Alveolitis associated with sulphamethoxypridazine

Dr J C Porter and others (September 1989; 44:766–7) report on a patient who developed alveolitis associated with the administration of sulphamethoxypridazine for bullous linear Iqg disease. The patient had previously had a reaction to dapsone. The dose of sulphamethoxypridazine was 250 mg thrice daily, increasing to 500 mg thrice daily, with prednisolone 15 mg daily for six months, during which time she became increasingly short of breath. Her drug induced alveolitis was reversed when the sulphonamide was stopped and the dose of prednisolone was raised to 60 mg daily.

The recommended dose of sulphamethoxypridazine for a urinary tract infection is, or was, 1–2 g immediately, followed by 500 mg daily. Because of the long plasma half life of the drug there is no advantage in giving the drug more frequently than once daily—indeed, peak plasma concentrations will be lower if the dose is split. Can the authors explain why they chose to give three times the recommended dose and why they used thrice daily dosage? And this to a patient with bullous skin disease who had already shown hypersensitivity to dapsone—and for six months . . .

The authors were fortunate that the daily prednisolone presumably damped down the progressive alveolitis and prevented any of the other severe reactions that might have been associated with prolonged overdosage.

IAN LENOX-SMITH
Rabby Heath, Welwyn, Herts AL6 9TE

AUTHOR’S REPLY Dr Lenox-Smith’s observations are correct concerning the use of sulphamethoxypridazine in urinary tract infections, for which it is no longer licensed, but they do not apply to bullous skin diseases. For over 30 years it has been prescribed in dermatitis herpetiformis.1 It is also used, on a named patient basis, in linear IgA disease, which is an intensely pruriit condition. Dose is titrated against clinical response and, in Oxford, there are 12 patients receiving doses of up to 1.5 g of this drug daily with good effect. It is commonly given when a patient is intolerant of dapsone. The alternative is sulphaspyridine, which causes nausea and is associated with renal failure and agranulocytosis. The main purpose of our letter and of the article by Dr C L Steinfeld and others (April 1989;44:310–1) was to report the alveolitis, which is a previously undetected but serious complication of sulphamethoxypridazine. As we suggested, routine three monthly spirometry and chest radiography may be indicated in patients receiving sulphamethoxypridazine.

The final point of Dr Lenox-Smith’s letter, concerning dosage interval, is entirely correct. The stated regimen in our letter is inadvertently incorrect and the patient actually received a once daily dose.

JS FRIEDLAND
JC PORTER
E WOJNAROWSKA
JGG LEDINGHAM
John Radcliffe Hospital, Oxford OX3 9DU

Significance of antibodies to cytoplasmic components of neutrophils

D J Harrison and colleagues (May 1989;44:373–7) cast further light on the usefulness of serum antibodies to neutrophil cytoplasmic antigens (ANCA) in the diagnosis of Wegener’s granulomatosis and other vasculitides, by their detailed description of the various different fluorescent patterns. Despite the seemingly high specificity of ANCA for certain diseases, their exact role is unclear. It might be a pathogenetic factor responsible for tissue injury or, alternatively, might simply be an immunological artefact resulting from the increased leucocyte turnover, which has been shown to occur in systemic vasculitides.1 To further address this issue we tested for the presence of ANCA in a group of patients who had lymphoproliferative diseases and had reduced leucocyte counts resulting from chemotherapy.

Serum samples from 18 patients, 10 male and eight female, ranging in age from 15 months to 81 years (median 39 years), were tested for presence of ANCA by indirect fluorescence as previously described.2 Nine patients had leukaemia, five multiple myeloma, three lymphoma, and one polycythaemia vera. Pretreatment leucocyte counts ranged from 4.0 to 26.0 (mean 31.8) × 109 cells/l and post-treatment lowest counts ranged from 0.1 to 3.2 (mean 2.1) × 109 cells/l. Serum from all patients was negative for ANCA, in contrast to the serum from our positive control subjects.

Thus patients with significant destruction and turnover of leucocytes do not appear to produce ANCA, strengthening the theory that these antibodies may be responsible for the pathological lesions in Wegener’s granulomatosis, possibly by activating neutrophils, rather than simply being a response to neutrophil destruction.

B RUDENSKY
J ASHKENAZI
A ABRAMOV
M ISACSOHN
Shaare Zedek Medical Centre, Jerusalem, Israel


Effect of inhaled leukotriene B4 alone and in combination with prostaglandin D2 on bronchial responsiveness to histamine in normal subjects

We read with interest the paper by Dr P Black et al (June 1989;44:491–5) and would like to support their findings with our own observations in the dog.

We measured the change in airway reactivity to methacholine and the cell content of bronchoalveolar lavage fluid one, three, and six hours after administration of aerosolised leukotriene (LTB4) in normal dogs. In contrast to previous reports in the dog,3 we found that airway responsiveness was reduced after LTB4 administration at each time point, despite a threefold increase in lavage fluid neutrophils.

These results show that the recruitment of neutrophils to the airways did not cause a concomitant increase in airway reactivity or methacholine. The mechanism by which LTB4 reduces airway responsiveness is unknown. A similar result has been reported in the guinea pig.4

MITSURU ADACHI
KOSTADIN S MAH
TERUMI TAKAHASHI
First Department of Internal Medicine, Shiga University School of Medicine, Shigarakamo, Otsu, Japan

Pulmonary eosinophilia

In the study reported in the two articles on pulmonary eosinophilia published in November,5 33 patients met the criteria for allergic bronchopulmonary aspergillosis and 32 were labelled as having "non-allergic broncho-pulmonary aspergillosis" (the latter being an unfortunate misnomer). The subsequent comparison of these two groups in respect of clinical and haematological features, response to prednisolone, and prognosis assumed a common pathophysiological basis within each group, which neither in fact possessed. The weakness of that assumption is reflected in the negative nomenclature of the "non" allergic bronchopulmonary aspergillosis group, and the authors themselves admit that this group “may be associated with several different syndromes whose underlying pathogeneses remain unclear.”

At first sight it might seem reasonable for the authors to assume that patients who met the criteria for allergic bronchopulmonary aspergillosis, unlike those in the other group, did indeed have disease with a common pathophysiological basis, but that too is open to question. Pathological differences within that group could have been recognised, or at least suspected, from the nature of the radiological