LETTERS TO THE EDITOR

Nebulised antipseudomonal therapy in cystic fibrosis

Mukhopadhyay *et al* (April 1996;51:364–8) have performed a thorough meta-analysis on the inhalation of antibiotics in cystic fibrosis. Their conclusions support ours that aerosol maintenance treatment can be recommended for patients with cystic fibrosis chronically infected with *Pseudomonas aeruginosa*.[1] We want to point, however, to two issues.

Firstly, the authors did not discuss the value of the addition of nebulised antibiotics to intravenous antibiotics during a pulmonary exacerbation. Several studies have addressed this issue and, in our view,[1] there are no data to support this treatment strategy. Secondly, the authors did not discuss the potential risks of long term inhalation of aminoglycoside antibiotics. Serum concentrations of aminoglycosides after inhalation have been determined in only a few studies with widely varying results. Smith *et al*[2] measured tobramycin levels in the urine of patients following inhalation of a dose of 600 mg and found very limited systemic resorption (0.008–1.4% of the dose administered), while Mukhopadhyay *et al*[3] and Zach[4] found serum concentrations ranging from <0.1 to 4.2 mg/l for tobramycin and gentamicin, respectively. These results are in line with those from a study we carried out in six patients with cystic fibrosis where maximum serum concentrations of 0.2–2.5 mg/l and a urinary recovery of 6–27% were found after the inhalation of a single dose of 600 mg tobramycin (unpublished results). These data indicate a widely varying and unpredictable systemic resorption of aminoglycosides after inhalation which, in some patients, may lead to serious toxicity when the much practised dose of 600 mg tobramycin three times daily is prescribed. It is therefore mandatory to monitor serum concentrations in every patient where such treatment is initiated.

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1 Touw DJ, Brimicombe RW, Hodson ME, Heijerman HGM, Bakker W. Inhalation of antibiotics in cystic fibrosis. *Eur Respir J* 1995;8: 1594–604.
2 Smith AL, Ramsey BW, Hedges DL, *et al*. Safety of aerosol tobramycin administration for three months to patients with cystic fibrosis. *Pediatr Pulmonol* 1989;7:265–71.
3 Mukhopadhyay S, Baer S, Blanshard J, Coleman M, Carswell F. Assessment of potential ototoxicity following high-dose nebulised tobramycin in patients with cystic fibrosis. *J Antimicrob Chemother* 1993;31:429–36.
4 Zach MS. Antibiotic treatment, aerosol therapy: discussion. *Chest* 1988;94:160–1S.

AUTHORS' REPLY The comments of Drs Touw and Bakker are very relevant. The effect of the addition of nebulised to intravenous antibiotics on pulmonary exacerbations was, however, not one of the clinical questions we addressed as part of our analysis; hence we are not in a position to comment on the likely effect of this intervention. We agree it is an important question, possibly requiring further clinical study.

The inadequacy of current evidence supporting the possibility of long term risks associated with tobramycin inhalation led us to limit our discussion of this issue carefully. In an earlier study (cited by Drs Touw and Bakker[3]) one of us (SM) was intrigued by apparently acute changes on evoked response audiometry with high dose nebulised tobramycin and identified at least one patient with a high serum concentration of tobramycin following the administration of a single 400 mg nebulised dose. We agree with the point raised by Drs Touw and Bakker that the current data are consistent with unpredictable systemic absorption of nebulised antibiotics in some patients with cystic fibrosis.

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Spontaneous regression of a giant pulmonary bulla

In the report by Bradshaw and colleagues (May 1996;51:549–50) of an almost complete spontaneous resolution of a giant pulmonary bulla the computed tomographic (CT) scans of the chest (unfortunately the two images are not from the same lung level) which the authors present do, indeed, show a reduction in the size of the thorax. One would therefore expect the total lung capacity (TLC) to decrease as a result of "near complete resolution of the bulla". Surprisingly, however, the TLC increased from 6.5 litres at the beginning of the observation to 8.36 litres at the end. Indeed, the plethysmographic method that one assumes the authors used (the method for measuring TLC is not mentioned) measures all the thoracic gas volume, be it in communication with the mouth or not. If, however, the helium dilution method was used it cannot explain the small increase in TLC of only 0.5 litres from 7.83 to 8.36 litres, measurements done simultaneously with the CT scan. Indeed, this method measures only the lung volume in communication with the mouth and, since lung parenchyma replaced the giant bulla, one would expect a large increase in TLC.

The authors emphasise that their case is of interest "because it was associated with such dramatic improvements in the radiological picture and lung function". However, no mention of any change in symptoms or quality of life is reported. These are, at least for the patient, even more important than changes in the radiological picture.

Looking at the figures in the table, unexpectedly the sum of the vital capacity and the residual volume – that is, the TLC – only equals the figure reported in the table at the end of the observation. Indeed, the sum is 7.14 litres (reported 6.5 litres) in 1989, 7.57 litres (reported 7.9 litres) in 1990, and 6.74 litres in 1993 (reported figure one litre higher (7.83 litres)). Finally, the abbreviations given in the table for FRC(He) and FRC(Pl) are forced residual capacity (helium dilution) and forced residual capacity (plethysmography), respectively. We presume it should be *functional* residual capacity.

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AUTHORS' REPLY We appreciate the interest and careful reading of our case report documenting the spontaneous regression of a giant lung bulla by Drs Stănescu and Veriter and are pleased to respond.

Firstly, although not identical cuts, the two CT images presented are both at the level of the aortic arch and are as closely matched as we could find.

Secondly, the sequential pulmonary function tests presented in the table require clarification. Total lung capacity (TLC) measurements from 1989 and 1993 were obtained by the helium dilution method (the patient had difficulty performing body box manoeuvres) while measurements from 1990 and 1991 were obtained using plethysmography. When one compares just the two studies performed by helium dilution the increase in TLC from 6.5 litres to 8.36 litres is consistent with the observed expansion of lung parenchyma which accompanied bulla regression. Additionally, the difference in functional residual capacity (FRC), as measured simultaneously by both helium dilution and plethysmography in 1990 and 1991, implies a large volume of non-communicating airspace as would be expected in the presence of a very large bulla.

Thirdly, Drs Stanescu and Veriter astutely point out that the sum of the residual volume (RV) and forced vital capacity (FVC) in our table do not equal TLC in the first three studies. In our laboratory patients perform both a "slow" or "relaxed" VC manuoeuvre in addition to a "forced" VC manoeuvre. We calculate TLC as the sum of RV and slow VC (data not included in the table). It is well known that the slow VC may be considerably larger than the FVC in patients with severe obstructive lung disease and this was the case in our patient. Interestingly, the FVC and slow VC were identical following bulla regression, suggesting resolution of air trapping.

Finally, Dr Stănescu was interested in the clinical/functional status of our patient. Our report focused on the physiological and radiographic changes simply because it was the marked improvement in pulmonary function tests that led to further investigation. The patient did note modest improvement in exercise tolerance but, perhaps, more telling was a comment by his son who remarked, "Dad sure has a lot more energy these days".

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