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 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 1.09 l (70% predicted), FVC to 1.72 l (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This case further demonstrates the good response of BOOP associated with nitrofurantoin once the offending drug is withdrawn and treatment given with oral corticosteroids.

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 BTS’ and the GINA guidelines. 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 fail 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 study 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 “...more 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.
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 investigators and support the well-documented dissociation between cough and bronchodysfunction, responses that are controlled by distinct neural pathways.

We have recently shown, however, that asthmatic subjects in whom cough is the sole or predominant symptom have significantly enhanced cough sensitivity compared with stable asthmatics without cough. I would therefore suggest that individuals with cough variant asthma are a distinct subgroup of asthmatics in whom the afferent airway receptors controlling cough are hypersensitive, whereas 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 but does not affect cough reflex sensitivity in patients with stable asthma without cough or in healthy volunteers.

P V DICPINIGAITIS
Albert Einstein College of Medicine, 1825 Eastchester Road, Bronx, New York 10461, USA


I would like to thank Dr Thomas for his interest in my article. He is critical that patient centred outcomes were not included in my discussions. Patient centred outcomes have been increasingly discussed, but a number of questions need to be answered before these are accepted. Just because health care practitioners and patients are using different words or terminology does not mean they are not interested in the same objective. A patient’s desire to be able to play sport and a practitioner’s aim to prevent exacerbation are just different ways of articulating the same goal. Furthermore, patients may have an incomplete understanding of their disease and the consequences of different treatment options. A patient may consider that an important outcome to them is to be able to stop all their inhalers and to smoke 20 cigarettes per day without getting wheezy, but I doubt that Dr Thomas would think that either of these were reasonable outcome measures to look at in a clinical trial. The physician must not only listen to patients’ concerns, but must also educate them as to the short and long term consequences of different treatment and treatment patterns. Unless care is taken, uncritical acceptance of patient centred outcomes may have negative as well as positive features. Furthermore, it needs to be established in well controlled clinical trials that adding patient centred outcomes makes a fundamental difference to clinical trial outcome. My paper was also about the interrelationship between different outcome measures. It is difficult to make comparisons when measures cannot be repeated frequently, and at present most research using quality of life questionnaires just administers these at the beginning and end of a trial, so comparisons with lung function, symptoms, and [f] agonist use which can be measured frequently and changes in quality of life are difficult.

N C BARNES
Department of Respiratory Medicine, The London Chest Hospital, London E2 9QH, UK

Capsaicin responsiveness in asthma and COPD

I read with interest the study by Doherty et al in which cough reflex sensitivity in asthmatic subjects and patients with chronic obstructive pulmonary disease (COPD) was examined. The authors found that subjects with asthma were more sensitive to the tussive agent capsaicin than were normal subjects and, furthermore, that capsaicin sensitivity was related to the subjective assessment of symptomatic cough. They concluded that an enhanced cough reflex is an important contributor to cough in asthma.

AUTHORS’ REPLY
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P A CALVERLEY
Pulmonary & Rehabilitation Research Group, Department of Medicine, Clinical Sciences Centre, University Hospital Aintree, Liverpool L9 7AL, UK

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 cardio-thoracic 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 7AL, UK. For further information contact Mr G Rocco, Consultant Thoracic Surgeon. Telephone +44 114 271 4950. Fax +44 114 261 0350. Email: grocco@tany.fasnet.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.nhlth@ic.ac.uk; www.med.ic.ac.uk/dh/div/ntsmts.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 Prof Dr Oktay Mutaf, Ege University Faculty of Medicine, Pediatric II Conference Department, 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: ALFA@hamptonmedical.com

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