LETTERS TO THE EDITOR

Improvement in sodium cromoglycate delivery from a spacer device

The study by Dr O'Callaghan *et al* (June 1993;48:603–6) is an interesting attempt to study some of the variables affecting drug delivery from holding chambers. Such studies are essential if we are to use these devices optimally, and it could be argued that it is unethical to proceed to radioisotope deposition studies without such basic data. It would, however, be wrong to make general recommendations based on a single study, particularly as previous studies assessing various chambers have shown that a number of factors, including chamber volume and valve design, can alter the dose delivered from a chamber.[1 2] Among other variables, this study attempts indirectly to assess the possible effect of static on the dose available from a holding chamber by using an "antistatic" spray. It should be noted, however, that the dose <5 µm available at one second with this spray is very similar to previously published results with a large volume chamber in which an antistatic spray was not used,[1] and the dose in particles <5 µm available at 20 seconds in this study when using the spray is very similar to the dose obtained in the previous study at 30 seconds without a spray.

The half life of the aerosol in the previous study was in the region of 15–20 seconds, which is significantly greater than that obtained in this study with the spray. Inspection of images produced with labelled aerosols would also suggest that impaction, influenced by gravity, is the principal cause of drug loss in large volume spacers.[3]

Similarly, the results with multiple actuations differ in magnitude from previously reported results. In a previous study[1] the "respirable" dose delivered per actuation when using four actuations in a large volume chamber was reduced, but only to that delivered from a metered dose inhaler alone, suggesting that, for certain chambers, two actuations can be used with little effect on efficiency.

It is possible that these discrepancies are due to the choice of chamber or formulation of metered dose inhaler, although my previous unpublished work suggests that the Fisonair performs at least as well as the other large volume spacers available. The formulation of the metered dose inhaler used delivers a relatively high dose and hence generates a denser aerosol than will be the case for most therapeutic metered dose inhalers; this may be relevant to the results. Alternatively, some other unrecognised factor may be influencing these results. Preliminary results with an electrometer suggest that variable static charge can be induced on a chamber by the way in which it is handled, but the relevance of this to clinical practice needs to determined. Reviewing the available evidence, further work is required to clarify these and other related issues.

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1 Clark AR. In-vitro assessment of spacer and reservoir devices. In: Dalby RN, Evans RM. *Respiratory drug delivery II*. Lexington: University of Kentucky, 1992:470–82.
2 Everard ML, Clark AR, Milner AD. Drug delivery from holding chambers with attached facemask. *Arch Dis Child* 1992;67:580–5.
3 Newman SP, Millar AB, Lennard-Jones TR, Moren F, Clarke SW. Improvement of pressurised deposition with Nebuhaler spacer device. *Thorax* 1984;39:935–42.

AUTHOR'S REPLY I strongly agree that studies of drug delivery from spacer devices are essential to optimise therapeutic effect, and that it may be unethical to proceed to radioisotope deposition studies without such basic data.

Delivery devices vary dramatically, as do drug formulations. We are in the process of analysing a large number of inhalational devices and drug formulations. Experiments have shown that static charge on spacers does, in fact, change considerably under the influence of several factors. It is therefore important to state whether a new or old spacer device is used, and the exact conditions of use in laboratory and clinical studies involving spacer devices.

Our recent work suggests that the Fisonair does perform at least as well as other large volume spacers, and our results are comparable to those obtained by Fisons in their laboratory in Loughborough (Dr A Clark, personal communication). We therefore feel that the increase in drug available for inhalation following the use of an antistatic agent in a new spacer is a real finding.

Multiple actuations into a spacer device should be avoided when using the Fisonair spacer with Intal, as recommended by the manufacturer. Subsequent work on Tilade endorses this finding.

Further work is certainly required to optimise drug delivery from spacer devices.

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Photodynamic therapy for treatment of bronchial carcinomas

We were interested to read the paper by Dr S G T Smith and coworkers (May 1993;48:474–80) in which the authors describe the effects of photodynamic therapy (PDT) on the tissue of the normal trachea in rats. The authors state that PDT has no effect on cartilage in the presence of granulation tissue. By two months the histology of the rat's trachea returned to normal.

Recently we had the opportunity to study the effect of PDT in human material.[1] A patient presented with shortness of breath caused by a tumour at the orifice of the right main bronchus. Histological investigation revealed typical bronchial carcinoid. After NdYAG laser treatment viable tumour tissue was still present in the dorsal wall of the right main bronchus. PDT was given to treat the residual tumour. After nine months follow up no tumour recurrence was seen, but the right main stem bronchus gradually developed a stenosis necessitating bronchoscopic dilatation. During one of these procedures a perforation of the dorsal wall of the right main bronchus occurred. A sleeve lobectomy was performed immediately afterwards.

