LETTERS TO THE EDITOR

BOOP associated with nitrofurantoin

Cameron et al reported two cases of bronchiolitis obliterans organising pneumonia (BOOP) associated with the use of nitrofurantoin. These patients had a favourable outcome after treatment with corticosteroids. We wish to report a similar case.

An 82 year old woman presented in 1997 with a two year history of a cough productive of white sputum and gradually increasing breathlessness. She gave a history of 41 pack years of smoking but had stopped 23 years previously. Before referral she had received treatment with inhaled steroids and bronchodilators but without any effect on her symptoms. She had been taking nitrofurantoin 50 mg at night for prophylaxis against urinary tract infection for the previous four years. Her general health was otherwise good, there was no previous history of lung disease, and no exposure to noxious fumes or dusts.

She was breathless on minimal exertion and had fine inspiratory crackles at both lung bases extending up to the mid zones; there was no finger clubbing. Her oxygen saturation dropped from 95% breathing air at rest to 87% after climbing two short flights of stairs. Her lung function showed a restrictive ventilatory defect with forced expiratory volume in one second (FEV₁) 0.941 (57% predicted) and forced vital capacity (FVC) 1.331 (65% predicted). Carbon monoxide transfer factor (TLCO) was reduced to 56% predicted. High resolution computer tomographic (CT) scans of the thorax showed marked mosaic perfusion affecting all areas with patchy ground glass opacification. There was associated mild interlobular thickening.

Nitrofurantoin related lung disease was suspected so the drug was stopped and an open lung biopsy was performed. Histological examination showed chronic interstitial pneumonia with interstitial chronic inflammatory cellular infiltration associated with the presence of occasional lymphoid follicles and aggregates of macrophages in several alveoli. In addition, there were some obtrusive changes associated with the presence of buds of oedematous fibroblastic tissue within terminal and respiratory bronchioles and extending into adjacent alveoli, which are features of BOOP (fig 1).

Treatment with oral prednisolone was given for four months starting at 30 mg daily for six weeks then slowly tailing off. There was clinical improvement within one month of starting oral steroids with reduction in cough and breathlessness, and eight months after starting treatment she felt that she had returned to her previous best. Her FEV₁ improved to 1.091 (70% predicted), FVC to 1.721 (88% predicted), and TLCO to 70% predicted. The chest radiograph showed improvement in the basal reticular shadowing; the CT scan was not repeated. She remains well three years after diagnosis.

This case further demonstrates the good response of BOOP associated with nitrofurantoin once the offending drug is withdrawn and treatment given with oral corticosteroids.

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Outcome measures in asthma

As Neil Barnes points out in his review of outcome measures in asthma, the selection of appropriate outcomes plays a key role in shaping clinical and research agendas. He relates widely used outcome measures to the aims of management as stated in current asthma guidelines, particularly in terms of parameters of long term asthma control such as prevention of symptoms, minimal requirement for reliever medication, normalisation of lung function, and prevention of exacerbations. These parameters correspond to the aims of asthma management in the BTS¹  and the GINA guidelines.² The importance of looking at a number of different outcomes and of recognising the different time scales over which these outcomes need to be measured is now widely recognised in the evaluation of medical interventions in asthma.

It could be argued, however, that even the wide range of parameters considered in the review fails to capture all the aims of asthma management, and particularly may miss those outcomes determined by the patients themselves. It is becoming increasingly clear that patients and their doctors do not always share the same perceptions of what is important in asthma management and what constitutes a successful outcome of asthma care. The AIR study² shows that patients are particularly concerned with functional outcomes—what matters most to them is what they can and can’t do because of their asthma, and how their asthma prevents them from doing the things they want to do. Although there is obviously an overlap with other outcome measures such as symptoms, patients frequently modify their lifestyle to prevent symptoms occurring, so asthma may disproportionately impair their quality of life even in the absence of reported symptoms.

Functional and patient determined outcomes are given surprisingly little attention in the stated aims of current guidelines. They are barely touched on in the aims statement of the BTS guidelines ("...minimisation of absence from school and work") and skirted over in the 1999 GINA guidelines ("... have productive, physically active lives"). The 1993 GINA guidelines aims statement covers the area more fully, with the aim to have "minimal limitation on activities, including exercise". Quality of life and health status tools, which are increasingly used as outcome measures in asthma clinical trials, are perhaps beginning to move us in the direction of patient centred outcomes. The Juniper AQLQ questionnaire in particular does include patient determined functional outcomes as part of the assessment of health status.

