volume in one second (FEV₁) was recorded. A supply of trial capsules and inhalers was issued at each visit.

All patients completed the trial and none required oral corticosteroids. The mean FEV₁ at the start of the trial was 1.54 (range 0.4-2.8 l). In each case the mean scores for diurnal and nocturnal wheezing were calculated for every treatment period. The three treatments were then ranked 1-3 (1=fewest symptoms) in order of efficacy for each patient in relation to the severity of diurnal and nocturnal wheezing. The totals of ranks for severity of symptoms on each treatment were then compared (see table). No statistically significant difference was shown between the totals for either of the treatments used alone or for the combined treatment. There were also no significant differences between the mean FEV₁ values recorded in the three treatment periods, though these recordings were, of course, made only at monthly intervals. Six patients were virtually without symptoms during the nine months of the study. The others continued to have symptoms, and separate analysis again failed to show any statistically significant differences between the three treatment regimens.

Symptom ranking and treatment given

Treatment regimen*	Total of ranks for wheeze		Mean FEV ₁ (l)
	Diurnal	Nocturnal	
SCG + placebo beclomethasone	29.5	34.5	1.80
Beclomethasone + placebo SCG	27.5	25.5	1.84
SCG + beclomethasone	27.0	24.0	1.76

*Doses (all four times daily): SCG 20 mg; beclomethasone 50 µg if aged less than 13 years, 100 µg if 13 years or over.

Comment

This small study showed no difference in efficacy between the two drugs or between either drug and the two drugs in combination. These results agree with those of Hiller and Milner.³ Our results are disappointing since SCG and corticosteroids, with their different modes of action, might have been expected to produce additive therapeutic effects when used in combination. Although such effects were not observed, the number of patients in this study and in Hiller and Milner's study may have been too small for a statistically significant advantage to be shown. It is notably difficult to find large numbers of patients suitable for this type of trial, for if the results are to be unbiased only patients who have not previously been treated with SCG or a corticosteroid aerosol—and this includes many asthmatic children—can be accepted. There may therefore be a case for mounting a large-scale study, possibly on a multicentre basis, before concluding that a combination of the two drugs is not more effective than either given alone.

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¹ *British Medical Journal*, 1972, **2**, 159.

² Godfrey, S, and König, P, *Archives of Disease in Childhood*, 1974, **49**, 591.

³ Hiller, E J, and Milner, A D, *British Journal of Diseases of the Chest*, 1975, **69**, 103.

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Desensitisation in a patient with chronic renal disease and severe allergy to allopurinol

Allergy complicates treatment in 15% of patients with renal disease given allopurinol. In such cases the risk of toxidermia requires immediate interruption of the treatment.¹ We tried to desensitise an allergic patient with gout because we thought that inhibiting uric acid synthesis might arrest the progression of renal failure. This approach was beneficial to the patient.

Case report

A 51-year-old man had suffered from gouty joint attacks since 1954. In 1962 tophi of multiple joints appeared and became unusually large. Several episodes of renal colic occurred. Renal failure (blood urea 13.3 mmol/l (80 mg/100 ml)) was detected in 1964 and progressed, with increasing blood pressure levels. In 1971 an intravenous pyelogram disclosed bilateral renal atrophy. Treatment with alkalinisation, colchicine, and benzodiarone were unsuccessful. In 1971 treatment with allopurinol was started but had to be interrupted within a month because of severe rash. The same was observed with thiopurinol.

The patient was referred to us in 1974. Clinical examination showed disseminated tumoral tophi and severe hypertension (200/140 mm Hg). Gouty attacks were practically continuous and were poorly influenced by colchicine. Blood urea was 13.3 mmol/l (80 mg/100 ml) and serum creatinine 239 to 283 µmol/l (2.7 to 3.2 mg/100 ml). Serum urate levels fluctuated between 0.54 and 0.71 mmol/l (9.1 and 12 mg/100 ml) with a 24-hour excretion of 5.4 mmol (900 mg). A third trial of allopurinol treatment was followed within 48 hours by a severe rash with spiking fever and had to be interrupted at once.

We then thought that without the use of a uric acid synthesis inhibitor the continuous renal tissue load with urate salts would lead to increasing kidney damage. The following treatment schedule was therefore started on 5 March 1975: 40 mg of allopurinol was dissolved in 500 ml of 14% sodium bicarbonate and for the next month the treatment was conducted as shown in the table.

There was no adverse reaction. Serum urate was measured every month. Levels were 0.71 mmol/l (12 mg/100 ml) at the beginning of the treatment with allopurinol and 0.4 mmol/l (6.9 mg/100 ml) one month later. From then on they stabilised at 0.32 mmol/l (5.4 mg/100 ml). Gouty attacks disappeared, and in February 1976 the tophi had diminished by about half their initial volume. Serum creatinine concentration was 212 µmol/l (2.4 mg/100 ml) and blood pressure was controlled (120/80 mm Hg) with pindolol and hydralazine.

Treatment regimen

Day	Dose		Day	Dose	
	Solution	Equivalent to		Solution	Equivalent to
1	0.1 ml	8 µg	16	12.0 ml	0.96 mg
2	0.2 ml	16 µg	17	14.0 ml	1.12 mg
3	0.3 ml	24 µg	18	16.0 ml	1.28 mg
4	0.4 ml	32 µg	19	20.0 ml	1.60 mg
5	0.5 ml	40 µg	20	25.0 ml	2.00 mg
6	0.6 ml	48 µg	21	32.0 ml	2.56 mg
7	0.7 ml	56 µg	22	64.0 ml	5.12 mg
8	0.8 ml	64 µg	23	128.0 ml	10.24 mg
9	0.9 ml	72 µg	24	250.0 ml	20.00 mg
10	1.0 ml	80 µg	25	$\frac{1}{4}$ tablet	50.00 mg
11	2.0 ml	160 µg	26	$\frac{1}{2}$ tablet	75.00 mg
12	4.0 ml	320 µg	27	1 tablet	100.00 mg
13	6.0 ml	480 µg	28	1 $\frac{1}{2}$ tablets	150.00 mg
14	8.0 ml	640 µg	29	2 tablets	200.00 mg
15	10.0 ml	800 µg	30	3 tablets	300.00 mg

Comment

Gouty nephritis is due to urate deposits in the renal interstitium and tubules. Alkalinisation of the urine prevents the formation of urate stones in the urinary tract but not of urate tophi in the renal tissue. As renal insufficiency progresses it increases the urate pooling and creates a vicious circle leading to destruction of the kidneys.² The xanthine oxydase inhibitor allopurinol can break this chain of events. Allergies to this drug are not uncommon and may lead to severe and sometimes lethal epidermolysis.^{3,4} In the present case, a very gradual increase enabled us to reach a dose of allopurinol that had induced reactions during three previous attempts. From then on the patient's clinical condition clearly improved. The rationale of this method of desensitisation is based on the probable formation of blocking antibodies. It has been successfully applied to patients with severe allergic reactions to penicillin.⁵

The schedule described here might be useful when xanthine oxydase inhibition is thought to be absolutely necessary in spite of an allergy to allopurinol.

¹ Frisch, J M, et al, in *Frontiers of Internal Medicine*, ed J H Blondheim, p 412. Basel, Karger, 1974.

² Emerson, B T, and Row, P G, *Kidney International*, 1975, **8**, 65.

³ Young, J L, et al, *Archives of Internal Medicine*, 1974, **134**, 553.

⁴ Ellman, M H, et al, *Archives of Dermatology*, 1975, **111**, 986.

⁵ Parker, C W, *New England Journal of Medicine*, 1975, **292**, 957.

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