# THORAX

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*President:* NEIL PRIDE



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Authors should follow the requirements of the International Steering Committee of Medical Editors (*BMJ* 1979;i:532–5). Papers must be typed in double spacing with wide margins for correction and on one side of the paper only. They should include a structured abstract on a separate sheet (see below). Papers should contain adequate reference to previous work on the subject. Descriptions of experimental procedures on patients not essential for the investigation or treatment of their condition must include a written assurance that they were carried out with the informed consent of the subjects concerned and with the agreement of the local ethics committee.

ABSTRACT Abstracts, which should be of no more than 250 words, should state clearly why the study was done, how it was carried out (including number and brief details of subjects, drug doses, and experimental design), results, and main conclusions. They should be structured to go under the headings "Background," "Methods," "Results," and "Conclusions."

STATISTICAL METHODS The Editor recommends that authors refer to Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. *BMJ* 1983;**286**:1489–93. Authors should name any statistical methods used and give details of randomisation procedures. For large numbers of observations it is often preferable to give mean values and an estimate of the scatter (usually 95% confidence intervals) with a footnote stating from whom the full data may be obtained. The power of the study to detect a significant difference should be given when appropriate and may be requested by referees. Standard deviation (SD) and standard error (SE) should be given in parenthesis (not preceded by ±) and identified by SD or SE at the first mention.

SI UNITS The units in which measurements were made should be cited. If they are not SI units the factors for conversion to SI units should be given as a footnote. This is the responsibility of the author.

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REFERENCES Responsibility for the accuracy and completeness of references rests entirely with the authors. References will not be checked in detail by the Editor but papers in which errors are detected are unlikely to be accepted. Reference to work published in abstract form is allowed only in exceptional circumstances—for example, to acknowledge priority or indebtedness for ideas. References should be numbered in the order in which they are first mentioned and identified in text, tables, and legends to figures by arabic numerals above the line. References cited only (or first) in tables or legends should be numbered according to where the particular table or figure is first mentioned in the text. The list of references should be typed in double spacing and in numerical order on separate sheets. The information should include reference number, authors' names and initials (all authors unless more than six, in which case the first six names are followed by *et al*), title of article, and in the case of journal articles name of journal (abbreviated according to the style of *Index Medicus*), year of publication, volume, and first and last page numbers. The order and the punctuation are important and should conform to the following examples:

1 Anderson HR. Chronic lung disease in the Papua New Guinea Highlands. *Thorax* 1979;**34**:647–53.
2 Green AB, Brown CD. *Textbook of pulmonary disease*. 2nd ed. London: Silver Books, 1982:49.
3 Grey EF. Cystic fibrosis. In: Green AB, Brown CD, eds. *Textbook of pulmonary disease*. London: Silver Books, 1982:349–62.

SHORT REPORTS Short reports of experimental work, new methods, or unique cases that illustrate an important principle may be accepted. These may be published as two page reports, in which case the report must be limited to 850 words, a maximum of two tables or illustrations, and no more than 10 references. Occasionally a one page short report is appropriate and this will need to be limited to 400 words, one table or illustration, and 10 references. Short reports should normally have a one or two sentence abstract at the beginning.

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# LETTERS TO THE EDITOR

## Sex differences in hypokalaemic and electrocardiographic effects of inhaled terbutaline

We were interested to read the paper by Dr ARA Rahman and coworkers (December 1992;47:1056–9) in which the authors reported gender related differences in the pharmacologically predictable side effects of the $\beta$ agonist drug terbutaline. Greater degrees of hypokalaemia, ST segment depression, and QTc interval prolongation were observed in women than in men following single doses of inhaled terbutaline. The authors concluded that women were more sensitive to $\beta$ agonist effects, and speculated on the relevance of this finding to the wider issue of the adverse effects of $\beta$ agonists.

In the light of this report we have carried out three further analyses of data from our own study which compared the effects of regular administration of $\beta$ agonist with "as needed" $\beta$ agonist in the management of asthma.[1 2] Overall control of asthma, baseline lung function, and changes in plasma potassium levels were reanalysed to identify any effect of gender on the results. Of the 64 evaluable patients 57 were better controlled during one or other of the two treatment periods; 17 when taking regular fenoterol and 40 when taking "as needed" bronchodilator ($p < 0{\cdot}005$). In table 1 this result has been stratified for gender, and $\chi^2$ testing shows that there were no significant differences between the sexes as far as overall asthma control was concerned. For the entire group (n = 64) the mean (SE) change in baseline $FEV_1$ during regular fenoterol treatment was $-0{\cdot}15$ (0·06) litres compared with "as needed" treatment (MANOVA: SPSSX). The changes in lung function were more marked in men than in women but the difference was not significant (table 2).

The only variable which correlated with the decline in $FEV_1$ during the period of regular $\beta$ agonist administration was that subjects experiencing more than six exacerbations of asthma during the treatment period had a significantly greater fall in $FEV_1$ than those patients who experienced six exacerbations or fewer (table 2).

