LETTERS TO THE EDITOR

Revision of BTS guidelines for treatment of asthma

The paper by Ward et al confirms the findings of Laitinen et al showing that airways inflammation is evident even in patients with mild asthma. This emphasises the importance of using anti-inflammatory drugs (steroids) as soon as the diagnosis of asthma has been confirmed, even in patients thought to have only mild asthma. Without anti-inflammatory treatment, symptoms resulting from bronchial hyperresponsiveness are never controlled and optimal lung function is never attained. Over time, structural changes (remodelling) occur leading to a progressive decline in lung function and the risk of fixed obstruction (chronic obstructive pulmonary disease). The present widespread dependence on bronchodilators in the UK may contribute to the fact that we have one of the highest respiratory death rates in Europe. The use of bronchodilators alone as in step 1 of the BTS guidelines should be discouraged, and treatment started at step 2 with regular inhaled corticosteroids to control symptoms and maximise peak flow rate. Bronchodilators should be used only as necessary for breakthrough wheezing. These principles have been used in Finland since 1994 with remarkable success in treating asthma. The new BTS guidelines would do well to follow their example.

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References

Authors’ reply

We would like to thank Dr Strube for his interest in our recent paper and his stimulating letter which is topical given that the new BTS guidelines on asthma management are currently in preparation. Our study was an attempt to investigate the interrelationships between airway inflammation, airway structural change (remodelling), lung function, and bronchial hyperreactivity to methacholine in patients with mild to moderate symptomatic asthma. Our paper is supportive of a further point, adding to work from others, which we feel is potentially substantive, of possible importance to future guideline considerations, and perhaps relates to some of Dr Strube’s concerns. The potential paradigm shift is in determining appropriate treatment only by reference to symptoms and lung function, as in current international and draft BTS guidelines, or even against indices of inflammation, may be oversimplified, with prolonged treatment necessary to benefit airway remodelling reflected by improvement in BHR. It should be recognised that this remains a hypothesis and, pragmatically, it is of interest that the inclusion of BHR as an asthma management tool in the UK is not resourced and is not currently practicable.

We also realise that the demanding and detailed preparation of the BTS asthma guidelines has followed a due process reliant on the available evidence base with “levels of evidence” leading to “grades of recommendation” and, in turn, to “recommended best practice”. If appropriate pathophysiological research relevant to the clinical questions does not exist, it cannot be included. We feel that longitudinal data that seek to integrate information on airway inflammation, airway remodelling, lung function, and bronchial hyperreactivity and the effects of treatment are required. Such work, though demanding, is possible and would require multidisciplinary cooperation, dialogue, and appropriate support.

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4 http://www.britthorac.org.uk/guide\_guidelines.htm
Chronic respiratory failure

The recent case report by Smyth and Riley describes an extremely uncommon chronic respiratory failure due to hyperventilation secondary to brainstem stroke, and documents a new treatment option with medroxyprogesterone acetate.

We recently saw two patients also with central hyperventilation resulting in chronic type II respiratory failure and treated both with, among other things, medroxyprogesterone acetate (30 mg twice daily) with good results.

The first patient, a 69 year old man with a medical history of glosus caroticus resection due to malignancy with postoperative radiotherapy, was referred to our outpatient clinic with polyglobulia. Arterial blood gas analysis revealed marked hypoxaemia (PaO2, 4.8 kPa) and hypercapnia (PaCO2, 6.9 kPa). An intensive search for the cause showed no abnormality in lung function indicating only marginal chronic obstructive pulmonary disease (FEV1/FVC 68%) but his hypoxic ventilatory response was markedly decreased and his hypcapnic ventilatory response was absent. The patient was treated with acetazolamide, theophylline, and medroxyprogesterone acetate and his blood gas tensions improved within days to normal values (PaO2, 10.3 kPa, PaCO2, 5.1 kPa).

The second patient, a 38 year old woman, was known from birth to have a hypothalamic pituitary gland deficiency with (stable) adipsositas (quiotet index 53). She had complete loss of peripheral and central RhE system. She had severe sleep apnoea on several occasions before being sent to our department. Arterial blood gas analysis revealed hypoxaemia and marked hypercapnia (PaO2, 8.0 kPa, PaCO2, 7.2 kPa). She probably suffered from Cushing’s disease of pituitary adenoma. She was treated with acetazolamide, theophylline, and medroxyprogesterone acetate and his blood gas tensions improved within days to normal values. Furthermore, she now follows an intense weight reduction programme and has lost more than 10 kg in weeks.

