

# Correspondence

## Effect of particle size of bronchodilator aerosols on lung distribution and pulmonary function in patients with chronic asthma

SIR,—We feel that we must comment on the recent paper by Dr DM Mitchell and others (June 1987;42:457-61), since its findings are likely to be misinterpreted by many readers.

Dr Mitchell and his colleagues nebulised salbutamol as aerosols of particles with mass median aerodynamic diameters (MMADs) of 1.4 and 5.5  $\mu\text{m}$  in eight patients with chronic and severe stable asthma. On the basis of their data from previous radioaerosol deposition studies, they set out deliberately to deliver the same amount of drug to the lungs for each of the two aerosols, and found no difference in bronchodilator response.

Although their methods were sound and their paper is of scientific interest, the study bears little relation to the clinical circumstances in which a fixed dose is placed in whatever nebuliser comes to hand and then nebulised "to dryness." Nebulisers differ widely in their droplet MMADs—from 1 to 12  $\mu\text{m}$ —and hence in the amounts of drug able to penetrate the oropharynx and reach the lungs. We have compared two commonly used nebulisers, producing particles with an MMAD of 3.3 and 7.7  $\mu\text{m}$  respectively: almost three times more radioaerosol was deposited in the lungs with the smaller aerosol and in a cumulative dose-response study using salbutamol bronchodilatation was significantly greater.<sup>1</sup> The use of the CIS-Optimist system seems a curious choice of nebuliser as this unit was designed to produce fine aerosols for ventilation scanning and achieves this by filtering out a very high proportion of the dose before it gets to the patient. Thus it would not be an ideal system for bronchodilator treatment.

Bearing these considerations in mind, we are concerned lest readers should conclude that nebuliser droplet size is of no importance in clinical terms. The importance of droplet size lies principally in the fact that it is not difficult to find nebulisers producing droplets so large that hardly any are capable of entering the lungs.

Surprisingly, Dr Mitchell and his colleagues were unable to detect a difference in the regional distributions of their two aerosols. Classically, the smaller aerosol should penetrate further into the lungs; less should be expected in a "central" zone and more in a "peripheral" zone. Failure to observe this may relate to the heterodisperse nature of the aerosols, the presence of airways obstruction, or the very simple division of the lungs into two zones (central one third and peripheral two thirds). Although the need to "target"  $\beta$  adrenergic bronchodilators to the small conducting airways is sometimes suggested, it may be that this is neither essential nor very practical, and that the main priority is to select a nebuliser system with a high yield of respirable droplets (less than about 5  $\mu\text{m}$  diameter). This is not necessarily the case with other types of drug, where targeting to some specific part of the bronchial tree may be appropriate. We urge nebuliser

manufacturers to assist clinicians by publishing full details of the droplet sizes yielded by their products.

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1 Johnson MA, Bloom R, Newman S, Clarke SW. The optimum aerosol size and dose of salbutamol in the treatment of asthma [abstract]. *Thorax* 1987;42:730.

\* \* \* This letter was sent to the authors, who reply below.

SIR,—We welcome the comments of Dr Newman and others, whose points concerning the effect of particle size on bronchodilator responses are, of course, quite correct. A major problem with assessing bronchodilator responses from nebulised medication, however, is that they will vary enormously, depending on the properties of a particular nebuliser and the distribution of particles produced. Thus the total drug dose deposited in the lungs will be unpredictable even if similar doses are put into different nebulisers. This important practical difficulty, we thought, still left open the question of whether differences in particle sizes when "put" into the lungs under controlled conditions really mattered. The study by Dr Newman and colleagues (ref 1 above) used two different particle sizes (3.3 and 7.7  $\mu\text{m}$  MMAD) and they will have achieved a greater bronchodilator effect with the smaller particles because they will have achieved a greater lung dose. In our study we deliberately compared two equal lung doses of two particle sizes and found no change in function or distribution. In these circumstances lung function did not change—a question not previously clearly answered. The lack of variability in particle distribution of the two sizes may be due to the severity of the airways obstruction in our patients, which was greater than in most of the studies by Dr Newman and his colleagues.

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## Low serum testosterone as an indicator of metastatic bronchial carcinoma

SIR,—Mr David Taggart and his colleagues make the interesting suggestion that a low serum testosterone concentration in patients with bronchial carcinoma may be an indicator of metastatic disease (September 1987;42:661-3). Further, they propose that sequential serum testosterone estimations could be valuable in the follow up of those who are thought to have undergone curative surgery.

