LETTERS TO THE EDITOR

Endobronchial nocardial infection

Further to the recent case report of Drs McNeil, Johnson and Oliver (December 1993;48:1281-2), we have seen another patient with nocardial chest infection and endobronchial involvement. This is the fifth reported case. A previously well 25 year old Australian aboriginal man presented with a non-resolving right lower lobe pneumonia. He had a five pack year history of smoking and had been admitted to a peripheral hospital and treated with intravenous amoxycillin and erythromycin for two weeks. Sputum cultures had subsequently grown *Nocardia* and he was therefore transferred to our hospital.

On examination he was febrile to 38°C, and auscultation revealed right lower zone crepitations. He produced 200 ml blood-stained sputum per day. Oral trimethoprim/sulphamethoxazole was commenced in a dose of 640 mg/3200 mg per day. The fever settled but sputum production and chest signs persisted. Bronchoscopic examination revealed a polypoid "tumour" partially obstructing the posterobasal segment of the right lower lobe. Biopsy material from this revealed filamentous organisms and florid active chronic inflammation. Culture of the biopsy specimen confirmed the organisms as *Nocardia* and bronchial washings also grew *Nocardia*. Intravenous amikacin was added with resolution of chest signs and cessation of sputum production.

No dissemination of *Nocardia* was seen after bronchoscopy, possibly because he had been on treatment for 10 days before the procedure. As with the previous case there was no underlying defect of humoral or cell-mediated immunity. However, he consumed an average of 200 mg alcohol per day. He will remain on trimethoprim/sulphamethoxazole for at least nine months.

This case shows once again that endobronchial "tumour" can be due to *Nocardia* even in patients with normal immune systems.

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Fluticasone propionate v beclomethasone dipropionate (BDP) in moderate to severe asthma

I read with interest the paper by L Fabbri *et al* (August 1993;48:817-23) which compared the above drugs in patients with moderate to severe asthma. The authors found a small (15 l/min) peak expiratory flow (PEF) advantage in the fluticasone group compared with BDP amounting to about 4% of the average morning PEF of these patients. I calculate from figure 1 and table 1 that the morning PEF of the fluticasone group increased from

74% predicted to 81% predicted, whereas in the BDP group PEF increased from 73% to 78% predicted.

The symptom scores were similar on both medications but there was said to be a slight excess of "severe" asthma (not clearly defined) in the group given BDP. There were 13 "severe" exacerbations in the BDP group and three "severe" exacerbations in the fluticasone group. However, a further four patients using fluticasone withdrew from the study because of poor asthma control compared with only one patient using BDP, and a further 15 patients (all using fluticasone) had to increase their dose of inhaled steroid because of poor asthma control. The total number of patients with poor asthma control was therefore 22 in the fluticasone group and 14 in the BDP group. Neither drug had any significant effect on adrenal function.

The authors conclude that fluticasone may be more effective than BDP and they recommend it for long term use in asthma because of the marginal benefits shown in the study, and also because of a theoretically superior side effect profile which was not demonstrated in their own study.

Surely it would be equally logical to conclude that both groups of patients fared very well on high dose inhaled steroid treatment and any difference between the two groups was disappointingly small considering that the fluticasone group was supposedly given twice the biologically effective dose of inhaled steroid. Most patients would have fared equally well on either preparation although there was a suggestion that a small number of patients who were prone to recurrent exacerbations might fare better on the more potent treatment.

Given that this trial was commercially commissioned and funded, one can understand the enthusiasm for the new agent which is expressed in the discussion. However, the discussion omits to mention that one year's treatment with fluticasone 1500 µg per day would cost £925 compared with £253 per year for the same dose of BDP. I feel that it would be premature (and very expensive) to transfer patients from BDP to fluticasone on the basis of this trial. I would have difficulty convincing my Pharmacy Therapeutics Committee that a 4% gain in peak flow with no difference in symptom scores or side effects was worth a 265% increase in cost.

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AUTHORS' REPLY Dr O'Driscoll suggests that the improvement in peak flow resulting from fluticasone propionate treatment in patients with moderate asthma is minimal when compared with that induced by beclomethasone dipropionate (BDP), particularly when one considers the associated increase in treatment cost. After reanalysing our data, Dr O'Driscoll also suggests that fluticasone was no more effective than BDP in reducing the overall exacerbation rate (as opposed to severe exacerbations). We thank him for his interest in our paper and welcome the opportunity to clarify, as far as possible, the issues he has raised.

Effect of treatment on PEF: patients entered this study at a time when their asthma was controlled, not during a period of exacerbation (an exclusion criterion). In addition, we compared the effect of treatment with fluticasone with that of high dose BDP—that is, the most effective antiasthma treat-

ment currently available. For these reasons we believe that we could not have expected anything other than a relatively small increase in PEF. Nevertheless, PEF increased from 74% to 81% after treatment with fluticasone, and from 73% to 78% after BDP treatment. For FEV₁, the increased effect was even greater (0.25 v 0.16 l increase with fluticasone and BDP respectively). Thus, while we did not observe the 2:1 efficacy ratio reported in previous studies,¹⁻³ we did find a greater effect of fluticasone on lung function.

