inhalation technique is not fully addressed, despite the FDA recommendation that the technique should be trained using an In-spirease, a spacer device. The problem of a consistent inhaler technique when patients use MDIs has been extensively reported⁹⁻¹¹ and hence could affect the reproducibility of any method related to lung deposition in asthmatics, despite extensive training of the technique. Furthermore, this variability of salbutamol deposition would be enhanced by the pathophysiology of a patient's respiratory tract.¹² Variability of the bioassay will also be introduced by the training effect of the inhalation technique with respect to steroid therapy, hyperresponsiveness due to previous bronchoprovocation, and the length of salbutamol washout periods. Furthermore, the protocol is very demanding on the asthmatic subjects and our projection is that the drop out rate will be high which, together with the strict inclusion criteria, may introduce bias. Nevertheless, to answer the criticism in the two letters, we are planning clinical studies to compare our urinary excretion method with a bronchoprovocation test and the influence of inhaler technique will be studied first.

In vivo deposition studies using a radio-label¹³ have indicated that the bronchodilator response seems to depend on the total amount delivered to the lungs.¹⁴⁻¹⁶ A recently reported abstract, using labelled salbutamol aerosols, has shown differences in regional lung deposition related to the technique and, when total lung deposition was high, there was a corresponding increase in the amount delivered to the different regions of the lungs.¹⁷ This is why we will evaluate the influence of inhaler technique in our bronchoprovocation studies. An ongoing study in our laboratories is showing a linear relationship between one, two, three, four, and five (n = 12 subjects) inhaled salbutamol doses from an MDI and the amount renally excreted. This suggests that an increase in dose delivered to the lungs produces a simultaneous increase in the renal elimination of salbutamol.

Finally, Drs Watson and Lewis state that a significant number of patients claim that they find generic salbutamol inhalers to be less effective than the original branded products. This information should be reported to the regulatory authorities. All inhaled products contain patient information leaflets describing the inhaler technique which should be used, and examination of these reveals different instructions. It may be the confusion created by these differences which causes patients to complain. If the pharmaceutical industry cannot agree on the standardisation of the information on how to use an MDI, then perhaps the British Thoracic Society should provide these guidelines. Any argument that different techniques are recommended because of the MDI formulations, characteristics, etc is not substantiated in the literature.

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Diffuse pulmonary fibrosis and Hermansky-Pudlak syndrome

Dr Reynolds and colleagues (June 1994;49: 617-8) report a case of interstitial fibrosis of the lung proven at necropsy in a patient with Hermansky-Pudlak syndrome (HPS). They mention that they had identified 18 more cases in the literature.

The exact number of patients with HPS and pulmonary fibrosis or restrictive lung disease is difficult to determine as several cases seem to have been published on more than one occasion without correct cross referencing. Based on our search of literature we estimate that approximately 50 patients with HPS and pulmonary fibrosis or restrictive lung disease have been observed (bibliographic data in two) including the two necropsic cases we published. Women seem to be affected more often than men. Only very few reports exist on pulmonary fibrosis in siblings with HPS.¹⁻³

Contradictory data exist regarding the identification of ceroid in lungs of HPS patients with pulmonary fibrosis. Pigment-laden macrophages were seen in some patients⁴ but not in others.⁵ In one case no ceroid was reported at open lung biopsy when fibrosis already existed, but was identified at necropsy.⁶

In the first of two brothers with HPS and interstitial fibrosis we observed numerous pigment-laden macrophages in the lungs at necropsy but none in the second, despite him having more severe pulmonary fibrosis. The deposition of ceroid cannot therefore be the only cause of pulmonary fibrosis in patients with HPS.

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Combined chemotherapy and radiotherapy in advanced pulmonary blastoma

We were interested to read the recent case report of Dr Chin *et al* (August 1994;49: 838-9) describing a case of pulmonary blastoma in an adult presenting as a chronic loculated effusion.

We admitted a 57 year old man in 1991 with left shoulder pain, hoarseness, dyspnoea and Horner's syndrome. Chest radiography revealed a 11 x 12 cm mass in the upper zone of the left hemithorax. At fibreoptic bronchoscopy the left vocal cord was paralysed and the left upper lobe bronchus obliterated with a necrotic lesion. Because of the localisation of the lesion, transthoracic lung biopsy was performed and histological examination revealed a pulmonary blastoma. A computed tomographic scan revealed mediastinal invasion by the mass. No distant metastases were detected. The patient was inoperable and conflicting results have been reported regarding the use of chemotherapy, radiotherapy alone, or in combination.¹⁻³ We gave combined modality treatment using cisplatin, etoposide, and adriamycin as chemotherapy.

After two cycles of chemotherapy 6000 cGy radiotherapy was given to the lesion and a 75% regression was noted in the tumour