*Table 1 Numbers of subjects with better overall control of asthma stratified for treatment and gender*

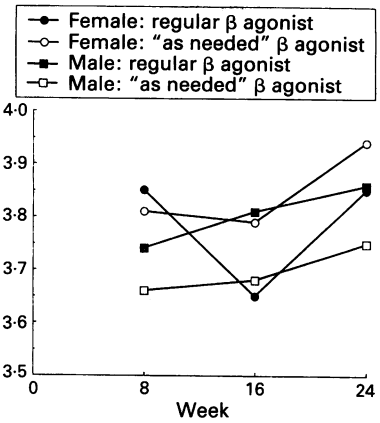
| | *Regular fenoterol* | *"As needed" β agonist* | *Total* |
|---|---|---|---|
| Men | 7 | 17 | 24 |
| Women | 10 | 23 | 33 |
| Total | 17 | 40 | 57 |

$\chi^2 = 0{\cdot}04$; $p = 0{\cdot}84$.

*Table 2 Mean (SE) changes in $FEV_1$ (litres) which occurred during first two months of treatment with regular β agonist (fenoterol)*

| *Group* | *n* | *$\Delta FEV_1$* |
|---|---|---|
| All subjects | 64 | −0·15 (0·06) |
| Men | 28 | −0·20 (0·07)* |
| Women | 36 | −0·12 (0·09)* |
| >6 exacerbations | 13 | −0·40 (0·17)** |
| ⩽6 exacerbations | 51 | −0·09 (0·07)** |

*NS; **$p \leqslant 0{\cdot}05$.




*Serum potassium levels by gender, week and treatment.*

We measured serum potassium levels every eight weeks throughout each of the two treatment periods and found no gender differences in these measurements (fig) nor, in fact, was there any significant difference in serum potassium levels between the regular and "as needed" treatment arms of the study. However, it requires to be noted that these measurements were made at least six hours after the most recent administered dose of inhaled $\beta$ agonist.

From our long term clinical study we therefore found no important gender related differences in the outcomes following regular use of an inhaled $\beta$ agonist.

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1 Sears MR, Taylor DR, Print CG, Lake DC, Li Q, Flannery EM, *et al.* Regular inhaled beta-agonist treatment in bronchial asthma. *Lancet* 1990;**336**:1391–6.
2 Taylor DR, Sears MR, Herbison GP, Flannery EM, Print CG, Lake DC, *et al.* Regular inhaled $\beta$ agonist in asthma: effects on exacerbations and lung function. *Thorax* 1993;**48**:134–8.

AUTHOR'S REPLY Dr Taylor and colleagues have reported on a subgroup analysis from their study comparing regular versus on-demand $\beta_2$ agonist use and showed no gender differences in serum potassium levels during the study. There are two possible explanations for this result. Firstly, as the authors have pointed out, they did not measure the peak hypokalaemic response which occurs at 30–60 minutes, returning to baseline by three hours, but performed their measurements at least six hours after dosing. Secondly, the dose of $\beta_2$ agonist used in their study was low (400 $\mu$g for fenoterol) and is not on the steep part of the dose-response curve for systemic effects. Indeed, in a study reported by Windom *et al* in asthmatics[1] it was shown that even a dose as high as 1600 $\mu$g only produced a group mean fall in potassium of 0·4 mmol/l. In order to assess systemic $\beta_2$ receptor responsiveness it is therefore important to choose a dose on the steep part of the dose-response curve which is why we chose a dose of 5 mg inhaled terbutaline in our study. It is also worth mentioning that after eight weeks of treatment systemic tachyphylaxis would have occurred due to downregulation of extrapulmonary $\beta_2$ receptors[2] which might conceivably have masked a small gender difference in response.

BJ LIPWORTH
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1 Windom H, Burgess D, Siebens RWL, *et al.* The pulmonary and expulmonary effects of inhaled $\beta$-agonists in patients with asthma. *Clin Pharmacol Ther* 1990;**48**:296–301.
2 Lipworth BJ, Struthers AD, McDevitt DG. Tachyphylaxis to systemic but not in airways responses during prolonged therapy with high-dose inhaled salbutamol in asthmatics. *Am Rev Respir Dis* 1989;**140**:586–92.

## Inhalation trauma due to overheating in a microwave oven

I enjoyed the report by Drs AL Zanen and AP Rietveld (March 1993;**48**:300–2) on inhalation trauma due to overheating in a microwave oven. I disagree with the conclusion that pet birds should not be kept in the kitchen because of their high sensitivity to toxic gases. The selfless parakeets gave their owner a half hour warning of the danger to her lungs. As long as the risks of ornithosis and extrinsic allergic alveolitis are considered, the authors should encourage the placement of birds in the kitchen.

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# NOTICES

**XII International Symposium of Respiratory Psychophysiology**
The XIIth International Symposium on Respiratory Psychophysiology will take place on 20–22 September 1993 at the Wellcome Centre, London. For further details contact: Miss Janette Shiel, Department of Medicine, Charing Cross & Westminster Medical School, Fulham Palace Road, London W6 8RF. Tel: 081 846 7176, Fax: 081 846 7170.

**Dr HM (Bill) Foreman Memorial Fund**
The Trustees of the above Fund invite applications for grants relating to study in respiratory disease. Limited funds are available for registered medical practitioners to assist in travelling to countries other than their own to study respiratory disease, and also for support of clinical research abroad. For further details contact Dr Brian H Davies, Llandough Hospital, Penarth, South Glamorgan CF6 1XX, UK.

**Tuberculosis in the 90s**
This conference will be held on 26 October 1993 at the Royal College of Nursing, London. Topics will include: The state of TB today; Immunotherapy; Immunology of TB; Tuberculosis: the global challenge. RCN members: £30.00, non-members: £45.00. Further details and an application form from Sandra Treadwell (071 409 3333 ext. 315).