography. Physical examination revealed blue toes and livedo racemosa. Laboratory investigation showed: serum creatinine concentration 700 μmol/l, white blood cell count 6780/mm³, with eosinophilia 710/mmol³. Atheroembolic disease was suspected but not proven by histology. Cutaneous symptoms and eosinophilia slowly improved but renal failure worsened. He was started on continuous ambulatory peritoneal dialysis (CAPD) in March 1997. CAPD was withdrawn 1 year later because of recurrent peritonitis. Haemodialfiltration was begun. Per-dialytic anticoagulation was proscribed because of the potential risk of atheroembolic disease with heparin.

Four months later, iterative coagulations of extracorporeal circulation responsible for anaemia led us to introduce low-molecular-weight heparin (enoxaparine 10 mg) at the beginning of dialysis. After the second session, the patient complained of abdominal pain with diarrhoea and general malaise. Physical examination revealed skin necrosis of his fingers and diffuse livedo reticularis. Eyeground showed cholesterol crystals. There was neither eosinophilia nor thrombocytopenia. Discontinuation of enoxaparine was followed by resolution of the abdominal symptomatology. Cutaneous lesions slowly improved. The patient died 3 months later because of pseudodemembranous colitis.

Atheroembolic disease is an infrequent disorder that occurs as a result of embolization of cholesterol crystals from atheromatous plaques lining the aorta and other major arteries. The prognosis is poor [1]. It occurs spontaneously in the majority of the cases, but adjuvant factors as invasive vascular procedures, thrombolysis, and anticoagulation are sometimes present [2]. Only one report describes the occurrence of atheroembolic disease following the subcutaneous administration of low-molecular-weight heparin [3], but never during haemodialysis. In this case, the diagnosis of atheroembolic disease is confirmed by the presence of cholesterol crystals on eye-ground. The close time relationship between the administration of enoxaparine and the manifestations of atheroembolic disease emphasizes the role of low-molecular-weight heparin in the pathogenesis of this disease. We think that low-molecular-weight heparin should
not be used for dialysis anticoagulation in patients with a past diagnosis of atheroembolic disease. When a patient with a past history of cholesterol crystal embolization needs extrarenal epuration, peritoneal dialysis or haemodialysis without anticoagulation should be used.

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An exploratory study examining the influence of religion on attitudes towards organ donation among the Asian population in Luton, UK

Sir, I would agree with G. Randhawa [1] that Moslems view organ donation in the light of religious teachings and ethics. Indeed a Moslem’s deeds are, or should be, greatly governed by the teachings of Islam. I wish to make the following comments in the light of our experience in the Kingdom of Saudi Arabia.

We would not have had a successful cadaveric programme in the Kingdom of Saudi Arabia without first obtaining religious leaders opinion (Fatwa) that Islam does not object to organ donation. We are now probably the leading Islamic country in transplantation from cadaveric donors (980 kidneys, 215 hearts (or heart valves) and 165 livers have been transplanted so far).

Saudis, before donating, always ask whether a fatwa has been passed to allow them donating their next of kins organs. Even when we assure them of this, they often seek the advice of a prominent religious person, whom they trust to seek his counsel.

Many fatwas have been passed by the Islamic Jurisprudence Council, which is made up of prominent religious scholars from all over the Islamic world allowing cadaveric organ donation, brain death and even xenotransplantation. Furthermore, they always, of course, stipulate that there is no harm done to the donor or desecration of his body, the chance of success outweighs failure and no other better alternative is available. They also stress willingness for donation by involved parties and refuse commercialism.

It may therefore be useful, in order to encourage Moslems in the west to donate organs, to have an intensive media campaign to inform them of its permissibility in Islam, to educate local Mosque Imams to support the campaign (since they will always be referred to for counselling) and also highlight to them that in many Moslem countries, especially Saudi Arabia where the sacred mosques exist and where Islamic Jurisprudence is applied as a way of life, that cadaveric organ donations is practiced routinely.

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Sir, Cyclosporin and tacrolimus (FK506) are both potent immunosuppressive agents which are characterized by a narrow range between blood concentrations that produce therapeutic efficacy and those which produce potentially serious side effects, such as nephrotoxicity, neurotoxicity, fluid retention and hypertension [1,2]. Since both drugs are extensively metabolized by the hepatic and intestinal cytochrome P-450 system, circulating levels may be greatly increased by inhibitors of these microsomal enzymes, including ketoconazole, cimetidine, erythromycin, danazol, methylprednisolone, diltiazem and verapamil [1,2]. We present two cases which suggest that metronidazole should also be added to this list.

**Case 1**: a 69-year-old man underwent cadaveric renal allograft transplantation in March 1998 for end-stage renal failure secondary to hypertensive nephrosclerosis. There was no prior history of other significant comorbid illnesses and he was on no medications, apart from calcitriol, calcium acetate, erythropoietin and nifedipine. His initial immunosuppressive therapy consisted of a combination of cyclosporin, prednisolone and sirolimus. On day 18, he developed acute vascular rejection, which responded promptly to 3 days treatment with intravenous methylprednisolone, followed by conversion of cyclosporin to tacrolimus and sirolimus to mycophenolate. The plasma cyclosporin stabilized at 0.21 mmol/l and mean ±SD trough tacrolimus levels in the blood were 10.4 ±1.6 μg/l on a daily dose of 5 mg (3 mg mane, 2 mg nocte). Two months after transplantation, he developed profuse, watery diarrhoea complicated by orthostatic hypotension. Stool cultures yielded *Clostridium difficile* and he was treated with a 2-week course of 400 mg of metronidazole three times daily *per os*. The patient’s diarrhoea settled after 2 days, but tacrolimus levels progressively rose from an initial value of 9.0–17.9 μg/l after 9 days (Figure 1). This was accompanied by an increase in plasma creatinine from 0.15 mmol/l to 0.21 mmol/l. His tacrolimus dosage was reduced accordingly to 1 mg twice daily, resulting in a fall in tacrolimus and creatinine concentrations over the next few days to 8.1 μg/l and 0.16 mmol/l, respectively. When his metronidazole was ceased at the completion of the 2-week treatment course, tacrolimus concentrations promptly fell further to a nadir of 5.2 μg/l. The dosage of tacrolimus was subsequently doubled to 2 mg b.d. to achieve a level of 8.8 μg/l, which has remained stable thereafter.

**Case 2**: a 50-year-old man received a left iliac fossa cadaveric renal allograft in February 1997 for end-stage renal failure secondary to glomerulonephritis. His post-operative course was uncomplicated and he remained well for 14 months. His immunosuppressive regime consisted of cyclosporin, azathioprine and prednisolone. During the second year post-transplantation, his cyclosporin dosage and trough whole blood levels had remained stable at 125 mg twice daily and 130–150 μg/l, respectively. On July 1 1998, he was admitted to hospital with a 3-day history of vomiting and diarrhoea associated with right iliac fossa tenderness. His serum creatinine was unchanged at 0.17 mmol/l and com-