Reduction in asthma exacerbations: table 2 of our paper lists the true exacerbation rates. Dr O'Driscoll selected only the severe exacerbations and then added to these those patients who withdrew and also those whose fluticasone dose had been changed during the study. It is invalid to do this, however, as these latter groups were, in fact, subsets of the patients who had exacerbations. For example, where the fluticasone dose had been increased this had been done as a result of an exacerbation and these patients would have been included in the table as such. In addition we have noticed an error in the original publication; the withdrawals were, in fact, four in the BDP group and one in the fluticasone group, rather than the reverse as described in the results section (p 820). We apologise for the oversight.

Costs: the study was designed to compare the efficacy of the two treatments rather than as a cost comparison. Such a comparison would require a more detailed analysis of the available data to investigate whether, for example, the reduction in costs of treating exacerbations of asthma would balance the increase in the cost of drug treatment. In addition, there are increasing numbers of published studies which show that fluticasone can be used at half the BDP dose with equivalent efficacy. It may therefore be more appropriate to leave the cost/benefit conclusions to the pricing authorities.

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- 1 Dahl R, Lundback B, Malo JL, *et al*. A dose-ranging study of fluticasone dipropionate in patients with moderate asthma. *Chest* (in press).
- 2 Barnes NC, Marone G, Di Maria GU, Visser S, Utama I, Payne SL. A comparison of fluticasone propionate 1 mg daily, with BDP 2 mg daily in the treatment of severe asthma. *Eur Respir J* 1993;6:677-84.
- 3 Woodcock AA. High-dose inhaled fluticasone propionate: clinical experience to date. *Eur Respir J* 1990;3(Suppl 10):250s-251s, S925.

Accuracy of CT appearances of fibrosing alveolitis

In answer to the question raised by Drs Selby and Brown (December 1993;48:1289) we have recalculated the sensitivity and specificity of the high resolution computed tomographic (CT) appearances of cryptogenic fibrosing alveolitis, including only those cases with histopathological confirmation of the diagnosis.¹ Contrary to their dogmatic assertion that the inclusion of cases without histological confirmation "results in an overestimate of the diagnostic usefulness of CT scanning", when this is done the performance of high resolution CT scanning actually improves: sensitivity 91% (compared with 89% for the whole group) and specificity

91% (compared with 87% for the whole group).

The logic behind their supposition that the accuracy of high resolution CT scanning would be diminished if only applied to cases which are biopsy proven is not clear. They might have supposed that only cases with atypical clinical presentation or radiographic features were confirmed by biopsy (in our practice some patients with typical fibrosing alveolitis may undergo biopsy for the evaluation of disease activity). In any event, we can dismiss the suggestion that including "biopsy unproven" cases in our study resulted in an overstatement of the accuracy of high resolution CT scanning in making the diagnosis of fibrosing alveolitis.

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1 Tung KT, Wells AU, Rubens MB, Kirk JME, Du Bois RM, Hansell DM. Accuracy of the typical computed tomographic appearances of fibrosing alveolitis. *Thorax* 1993;48:334-8.

BOOK NOTICES

New Concepts in Asthma. J P Tarayre, B Vargaftig and E Carilla. (Pp 310; £70.00.) Basingstoke: Macmillan, 1993. 0 333 65430 8.

The number of books on asthma is increasing almost as rapidly as the number of cytokines identified. This book contains contributions to a meeting on asthma organised by a French pharmaceutical company and held in France in 1991. Research in asthma is moving very fast and some of the chapters now appear somewhat dated. Several chapters are concerned with animal models of asthma and conclude that there is no ideal experimental model that closely mimics the features of asthma. Several chapters discuss the potential role of cytokines and adhesion molecules in chronic asthmatic inflammation, but some of these chapters are inevitably out of date. As is usual with a book made up of contributions to a meeting there is a fair amount of overlap, and several of the chapters are a rehash of previously published chapters or reviews. There are relatively few illustrations.

This book provides a good selection of chapters on the immunopathology of asthma, but several important areas are neglected including the role of nerves, structural remodelling, plasma exudation, and airway smooth muscle. The title is therefore somewhat misleading. The book is expensive at £70.00 and many other books on asthma which are more comprehensive are a better buy. – PJB

Fungal Diseases of the Lung. 2nd edition. George A Sarosi and Scott F Davies. (Pp 351; \$120.00.) New York: Raven Press, 1993. 0 7817 0001 9.

