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 SaO2 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 anaerobic output (Q/T) during exercise. In patients with PCP this patient might result 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 (VA/Q) ratio (shunt) due to low VA/Q ratio, thereby inducing arterial oxygen desaturation. Increased intrapulmonary shunt is the most influential intrapulmonary factor governing gas exchange in patients with pneumonia. In contrast, in the non-PCP group the contention would be that the increments of Qr could have preferentially increased the mixed venous Po2, hence favouring a better PaO2, other things being equal. However, this explanation was not based on the fact that any increase in Qr also augments the mixed venous oxygen saturation in patients with PCP, thereby tending to increase SaO2 and, alternatively, increase the amount of blood flow to areas of the lung and low VA/Q ratio in those with non-PCP, thereby tending to decrease SaO2. It seems difficult to reconcile these two potential mechanisms with the different SaO2 responses observed during exercise. The shunt explaining could be that patients with PCP have, in addition to shunt and VA/Q mismatch, alveolar to end capillary diffusion limitation to oxygen, predominantly attributed to a decrease in the component of the membrane diffusing capacity (Dm) of transfer factor (TL,co), possibly resulting from attachment of trophozoites to type I 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 SaO2 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. Interestingly, despite the fact that Qr was augmented during exercise, mixed venous Po2 fell. We hypothesised that a decrease in mixed venous Po2, or a reduction in the transit time, or both, increases the vulnerability of pulmonary gas exchange to become limited by diffusion. During exercise VA/Q mismatch did not worsen but the diffusion limitation component of arterial hypoxaemia increased significantly as shown by changes in the alveolar to arterial oxygen gradient (A-AD) from 6 mm Hg (at rest) to 21 mm Hg (during exercise). We also noted that oxygen associated disturbances of the pulmonary vasculature play a pivotal part in modulating pulmonary gas exchange, especially during exercise.1 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 SaO2 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 However, in patients suffering from bacterial pneumonia there is also ventilation-perfusion (VA/Q) mismatching, but only about half that of the shunt.1 In our study in patients with HIV we did not conclude that cardiac output (Qr) acted differently in patients with Pneumocystis carinii pneumonia (PCP) compared with those with other pneumonias (non-PCP). It is probable that Qr had similar qualitative effects in both groups. The expected rise in Qr would have resulted in a tendency to increase Po2 (and therefore PaO2). However, it could be expected that the rise in Qr would result in both an increase in blood flow to shunt and low VA/Q areas, tending to decrease PaO2, and a reduction of transit time in lung capillaries. The former mechanisms would be present in both groups, but their relative weight and final effect on PaO2 may be 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. 1 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). 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 PaO2 in PCP patients was lower than PaO2, predicted from PAQ distributions and Po2, other factors such as oxygen diffusion limitation would be present. Nevertheless, MIGET has shown that, whilst TlCO may be reduced in bacterial pneumonia, oxygen diffusion limitation appears to be present.2

Finally, we agree on the role of pulmonary vessels in modulating gas exchange during exercise in patients with interstitial damage. 2 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 PCP could account for these differences. Unfortunately, as this was not a physiopathological study designed to elucidate the mechanisms of pulmonary gas exchange in the two groups of patients, only speculation is possible. On the contrary, our was a clinical trial to demonstrate the usefulness of a simplified exercise test for the initial diagnosis of PCP.

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NOTICE

Pharmacology of asthma

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: Post-graduate Education in the two, National Heart and Lung Institute, Dovehouse Street, London SW3 6LY, UK. Tel: 011 351-8172. Fax: 071 376-3442.