Dear Sir,

Because of the current large use of sulfinpyrazone (SP) in the prevention of cardiac death after myocardial infarction, the possibility that this drug can cause renal impairment would certainly be an important information to be brought to the attention of the nephrologist. We would like, therefore, to report one more case of acute renal failure (ARF) temporally associated with SP treatment.

Case Report

A 51-year-old man was hospitalized with an acute anteroseptal myocardial infarction. On admission, the findings of clinical examination were unremarkable. The blood pressure was 130/80 mm Hg, pulse 75/min and temperature 36 °C. Rare premature ventricular beats were observed on the ECG. X-ray films of the chest were normal. The patient was devoid of known previous renal disease and gross metabolic abnormalities. 40 mg/day isosorbide dinitrate was the patient’s only other medication, and he had been taking it regularly for almost 1 year. His blood urea nitrogen (BUN) was 9.3 mg/dl, serum creatinine 0.8 mg/dl and serum uric acid 5.8 mg/dl. Daily urinary output ranged from 1,500 to 1,900 ml. Urinalysis was normal.

7 days after admission, 800 mg/day SP was started. On the 4th day of treatment, when the renal function was checked again, BUN had risen to 39 mg/dl and serum creatinine to 3.7 mg/dl. Serum uric acid was 5.9 mg/dl. Whole blood count was normal, with normal differential count; the erythrocyte sedimentation rate was 22 mm/h. Urinary output remained unchanged. Repeated urinalyses were normal; crystalluria was never seen. Interestingly, the ratio of urinary uric acid to creatinine was low (0.49) and a fractional sodium excretion of 0.39 was calculated. No fever, cutaneous rash or ecchy-moses were observed. Serum electrophoresis, immunoelectrophore-sis and complement were normal; cryoglobulins and antinuclear antibodies were not detected. The blood pressure remained stable throughout hospitalization; no significant arrhythmias, signs of heart failure or other causes of low cardiac output were seen at any time. Renal ultrasonography was normal. Kidney biopsy was not performed because of the recent myocardial infarction.

Following SP discontinuation, the patient made a rapid uneventful recovery. 3 days later, BUN was 29 mg/dl and serum creatinine 2.3 mg/dl. At discharge, 3 weeks after hospitalization, kidney function tests had spontaneously returned to pretreatment levels.
Comment
We present 1 case of nonoliguric ARF that occurred shortly after the institution of SP treatment after myocardial infarction. Although a direct proof of a cause and effect relationship (e.g., by rechallenge) between the administration of the drug and the occurrence of ARF was lacking, the short interval between these two events in an otherwise uncomplicated case makes this connection likely.

There is already a number of anecdotal reports of ARF attributed to SP [1–8]. A massive precipitation of uric acid crystals within the renal tubules secondary to the drug-induced uricosuria or an immunologically mediated acute interstitial nephritis could be involved. The absence of any extrarenal signs suggestive of hypersensitivity and the lack of any alterations suggesting an immunological involvement do not support the later hypothesis. On the other hand, the lack of crystalluria and the low urinary uric acid to creatinine ratio speak against the occurrence of an acute uric acid nephropathy in our patient [9]. A third explanation that comes in mind is that SP may exert a direct nephrotoxic effect, similar to that described with phenylbutazone, the parent drug [10]. ARF following SP therapy, however, does not seem to be a dose-related phenomenon, having occurred in patients who had been taking the drug at doses ranging from 400 to 800 mg/day, with no relationship between the cumulative dosage and the degree of renal impairment. Moreover, the low fractional sodium excretion documented in our patient is not consistent with an acute tubular necrosis [11].

More recently, Lijnen et al. [12] reported a new hypothesis for the pathogenesis of ARF secondary to SP treatment after myocardial infarction. They suggested the possibility of an acute reduction of renal blood flow due to the inhibition of renal prostaglandin synthesis and kallikrein activity by the drug when administered within the early postinfarction period. Therefore, the consequent renal ischemia, rather than a parenchymal damage, would be responsible for the impairment in renal function in this clinical setting. In our patient, SP treatment was started 7 days after acute myocardial infarction. In view of the low fractional sodium excretion, which is compatible with renal ischemia [11], extrarenal causes of renal hypoperfusion excluded, such a mechanism is likely to be involved in this case.

References