



Specific conductance against time after challenge with nebulised normal saline and unit dose phial ipratropium bromide

saline and ipratropium bromide. There was no change in specific conductance after nebulised normal saline. In the group as a whole there was a significant decrease in specific conductance at one minute after nebulisation of the ipratropium bromide (from a mean of 0.083/cm H<sub>2</sub>O/s to 0.066/cm H<sub>2</sub>O/s;  $p < 0.05$ ). Twenty minutes after nebulisation of ipratropium bromide specific conductance was significantly greater (0.11 cm H<sub>2</sub>O/s) than baseline values ( $p < 0.05$ ). The osmolality of nebulised normal saline changed from 280 to 320 mmol/kg during nebulisation and that of the nebulised ipratropium bromide from 285 to 318 mmol/kg. There was no change in the pH of the solutions with nebulisation.

#### Comment

Ipratropium bromide nebuliser solution was reformulated in an iso-osmolar form after episodes of bronchoconstriction in adults that were shown to be related to its hypo-osmolality.<sup>2</sup> The unit dose phial of ipratropium bromide has had preservatives removed

and is osmolar. The preservatives present in the previous isotonic ipratropium solution as bacteriostatic and stabilising agents, (benzalkonium chloride and ethylenediaminetetra-acetic acid (EDTA)), cause bronchoconstriction in adult asthmatics.<sup>3</sup>

There are two possible explanations for the bronchoconstriction seen in our infants after ipratropium bromide. Firstly, the unit dose phial solution of ipratropium bromide is acidic, with a pH of 3.6, and acidic solutions may cause bronchoconstriction.<sup>4</sup> Secondly, ipratropium bromide is a non-selective anticholinergic drug which blocks prejunctional (M<sub>2</sub>) and postjunctional (M<sub>3</sub>) muscarinic receptors with equal affinity. Blockade of the muscarinic autoreceptor (M<sub>2</sub>) means that more acetylcholine will be released during cholinergic nerve stimulation. This may precede and may overcome postjunctional blockade of the M<sub>3</sub> receptor. This supports the idea that non-selective muscarinic antagonists might exacerbate bronchoconstriction by an action on prejunctional M<sub>2</sub> receptors. Nevertheless, paradoxical bronchoconstriction was not seen in a group of wheezy infants after administration of ipratropium bromide through a metered dose inhaler.<sup>5</sup> While we cannot directly compare these groups, the results suggest that the acidity of the solution may be related to the paradoxical bronchoconstriction seen.

- O'Callaghan C, Milner AD, Swarbrick A. Paradoxical deterioration in lung function after nebulised salbutamol in wheezy infants. *Lancet* 1986;ii:1424-5.
- Mann JS, Howarth PH, Holgate ST. Bronchoconstriction induced by ipratropium bromide in asthma: relationship to hypertonicity. *Br Med J* 1984;289:469.
- Beasley R, Rafferty P, Holgate ST. Bronchoconstriction properties of preservatives in ipratropium bromide (Atrovent) nebulizer solution. *Br Med J* 1987;294:1197-8.
- Utall MJ, Marrow PE, Speers DM, Darling J, Hyde RW. Airways response to sulphate and sulphuric acid aerosols in asthmatics. *Am Rev Respir Dis* 1983;128:440-50.
- O'Callaghan C, Milner AD, Swarbrick A. Spacer device with face mask attachment for giving bronchodilators to infants with asthma. *Br Med J* 1989;298:160-1.

(Accepted 4 September 1989)

## Use of oestrogen replacement therapy in high risk groups in the United Kingdom

Tim D Spector

Department of Environmental and Preventive Medicine, St Bartholomew's Hospital Medical College, London EC1M 6BQ  
Tim D Spector, MRCP, lecturer in epidemiology

*Br Med J* 1989;299:1434-5

Hormone replacement therapy is used less in the United Kingdom than in North America and other European countries. Recently both the media and medical journals<sup>1</sup> have urged that it be prescribed for more women in the United Kingdom. To assess the levels of current use I carried out a survey among menopausal women and women who had had a hysterectomy or oophorectomy in three general practices in Greater London.

#### Subjects, methods, and results

I obtained the names and addresses of 5025 women aged between 45 and 65 from the practices' age-sex registers. The women were sent a questionnaire that asked whether they had received hormone replacement therapy and if so for how long and when they had started it; and whether they had had a hysterectomy or oophorectomy and for details of any gynaecological operations. Altogether 3238 replied. The table gives the results.

The mean age of the women was 52, and 1858 were no longer having periods. Altogether 330 had received

hormone replacement therapy (10% of all the respondents and 18% of the postmenopausal respondents). The mean duration of use was only 21 months (median 11 months) in the women overall and 28 months (median 24) in the women who had had a bilateral oophorectomy.

#### Comment

The survey showed that most of the menopausal women questioned had never received hormone replacement therapy and those who had had received it for only short periods. Those who would have benefited most—namely, women after hysterectomy and oophorectomy—had generally not been prescribed it despite a lack of medical contraindications. The practices that I studied were probably reasonably representative of practices in general, and no major differences were noted in their rates of hysterectomy or oophorectomy compared with national rates.<sup>2</sup>

The observations that 70% of women who had had a

Number (percentage) of menopausal women and women who had had hysterectomy or oophorectomy who had received hormone replacement therapy (HRT)

	Total No	Women who had received HRT
All women	3238	330 (10)
Women after hysterectomy	464	112 (25)
Women after oophorectomy:		
Unilateral	112	29 (26)
Bilateral	119	36 (30)
Bilateral before age 40	31	7 (23)

bilateral oophorectomy had never received hormone replacement therapy is important. Women without ovaries are those most at risk of subsequent osteoporosis<sup>3</sup> and cardiovascular problems,<sup>4</sup> and bilateral oophorectomy is regarded by most gynaecologists as an absolute indication for oestrogen treatment. Most of the women who had had a hysterectomy had also never received hormone replacement therapy, and these women, even with intact ovaries, are believed to be at moderately increased risk of osteoporosis and ischaemic heart disease,<sup>5</sup> can safely receive unopposed oestrogens, and have a higher ratio of benefit to risk associated with the therapy.

