LETTERS TO THE EDITOR

Nasal provocation with AMP

We read with interest the article on histamine release following nasal provocation with adenosine 5'-monophosphate (AMP) recently published in *Thorax* by Polosa *et al*.[1] This is a further in vivo demonstration of the histamine releasing ability of adenosine in the respiratory tract. However, in contrast to the in vitro studies described in the paper where adenosine exerts a modulatory effect on mast cell mediator release, we have demonstrated the direct histamine releasing ability of this molecule on mast cells in the bronchoalveolar lavage (BAL) fluid.[2 3] In samples of BAL fluid from 37 of 54 patients attending hospital for routine bronchoscopy, adenosine alone caused histamine release (maximum 20.6 (2.5)% of the total cellular content of the amine). The adenosine receptor agonists R-PIA, NECA, and CGS21680 also induced histamine release from BAL fluid mast cells. Preincubation of BAL fluid mast cells with the adenosine receptor antagonist xanthine amine congener caused significant inhibition of the response to adenosine ($p = 0.007$).

Our findings indicate a means by which adenosine challenge of the airways can induce bronchoconstriction and support a role for adenosine in the pathophysiology of asthma. The results suggest that cells obtained from BAL fluid may provide the ideal model for the testing of novel, adenosine receptor, targeted therapies for asthma. The inter-individual variability in response to adenosine and adenosine agonists is therefore most probably due to the variation in the clinical histories of this unpreselected population. Previously we have found a wide variation in response to substance P in such unpreselected patients, although the variation in response was not present in further studies in a clearly defined asthmatic population.[4 5] We are currently investigating the action of adenosine on BAL fluid cells employing carefully defined subject groups of atopic asthmatic subjects, atopic non-asthmatic subjects, and non-atopic non-asthmatic controls.

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1 Polosa R, Pagano C, Prosperini G, *et al*. Histamine release upon adenosine 5'-monophopshate (AMP) nasal provocation in allergic subjects. *Thorax* 1999;**54**:230–3.
2 Forsythe P, McGarvey LPA, Heaney LG, *et al*. Adenosine mediated histamine release from human bronchoalveolar lavage mast cells. *Am J Respir Crit Care Med* 1996;**153**:A211.
3 Forsythe P, McGarvey LPA, Heaney LG, *et al*. Adenosine induced histamine release from human bronchoalveolar lavage mast cells. *Clin Sci* 1999;**96**:349–55.
4 Heaney LG, Cross LMJ, Stanford CF, *et al*. Substance P induces histamine release from human pulmonary mast cells. *Clin Exp Allergy* 1995;**25**:179–86.
5 Heaney LG, Cross LMJ, Ennis M. Histamine release from bronchoalveolar lavage cells from asthmatic subjects after allergen challenge and relationship to the late asthmatic response. *Clin Exp Allergy* 1998;**28**:196–204.

AUTHOR'S REPLY That airway responsiveness to nebulised adenosine is a more selective indicator of allergic inflammation than other non-specific stimuli such as histamine or methacholine is supported by a number of clinical studies.[1] Although activation of neural pathways[2 3] and the intrinsic hyperresponsiveness of the bronchial smooth muscle to adenosine[4] may also contribute to adenosine induced bronchoconstriction in asthma, enhanced mast cell releasability in vivo is a primary determinant for these responses.

We are glad to learn that, in keeping with our previous findings in the lower[5] and upper airways,[6] Ennis *et al* have recently shown that adenosine elicits a significant histamine release from BAL fluid mast cells in 37 out of 54 consecutive patients undergoing routine bronchoscopy.[7] It would be of interest to know whether adenosine potentiates histamine releasability in those BAL fluid mast cells obtained from atopic individuals and to investigate whether PC_{20} adenosine correlates with the extent of mast cell releasability. This would further substantiate the view of adenosine bronchial provocation as a potential new marker of airway inflammation in asthma.

