LETTERS TO THE EDITOR

Investigation of pulmonary disease in HIV infection

The titles of two of your recent reviews from the AIDS and the lung series (Nos 4 and 5, January 1990;45:57–65) refer to the investigations and diagnosis of pulmonary disease in patients infected with HIV; but both papers direct their attention to the problems of the late stage of infection only—namely, AIDS. This emphasis presumably reflects the clinical experience in London, where more advanced disease is prevalent; but your readers must not equate HIV infection with AIDS. There are many causes of pulmonary symptoms within the ever lengthening incubation period preceding AIDS, and the importance of these is not addressed adequately in these reviews.

At the regional infectious diseases unit in Edinburgh, where drug users comprise 78% of the 451 HIV infected individuals under review, there have been 180 admissions in the last four years for respiratory symptoms, and most of these have been in patients without AIDS. Forty nine per cent of these admissions were for microbiologically proved bacterial chest infections, 14% for suspected bacterial infection, and only 27% for *Pneumocystis carinii* pneumonia. Drug users were well recognised as having increased susceptibility to bacterial chest infections and tuberculosis even in the pre-HIV era, and against a background of HIV infection these have become predominant causes of respiratory pathology.[1,2] In New York they are a significant cause of HIV associated mortality in drug users before the development of AIDS.[3] Our data suggest that there is a similar phenomenon occurring in the UK in susceptible groups.

As part of our assessment of patients we find it useful to obtain serial $CD4^+$ lymphocyte counts, which can serve as a marker for susceptibility to infection. In individuals with $CD4^+$ counts above $0{\cdot}2 \times 10^9$/l we have obtained a negative predictive value of 95% for a diagnosis of pneumocystis pneumonia as a cause of respiratory symptoms (that is, there is a 95% chance that pneumocystis pneumonia is not the cause). This indicates the importance of other, more pathogenic organisms in the earlier stages of HIV infection. Appropriate analysis of sputum, which need not be induced if patients have a productive cough, can result in the diagnosis of many bacterial pathogens, including tuberculosis. These procedures are non-invasive and should not be forgotten. Chest radiographs may be normal in a greater proportion of patients than suggested in your review, with only half of our proved bacterial chest infections showing radiological changes.

As the HIV epidemic evolves, greater emphasis should be placed on diagnostic and interventive measures earlier in the natural history of HIV, and this will shift the bias away from the advanced disease seen in homosexuals and bisexuals to earlier disease in the other groups of patients, who are becoming more numerous. Hence it is important to recognise the spectrum of respiratory problems that will occur so as to investigate and treat these appropriately. Philip Hopewell's review on prevention (December 1989;44:1038–44) achieves a more balanced perspective, perhaps because in the United States the infections occurring in drug users are more widely recognised, and we endorse his recommendations for the prevention of bacterial chest infections.

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1 Selwyn PA, Feingold AR, Hartel D, *et al.* Increased risk of bacterial pneumonia in HIV-infected drug users, without acquired immunodeficiency syndrome. *AIDS* 1988; 2:267–72.
2 Selwyn PA, Hartel D, Lewis VA, *et al.* A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. *N Engl J Med* 1989;320:545–50.
3 Stoneburner RL, Des Jarlais DC, Benezra D, *et al.* A larger spectrum of severe HIV-1-related disease in intravenous drug users in New York City. *Science* 1988;242:916–9.

AUTHORS' REPLY (1) We thank Dr Flegg and others for their comments on our review article (January 1990;45:57–61) and for documenting their experience. We differ, however, on several issues. We do not find the CD4 count of particular value at the clinical level as it is a relatively insensitive marker for specific pulmonary infections and we have many patients who had pneumocystis pneumonia with relatively high CD4 counts and also patients who had only bacterial infection but relatively low CD4 counts. Undue diagnostic reliance on the CD4 count would be misplaced. In addition, though conventional sputum examination is routinely performed in most respiratory units in the United Kingdom, we have not found this useful in the context of HIV positive patients. Negative results for *Pneumocystis carinii* in conventional sputum samples have been followed by positive findings in induced sputum.