Why do so many women at high risk never receive this treatment? One reason might be a lack of communication between the gynaecologist, general practitioner, and patient after the operation or, alternatively, ignorance of the indications for and contraindications to treatment. Before the general

use of hormone replacement therapy is considered attention should be focused on those women who undoubtedly need such treatment.

I thank the doctors and staff of the participating general practices for their cooperation, Mr Roy Ide for collecting data, and Professor Nicholas Wald for comments on the manuscript. This work was supported by Research into Ageing and the Oliver Bird Fund.

- 1 Belchetz P. Hormone replacement. *Br Med J* 1989;298:1467-8.
- 2 Coulter A, McPherson K. The hysterectomy debate. *Quarterly Journal of Social Affairs* 1986;2:379-96.
- 3 Aitken JM, Hart DM, Lindsay R. Oestrogen replacement therapy for prevention of osteoporosis after oophorectomy. *Br Med J* 1973;iii:515-8.
- 4 Colditz GA, Willett WC, Stampfer MJ, Rosner B, Speizer FE, Hennekens CH. Menopause and the risk of coronary heart disease in women. *N Engl J Med* 1987;316:1105-10.
- 5 Gordon T, Kannel WB, Hjortland MC, McNemara PM. Menopause and coronary heart disease: the Framingham study. *Ann Intern Med* 1978;89:157-61.

(Accepted 15 September 1989)

## Two management policies for patients after myocardial infarction: Does exercise testing and a more intensive approach make any difference?

J E Sanderson, E Whiteley, K Neubauer, M Barry

Taunton and Somerset Hospital, Musgrove Park, Taunton TA1 5DA  
J E Sanderson, MD, consultant physician and cardiologist  
E Whiteley, PHD, research assistant  
K Neubauer, MRCP, medical registrar  
M Barry, FRCP, consultant physician

Correspondence to: Dr Sanderson.

*Br Med J* 1989;299:1435-6

The management of patients after a myocardial infarction varies widely among doctors. To determine if this affects the outcome long term we studied two groups of patients admitted to a district general hospital under the care of two doctors with different policies on managing infarction. In no previous study has management been compared in this way.

### Patients, methods, and results

A total of 234 patients under age 70 with proved myocardial infarction were admitted as emergencies into the coronary care unit under two doctors—group A (121 patients) and group B (113 patients). The average age was similar in the two groups (group A: 56.5 years, range 22-70, 109 men; group B: 59 years, range 33-70, 95 men). All patients in group A performed a limited exercise test before discharge from hospital (stage II modified Bruce protocol), and 86 of these patients also had a full exercise test limited by their symptoms one month after discharge. All patients in group B were managed in the standard way and had a one month follow up appointment in the clinic. If the patients were well they were discharged back to the care of their general practitioner. Follow up data were available from 96 patients in group A and from 84 patients in group B. The minimum follow up was 12 months after discharge from hospital with a mean of 30 months (range 12-47 months). The sites of infarction were identical in the two groups, and the percentage of smokers was similar (47% and 49%).

Fifty four patients in group A and 16 patients in group B were discharged taking a  $\beta$  blocker. There was no significant difference between the number of patients in each group receiving treatment with thrombolytic drugs during the last year of the study. Angiography was considered for patients in group A with strongly positive exercise tests. No operations

were done for prognostic reasons only. The decision to carry out angiography or surgery in group B patients was taken on clinical grounds only.

The table shows that there was a significant difference in the numbers of patients who were free of symptoms, patients in group A having fewer symptoms, and numbers of deaths. Thirty nine

Findings in two groups of patients at a mean follow up of 30 months after myocardial infarction

State	Group A (n=96)	Group B (n=84)
No symptoms	67	45
Symptoms:	20*	27*
Angina	16†	17
Further infarction	2	4
Heart failure	1	2
Arrhythmias†	0	3
Claudication	1	1
Angiography	15	3
Cardiac artery bypass grafting	11	1
Dead	9	12

\*Difference  $p < 0.05$  ( $\chi^2$  test).

†Symptomatic supraventricular tachycardia and heart block.

‡Two after cardiac artery bypass grafting.

patients in group A and 25 patients in group B had angina before their infarction. Of those patients, 26 in group A and 13 in group B were free of angina after their infarction. Thirty seven patients in group A were considered to have angina immediately after their infarction against 18 patients in group B. (This probably represents increased awareness because angina was detected on exercise testing.) At follow up 11 of these 37 patients in group A still had angina compared with 13 of the 18 patients in group B. The rate for coronary artery bypass grafting in group A (10.5%) is comparable to the rate reported in other studies of 10-15%.<sup>1</sup>

### Comment

Most of the conflicting results from studies on the role of exercise testing after myocardial infarction focus on the effectiveness of detecting ischaemia and relate this to prognosis.<sup>1-4</sup> But in the United Kingdom most patients do not have an exercise test after myocardial infarction, and we do not know if the current cardiological management is of proved benefit. The results of this study suggest that the more intensive approach is worth while. The increased use of  $\beta$  blockers may be a factor,<sup>5</sup> but we think that exercise testing is an important part of management and is the main reason for the differences. In practice, it seems to