effects, and the substantially lower dose. The main long-term hazardcarcinogenesis or leukaemogenesis-should be lower, possibly no more than a lifetime fatal cancer risk of 1% after 25 years.<sup>5</sup>

This case provides further evidence that total body irradiation may provide a useful additional form of management in cases of polymyositis resistant to conventional drug treatment, although a lasting effect has not been demonstrated.

We thank Mrs J Coppen, senior physiotherapist, and members of the Jerry Lewis Muscle Research Laboratories, Royal Postgraduate Medical School, London, for their help with this case.

- <sup>1</sup> Kotzin BL, Strober S, Engelman EG, et al. Treatment of intractable rheumatoid arthritis with total lymphoid irradiation. N Engl J Med 1981:305:969-75.
- <sup>2</sup> Fuks Z, Slavin S. The use of total lymphoid irradiation as immunosuppressive therapy for organ allotransplantation and autoimmune disease. Int J Radiat Oncol Biol Phys 1981;7:79-82.
  Engel WK, Richter AS, Galdi AP. Polymyositis: remarkable response to
- total body irradiation. Lancet 1981;i:658.
- <sup>4</sup> Edwards RHT, McDonnel M. Hand-held dynamometer for evaluating voluntary muscle function. Lancet 1974;ii:757.
- <sup>5</sup> United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and effects of ionizing radiation. New York: United Nations, 1977.

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# Effect of nifedipine on histamine reactivity in asthma

The release of mast-cell mediators and the contraction of smooth muscle are associated with influx of calcium ions. Williams et al1 reported that the calcium antagonist nifedipine given sublingually modified histamine-induced bronchoconstriction in asthma. Our observations, however, show that the calcium antagonist verapamil given by inhalation does not modify histamine or methacholine bronchoconstriction in asthma.<sup>2</sup> We report the effect of 20 mg nifedipine and a matched placebo on histamine reactivity in eight patients with allergic asthma.

#### Patients, methods, and results

We studied eight patients aged between 17 and 33 years with allergic

asthma and reversible airflow obstruction. Sodium cromoglycate and bronchodilators were discontinued for at least 24 hours before each test was carried out. Forced expiratory volume in one second was measured with a water-sealed spirometer (Godart Pulmotest) and values corrected for body temperature, pressure, and saturation. Each subject was then given 20 mg nifedipine or a matched placebo sublingually on a double-blind basis. Pulse rate and blood pressure were recorded at five-minute intervals for 30 minutes. Measurement of forced expiratory volume in one second was repeated at 30 minutes and followed by two-minute inhalations of histamine dihydrochloride through a Wright nebuliser in doubling concentrations from 0.025 to 8 g/l at tidal breathing.

After each inhalation forced expiratory volume in one second was recorded at 0.5, one, three, and five minutes and subsequent intervals of two minutes to obtain the lowest value after inhalation. Inhalation of histamine was continued until the forced expiratory volume in one second had fallen by 20% or more. The responses were expressed in terms of the provocative concentration of histamine producing a 20% fall in forced expiratory volume in one second (PC20H) and calculated as described previously.<sup>2</sup> Results of the study are shown in the table. There was no significant difference in the mean baseline forced expiratory volume in one second before and after nifedipine or a matched placebo. Furthermore, the mean percentage changes in forced expiratory volume in one second and the  $PC_{20^{11}}$  for histamine were not significantly altered by nifedipine. Pulse rate and blood pressure changes were also not significant.

#### Comment

In contrast to the results reported by Williams et al,<sup>1</sup> nifedipine did not modify histamine reactivity in the patients we studied. We did not observe the significant changes in blood pressure or pulse rate reported by Millar and Struthers<sup>3</sup> in normal subjects with a similar dose of nifedipine. Our observations with verapamil and nifedipine suggest that the effect of calcium antagonists on the bronchial smooth muscle in patients with asthma is minimal. The beneficial effect of verapamil and nifedipine in exercise-induced asthma<sup>4</sup> <sup>5</sup> is probably on mast-cell degranulation, which is calcium dependent.

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- <sup>1</sup> Williams DO, Barnes PJ, Vickers HP, Rudolf M. The effect of nifedipine on bronchomotor tone and histamine reactivity in asthma. Br Med J 1981:283:343.
- <sup>2</sup> Patel KR. The effect of verapamil on histamine and methacholine induced bronchoconstriction. Clin Allergy 1981;11:441-7.
- <sup>3</sup> Millar JA, Struthers AD. Effect of nifedipine on bronchomotor tone and histamine reactivity in asthma. Br Med J 1981;282:796.
- <sup>4</sup> Patel KR. Calcium antagonist in exercise-induced asthma. Br Med J 1981;282:932-3.
- <sup>5</sup> Cerrina J, Denjean A, Alexandre G, Lockhart A, Duroux P. Inhibition of exercise-induced asthma by a calcium antagonist, nifedipine. Am Rev Respir Dis 1981;123:156-60.

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Effect of nifedipine on histamine-induced fall in forced expiratory volume in one second and  $PC_{20H}$  in eight asthmatic patients

|                   |         | Placebo                           |                    |                 |                              | Nifedipine                |                    |                           |                             |
|-------------------|---------|-----------------------------------|--------------------|-----------------|------------------------------|---------------------------|--------------------|---------------------------|-----------------------------|
| Case No           | Sex/Age | Baseline                          |                    |                 |                              | Baseline                  |                    |                           |                             |
|                   |         | Before<br>treatment               | After<br>treatment | % Fall          | $\substack{PC_{20}H\\(g/l)}$ | Before<br>treatment       | After<br>treatment | -<br>% Fall               | РС <sub>20</sub> н<br>(g/l) |
| 1                 | M 18    | 5.22                              | 5.29               | 34.2            | 0.12                         | 5.04                      | 4.97               | 27.2                      | 0.07                        |
| 2<br>3            | F 33    | 1.87                              | 1.91               | 34.6            | 0.03                         | 1.67                      | 1.66               | 33.7                      | 0.06                        |
| 3                 | M 21    | 4.45                              | 4.55               | 33·0            | 0.15                         | 4.59                      | 4.79               | 36.3                      | 0.88                        |
| 4                 | F 22    | 1.87                              | 1.77               | 29.9            | 0.03                         | 1.67                      | 1.74               | 36.8                      | 0.02                        |
| 5                 | M 18    | 4.55                              | 4.54               | 32.8            | 3.05                         | 4.57                      | 4.54               | 20.7                      | 2.90                        |
| 6                 | M 21    | 2.74                              | 2.78               | 20.1            | 0.10                         | 2.38                      | 2.51               | 21.5                      | 0.02                        |
| 7                 | M 32    | <b>4</b> ·70                      | 4.69               | 23.7            | 0.68                         | 4.62                      | 4.82               | 20.7                      | 1.54                        |
| 8                 | M 19    | 3.02                              | 2.98               | 32.2            | 0.06                         | 2.99                      | 3.25               | 28.0                      | 0.29                        |
| Mean±<br>SEM<br>p | 23      | $\textbf{3.55} \pm \textbf{0.47}$ | 3·56 ±0·48<br>NS   | $30.1 \pm 1.88$ | 0·52 <u>±</u> 0·37           | $3{\cdot}54\pm0{\cdot}50$ | 3·54 ±0·50<br>NS   | $28{\cdot}1\pm2{\cdot}42$ | 0·73 ± 0<br>NS              |

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