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Letters to the Editor

Dear Editor

Menthol and aspirin-induced asthma

I read with interest the recent short report by Tamaoki *et al.* on the effect of menthol vapour in mild asthmatics (1). However, they did not comment on the effect of menthol in aspirin-induced asthma. Subiza *et al.* reported on an aspirin-sensitive patient whose asthma was exacerbated by the mint flavour contained in her toothpaste (2). They performed the challenge test and showed that the mint and menthol contained as flavouring in toothpastes may act as asthma-inducing agents.

I have experienced three patients with aspirin-induced asthma who also complained of dyspnoea when they brushed their teeth, chewed gum with mint flavour, or had a cough drop. I pointed out the resemblance of chemical structures in aspirin, parabens, and artificial flavours (3). Recently I encountered two more patients with aspirin-induced and mint-flavour-sensitive asthma. In one patient, the challenge test with his flavoured toothpaste was performed. Immediate response (decrease in FEV_1 from 4·30 l to 3·81 l) was obtained after he had used his toothpaste. A challenge was then performed with menthol, one of the components of the patient's toothpaste. The patient was instructed to rinse his mouth with 25 mg of menthol diluted in 50 ml of 5% alcohol for 1 min and then spit it out. Five minutes later, FEV_1 was decreased from 4·49 l to 4·08 l. The patient complained of tightness.

Therefore, it seems that menthol vapour does not have a beneficial effect on aspirin-induced asthma.

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Reply to Dr Kawane

We thank Dr Kawane for raising the possibility that menthol could deteriorate asthmatic symptoms in patients with aspirin- and mint-flavour-sensitive asthma. Although such patients were not included in our study, two patients complained of uncomfortable sensation in the upper airway immediately after menthol inhalation. These patients were withdrawn from our study protocol and, thus, we did not assess their airway reactivity. The mechanism of efficacy of menthol on airway hyper-responsiveness remains unknown, but this cyclic alcohol stimulates laryngeal cold receptors (1), inhibits cough reflex (2), stimulates airway epithelial Cl secretion through a Ca^{2+}-dependent mechanism (3,4) and directly relaxes airway smooth muscle (unpubl. data). We speculate that these actions could be involved in the observed effect of menthol in our study.

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Dear Editor

Raised brain natriuretic peptide in pulmonary hypertension

The interesting observations on brain natriuretic peptide (BNP) in association with pulmonary hypertension as described recently (1) raises the issue

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of whether the secretion of this group of peptides could be beneficial, and whether hypoxia or hyperventilation plays a role in their release. It prompts me to report our findings when we investigated the acute effects of these stimuli upon plasma ANP levels, previously only published in abstract form (2).

Six normal volunteers were studied using a rebreathing circuit with a spirometer to measure rate and minute volume. A soda lime CO_2 absorber with variable bypass controlled inspired carbon dioxide, as measured by end-tidal (ET) CO_2. Inspired O_2 content was monitored at the inspiratory limb of the circuit. Oxygen saturation (SaO_2) was measured by pulse oximetry. The subjects were allowed 10 min run-in period, then rebreathed 6 l of air for 20 min and baseline values obtained. Hypoxia was induced by replacing 4 l of the air with nitrogen to attain a SaO_2 level of 75–80% for 20 min, additional O_2 being added as required. End-tidal CO_2 was maintained at 5–5·5 kPa. After a recovery period of 10 min, hypocapnic hyperventilation was voluntarily induced and the subject maintained his ET CO_2 at 3–3·5 kPa for 20 min. After a further 10-min recovery period, combined hypoxia and hypocapnic hyperventilation was studied for 20 min using the same variables. The experiment was concluded by a further 10 min recovery while still breathing through the apparatus. Venous blood for plasma ANP was collected throughout at 10-min intervals. Statistical analysis was by the Friedman statistic for non-parametric data.

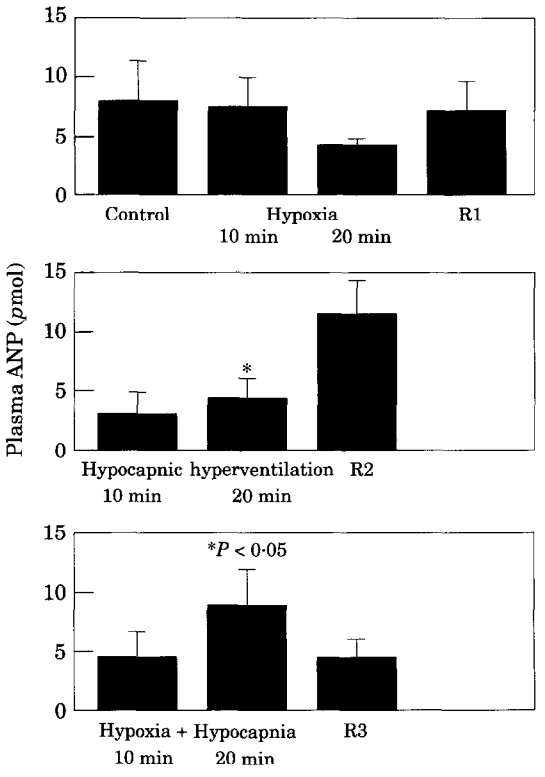

Fig. 1 Effect of hypoxia, hypocapnic hyperventilation and both stimuli combined upon plasma ANP levels. R, recovery period. Studies were run sequentially.

