days prior to admission, he was diagnosed as having a recurrence of pulmonary tuberculosis and was started on the same four medications at a local clinic. One day after the initiation of this treatment, he noted jaundice, abdominal pain and oliguria. Admission laboratory data were as follows: blood urea nitrogen, 71.6 mg/dl (25.5 mmol/l); creatinine, 5.2 mg/dl (459 μmol/l); albumin, 4.0 g/dl (40 g/l); total bilirubin, 14.0 mg/dl (238 mmol/l); direct bilirubin, 9.8 mg/dl (166 mmol/l); aspartate aminotransferase, 170 IU/l; alanine aminotransferase, 28 IU/l; urine pH 7.0, specific gravity 1.010, proteinuria 3þ; and the urine sediment contained many red cells and 3–5 white cells per high-power field. Sputum stained positive for acid-fast bacilli. All four antituberculosis medications were stopped on the day of admission.

Anuria persisted for 4 days. On the 8th and 15th day after initiation of antituberculosis medication, isoniazid and rifampicin were reintroduced without development of anuria or other intolerance reactions. On the 24th day after initiation of antituberculosis medication, ethambutol was reintroduced, and abdominal pain, fever and general weakness occurred on the same evening. The serum creatinine level increased to 8.6 mg/dl and urine output decreased; therefore, haemodialysis was initiated (Figure 1). A renal biopsy performed on the 39th day after initiation of antituberculosis medication showed features characteristic of acute tubular necrosis that were more prominent than interstitial infiltration. The patient completely recovered his renal function after receiving isoniazid, rifampicin, pyrazinamide and cycloserine.

Comment. Ethambutol-induced acute renal failure is very rare; we know of only three reported cases of tubulointerstitial nephritis due to ethambutol administration [1,2]. In those cases, the renal function deteriorated only after administration of antituberculosis medication over several months, and liver function tests were normal. The clinical characteristic findings of ethambutol-induced acute renal failure were sudden onset of oliguria and renal failure, association with hepatotoxicity, and development after re-exposure to ethambutol. On the basis of the histological appearance and the time course of the disease, we suggest that the renal damage in our patient was due to a toxic rather than an allergic effect producing a tubular lesion and interstitial nephritis.

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Dobutamine-induced myoclonia in severe renal failure

Sir,

Dobutamine is a catecholamine with β1-, β2- and α1-adrenergic properties. This drug is marketed as a racemic mixture containing two stereoisomers having different distribution and elimination properties. Pharmacological activity also differs: the L-enantiomer is a potent α1-agonist whereas the D-enantiomer is a potent β1-agonist [1]. Dobutamine is widely used in the treatment of severe heart failure. Tachycardia is the most common effect. To our knowledge, no neuromuscular disturbances with dobutamine administration have been reported.

We observed six cases of dobutamine-induced myoclonia in four women and two men (68.6 ± 6.35 years old) hospitalized for congestive cardiac failure responsible for severe renal insufficiency (creatinine clearance: 15.5 ± 2.5 ml/min/1.73 m2). Mean arterial pressure was 62 ± 5 mmHg. Serum ASAT and ALAT were increased by 25% above normal range and total bilirubin and alkaline phosphatases were normal. The patients had moderate hypotension (127 ± 3 mmol/l). Plasma potassium was normal, mean plasma total calcium was decreased (2.17 ± 0.05 mmol/l) and serum magnesium was slightly increased (1.3 ± 0.1 mmol/l). All patients had metabolic acidosis, with
In such patients the described side effect of dobutamine is associated condition to induce myoclonia. It is possible that failure. Severe renal failure appears to be an obligatory consideration. The well-known prevalence of congestive heart failure and impaired hepatic drug metabolism has been reported [2]. In uraemic patients, O-methylation could be altered by non-competitive erythrocyte COMT inhibition due to larger amounts of endogenous methyl acceptors in uraemic plasma than in normal plasma [3]. This mechanism could prolong dobutamine half-life.

Pgp activity has been shown to be reduced in rats with acute renal failure [4], together with a suppression of its brain function [5]. Pgp inhibition could be enhanced by furosemide [6], which was part of patients’ treatment. It is admitted at present that Pgp, which is expressed at the site of the blood–brain barrier, limits the entry of xenobiotics and prevents them from reaching toxicological concentrations. Therefore, Pgp inhibition could increase brain delivery of dobutamine.

Our hypothesis would explain a longer dobutamine half-life and a more marked penetration of the drug into the nervous system, ultimately responsible for myoclonia. As for other β1 adrenergic drug-like tricyclic antidepressants, stimulation of β1 post-synaptic adrenergic receptors leads in turn to an activation of serotoninergic neurons. This could induce myoclonia, when occurring at the cortical level. To our knowledge, dobutamine-induced myoclonia has not been reported before, despite the wide utilization of this drug, considering the well-known prevalence of congestive heart failure. Severe renal failure appears to be an obligatory associated condition to induce myoclonia. It is possible that in such patients the described side effect of dobutamine is likely to be underestimated or neglected because of other major signs and symptoms caused by severe cardiac failure.

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The impact of visceral fat on multiple risk factors and carotid atherosclerosis in chronic haemodialysis patients

Sir,

We read with much interest the original article by Yamauchi et al. [1] reporting the importance of visceral fat (VF) in carotid atherosclerosis, lipid abnormalities and hyperinsulinemia in maintenance haemodialysis patients. In their study, the patients were separated into three groups according to VF content, and three groups were compared for well known atherosclerotic risk factors such as age, blood pressure, lipid levels, duration of haemodialysis, haemodialysis efficiency (Kt/V urea), fasting plasma glucose and insulin levels. They evaluated systemic atherosclerosis with carotid intima media thickness (CIMT), plaque score (PS) and stiffness parameter (SP) by high-resolution B-mode ultrasonography. All three methods shows that patients with higher VFA had greater carotid atherosclerotic changes. In this study, although VFA was not correlated with CIMT, it was correlated with PS and SP. Using multivariate regression analysis, they found that VFA was the strongest predictor of PS, but not SP and CIMT.

When looking at the relationship between VFA and lipid abnormalities and hyperinsulinemia, it was clear that VF was a good predictor of metabolic disorder as it was shown in non-dialysis subjects. However, as stated in the Discussion (para 3), it seems to be difficult to conclude that VF had an additional risk for atherosclerotic disease and contributed to the accelerated atherosclerosis. As shown, VFA was highly correlated with well-known risk factors such as low high-density lipoprotein (HDL), high triglyceride and high plasma insulin levels. If there were a correlation analysis between these factors (HDL, plasma insulin, fasting glucose and triglyceride) and systemic atherosclerosis (CIMT, PS and SP), one would expect the existence of a correlation between metabolic factors and systemic atherosclerosis. In addition, the multivariate regression models including body mass index (BMI), SFA and VFA (independent variables) were performed to clarify which was the most strongly related to carotid atherosclerosis (PS, SP and CIMT taken as dependent variables). They found that only PS seems to