Interestingly, Ennis *et al* provide evidence for an A_{2A}-mediated mechanism for the adenosine induced histamine release from BAL fluid mast cells (since CGS21680 is a selective A_{2A} agonist), whereas A_{2B} receptors are mainly indicated to be involved in the activation of human mast cells.[8] This needs to be carefully investigated as the appreciation of the potential role of A_{2A} receptors in mediating adenosine induced responses in human mast cells raises the possibility that these receptors could become the target for future drug development.

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1 Polosa R, Holgate ST. Adenosine bronchoprovocation: a promising marker of allergic inflammation in asthma? *Thorax* 1997;**52**:919–23.
2 Polosa R, Phillips GD, Rajakulasingam K, *et al*. The effect of inhaled ipratropium bromide alone and in combination with oral terfenadine on bronchoconstriction provoked by AMP and histamine in asthma. *J Allergy Clin Immunol* 1991;**87**:939–47.
3 Polosa R, Rajakulasingam K, Church MK, *et al*. Repeated inhalation of bradykinin attenuates adenosine 5'-monophosphate (AMP) induced bronchoconstriction in asthmatic airways. *Eur Respir J* 1992;**5**:700–6.
4 Bjorck T, Gustafsson LE, Dahlen SE. Isolated bronchi from asthmatics are hyperresponsive to adenosine, which apparently acts indirectly by liberation of leukotrienes and histamine. *Am Rev Respir Dis* 1992;**145**:1087–91.
5 Polosa R, Ng WH, Crimi N, *et al*. Release of mast cell-derived mediators after endobronchial adenosine challenge in asthma. *Am J Respir Crit Care Med* 1995;**151**:624–9.
6 Polosa R, Pagano C, Prosperini G, *et al*. Histamine release upon AMP nasal provocation in allergic subjects. *Thorax* 1999;**54**:230–3.
7 Forsythe P, McGarvey LPA, Heaney LG, *et al*. Adenosine induced release from human bronchoalveolar lavage mast cells. *Clin Sci* 1999;**96**:349–55.
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BOOK REVIEW

Key Topics in Respiratory Medicine. Kinnear W, Johnston I, Hall I. (Pp 169; £18.95). UK: BIOS Scientific Publishers Ltd, 1999. ISBN 1 85996 271 8.

This book from the Key Topic Series is aimed at postgraduate students in medicine (those sitting MRCP examinations) and other trainees (including intensivists and anaesthetists) who come into contact with respiratory medicine during their clinical practice. It is divided into discrete, although overlapping, topics in a standard format covering respiratory symptoms, pathologies and clinical scenarios.

The schematic radiograph on the front cover belies the conspicuous absence of pictures, diagrams or radiographs throughout the rest of the book. It is particularly remarkable that the chapters on chest *x* rays and diagnostic imaging are thus unfurnished. Similarly, lung function tests are explained with great clarity and serve as a useful revision tool, but without the assistance of any diagrams their value to the novice is limited. The chapters on *Aspergillus*, diffuse parenchymal lung disease and pneumoconiosis were, however, very helpful in clarifying what can be confusing nomenclature. The common respiratory problems (particularly asthma, chronic obstructive pulmonary disease (COPD), lung cancer, and pneumonia) are all covered excellently with clear, up to date overviews. Their management sections are well supported by references to the British Thoracic Society guidelines which enhances the usefulness of the book in clinical practice. Other chapters which deal with respiratory disease in special situations add to the interest and breadth of the text.

I would reiterate the recommendation of the book as a useful text in preparation for both the written and clinical sections of the second part of the MRCP examination. It admirably fulfils its intentions by providing a concise, exceptionally factual, account of clinical respiratory medicine, despite the conspicuous absence of illustrations.—SS

NOTICES

20th International Symposium on Intensive Care and Emergency Medicine

The 20th International Symposium on Intensive Care and Emergency Medicine will be held on 21–24 March 2000 at the Congress Center in Brussels, Belgium. For further information contact Carl Vanhaesendonck, Telephone: 322 555 3215/3631. Fax: 322 555 4555. email: sympicu@ulb.ac.be.