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- 2 Green AB, Brown CD. *Textbook of pulmonary disease*. 2nd ed. London: Silver Books, 1982:49.
- 3 Grey EF. Cystic fibrosis. In: Green AB, Brown CD, eds. *Textbook of pulmonary disease*. London: Silver Books, 1982:349-62.

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LETTERS TO THE EDITOR

Pneumocystis pneumonia in HIV antibody positive patients

The impression was given by Dr J Sauleda and colleagues (February 1994;49:112-5) that the significant decrease in SaO_2 observed in patients with *Pneumocystis carinii* pneumonia (PCP) with antibodies against human immunodeficiency virus (HIV), and the mild increase shown in the group with "other pneumonias" (non-PCP), was the result of different responses to an increase in cardiac output (\dot{Q}_T) during exercise. In patients with PCP this could have resulted in both a reduction in the time that the red blood cell spends in the pulmonary capillary (transit time), and an increased blood flow to lung units with zero ventilation-perfusion (\dot{V}_A/\dot{Q}) ratios (shunt) and also with low \dot{V}_A/\dot{Q} ratios, thereby inducing arterial oxygen desaturation. Increased intrapulmonary shunt is the most influential intrapulmonary factor governing gas exchange in patients with pneumonia.¹ In contrast, in the non-PCP group the contention would be that the increments of \dot{Q}_T could have preferentially increased the mixed venous PO_2 , hence favouring a better Pao_2 , other things being equal. However, this explanation seems to ignore the fact that any increase in \dot{Q}_T also augments the mixed venous oxygen saturation in patients with PCP, thus tending to increase SaO_2 or, alternatively, increase the amount of blood flow to areas of shunt and of low \dot{V}_A/\dot{Q} ratio in those with non-PCP, thereby tending to decrease SaO_2 .¹ It seems difficult to reconcile these two potential mechanisms with the different SaO_2 responses shown during exercise.

A more compelling explanation could be that patients with PCP have, in addition to shunt and \dot{V}_A/\dot{Q} mismatch, alveolar to end capillary diffusion limitation to oxygen, predominantly attributable to a decrease in the component of the membrane diffusing capacity (DM) of transfer factor (TLCO),² possibly resulting from attachment of trophozoites to type 1 pneumocytes found in the biopsy specimens of patients with PCP. Implicit in this concept is a lengthening of the diffusion pathway of oxygen between alveolar gas and pulmonary capillary blood, thus causing SaO_2 to fall during exercise. In contrast, the patients with non-PCP did not show findings consistent with the concept of oxygen diffusion limitation.²

We also have shown the presence of diffusion limitation to oxygen both at rest and during exercise in patients with cryptogenic fibrosing alveolitis using the multiple inert gas elimination technique.³ Interestingly, despite the fact that \dot{Q}_T was augmented during exercise, mixed venous PO_2 fell. We hypothesised that a decrease in mixed venous PO_2 , or a reduction in the transit time, or both, increases the vulnerability of pulmonary gas exchange to become limited by diffusion.³ During exercise \dot{V}_A/\dot{Q} mismatch did not worsen but the diffusion limitation component of arterial hypoxaemia increased sig-

nificantly as shown by changes in the alveolar to arterial oxygen gradient (A-a DO_2) from 6 mm Hg (at rest) to 21 mm Hg (during exercise). We also observed that the associated disturbances of the pulmonary vasculature play a pivotal part in modulating pulmonary gas exchange, especially during exercise.³ If most HIV antibody positive patients with PCP in the study of Dr Sauleda and coworkers were intravenous drug addicts (a not reported finding), in whom obliteration of pulmonary capillaries by previously injected material can be frequent, these vascular abnormalities would have further enhanced the fall of SaO_2 in patients with PCP during exercise.

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AUTHORS' REPLY We find the comments of Rodriguez-Roisin and colleagues very interesting. These comments mainly refer to mechanisms of pulmonary gas exchange in patients with pneumonia.

It is true that pulmonary shunt is the main and almost unique mechanism involved in gas exchange abnormalities in experimental pneumonia.^{1,2} However, in patients suffering from bacterial pneumonia there is also ventilation-perfusion (\dot{V}_A/\dot{Q}) mismatching, but only about half that of the shunt.³ In our study in patients with HIV we did not conclude that cardiac output (\dot{Q}_T) acted differently in patients with *Pneumocystis carinii* pneumonia (PCP) compared with those with other pneumonias (non-PCP). It is probable that \dot{Q}_T had similar qualitative effects in both groups. The expected rise in \dot{Q}_T would have resulted in a tendency to increase $P\dot{V}O_2$ (and therefore Pao_2). However, it could be expected that the rise in \dot{Q}_T would result in both an increase in blood flow to shunt and low \dot{V}_A/\dot{Q} areas, tending to decrease Pao_2 , and a reduction of transit time in lung capillaries. The former mechanism should be present in both groups, but their relative weight and final effect on Pao_2 may have been different. However, as Rodriguez-Roisin and colleagues point out, the latter mechanism for hypoxaemia would only affect patients with interstitial damage (mainly PCP) where diffusion limitation for oxygen is present.^{4,5} Although we agree with this hypothesis to explain differences between the groups in our study, oxygen diffusion limitation has not been directly shown in PCP and its existence is based on studies showing a reduction in carbon monoxide transfer factor (TLCO).⁴ This is usually used as a synonym for oxygen diffusion limitation, but it is not a direct measure. Studies using the multiple inert gas elimination technique (MIGET)

may confirm the presence of oxygen diffusion limitation. If the measured Pao_2 in PCP patients was lower than Pao_2 predicted from \dot{V}_A/\dot{Q} distributions and $P\dot{V}O_2$, other factors such as oxygen diffusion limitation would be present.⁶ Nevertheless, MIGET has shown that, whilst TLCO may be reduced in bacterial pneumonia, oxygen diffusion limitation appears to be preserved.¹

Finally, we agree on the role of pulmonary vessels in modulating gas exchange during exercise in patients with interstitial damage.^{5,6} The percentage of intravenous drug abusers was very similar in the two groups. So, if previous obliteration of pulmonary capillaries had occurred, this factor was probably equivalent in both groups of patients. Only additional interstitial and vascular damage due to PCP⁷ could account for these differences.

Unfortunately, as this was not a physiological study designed to elucidate the mechanisms of pulmonary gas exchange in the two groups of patients only speculation is possible. On the contrary, ours was a clinical trial to demonstrate the usefulness of a simplified exercise test for the initial diagnosis of PCP.

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NOTICE

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A course on the pharmacology of asthma organised by Professor Peter Barnes will be held from 28 November to 1 December 1994 at the National Heart and Lung Institute. Enquiries should be addressed to: Postgraduate Education Centre, National Heart and Lung Institute, Dovehouse Street, London SW3 6LY, UK. Tel: 071 351-8172. Fax: 071 376-3442.

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