In the resected specimen no residual tumour was seen. Bronchial cartilage and epithelium were intact, with fibrosis in the resected specimen of the bronchial ring between the cartilage tissue (figure).

Our histological finding confirms the data reported by Smith in rats. This observation is important, especially if any bronchoscopic therapy is attempted to improve resectability, or in cases with operable tumours in which too much damage to normal tissue may compromise any additional surgery.[2 3]

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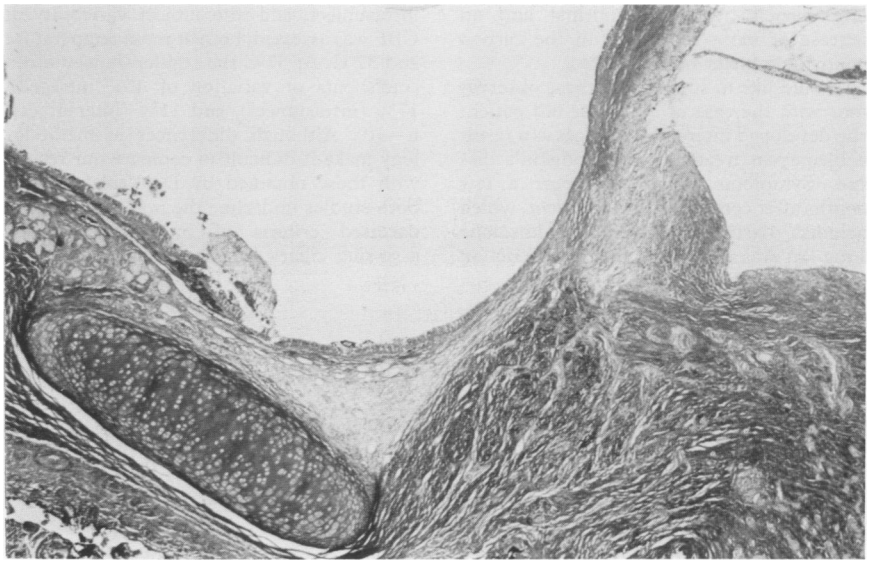

Histology of the right main bronchus after sleeve lobectomy.

1 Sutedja T, vd Heyden A, van Mourik J, Postmus PE. Haemoptysis and wheezing in a young woman. Case for diagnosis. *Eur Respir J* (in press).
2 Sutedja TG, Kwa B, van Kamp H, van Zandwijk N. Photodynamic therapy as an alternative for surgery in a patient with lung cancer undergoing bone marrow transplantation. *Chest* 1993;**103**:1908–9.
3 Edell ES, Cortese DA. Photodynamic therapy in the management of early superficial squamous cell carcinoma as an alternative to surgical resection. *Chest* 1992;**102**:1319–22.

AUTHORS' REPLY We were very interested to read the letter by Dr Postmus *et al*. This case report is very encouraging since it supports the findings in our animal study.

It is, of course, worrying that a fibrotic stenosis developed after treatment, but this may have been due to the preliminary treatment with the NdYAG laser and not the PDT.

PDT with haematoporphyrin derivative or phthalocyanines does, nevertheless, cause some fibrosis, but we are currently studying, in the same animal model, the role of amino laevulinic acid (ALA), a natural precursor in the synthesis of haem. When given in excess this leads to an accumulation of protoporphyrin IX, which is an effective photosensitiser when illuminated with red laser light. ALA appears to have much better selectivity for tumour cells and for mucosa and may therefore give a much better result than is currently possible.

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Reversal of bleomycin lung toxicity with corticosteroids

In their paper Drs Maher and Daly (January 1993;**48**:92–4) describe the case of a man with interstitial changes in the lungs after bleomycin treatment in whom they obtained a reduction in clinical symptoms and an improvement in the chest radiograph after long term high dose corticosteroids plus azathioprine. They also measured an improvement in the lung function with total lung capacity becoming normal and an increase of more than 50% in the carbon monoxide transfer factor (TLCO).

I would like to supplement these observations with the case of a 42 year old patient who developed interstitial changes as a result of bleomycin treatment for Hodgkin's disease. Symptoms began to appear a few months after completion of treatment, which included 420 mg bleomycin. Prednisolone (1 mg/kg) was given and the lung function changes are shown in the table. After one month of treatment there was a reduction in clinical symptoms and an improvement in the chest radiograph, as well as a return to normal of spirometric values and an improvement in the TLCO.

