Inhaled fluticasone

I read with interest the article on the effects of inhaled fluticasone propionate and oral prednisolone on markers of airway inflammation in asthma recently published in Thorax by Meijer et al.1 In particular, it was interesting to read that the magnitude of reduction in airway hyperresponsiveness after fluticasone was more pronounced for adenosine 5'-monophosphate (AMP) than for methacholine. Ketchell et al2 have recently reported that sensitive prediction of the AMP response to inhaled corticosteroids is already apparent as early as 48 hours. Taken together, these findings further support the use of adenosine challenge as a sensitive and convenient non-invasive test of asthmatic inflammation for potential use in diagnosis, monitoring disease activity, and evaluating treatment efficacy.3

In asthmatic airway the ability of this test to discriminate the changes in airway reactivity with anti-inflammatory treatment better than histamine or methacholine has also been validated with inhaled budesonide and the new non-invasive test of asthmatic inflammation is more specific in assessing changes in airway inflammation than methacholine.4-6 So far, the test has been shown to be a sensitive non-invasive test of asthmatic inflammation with potential use in diagnosis, monitoring disease activity, and evaluating treatment efficacy in asthma.7

In that study the mean (SD) improvement in PC20 methacholine and AMP might therefore be a better predictor of efficient anti-asthma therapy.

AUTHORS’ REPLY We have read the letter by Dr Polosa with great interest. We support his view that adenosine challenge appears to be a sensitive non-invasive test of asthmatic inflammation than methacholine. Improvement in PC20 AMP is more specific in assessing changes in different components of airway inflammation than methacholine. Improvement in PC20 AMP might therefore be a better predictor of efficient anti-asthma therapy.


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Figure 1 Improvement in PC20 methacholine and AMP with salmeterol (solid bars) and fluticasone (open bars) both during active treatment and 12 hours after stopping the drugs. *p<0.05, fluticasone versus salmeterol.

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than changes in the conventionally used parameters, as advised in current guidelines.

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Gender differences in airway behaviour

We were surprised to read in the exhaustive and, some might say, exhausting review of gender differences in airway behaviour by Becklake and Kauffman1 that the most common respiratory symptom—namely, cough—deserved only a single sentence and was then dismissed. In fact, the most dramatic gender difference in airway sensitivity is seen with the cough reflex. We studied 163 consecutive, healthy, non-smoking volunteers (90 women, mean age 32 years) with an inhalation cough challenge of five one-second inhalations of 10% citric acid delivered from a Mefar dosimeter. Women coughed over 50% more than men (mean total cough score 19.1 versus 12.0, p<0.001). This confirms several other observations in the literature with both acid1 and capsaicin2 inhalation.

It could be argued that the smaller airways of women allow for greater deposition of the irritant agent, but this cannot explain the twofold difference between the sexes in the incidence of ACE inhibitor–induced cough. Unlike many of the observations quoted in their review, this gender difference in the cough reflex sensitivity has important clinical implications. In the Hull Cough Clinic we see twice as many women as men (64 versus 33 completed episodes last year). Other reported series have similar experiences.3,7

The fact that a review of 20 pages and 211 references did not comment on these observations is alarming. Surely the objective to sift the literature, or is the policy now to publish gargantuan articles of the kind seen earlier last year on cytokines in asthma3 in order to enhance the journal’s impact factor?

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Cell and cytokine markers in COPD

We read with interest the paper by Dr Wedzicha and colleagues on cell and cytokine measurements in exacerbations of COPD.1 We feel there are two factors which are worthy of comment. The authors described their patients as being predominantly those with chronic bronchitis. This is consistent with an exacerbation that consisted of the cardinal features described by Anthonisen and colleagues—namely, combinations of increased breathlessness, increased sputum volume, and increased sputum purulence.2 In view of the fact that increased sputum purulence is a feature of exacerbations, we are surprised at the lack of increase in neutrophils seen in the exacerbation paper. Even if half the patients did not have purulent sputum, we would have expected to have seen an overall increase in the number of neutrophils in the samples obtained.