The results are summarized in Fig. 1. Acute normocapnic hypoxia caused no significant change in plasma ANP. Acute hypocapnic hyperventilation caused a fall in ANP after 10 and 20 min, from the mean baseline of $8{\cdot}2 \pm 2{\cdot}2$ pmol l^{-1} to $2{\cdot}1 \pm 1{\cdot}0$ at 10 min and $4{\cdot}2 \pm 1{\cdot}7$ at 20 min ($P<0{\cdot}05$ comparing control with both hypocapnic values). The combined stimulus caused an initial fall in ANP to $4{\cdot}4 \pm 2{\cdot}1$ pmol l^{-1} at 10 min followed by a return to control levels at 20 min ($8{\cdot}7 \pm 2{\cdot}8$ pmol). There appeared to be an inverse relationship between the rate of ventilation and the level of plasma ANP but only during control, recovery and hypocapnic hyperventilatory states.

As noted by Prasad *et al.* (1), *in vitro* work has suggested that acute, severe hypoxia may cause a rise in the secretion of ANP, and chronically hypoxic rats appeared to deplete right atrial ANP and have elevated levels of plasma ANP (4,5). Studies in man have, however, failed to reveal a clear relationship between hypoxia and release of ANP. One study of hypoxia in man showed a gradual rise in plasma ANP reaching significance at 120 min (6) but the same group were unable to reproduce this result in dogs. Comparable levels and duration of hypoxia were used in a study which showed a small rise in ANP (7).

Our acute study did not show a rise in ANP with acute hypoxia. It did, however, suggest that an increase in ventilatory rate causes a fall in venous ANP acutely, which is only detectable during hypocapnia. It is quite possible that increases in plasma ANP are consistent only in chronic hypoxia and are related to the development of pulmonary hypertension rather than hypoxia alone. The case reports described raise the possibility that there may be a similar stimulus for BNP secretion, although factors acting on the ventricle may be more important.

The ANP assay was generously supported by the British Lung Foundation.

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Dear Editor

Bronchiectasis and Felty's syndrome

Following Takanami *et al.*'s case report (1) and discussion regarding an association between rheumatoid arthritis (RA) and bronchiectasis (BR), we would like to report a case of BR in a patient known to suffer from Felty's syndrome, an association not previously described. Felty's syndrome is characterized by a combination of RA, splenomegaly and leucopaenia and in this case the patient was also suffering from Sjögren's syndrome (dry eyes, confirmed by a positive Schirmer's tear test plus an auto-immune disease, e.g. RA).

A 74-year-old man presented to our chest clinic complaining of a persistent cough productive of purulent sputum and associated with increasing breathlessness over a period of several years. He had suffered from seropositive nodular RA and Sjögren's syndrome for approximately 40 yr and had been admitted to hospital on one occasion following an episode of bronchopneumonia during which *Staphylococcus aureus* was isolated in large numbers from sputum samples. No immunosuppressive therapy had ever been instituted. Physical examination revealed bibasal crackles on auscultation of the chest and moderate splenomegaly on abdominal palpation.

Lung function tests revealed an FEV_1 of 1·30 (55% predicted), FVC 2·43 (79% predicted) and FEV_1/FVC ratio of 0·53. Chest radiography showed slight bibasal shadowing, (a radiograph in 1989 had been reported as normal), but CT scanning of the thorax revealed severe BR with loss of volume within the left and right lower lobes and right middle lobe. A full blood count revealed a pancytopaenia with haemoglobin 11·4 g dl^{-1}, white cell count $1{\cdot}3 \times 10^9\,l^{-1}$ and platelets $99 \times 10^9\,l^{-1}$.

In our patient, as in Takanami *et al.*'s case, the onset of RA almost certainly predated the development of BR. However, the presence of Felty's syndrome would result in a greatly increased susceptibility to infection (due to neutropaenia), in addition to the increased risk in RA discussed by Banji and Cooke (2). This association may lend some weight to their hypothesis that RA increases the incidence of respiratory infection, resulting in the development of BR.

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