In daily clinical practice we aim to elucidate and address our patients’ goals and aspirations, and they form a major part of our clinical decision making process. Perhaps the time has come for us to develop and validate tools to capture these important outcomes in clinical trials of asthma interventions. The outcome measures outlined in the review all reflect different and complementary aspects of overall asthma management, but they are generally physician centred. There is also a need to capture data on patient centred and functional outcomes. This is particularly true of the pragmatic real world studies that are needed to clarify the position and merits of the increasingly wide array of therapeutic options open to us in the everyday management of asthma.

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Figure 1 Section from the open lung biopsy showing an area of BOOP. Stain: haematoxylin and eosin; original magnification ×160.
I wish to share my own experience in this field, which has led me to a somewhat different conclusion. In our laboratory measurement of capsaicin sensitivity in over 200 healthy volunteers, as well as in a smaller group of stable asthmatic patients in whom cough was not a reported complaint, demonstrated no significant difference in cough reflex sensitivity between these two groups. Our findings are consistent with those of previous investigations which support the well documented dissociation between cough and bronchoconstriction, responses that are controlled by distinct neural pathways.

We have recently shown, however, that asthmatic subjects with cough in the sole or predominant symptom have significantly enhanced cough sensitivity compared with stable asthmatics without cough. We therefore suggest that individuals with cough variant asthma may be a distinct subgroup of asthmatics in whom the afferent airway receptors controlling cough are hypersensitive, whereas in those in whom cough is not a significant feature do not differ from normal subjects in terms of cough reflex sensitivity. Lending further support to this concept is our recent demonstration that the leukotriene receptor antagonist zafirlukast inhibits capsaicin sensitivity and symptomatic cough in subjects with cough variant asthma (14) but does not affect cough reflex sensitivity in patients with stable asthma without cough (15) or in healthy volunteers.

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“Cough as a reported complaint with lung function, symptoms, and support from normal subjects in terms of cough reflex sensitivity. Lending further support to this concept is our recent demonstration that the leukotriene receptor antagonist zafirlukast inhibits capsaicin sensitivity and symptomatic cough in subjects with cough variant asthma but does not affect cough reflex sensitivity in patients with stable asthma without cough or in healthy volunteers.”

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NOTICES

The Sheffield Seminar

“The Sheffield Seminar” will take place in Sheffield, UK, yearly starting next May. The meeting will focus on all aspects of cardiothoracic surgery, starting next year with general thoracic surgery topics. It will take place on 31 May and 1 June 2001 at the Postgraduate Medical Centre, Northern General Hospital, Herries Road, Sheffield S5 7AJ, UK. For further information contact Mr G Rocco, Consultant Thoracic Surgeon. Telephone +44 114 271 4950. Fax +44 114 261 0350. Email: grocco@tany.fsnet.co.uk

Basic and Clinical Allergy 2001

Basic and Clinical Allergy will be held at the National Heart & Lung Institute, Imperial College School of Medicine, London on 2–6 April 2001. CPD/CME approval pending (2000 course maximum 28 credits). Further details are available from the Short Courses Office, Education Centre, National Heart & Lung Institute, Imperial College School of Medicine, Dovehouse Street, London SW3 6LY, UK. Telephone +44 207 351 8172; fax +44 207 351 8246; email: shortcourses@nhli.ic.ac.uk; www.med.ic.ac.uk/th/dh/divnts.htm.

Pediatric Pulmonology

The 2nd World Congress of Pediatric Thoracic Disciplines will take place in Izmir, Turkey on 26–28 April 2001. For further information contact Professor Dr Oktay Mutaf, Ege University Faculty of Medicine, Pediatric Surgery Dept, Izmir, Turkey. Fax +90 232 3751288; email: omutaf@med.rgr.edu.tr

4th International Symposium on Angiotensin II Antagonism

The 4th International Symposium on Angiotensin II Antagonism will be held at the Queen Elizabeth II Conference Centre, London, UK on 3–5 April 2001. For further information contact the Secretariat, Hampton Medical Conferences Ltd, 127 High Street, Teddington, Middlesex TW11 8HH, UK. Telephone +44 020 8977 0011; fax +44 020 8977 0055; email: AIFA@hamptonmedical.com
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