Exhaled carbon monoxide in lung disease

To the Editor:

We read with interest the paper by ZETTERQUIST *et al.* [1] in which the levels of exhaled nitric oxide (NO) and carbon monoxide (CO) were measured in a group of asthmatic and cystic fibrosis (CF) patients using two different methods. A new fast-response nondisperse infrared (NDIR) CO analyser was used alongside the old electrochemical method and the results obtained with the two methods were compared.

Surprisingly, contrary to what has previously been shown by our own and other groups [2–6], as shown by both methods, the levels of exhaled CO were found to be similar in a group of asthmatic patients and patients with CF compared with normal subjects. The authors conclude that exhaled CO is not a marker of airway inflammation and may derive predominantly from the alveoli, as its exhaled concentrations are not flow-dependent and increase after a breath-hold.

Even though we previously acknowledged that the measurement of exhaled CO may be of more interest in patients with severe asthma compared to those with the mild form of the disease [7, 8], we feel that the measurement of exhaled CO maybe useful in CF patients [5, 6, 8]. We suggest that the discrepancies found may be mainly attributed to different techniques and, ultimately, different methods.

First, ZETTERQUIST *et al.* [1] used the basic Bedfont analyser for the measurement of CO. However, in our previously published studies by us a modified version of the Bedfont analyser was used. In this altered version, the exhalation flow rate was standardised and controlled, and a resistance was added to the exhalation flow to produce enough mouth pressure to close the soft palate allowing the separation of nasal air from exhaled air. Besides controlling these parameters, contrary to what is stated in this paper, we did connect the analyser to a computer and the exhaled CO traces could be studied point by point and in relation to exhaled volumes.

Secondly, in our studies, the exhalation manoeuvre was different from that used in the paper by ZETTERQUIST *et al* [1]. We used a single-breath technique without breath-hold. We agree with the authors that breath-hold increases exhaled CO levels, but in addition, this may also eliminate the bronchial contribution to the total production of CO, which would be biased towards the alveolar component because of alveolar CO diffusion in the bronchial space during the time of breath-hold. This may explain the similar levels of exhaled CO in the studied groups compared to normal subjects.

Thirdly, in this paper, the contamination of exhaled CO with ambient CO was taken into account only in the NDIR method, in which the patients were asked to breathe CO (and NO)-free air. We have previously shown that exhaled CO may be affected by ambient CO and that this influence may be reduced by subtracting ambient CO from exhaled CO [6]. Unfortunately, in this study, this was not considered when analysing the levels of CO obtained with the Bedfont analyser.

In conclusion, the authors of the paper compared the results obtained with two different methods and exhalation techniques. The effect of ambient contamination and breath-hold were not taken into account. Both these variables and the use of different exhalation techniques may explain the discrepancy in the data obtained by ZETTERQUIST *et al.* [1] and the other investigators in this area. Using fast analysers like the nondisperse infrared analyser may not be beneficial by itself if the exhalation technique is not standardised. Furthermore, comparisons of the data obtained by other numerous groups may only be possible if the same technique and methods are used.

P. Paredi, S.A. Kharitonov, P.J. Barnes
Dept of Thoracic Medicine, National Heart and Lung Institute, Imperial College School of Science, Technology and Medicine, London, UK.

References

1. Zetterquist W, Marteus H, Johannesson M, *et al.* Exhaled carbon monoxide is not elevated in patients with asthma or cystic fibrosis. *Eur Respir J* 2002; 20: 92–99.
2. Zayasu K, Sekizawa K, Okinaga S, Yamaya M, Ohrui T, Sasaki H. Increased carbon monoxide in exhaled air of asthmatic patients. *Am J Respir Crit Care Med* 1997; 156: 1140–1143.
3. Horvath I, Donnelly LE, Kiss A, Paredi P, Kharitonov SA, Barnes PJ. Raised levels of exhaled carbon monoxide are associated with an increased expression of heme oxygenase-1 in airway macrophages in asthma: a new marker of oxidative stress. *Thorax* 1998; 53: 668–672.
4. Yamara M, Sekizawa K, Ishizuka S, Monma M, Sasaki H. Exhaled carbon monoxide levels during treatment of acute asthma. *Eur Respir J* 1999; 13: 757–760.
5. Paredi P, Shah PL, Montuschi P, *et al.* Increased carbon monoxide in exhaled air of patients with cystic fibrosis. *Thorax* 1999; 54: 917–920.
6. Antuni JD, Kharitonov SA, Hughes D, Hodson ME, Barnes PJ. Increase in exhaled carbon monoxide during exacerbations of cystic fibrosis. *Thorax* 2000; 55: 138–142.
7. Stirling RG, Lim S, Kharitonov SA, Chung KF, Barnes PJ. Exhaled breath carbon monoxide (CO) is minimally elevated in severe but not mild atopic asthma. *Am J Respir Crit Care Med* 2000; 161: A922.
8. Kharitonov SA, Barnes PJ. Exhaled markers of pulmonary disease. *Am J Respir Crit Care Med* 2001; 163: 1693–1722.

From the authors:

We appreciate the interest P. Paredi and colleagues have shown in our article. In their letter, they describe