In the UK chest disease has not been a particular problem in HIV positive patients before the development of AIDS except for a small increased risk of pneumococcal infections. The exception, of course, is intravenous drug misusers, as stated by Dr Flegg and others, but here it is uncertain whether this is due to HIV or intravenous drug misuse, as the latter in its own right causes a high incidence of respiratory complications. Intravenous drug misuse is a greater problem in the United States, as reflected in Dr Hopewell's article on prophylaxis (December 1989;44:1038–44), which gains Dr Flegg's approval. Although things may change in the future, only 1876 of the 13 632 cases of HIV infection in the UK at the end of March 1990 had intravenous drug use as their exposure factor.[1] The pulmonary problems of this group, though important, remain in the minority.

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1 Public Health Laboratory Service. *Communicable Disease Reports* 1990;No 16.

AUTHORS' REPLY (2) We welcome Dr Flegg's comments and agree with the need for greater emphasis to be placed on diagnostic and interventional measures earlier in the natural history of HIV infection. Our aim was to review invasive investigative measures in patients who had advanced HIV infection. Clearly when patients are spontaneously expectorating purulent sputum a bacterial pathogen may be identified. In our experience, however, failure to attempt sputum induction with hypertonic saline in this situation may mean that diagnosis of *Pneumocystis carinii* with a bacterial coinfection is missed. We would therefore recommend routine induction of sputum in HIV positive patients presenting with fever or dyspnoea, regardless of the chest radiographic appearances. In the future use of *Pneumocystis carinii* specific DNA probes[1,2] may mean that pneumocystis pneumonia can be diagnosed from spontaneous expectorated sputum. Until these probes are routinely available excessive reliance should not be placed on spontaneously expectorated sputum samples.

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1 Wakefield AE, Hopkin JM, Burns J, *et al.* Cloning of DNA from *Pneumocystis carinii*. *J Infect Dis* 1988;158:859–62.
2 Wakefield AE, Pixley FJ, Banerji S, *et al.* Detection of *Pneumocystis carinii* with DNA amplification. *Lancet* 1990;ii:451–3.

BOOK NOTICES

Classic Papers in Asthma. Volume 1. Edited by RAL Brewis. (Pp 208; £39.50.) London: Marston Book Services, 1990. ISBN 1-870026-16-0.

Alistair Brewis has brought together some of the landmark papers in the history of asthma. These classics are reproduced as facsimiles of the original papers and provide a fascinating insight into the way asthma has been perceived over the years. Dr Brewis provides a brief introductory history of asthma from Hippocrates to modern times, highlighting

why he has chosen particular papers. I am in agreement with most of his selection, which begin with the writings of Aretaeus the Cappadocian from the 1st century AD (rediscovered only in the 16th century). Aretaeus clearly recognised asthma as a disease entity and described exercise induced asthma and coughing as a common symptom of asthma, and understood that death might occur in an asthma attack. Then follows a surprisingly clear account of asthma from the 17th century Belgian physician Jean Baptiste van Helmont, who did much to liberate medical thought from the dogma of Galen, which held sway from the early Christian era. This is followed by the classic and well known accounts of Thomas Willis and John Floyer (who wrote the first book devoted to asthma). Other chapters include the 18th century observations of Ramazzini, described as the father of occupational asthma, on baker's asthma, Miller's description of fatal asthma, and Cullen's clinical description. The highlight of the book is the marvellous description of asthma by Henry Hyde Salter, which deserves to be read by everyone interested in asthma. There could hardly be a clearer and more articulate description of the symptoms of asthma. The 20th century contributions include Metzer's classic paper, which likens asthma to anaphylaxis and shifts the emphasis away from neural mechanisms towards mediators. Other papers include Tiffeneau's remarkable studies on bronchial challenge and bronchodilators. The most recent three papers were all published in 1967 and include Voorhorst's description of mites as the major house dust allergen, the Ishizakas' identification of reagin as IgE antibodies, and the paper by Lands *et al* on beta adrenoceptor subtypes (though I believe that Ahlquist's classic paper, which distinguished alpha and beta adrenoceptors in 1941, would have been a more appropriate classic to include). This is a splendid collection of papers, which deserve careful reading because so much of what we now consider as modern thinking has already been clearly expressed, albeit without the details made possible by modern technology. Dr Brewis is to be congratulated on this excellent compendium, which I can thoroughly recommend. It is also excellent value for money.—PJB

Introduction to Respiratory Medicine. Meir H Kryger. (Pp 402; £19.95.) New York: Churchill Livingstone, 1990. ISBN 0-4435-08695-8.

