Correspondence

Transfer factor for carbon monoxide in patients with diabetes with and without microangiopathy

SIR,—We note with interest the observations made by Dr DC Weir and colleagues (September 1988;43:725-6), but feel that the results and conclusions merit further discussion.

The main conclusion from the study appears to be that a reduction in transfer coefficient in patients with diabetes mellitus is related to pulmonary microangiopathy and that this is independent of duration of diabetes. It is likely that this interpretation reflects study size and the heterogeneous nature of the patient groups studied. We know that the presence of diabetic complications, including microangiopathy, is at least in part related to duration of diabetes.¹ Sandler *et al.*² in a larger study of respiratory function in patients with diabetes mellitus, showed a reduction in transfer factor which related to duration of diabetes but not to the presence of diabetic complications. To say that Weir's group had a greater degree of microangiopathy does not adequately explain the difference. In Sandler's study subgroup analysis of patients with diabetic complications, including late retinopathy, did not show any correlation with abnormalities of lung function. In addition, we have shown a reduction in FEV₁ and forced vital capacity in a group of male insulin dependent diabetic patients³ that correlated with duration of diabetes.⁴ These patients had a longer duration of diabetes and were younger, with less evidence of microangiopathy. They did not show a reduction in transfer coefficient, although this was lowest, as one would expect, in diabetic smokers.⁵ It is therefore possible that the absence of a correlation between the reduction in transfer factor and duration of diabetes reflects the small study numbers and the mixed patient population group studied.

A small point is that it seems unnecessary to express the results as % predicted as there is a control group and it makes further analysis of the results difficult. It would have been interesting to see the distribution of transfer coefficient data as an unpaired *t* test does not separate the two groups.

The alterations in lung function seen in diabetic patients may reflect not only the presence or absence of microangiopathy but also alterations to collagen. Collagen is the most abundant structural protein within the lung, being found not only in the bronchi and major blood vessels but also within the interstitium.⁶ Diabetes leads to thickening of alveolar epithelial and capillary basal lamina,⁶ but may also lead to thickening of the alveoli.⁷ These changes may result from non-enzymatic glycosylation of the collagen with a subsequent reduced turnover and alteration in mechanical properties. These changes, as well as the duration of disease and the presence of microangiopathy, may be important in the abnormalities of lung function which have been described in diabetes mellitus.

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AUTHORS' REPLY The development of diabetic complications is believed to be related at least in part to the duration of diabetes. The lack of a significant correlation between Kco and duration of the disease is likely to be due to the small numbers studied, as the group with complications had a mean duration of the disease which was nearly twice that of the group without complications.

We believe the differences between our results and those of Sandler *et al.*² above reflect both the greater severity of the complications of diabetes in our group and the method of analysis. We used a more powerful statistical test to compare the values of Kco between the two groups of patients directly. Sandler *et al.* identified those patients with and without various complications of diabetes who had abnormal transfer coefficients (below the 90% confidence limits for the regression equation used) and compared the numbers with abnormal values in the two diabetic groups by a χ^2 test. This may mask actual differences which exist. The reduction in Kco in our patients was small. An analysis similar to that of Sandler gives results which are statistically not significant. The number of patients with an absolute Kco that are ≥ 1.65 standardised residuals from the predicted value was: "uncomplicated" group 1/9, "complicated" group 4/9 ($p = 0.13$, Fisher's exact test).

We would agree that the changes seen in our study and by other investigators probably reflect various alterations to the lung tissue architecture, but pulmonary microangiopathy is an attractive explanation for the differences we observed.

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