LETTERS TO THE EDITOR

Use of nitric oxide inhalation in COPD

Ashutosh *et al*[1] report that inhaled nitric oxide (iNO) lowers pulmonary vascular resistance (PVR) in stable patients with chronic obstructive pulmonary disease (COPD) receiving long term oxygen therapy (24 hours' treatment, randomised, double blind, crossover study). Oxygen was delivered via face mask at a rate of 2 l/min into which NO was diluted down from 200 ppm (cylinder) to achieve a final concentration of 25 ppm inspired. The authors conclude that vasodilation and relaxation of the pulmonary arterial bed is responsible for the fall in PVR.

Pulmonary arterial pressures were measured by cardiac catheterisation. Expired air was collected for five minutes and carbon dioxide output ($\dot{V}CO_2$) and deadspace/tidal volume ratio (Vd/Vt) were measured. Cardiac output (CO) was determined by the Fick equation using $\dot{V}CO_2$ and calculations of arterial and mixed venous carbon dioxide contents from directly measured mixed venous and arterial oxygen and carbon dioxide (PO_2 and PCO_2) based on McHardy's equations. Although these measurements were validated against the thermodilution technique in 24 samples obtained from four patients, the correlation was very low (r = 0.6; $p<0.01$) and individual values agreed within one litre of each other. PVR values obtained by two methods were better with a correlation of r = 0.96, but this is dominated by the pulmonary artery pressure (PAP).

Analysis of table 2 shows that, of all the haemodynamic parameters recorded, only CO was shown to increase after 24 hours of NO inhalation (by up to 80% in some patients). Pulmonary artery pressure (PAP) and pulmonary wedge pressure (P wedge) were unchanged. The fall in PVR can therefore be mostly attributed to the increase in CO and not to vasodilation of the pulmonary arterial bed. They also suggest that iNO may have improved CO by reducing the right ventricular afterload in these patients with severe COPD (forced expiratory volume in one second (FEV_1) = 0.89 (0.4) 1 (25.8 (9.4)% predicted); forced vital capacity (FVC) = 2.1(0.75) 1).

We and others have reported no effect on CO of short term iNO.[2 3] Dosing iNO in patients with COPD is a challenging task. Matching inhaled gas flow rate to the frequency of breathing is limited with continuous NO delivery systems, but this problem is minimised by pulsing a small volume of NO at the beginning of the breath.[4] Trials of long term exposure to iNO in ambulatory patients have started, and preliminary data suggest that chronic exposure to pulsed NO does not affect CO in hypoxaemic patients. The positive inotropic effect reported by Ashutosh *et al* (reduction in right ventricular afterload, thus increase in CO) is interesting and worthy of further investigation but, given the caveats of their methods to measure CO, must remain preliminary at the best. These results must be confirmed by others before we give too much credence to the authors' observations.

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AUTHORS' REPLY We thank Dr Higenbottam and colleagues for their interest in our work and appreciate their thoughtful comments. We would like to address some of their concerns as follows.

The non-invasive CO_2 Fick method is considered to be a reliable technique both on theoretical and experimental grounds for measurement of cardiac output (CO).[1–3] The correlation between the CO measured by the two techniques as noted by us was sufficiently significant to allow the use of the CO_2 Fick method with reasonable confidence.[4]

Our study was not designed to investigate the possible mechanisms for the observed changes in CO. We can only speculate that our patients had underlying cardiac dysfunction from an increased afterload due to pulmonary hypertension that responded to the administration of nitric oxide (NO), leading to the rise in CO. A fall in the pulmonary artery pressure (PAP) was prevented by a concomitant rise in CO. Although pulmonary vascular resistance (PVR) is a derived measurement, its fall in the face of a rising CO can only indicate a relaxation of the pulmonary arterial vasculature to accommodate the increased flow without a rise in pressure. We wish to point out that a similar rise in CO with little change in PAP has also been noted by other workers.[5 6] In a recent study Robbins and colleague noted an increase in CO with a fall in PVR without a fall in PAP in two of three patients with the use of NO and in one of three patients with epoprostenol.[7]

We fully agree with their final comment that our study results need to be evaluated and confirmed by larger and more rigorous studies.

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NOTICE

The Sheffield Seminar

"The Sheffield Seminar" will take place in Sheffield, UK, yearly starting next May. The meeting will focus on all aspects of cardiothoracic surgery, starting next year with general thoracic surgery topics. It will take place on 31 May and 1 June 2001 at the Postgraduate Medical Centre, Northern General Hospital, Herries Road, Sheffield S5 7AU, UK. For further information contact Mr G Rocco, Consultant Thoracic Surgeon. Telephone +44 114 271 4950. Fax +44 114 261 0350. Email: grocco@tany.fsnet.co.uk

CORRECTION

CFC transition

In the editorial entitled "CFC transition: the Emperor's new clothes—each class of drug deserves a delivery system that meets its own requirements" published on pages 811–4 of the October 2000 issue of *Thorax* an error appeared in the first sentence of the second paragraph on page 811. This should have read "It seems probable that, during the later part of **2001**, the FDA will grant a licence to deliver insulin as an aerosol."