It has been stressed that TLCO is a more sensitive parameter of lung damage than vital capacity after bleomycin.[1,2] The improvement in diffusion seen in the patient treated by Drs Maher and Daly also suggests improvement in the interstitial changes. However, the continuing reduced TLCO indicates that there was residual damage. This was confirmed in our case by a reduction in static compliance. It appears that static compliance in these patients may be a useful measurement of persistence of interstitial changes in patients treated with bleomycin.

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1 Comis RL, Kuppinger MS, Ginsberg SJ, *et al*. Role of single breath carbon monoxide diffusing capacity in monitoring the pulmonary effects of bleomycin in germ tumor patients. *Cancer Res* 1979;**39**:5076–80.
2 Ginsberg SJ, Comis RL. The pulmonary toxicity of antineoplastic agents. *Semin Oncol* 1982; **9**:34–51.

Lung function parameters in patients with interstitial lung changes as a function of the duration of the disease and treatment

Timing of examination	*FVC (% pred)*	*TLCO (% pred)*	*Compliance (% pred)*	*Dosage of prednisolone*
On admission	59	39	16·3	50 mg/day
One week	75	—	—	50 mg/day
One month	93	71	33	50 mg/day
Three months	93	—	—	25 mg/day
Seven months	100	80	34	10 mg/day

FVC = functional vital capacity; TLCO = carbon monoxide transfer factor.

Variability in ciliary beat frequency in bronchiectasis

I read with great interest the paper by Dr D Veale and coworkers (October 1993; **48**:1018–20) in which the authors reported results on the in vitro variability of nasal ciliary beat frequency (CBF) in normal subjects and bronchiectatic patients. In 1990 my group conducted a study in which the variability of nasal CBF was investigated in healthy subjects.[1] Samples of nasal epithelium were collected and transferred to either sealed microscope coverslip slide preparations or tissue culture chamber. By using a photometric technique and rigorous randomisation criteria for the measurements, the intracell, intrasubject, and intersubject variability of CBF was assessed, both at room temperature and 37°C. At 37°C the results showed mean coefficients of variation of 4% (intracell), 17% (intrasubject), and 11% (intersubject; n = 10). Although differences in methodology make it difficult to compare our results with those obtained by Dr Veale's group, both studies underline the necessity of standardised criteria of investigation when assessing ciliary function. The wider question remains as to when a small but statistically significant difference in CBF in vitro also constitutes a physiologically meaningful difference in vivo.

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1 Di Benedetto G, Manara-Shediac FS, Mehta A. Variability of human ciliary beat frequency in vitro. *Eur Respir J* 1990;**3**(Suppl 10):257S.

BOOK NOTICE

Pulmonary Radiology. EJ Potchen, RG Grainger and R Greene. (Pp 412; £57.00). Philadelphia: Saunders, 1993. 0 7216 4821 5.

The Fleischner Society was named after the late Felix Fleischner in recognition of his outstanding contribution to the development of chest radiology. One of the Society's aims was to have a multidisciplinary approach to give a better understanding of disease processes to chest radiologists. The original contributions were published in *Frontiers of Pulmonary Radiology*.

Pulmonary Radiology is the second book published by the Society and exemplifies this multidisciplinary approach throughout the chapters which include: The developing lung; Interstitial lung diseases; Lung transplantation; Vascular diseases; The pleura; Acute lung injury; Airway disease; AIDS; Lung cancer; and New imaging modalities.

This is an excellent book which is intended to update and inform rather than being comprehensive, and is written by experts who explain the radiological appearances on the basis of morphology and pathophysiology. Not only does it do this, but it is a pleasure to read.

The chapter on Pathology of the developing lung by Lynne Reid is dealt with in a very clear and comprehensive way, aided by excellent illustrations and line drawings. I also enjoyed the chapter on Problems and pitfalls in the early diagnosis of lung cancer which is an excellent review, and the informative and refreshing way in which such a basic topic as lobar collapse is discussed. Lung physiology features highly, particularly in the section on acute lung injury, but such is the wealth of experience of the authors and variety of the subject matter that I am sure all chest physicians or radiologists who read this book will have their understanding or knowledge enhanced.

The book is well referenced, up to date, and has a comprehensive index. The illustrations are of a very high standard and all imaging modalities are included. The role of MRI in chest radiology is well presented, and there is an interesting final section on current concepts in thoracic CT scanning which includes spiral scanning, 3D reconstructions of the central airways, and the possibilities for physiological scanning.

This book should be an essential purchase to all thoracic and imaging departments at only £57, and I recommend it unreservedly to all those interested in a better understanding of chest radiology. – PS