Before their suggestions can be accepted, further information is necessary regarding the patients they studied. As Mr Taggart and his colleagues acknowledge, serum testosterone concentrations decline with age and it would therefore be reassuring to know that the patients in the "curative surgery" and "palliative surgery" groups were not significantly different in age, and that the control group undergoing minor elective surgical procedures was age matched. Hypoxia also

results in low serum testosterone concentrations,<sup>1</sup> and while severely hypoxic patients are unlikely to have undergone surgery it is nevertheless important to establish that the findings of Mr Taggart and colleagues cannot be attributable to this factor. From the point of view of follow up of apparently cured patients to detect metastasis, the post-operative reduction of lung function, the further diminution with passage of time, and indeed the mere aging of the patient are all factors that would make the interpretation of such measurements of serum testosterone extremely difficult.

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- 1 Semple Pd'A, Watson WS, Beastall GH, Bethel MIF, Grant JK, Hume R. Diet, absorption and hormone studies in relation to body weight in obstructive airways disease. *Thorax* 1979;**34**:783-8.

\* \* \* This letter was sent to the authors, who reply below.

SIR,—In reply to the points raised by Dr Moore-Gillon, we apologise for the oversight in not having stated the ages of the patients in the various groups. The mean was 60 (SD 5) years for patients undergoing curative surgery, 62 (8) for patients undergoing palliative surgery, and 58 (13) for patients undergoing minor elective surgical procedures; there was no significant difference in age between these groups.

Lung function tests are performed routinely to ensure that our potential surgical candidates have sufficient respiratory capacity to tolerate the proposed operation. Although a degree of chronic obstructive airways disease is commonly present, none of our operated patients had the severity of obstructive airways disease known to produce a low serum testosterone concentration<sup>1</sup> as these patients would be very unlikely to survive pneumonectomy or even lobectomy.

Although there is a decline in circulating testosterone concentrations in older men, the serum concentration remains within the normal range until the eighth decade.<sup>2</sup> The mean age of our surgical candidates was 60 years in the curative group and 62 in the palliative group, and a useful period of follow up is therefore available before the development of a serum testosterone concentration outside the normal range.

Finally, we would like to re-emphasise a point made in our paper—that, until further evidence is available, a low serum testosterone concentration should be used only in conjunction with the results of other investigations, as an early indicator of recurrent disease in patients after “curative” surgery.

- 1 d'A Semple P, Watson WS, Beastall GH, Bethel MIF, Grant JK, Hume R. Diet, absorption, and hormone studies in relation to body weight in obstructive airways disease. *Thorax* 1979;**34**:783-8.  
2 Bremner WJ, Vitiello MV, Prinz PN. Loss of circadian rhythmicity in blood testosterone levels with aging in normal men. *J Clin Endocrinol Metab* 1983;**56**:1278-81.

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## Book review

*Pulmonary pathology*. 2nd ed. MS Dunnill. (Pp 632; £95.) Edinburgh: Churchill Livingstone, 1987. ISBN 0-443-03396-X.

The first edition of *Pulmonary Pathology* appeared in 1982, and rapidly established itself as a standard reference work. In this second edition the number of pages has been increased from 496 to 631 by the addition of new chapters on small biopsy specimens and pulmonary cytology. The text has been extensively revised, and the references updated. The opening chapter on pulmonary defence mechanisms is followed by sections dealing with chronic bronchitis, asthma, bronchiectasis, and emphysema. Subsequent topics include pneumonia, pulmonary fibrosis, and pulmonary vascular disease. Carcinoma and other neoplasms are considered, and a chapter is devoted to pulmonary lymphomas, lymphoproliferative disorders, and granulomatous vasculitis. Twenty or so pages deal specifically with neonatal and paediatric pulmonary disease. Miscellaneous disorders, including pulmonary amyloid, alveolar microlithiasis, and idiopathic pulmonary haemosiderosis, are also covered. The text concludes with a brief appendix on pulmonary anatomy and histology. The new chapter on small biopsies reviews the techniques that have become available as a result of recent developments in instrumentation. The handling of fibreoptic, drill, and transbronchial biopsy specimens is outlined, together with their limitations and likely yield. The older established methods of pleural biopsy and open lung biopsy are also dealt with. An additional chapter on pulmonary cytology has been contributed by Dr Winifred Grey. As well as describing the microscopy of cytological material in the commoner neoplastic and non-neoplastic diseases, Dr Grey comments on technical aspects and describes how appearances vary with the type of specimen. Like the first edition, this book is an important contribution to pulmonary pathology. The text is clear and concise, the illustrations of a high standard, and the references comprehensive and up to date. It will be of value not only to general and specialised histopathologists but also to physicians and surgeons with an interest in chest disease.

## Notice

### Scandinavian Association for Neonatal Extracorporeal Membrane Oxygenation (ECMO)

Experiences in neonatal ECMO and research in long time perfusion will be the subject of the association's meeting on 27-29 May 1988 at the Riverton Hotel, Gothenburg. The deadline for abstracts is 20 March. Details from the association's secretariat (Dr LG Friberg), Paediatric Surgical Clinic, Östra sjukhuset, S-416 85 Gothenburg, Sweden (tel 046-031-374620).