This book, based on the undergraduate teaching course of the University of Manitoba, aims to provide a self contained introduction to respiratory medicine for students and junior doctors. The chapters are well written by recognised experts and move logically from physiological principles to pathophysiological adaptations and alterations due to disease. Of the 18 chapters, seven deal with basic concepts of pulmonary physiology and the remainder with clinical conditions, including a section on symptoms and clinical signs. The text is clear and straightforward and avoids prejudice, with good use of tables and diagrams, often taken from original publications. Where appropriate, questions are raised in areas where understanding of disease mechanisms exists and further research is needed. Common respiratory conditions are well covered with good chapters on airflow obstruction, pulmonary restriction, lung cancer, and respiratory infections. The three chapters on respiratory failure are excellent reviews of pathophysiology, but will be too detailed for the average undergraduate. There is a useful chapter on paediatric lung disease, which is rarely covered in texts aimed at physicians concerned with adult disease. The pathophysiological approach of this book ought to appeal to medical students and junior doctors. It should be particularly useful for those sitting the first part of the MRCP; part 2 candidates will need to know more about the treatment of pulmonary disease than is covered, though this is not a great disadvantage as treatment strategies in North America often differ from those in Europe. This is one of the best introductory textbooks of respiratory medicine that I have read, and the authors and editor are to be commended for the content and clarity of presentation. Teachers, trainees, and students should find it a useful addition to their libraries.—SE

Pulmonary Blood Vessels in Lung Disease. J Widimsky, J Herget. (Pp 150; £56.30.) Basel: Karger, 1990. ISBN 3-8055-5155-X.

Aficianados of the pulmonary circulation will know that once every five years clinicians, physiologists, pathologists, biochemists, and others gather in Prague to discuss the latest research in their field at one of the renowned pulmonary circulation symposia. For a few days little groups of lung enthusiasts throng the banks of the Vltava deep in earnest conversation or gather at the sessions to engage in the cut and thrust of the discussions following the papers. No book can replace actual participation in this quintennial pilgrimage to the Czech capital, but the organisers take care to see that highlights of the meeting are published as proceedings to be available to those unfortunate enough not to have been able to attend. This volume records 16 of the papers read at the fifth symposium in 1989. Atmosphere is lost by not including some of the discussions following the presentations. Eleven of the papers are grouped as a mini symposium on the pathophysiology of the pulmonary vascular wall and the remaining five deal with clinical problems of pulmonary hypertension. The quality of the papers is high, as one would anticipate from leading authorities—predominantly from Czechoslovakia and the United States with smaller contributions from Western Europe. Subjects range from deposition of arterial collagens in pulmonary hypertension and the putative role of growth factors derived from the circulation to impaired prostacyclin synthesis of endothelial cells derived from pulmonary arteries of calves with pulmonary hypertension. The volume is slim, comprising only 150 pages, so that at £56 it is not cheap. These symposia on the pulmonary circulation reflect great credit on Czechoslovak medicine and especially on Professors Widimsky and Herget, who have initiated meetings of such quality and maintained their high standard.—DH

NOTICE

Mediastinal tumours: Pandora's box

A two day symposium on mediastinal tumours will be held at the National Heart and Lung Institute in association with the Royal Brompton and National Heart Hospital, London, on 3 and 4 December 1990. It is designed for radiologists, respiratory physicians, surgeons, oncologists, and pathologists, but should be of interest to others concerned with thoracic medicine. Topics will include thymomas, lymphomas, germ cell and neural endocrine and rarer connective tissue tumours. There will be an emphasis on imaging and treatment. Further details are available from the Postgraduate Education Centre, National Heart and Lung Institute, London SW3 6LY (telephone 071-351 8172 (24 hours), fax 071-376 3442).