Correspondence

Desensitisation to allopurinol

SIR, We read with interest the report by Kelsey *et al* of successful desensitisation to allopurinol.¹ We have recently treated a patient with massive tophaceous deposits, but no attacks of acute crystal synovitis, using this regimen, with useful lowering of uric acid and regression of tophi. The patient had chronic renal impairment which rendered alternative hypouricaemic therapy ineffective.²

The patient, a 73 year old woman, was found to have nodal osteoarthritis and hypertension in 1969; the serum urate at this time was 0.4 mmol/l. In 1963 after hip replacement she was referred for a rheumatological opinion with symptoms of median nerve compression, almost certainly due to walking stick pressure, and was found to have large tophaceous deposits in her fingers. She had a history of several years congestive cardiac failure treated with diuretics. When subsequently admitted for median nerve decompression her uric acid was 0.8 mmol/l, urea 24.4 mmol/l, and creatinine 185 µmol/l. Treatment with allopurinol 300 mg/day was started. Over the next two weeks she was unwell with malaise, gastrointestinal upset and subsequently developed a pruritic macular rash over the trunk and limbs. Her uric acid had fallen to 0.44 mmol/l, but the renal function was unchanged. Allopurinol was stopped, and her rash and other symptoms resolved. A further attempt to initiate allopurinol at 100 mg/day resulted in a prompt recurrence of the rash.

Over the next two years azapropazone and probenecid were tried without benefit, indeed her hyperuricaemia and tophi slowly enlarged and became increasingly painful. In 1986 she was admitted for management of an infected foot ulcer aggravated by subcutaneous tophi and peripheral oedema. Investigation showed uric acid 0.51 mmol/l, urea 18.8 mmol/l, creatinine 155 µmol/l. Attempts to control the oedema with increased diuretic therapy promptly increased her uric acid and caused the tophi to enlarge and ulcerate. It was decided to make a further attempt to reinstitute allopurinol, using the desensitisation regimen of Meyrier.³ This was completed without any recurrence of side effects, and she was eventually maintained on 200 mg/day. On this regimen her uric acid fell to 0.46 mmol/l and her tophi healed and have regressed markedly; her renal function is stable.

As Kelsey *et al* point out,¹ the significant incidence of adverse reactions with allopurinol limits its use. Such reactions are more common in patients with renal impairment, possibly because of greater accumulation of the allopurinol metabolite oxypurinol.⁴ It is possible that the initial adverse reaction in our patient was in part due to the high initial dose of allopurinol, and this illustrates the importance of starting the drug in low doses in the presence of renal impairment. Our case, however, also shows that should such a reaction recur on a low dose rechallenge, the patient can still be successfully desensi-

tised to the drug. As the source of stock preparations of allopurinol held by the hospital pharmacy differed in 1986 from 1983 we cannot exclude the possibility that there could be a difference in excipients to account for the absence of drug sensitivity in 1986. We agree that this regimen, though not without precedent,⁵ is a useful measure and deserves wider application when non-life-threatening sensitivity to allopurinol has occurred. It is particularly relevant in the context of renal impairment when other hypouricaemic agents usually prove ineffective.

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Oral methotrexate in the treatment of rheumatoid arthritis: Allergic agranulocytosis?

SIR, We have recently observed a patient who developed agranulocytosis after oral administration of methotrexate (MTX) in the treatment of rheumatoid arthritis (RA).

This 61 year old man had a 10 year history of progressive seropositive RA. The RA had been previously treated with auranofin, which had been discontinued because of an allergic exanthema. In September 1986 he was given a trial of oral MTX to control the progression of his disease. A dose of 15 mg MTX was to be given weekly. The patient, however, was accidentally administered 45 mg MTX over three days. Other concurrent medications were fluocortolone, ketoprofen, and oral ferrous sulphate.

Fig. 1 shows the peripheral neutrophils and precursors of this patient before, during, and after the administration of