In this short textbook on fungal diseases of the lung the general chapters are excellent, dealing with the life cycle in different fungal

diseases. The illustrations are particularly good, demonstrating the morphology and life cycle of the various fungi. The chapter on the clinical laboratory diagnosis is also excellent, giving tables which greatly aid in separating the individual fungi from each other by both morphological and cultural characteristics. It is interesting to note that a fluorescent stain can be used immediately to enable rapid diagnosis in many cases. There is also a detailed chapter on serological tests which indicates that, while the tests are excellent for histoplasmosis, coccidioidomycosis, aspergilloma/allergic bronchopulmonary aspergillosis, and central nervous system cryptococcosis, they are less useful for blastomycosis, candida, and disseminated aspergillosis. The application and limitations of tests for individual fungi are discussed in detail. Specific chapters on the various fungi follow, which are excellent in their clinical details, symptomatology, radiology, diagnostic tests, and latest treatment methods. All this is clearly written with good illustrations. The chapters on allergic bronchopulmonary aspergillosis and farmer's lung are short, while the chapter on AIDS is poor, giving just a very broad outline of the damage to the immune system in this condition. There follow several chapters on AIDS and specific fungal infections which are repetitious of earlier chapters. The two chapters on fungal infection in lymphoma and leukaemia and organ transplantation are also repetitious, but may be of interest for specific problems faced in these conditions. The final two chapters deal with methods of treatment, with particular reference to Amphotericin B and the azole antifungal agents. They are excellent, dealing with the actions, pharmacokinetics, effects on the immune system, side effects, and methods of administration of these drugs, and are clinically very useful.

This book is value for money at approximately £60, and will give information on specific fungal infections which affect the lung, as well as details of the extrapulmonary manifestations. Even though the later parts of the book are repetitious it is concise and gives useful information on fungal disease with specific reference to the lung. I would recommend it. – MS

Principles and Practice of Pulmonary Rehabilitation. R Casaburi and TL Petty. (Pp 508; £57.00.) Philadelphia: Saunders, 1993. 0 7216 3304 8.

Do not be misled by the title of this book. Its purpose is to provide a rational and scientific approach to rehabilitation in chronic lung disease but, in the process its authors and contributors have produced a highly authoritative reference work on chronic obstructive airways disease. Its scope is broad – from disturbances of basic pulmonary function, through cardiovascular consequences, to sleep disorder, psychological and cognitive dysfunction. The aggregation of these review chapters together under one cover would alone be almost sufficient reason for buying it. The remainder of the book covers all aspects of the care and management of patients with chronic pulmonary disease. While it concentrates on chronic obstructive pulmonary disease, it includes worthwhile chapters on non-obstructive lung diseases, asthma, cystic fibrosis, and rehabilitation related to lung transplantation. Whilst it is an

extremely valuable reference for those with a specialist interest in rehabilitation of patients with lung disease, it is equally useful for those with any form of involvement with such patients, whether at a clinical or research level. Therapeutic topics range from standard pharmacology and long term oxygen therapy to smoking cessation and breathlessness desensitisation.

The core of the book, but not its bulk, is concerned with the components of a pulmonary rehabilitation programme. The reader is provided with a wealth of advice and comment in this area, yet it is here that the greatest disappointments lie. Despite the high level of scientific analysis of the processes underlying the development of disability and impaired health and well being, there is a clear shortage of critical analysis and identification of the important components of an effective rehabilitation regime. This is not the fault of the authors but a reflection of the current state of knowledge. I also felt that, in a book with such a broad scope, there was only a limited analysis of the impact of the disease from the patient's perspective, and insufficient discussion of the process of setting realistic goals for rehabilitation and methods by which these could be achieved most efficiently.

Having made these small criticisms, it is hard to fault. It is very comprehensive and should be accessible to readers from a wide range of backgrounds. All chest physicians, nurses, and physiotherapists concerned with the care of patients with chronic lung disease would gain much from it. One of its greatest contributions is to highlight the fact that, once maximum bronchodilatation has been achieved, the care and management of these patients has only just begun. – PWJ

NOTICE

Testing drugs for asthma

The recommendations of the Society of Pharmaceutical Medicine (SPM) Working Party on Testing Drugs for Asthma will be presented at a meeting at The Scientific Societies' Lecture Theatre, Savile Row, London W1 on 20 April 1994. For further details contact: Mrs B Cavilla, Society of Pharmaceutical Medicine, The Institute of Biology, 20-22 Queensbury Place, London SW7 2DZ. Telephone: 071 581 8333. Fax: 071 823 9409.

CORRECTION

BTS Asthma Guidelines

An error occurred on page S16 of the BTS Asthma Guidelines (*Thorax* 1993;48 (Suppl)). In the section on "Special points about management of acute asthma in general practice" under the subheading "Children" the correct dose of terbutaline that may be administered subcutaneously in severe episodes is 0.25 mg and not 2.5 mg as published.