Acetazolamide has been shown to augment both the hypoxic and hypcapnic ventilatory response and to decrease PaCO2 levels significantly in patients with chronic obstructive pulmonary disease (COPD). The mechanism of the effect is possibly due to a direct effect on the peripheral chemoreceptors (arterial chemoreceptors) as well as an effect on the central respiratory control centre.

It has been shown that medroxyprogesterone acetate also acts on the peripheral chemoreceptors (arterial chemoreceptors) as well as on the central chemoreceptors (indirectly) and prostaglandin synthesis and hypothalamic in cats. It was also found in hypercapnic COPD patients, indicating that medroxyprogesterone acetate acts centrally on the respiratory centres. This support the hypothesis of medroxyprogesterone acetate in central hyperventilation. Furthermore, the combined treatment of acetazolamide and medroxyprogesterone acetate increases ventilation and improves arterial blood gas values—that is, it decreases PaCO2, to normocapnic values and increases PaO2 to almost normocapnic values in hypcapnic and hypoxic patients with COPD.

In conclusion, we agree with Smyth and Riley that medroxyprogesterone acetate can be used in patients with central hyperventilation disorders.

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References

Caffeine and exhaled nitric oxide

We read with interest the paper by Bruce et al which reported a significant decrease in exhaled nitric oxide (NO) levels 1 hour after caffeine consumption. However, we do not believe that this study has fully clarified the relationship between caffeine consumption and exhaled NO levels.

When ascertaining the normal ranges for offline exhaled NO measurements we observed that some individuals had raised exhaled NO levels 1 hour after caffeine consumption. To further clarify this effect, exhaled NO (parts per billion (ppb)) levels were measured at baseline and 0.5 and 1 hour after drinking a hot cup of coffee in 18 healthy non-smokers, aged 17–56 years.

Exhaled NO was measured by chemiluminescence. No difference was observed at baseline and 0.5 hour. However, a significant decrease in exhaled NO was observed 1 hour after caffeine consumption (4.7 (2.6–8.3) ppb, difference between medians 2.9 ppb (95% CI 1.4 to 4.3), p = 0.007). There was a significant difference between baseline levels and the levels 1 hour after caffeine consumption (4.7 (2.6–6.6) ppb, p < 0.001).

We can conclude that levels of exhaled NO are decreased 1 hour after caffeine consumption (case 1) was morbidly obese. Athenaeus reported that Magas “was weighted down with monstrous masses of flesh in his last days; in fact, he choked himself to death.” 2 Ptolemy II (case 2) and his sister Arsinoe III were extremely obese. Ptolemy II was not an energetic man and he disliked physical exertion. Although he lived to the age of 62, he was troubled by ill health throughout most of his life. 3 Ptolemy IV, the Philopater (case 3),
was described as licentious even by the standards of his contemporaries. Calvin Wells reported that he was obese and he languished in habitual lethargy, perhaps because of chronic illness. Ptolemy VI Philometor (case 5) was portrayed also developed extreme obesity and used to fall asleep during social and political events. From these descriptions it is clear that obesity was present in all of them and, at least four of the seven kings, there were reports of daytime somnolence. This dynasty was probably the first reported family with sleep disordered breathing that had a familial predisposition.

Figure 1 The pedigree of the Ptolemaic dynasty (shading indicates affected members).

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3. Strabo. XVII. 1. 5.

BOOK REVIEW
Clinical Management of Chronic Obstructive Pulmonary Disease

According to the publishers, this book is a comprehensive review of recent evaluative and management strategies aimed at practising clinicians. In the past, most of the volumes from this epic series have concentrated on selective aspects of the scientific basis of respiratory disease and therefore attracted the interested specialist. As on previous occasions, the format follows the pattern of a series of reviews written by acknowledged scientific experts. As usual the book is expensive, and is wide in scope with over 90 collaborators and more than 1000 pages. Unlike a textbook, however, the content lacks strong editorial control and it is effectively a collection of individual reviews. The quality of the chapters is therefore inconsistent. Some authors have clearly accepted their brief and produced excellent reviews. In particular, the chapters on radiology, dyspnoea, genetics, and trial methodology are outstanding. However, many other chapters fall short and there is evident “resting on laurels” in some areas. The book does cover many other interesting facets of COPD but clinicians who purchase this book will also be aware of substantial omissions in clinical areas of COPD care that are currently being developed. There is, for example, very little on rehabilitation or the organisation of services. There is nothing at all on nursing intervention, terminal care, travel, or self-management. There is, however, a welcome attempt to cover the global issues surrounding COPD.

This is an expensive book which contains some excellent chapters. However, the overall volume is slightly disappointing and would compare badly with a thoughtfully structured comprehensive textbook. In the past this series has worked well where it examines the leading edge of research. In this instance the more general reader may find better value in a textbook but could still profit from borrowing a copy from the library.

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