of calcium salts under these circumstances is common in the UK, in keeping with clinical teaching and a number of available guidelines (e.g. http://www.clinicalschool.swan.ac.uk/wics/itugl/hi.htm and West Mercia Guidelines Partnership: Medical Guidelines, 2003) which advise using intermittent injections of 10 ml of 10% calcium gluconate and/or calcium chloride. This advice has also been promulgated and considered in Emergency Medicine literature [2], yet it is based on the evidence of anecdote, extrapolation and experience rather than any randomized prospective trial. The extrapolations which carry most weight are from cardiac surgery, where directly applied calcium salts help restore sinus rhythm intraoperatively, and the indubitable correction of the hyperkalaemic ECG abnormalities that many of us have observed first hand using calcium salts under these circumstances. Unfortunately, the ECG improvement and inferred membrane stabilization do not often persist, hence the advice to repeat doses as necessary. Tempting as it is to jump logically from an improved ECG appearance to a reduced chance of an adverse outcome, there is no hard evidence to show that such a manoeuvre does actually diminish the incidence of life-threatening dysrhythmia. One of the main supports for the advice may be guilty of succumbing to this temptation [3]: in a case series of five instances of treating severe hyperkalaemia with intravascular calcium, ECG improvement was seen every time. Unfortunately, the outcomes were: immediate death (case 3), death within an hour (case 2), death within a few days (case 4), death after a couple of months (case 5) and only in one case did long-term survival ensue (case 1). Given such outcomes, particularly in the absence of randomization, it is only a speculation that the calcium was actually helpful. It can properly be argued that ‘if calcium does no harm but may save a life in a minority of cases then surely its use is worthwhile?’ This might be so, but then we can go on to ask whether a calcium-containing infusion, giving steadier calcium levels, would yield better outcomes. One of the largest studies, again non-randomized and essentially observational, would suggest so [4]. The successful management of 46 cases of battlefield acute renal failure in Korea by the US army employed a continuous infusion containing calcium gluconate, sodium bicarbonate, dextrose and insulin.

At the end, I do not know the answer regarding the place of calcium salts in the acute management of hyperkalaemia with ECG changes, but would certainly value the opinion of the authors.

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Chronic overdose of leflunomide inducing interstitial nephritis

Sir,

Leflunomide (LFM) is one of the relatively new drugs in the treatment of rheumatoid arthritis (RA) [1]. It has been reported as causing anaphylaxis, hepatic failure, Stevens–Johnson syndrome and toxic epidermal necrolysis [2], but never as causing renal tubulointerstitial disease. We report a case of a man who was taking a higher dose than prescribed of LFM (equivalent to 34 mg/day) and developed acute on chronic reversible renal impairment secondary to interstitial nephritis.

Case. A 70-year-old male patient was diagnosed at the age of 55 with chronic active RA. He was tried on many medications including anti-inflammatory drugs, steroids, weekly intramuscular gold injections and finally oral methotrexate (stopped due to elevated liver enzymes). The patient had another disease flare up and was started on LFM 100 mg loading dose for two doses and 10 mg/day for maintenance. The initial response was modest, so the LFM dose was increased to 20 mg per os per day. The patient was reviewed every 3 months and it was noted that his creatinine was increasing gradually from a baseline of ~140 mol/l to 287 mol/l over 2 years. The baseline creatinine was elevated because of uncontrolled hypertension. The patient was reluctant to bring his medication to clinic, but when he finally brought his regular prescription, it became clear that he was taking LFM 100 mg once a week in addition to his 20 mg daily maintenance dose. This equated to an average of 34 mg of LFM for the day for the past 26 months. His other medications were bumetanide, furosemide, atenolol, aspirin, amiodarone and lisinopril. Urinalysis showed low-grade proteinuria and negative urine sediment, and renal ultrasound was normal. Because of continuously rising creatinine, a renal biopsy was performed and revealed patchy chronic tubulointerstitial nephritis (non-cosinophilic), 10% glomerulosclerosis and hypertensive vascular changes with no immunoglobulin deposition (see Figure 1). LFM was stopped immediately and he was started on daily 20 mg prednisolone, mainly to control his RA and for the possible benefit from steroids, although the evidence for this in the literature is weak. Plasma creatinine started to decrease after 1 month and returned to 160 mol/l (close to the patient’s baseline) after 5 months. No other drug changes were made.

Comments. RA, a chronic systemic inflammatory disease, affects, in addition to the joints, many vital organs such as the eyes and the heart. Severe kidney disease in patients with RA is rare, and most commonly is either secondary amyloidosis or membranous/analgesic nephropathy as a side effect of medications (gold, penicillamine, non-steroidal anti-inflammatory drugs, acetaminophen, mesalazine and cyclosporine). RA itself, as opposed to the effects of systemic inflammation or drug toxicities, is rarely known to cause primary interstitial disease, although focal glomerulonephritis is not an uncommon finding [3].

LFM has, in contrast to many disease-modifying agents in rheumatoid disease, no known renal side effects. LFM has been incriminated once as causing IgA glomerulonephritis [4] and anti-glomerular basement membrane disease [5] in two RA patients, but not interstitial nephritis. Many other drugs can cause interstitial nephritis, but this patient was not taking any of them (e.g. non-steroidal or acetaminophen).

Our patient was on a higher dose than that which is generally prescribed for RA patients (the patient was on 34 mg/day for 26 months; maximum recommended dose is
20 mg/day), and his creatinine started to increase 1 year after the drug was introduced and returned to baseline 5 months after LFM was withdrawn (positive dechallenge). This, and the previous safety record for LFM, suggests that the interstitial nephritis was related to the chronic overdosage which persisted for many months especially as LFM has a very long half-life lasting for 15 days. Furthermore, the time course of the deterioration in renal function was very long, which argues against an idiosyncratic response.

The patient had uncontrolled hypertension which was the cause of his initial elevated creatinine. In addition, the renal biopsy showed mainly interstitial fibrosis and minimal glomerulosclerosis which is a typical lesion in hypertension-induced renal dysfunction.

Steroids are not proven in uncontrolled trials to be efficacious in the treatment of interstitial nephritis. The evidence for their benefit comes from two small trials where they induced quicker recovery, lower creatinine on follow-up, and less interstitial fibrosis in repeat renal biopsy [6,7].

This case emphasizes the importance of physicians supervising the treatment of patients having a precise knowledge of the type and dosage of drugs their patients are actually taking.

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Ethambutol-induced acute renal failure

Sir,

Ethambutol can cause ocular toxicity and hyperuricaemia, but ethambutol-associated acute renal failure during treatment of pulmonary tuberculosis is extremely rare [1,2]. Here we report the case of a man who manifested with oliguric acute renal failure and jaundice associated with ethambutol.

Case. A 33-year-old man was referred to our university hospital from a local clinic because of oliguria for the previous 2 days. Five years previously he had been treated for pulmonary tuberculosis with the antituberculosis medications rifampicin, pyrazinamide, isoniazid and ethambutol. Three