

**Comment**

The cause of uraemic pruritus is unknown. In some cases it may be due to secondary hyperparathyroidism. Only in these patients is parathyroidectomy indicated.<sup>2</sup> The mechanisms of other treatments such as ultraviolet light<sup>3</sup> or cholestyramine<sup>4</sup> are unknown and are effective in only some cases. In our patient the rapid and complete disappearance of pruritus after lowering the dialysate magnesium concentration suggests a causative relation between itching and serum magnesium concentration. Lowering the dialysate magnesium concentration is known to restore nerve conduction velocity towards normal in patients receiving CHD,<sup>5</sup> and this could be the reason for the complete disappearance of the pruritus in our patient.

<sup>1</sup> Easton, P, and Galbraith, P R, *New England Journal of Medicine*, 1978, **299**, 1134.

<sup>2</sup> Massry, S G, *et al*, *New England Journal of Medicine*, 1968, **279**, 697.

<sup>3</sup> Gilchrist, B A, *et al*, *New England Journal of Medicine*, 1977, **297**, 136.

<sup>4</sup> Silverberg, D S, *et al*, *British Medical Journal*, 1977, **1**, 752.

<sup>5</sup> Stewart, W K, *et al*, *Proceedings of the European Dialysis and Transplant Association*, 1967, **4**, 285.

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## A tube spacer to improve inhalation of drugs from pressurised aerosols

Inhalation from pressurised aerosols provides an effective means of drug administration with a low incidence of side effects, but many patients cannot co-ordinate inhalation with aerosol actuation.<sup>1</sup> Another potential disadvantage of pressurised aerosols is the deposition of drug on to the mucosa of the mouth and oropharynx caused by the high velocity of the flow of drug particles produced by aerosol actuation directly into the mouth. It has been shown,<sup>2</sup> however, that the interposition of a tube spacer between the aerosol and the mouth reduces deposition of drug and also that the drug remains suspended in the system for several seconds, thus enabling inhalation to be delayed after aerosol actuation. This study was designed to test the hypothesis that a tube spacer could improve drug inhalation in patients unable to use aerosols efficiently.

**Patients, methods, and results**

Sixteen patients with chronic asthma (age range 62-77 years, 10 men) were studied. All had a forced expiratory volume in one second (FEV<sub>1</sub>) less than 70% of predicted normal, and the pretreatment FEV<sub>1</sub> did not vary by more than 12.5% between study days. Each patient received four separate treatments on different days. All bronchodilator treatment was withheld for 12 hours before each test. The order of treatment was randomised. The four treatments were: (a) 500 µg terbutaline from the conventional aerosol with actuation of aerosol at the beginning of inspiration; (b) 500 µg terbutaline from a conventional aerosol with a spacer 10 cm long and 3.2 cm in diameter attached—inhalation and actuation were co-ordinated; (c) 500 µg terbutaline from a conventional aerosol with a spacer 10 cm long and 3.2 cm in diameter attached—inhalation was delayed two seconds after actuation of aerosol; (d) 500 µg terbutaline from a conventional aerosol—inhalation was delayed two seconds after actuation of aerosol. FEV<sub>1</sub>, forced vital capacity (FVC), peak expiratory flow rate (PEFR), and pulse rate were measured before and 5, 10, 20, 30, 60, 120, 180, 240, and 300 minutes after drug administration. Statistical analysis was carried out using a *t* test for paired comparisons.

The mean maximum increases in FEV<sub>1</sub>, FVC, and PEFR are shown in the table. All treatments produced significant improvements at five minutes and the values remained above pretreatment levels for up to five hours. The rates of onset and duration of effects were similar for all treatments. The mean maximum increases in FEV<sub>1</sub>, FVC, and PEFR were consistently higher after the co-ordinated use of the conventional aerosol and were significantly greater than the mean maximum improvements produced by

*Influence of tube spacer and co-ordination on airways response to inhaled terbutaline sulphate. Results are means of maximum improvement (±SD), with statistical significance calculated as paired comparison to inhalation from aerosol co-ordinated*

	Aerosol co-ordinated	Tube spacer co-ordinated	Tube spacer uncoordinated	Aerosol uncoordinated
FEV <sub>1</sub> (ml)	346 ± 180	325 ± 171 (NS)	319 ± 173 (NS)	238 ± 171 (P < 0.02)
FVC (ml)	504 ± 309	432 ± 392 (NS)	459 ± 193 (NS)	316 ± 223 (P < 0.05)
PEFR (l/min)	64 ± 33	58 ± 38 (NS)	46 ± 37 (NS)	43 ± 35 (P < 0.05)

NS = Not Significant.

the conventional aerosol uncoordinated. The mean maximum increases in the measurements of ventilatory function produced by the conventional aerosol used efficiently were not, however, significantly better than those after the use of the tube spacer co-ordinated or uncoordinated. The differences between the mean maximum increases in FEV<sub>1</sub>, FVC, and PEFR after the use of the tube spacer co-ordinated and the conventional aerosol uncoordinated were not significant.

**Comment**

Many patients with bronchial asthma cannot use inhalers efficiently. At worst they expire at the time of actuation or at best actuation is not co-ordinated with the beginning of inspiration. In this study we used a compromise for inefficient administration of an inhaler in that inspiration was delayed by two seconds after aerosol actuation and this caused a significant reduction in efficacy when compared with the co-ordinated use of the aerosol. Nevertheless, there was no significant difference between the improvements in ventilatory function produced by the tube spacer without co-ordination and those produced by the conventional aerosol co-ordinated, though the mean values were consistently lower for the spacer.

These results show that the tube spacer can at least partially compensate for the artificially poor inhalation technique used in this study and suggest that this device may have a useful role in clinical practice. If further clinical studies confirm this the tube spacer will provide a much needed alternative to the dry powder inhaler.<sup>3</sup>

<sup>1</sup> Paterson, I C, and Crompton, G K, *British Medical Journal*, 1976, **1**, 76.

<sup>2</sup> Moren, F, *International Journal of Pharmaceutics*, 1978, **1**, 205.

<sup>3</sup> Hallworth, G W, *British Journal of Clinical Pharmacology*, 1971, **4**, 689.

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## Clostridium difficile-associated colitis after neomycin treated with metronidazole

*Clostridium difficile*-associated colitis is being increasingly recognised after antibiotic treatment. The following case is the first to be documented after oral neomycin and was successfully treated with oral metronidazole.

**Case report**

A 65-year-old man with longstanding alcoholic cirrhosis was admitted with hepatic decompensation causing ascites and encephalopathy. Protein and salt restriction, oral lactulose, spironolactone, and neomycin (1 g four times daily) produced good improvement and he was discharged. Eight days after stopping neomycin he developed abdominal pain and bloody diarrhoea 8-10 times daily. This failed to settle over the next seven days, and on re-admission he was dehydrated, febrile, and jaundiced but had no encephalopathy. Sigmoidoscopy showed grossly active colitis with ulceration, pus, and bleeding to the limit of examination, but there was no pseudomembrane. A stool sample was cultured in Reinforced Clostridial Medium with 0.2% paracresol<sup>1</sup> and grew *Cl difficile* as identified morphologically and biochemically.