In addition, the authors’ use of sputum induction when most of the patients must have presented with spontaneous sputum production in order to have increased sputum volume or sputum purulence. Surely the use of sputum induction in such patients would lead only to dilution of the bronchial secretion obtained, and this may explain some of the negative neutrophil results. Indeed, in our own studies of approximately 140 exacerbations in a similar setting, two thirds of them were purulent in nature and were associated with increases in cytokines in the spontaneously expectorated sample. The purulent samples were associated with an increase in myeloperoxidase concentration and in neutrophil numbers seen on Gram staining. We would have expected the same findings in the paper by Wedzicha and colleagues if the exacerbations were similar.

We consider that it may be appropriate to stratify exacerbations, particularly when trying to assess the role of intervention treatments and the nature of the cytokines present.

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AUTHORS’ REPLY We appreciate the comments of Professor Stockley and Dr Hill that neutrophils should increase during COPD exacerbations and their hypothesis that this was not found in our study because of a possible dilutional effect of the induced sputum technique on lower airway secretions.

Eleven of the 37 sampled exacerbations (29.7%) in our study1 were associated with purulent sputum, whereas 24 (64.7%) were associated with increased sputum volume and 10 patients had no sputum production at exacerbation. This indicates that 31% (33% of COPD exacerbations are not associated with sputum production.

We have shown previously that the number of viable cells was greater in induced sputum than in spontaneous sputum (65% versus...
Diagnosis and assessment of DPLD

In this excellent report the transfer factor (Tl) in untreated cryptogenic fibrosing alveolitis is reported as reflecting the extent of fibrosis; it is noted that Kco (Tl/Va) does not. Given more space, the authors might have added that Kco can mislead by being normal or increased when alveolar volume is restricted. This is because Kco is based on a proportional model that does not make valid allowance for alveolar volume. An alternative linear model is available and should be used instead.

BOOK REVIEW


This book represents the ninth publication in the Clinical Physiology series published for the American Physiological Society and provides a comprehensive review of the multiple facets of lung growth and development in both health and disease. Particular emphasis has been placed on recent advances at the cellular and molecular level with respect to the complex series of controlled interactions involving genetic, hormonal, and cell-cell interactions that are required for lung development. Each chapter is extensively referenced and presents a succinct review of selected topics relevant to lung development by experts in the field.

Inevitably with a multi-author book such as this, there is considerable variability in presentation style with some chapters more accessible to the non-specialist than others. The inclusion of a glossary would have been beneficial in view of the increasing use of abbreviations in this field. Nevertheless, most of the authors have provided an excellent review of their topic and have clearly indicated, not only the current state of knowledge and the clinical significance of recent research findings, but what still needs to be investigated.

The first part of the book is devoted to lung branching morphogenesis, development of the lung elastic matrix and the importance of elastin in lung structure and function, differentiation of airway epithelial cells, and gene expression in alveolar development. Lung development and angiogenesis, including sections which emphasise the importance of postnatal microvascular maturation and the potential impact of exogenous risk factors such as impaired nutrition and glucocorticoid therapy on lung development and alveolarisation, are the subject of an important chapter. Other authors have reviewed the developmental aspects of the pulmonary vasculature and circulation, cellular host defence mechanisms, lung epithelial ion transport (including a fascinating overview of its dysfunction in neonatal lung diseases), cell growth and tissue repair, and the role of bioactive peptides.

COPD: New Developments and Therapeutic Options

A course on “COPD: New Developments and Therapeutic Options” organised by Professors Peter Barnes and Neil Pride will be held on 26–28 September 2000 at Imperial College School of Medicine at the National Heart & Lung Institute in collaboration with the Royal Brompton Hospital, Dovehouse Street, London SW3 6LY. Enquiries to: Postgraduate Education Centre, National Heart & Lung Institute, Imperial College School of Medicine, Dovehouse Street, London SW3 6LY. UK. Telephone: 020 7351 8172. Fax: 020 7351 8246. Email: shortcourses.nhli@ic.ac.uk

Pharmacology of Asthma

A course on “Pharmacology of Asthma” organised by Professor Peter Barnes will be held on 20–23 November 2000 at Imperial College School of Medicine at the National Heart & Lung Institute in collaboration with the Royal Brompton Hospital, Dovehouse Street, London SW3 6LY. Enquiries to: Postgraduate Education Centre, National Heart & Lung Institute, Imperial College School of Medicine, Dovehouse Street, London SW3 6LY. UK. Telephone: 020 7351 8172. Fax: 020 7351 8246. Email: shortcourses.nhli@ic.ac.uk