

# 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