Alveolitis associated with sulphamethoxypyridazine

Dr J C Porter and others (September 1989; 44: 766–7) report on a patient who developed alveolitis associated with the administration of sulphamethoxypyridazine for bullous linear IgA disease. The patient had previously had a reaction to dapsone. The dose of sulphamethoxypyridazine 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 sulphamethoxypyridazine 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 dampened down the progressive alveolitis and prevented any of the other severe reactions that might have been associated with prolonged overdosage.

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AUTHOR'S REPLY Dr Lenox-Smith's observations are correct concerning the use of sulphamethoxypyridazine 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. It is also used, on a named patient basis, in linear IgA disease, which is an intensely pruritic 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 sulphapyridine, 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 sulphamethoxypyridazine. As we suggested, routine three monthly spirometry and chest radiography may be indicated in patients receiving sulphamethoxypyridazine.

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.

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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 responsiveness to methacholine and the cell content of bronchoalveolar lavage fluid one, three, and six hours after administration of aerosolised leukotriene (LTB4) to beagle dogs. In contrast to previous reports in the dog, 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 responsiveness to methacholine. The mechanism by which LTB4 reduces airway responsiveness is unknown. A similar result has been reported in the guinea pig.

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Pulmonary eosinophilia

In the study reported in the two articles on pulmonary eosinophilia published in November 1989, 33 patients met the criteria for allergic bronchopulmonary aspergillosis and 32 were labelled as having "non-allergic broncho-pulmonary aspergillosis" (the latter parameter being unfortunatly misnomer). The subsequent comparison of these two groups in respect of clinical and haematological features, response to prednisolone, and prognosis assumed a common pathological 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 pathogenesis 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 pathological 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
are two physiologists, an anaesthetist and a professor of medicine. In the preface they state that the book is most suitable for medical (and non-medical) graduates. This is a broad remit within medicine, I think that the book would be most useful for those studying anaesthetics or intensive care rather than respiratory medicine. It covers areas that are not usually found in physiology textbooks, in particular the pulmonary and bronchial circulations, lung fluid balance, the use of ventilators, and the physiology of high altitude and diving medicine. I found these very welcome, and the section on the clinical use of pulmonary function test was also good. I have some criticisms about the other sections. For example, in the discussion of ventilation the only spirometer mentioned was a water meter, a piece of equipment not generally found outside physiology laboratories. In the section on diffusion there was no mention of specific gas transfer. In the section on oxygen transport there was no mention of the relation of cardiac output to oxygen delivery. The chapter on ventilatory control had little on the sleep apnoea syndrome, Cheyne Stokes respiration, or exercise physiology. The drawings are clear and the biopsy specimens presented. Photographs are mostly lift from other texts but are not for worse for that. Each chapter is followed by a series of questions related to that chapter, which are meant to be problem solving within the subjects covered by the chapter but are actually calculations based on data presented in the chapter. Overall this is a well written and well presented book, which suffers slightly, I think, from a lack of direction. It is not clear whether it is meant for those studying physiology, those studying medicine, or those who graduated in medicine and are studying for specialties, such as anaesthetics or respiratory medicine, where a good knowledge of clinical respiratory physiology is essential. The book would be most useful for those interested in anaesthetics, because of the chapters on fluid balance and ventilators. As a respiratory physician I would have liked to see more on the relevance of the various aspects of clinical physiology to the common and less common diseases affecting the patients we see.—AP


BOOK NOTICES


This is the latest volume in the series currently published by Chapman and Hall Medical. These books are aimed primarily at the practising pathologist, and are intended to be used more as bench books than as definitive reference works. Professor Wagenvoort and Dr Mool are international authorities on the pathology of pulmonary vascular disease, and this book is in many ways an update of Pathology of Pulmonary Hypertension, which first appeared in 1977. Its emphasis, however, is orientated towards the open lung biopsy diagnosis of the whole spectrum of pulmonary vascular disease rather than hypertensive states alone. The first three chapters deal with the microanatomy of the normal pulmonary vascular bed, and with techniques for obtaining and processing biopsy specimens. Specific details of the changes in various disorders are covered in the ensuing chapters, which include sections on pleuropneumonic pulmonary hypertension, hypoxic pulmonary vascular disease, and the vasculopathies associated with chronic congestive states and conditions in which blood flow and pulse rate are abnormally high. Many of the diseases discussed are uncommon, and the book is not without its share of surprises and discussions which had not previously been considered in any text. As such, it is of considerable interest to those who deal with unusual or very difficult cases. It is a well-produced, well-illustrated book which will be of value to all who deal with these disorders, either as a reference text—or as an outstanding example of how simple techniques allied to clear thinking can elucidate the most complex problems.—CWE


This book describes current research into the development of drugs which, through modulating allergic responses, are potential treatments for asthma. It also intends to give the reader new ideas and methods available in the field of immunotherapy. It contains a number of manuscripts gathered from a meeting in November 1987 and includes some of the audience discussion. About half of the contributors are from the pharmaceutical industry. The book is divided into three sections, the first describing lipid mediators and their antagonists, the second modulation of the specific immune response, and the third agents that suppress inflammation. Of the three sections, the first is the most successful, with good reviews of the potential for development of drugs inhibiting lipid mediators. I particularly enjoyed the chapter from Dr Philips, a clearly published in physiology text that would act as a good model for discussing the inhibitors of any other mediators. The section on immunotherapy was the most disappointing and suffers from the time lapse between the meeting and publication of the book, and also from a rather uncritical assessment of immunotherapy by Dr Dreborg. Potentially the most exciting section on anti-inflammatory drugs confines itself to discussing nedocromil sodium, antihistamines, budesonide, azelastine, and the steroid derived peptide lipicortin. The chapters on nedocromil, lipocortin, and citizine provide a balanced review of inflammation available at the time of writing. In the chapter, however, the authors allow themselves some rather uncritical speculation about the clinical benefit of the drug. Overall the book would be of value for obtaining some background information on the subject for those starting out. Its lack of up to date information on rapidly changing subjects, however, makes it of little value to the established scientist, and its non-clinical bias makes it of no help to the clinician.—RWF

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