nitrogen dioxide is defined as: "The 98th percentile of hourly means should not exceed 104·6 ppb." The underlying reason for specifying an upper percentile rather than an absolute limit is that extreme values are liable to be erratic, occurring in a highly local or transient manner or even as a result of instrument malfunction. In one year there are 8760 hours; the 98th percentile of hourly means is defined as the 176th highest hourly mean measured. Only if this exceeds 104·6 ppb is the relevant ED directive contravened. The limit value, designed to safeguard health with regard to exposure to nitrogen dioxide, was set with knowledge of the likely log-normal distribution of hourly mean concentrations. Though hourly means could exceed 104·6 ppb on 175 occasions per year, with occasional maxima up to three or four times that value, damage to health would not be expected.

In discussing WHO air quality guidelines for sulphur dioxide and smoke Dr Britton fails to point out that safety factors of 2 for effects on morbidity and mortality and of 1·5 for decrements of lung function were included when the guidelines for combined exposure to sulphur dioxide and particulate matter were defined.[2]

It should also be noted that the data on which the joint guideline was defined did not permit separation of sulphur dioxide and black smoke in terms of effects; it would thus be more appropriate to quote the number of days when the joint guidelines were exceeded than each one separately. Furthermore, WHO guidelines for black smoke[2] have not been defined on an hourly basis and the 24 hour guideline is currently quoted[2] as 125 $\mu g/m^3$ rather than 100 $\mu g/m^3$. The figure of 100 $\mu g/m^3$ occurs in the World Health Organisation report of 1979.[3] In that report a range of 100–150 $\mu g/m^3$ was defined.

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The above are the opinions of the authors and should not be taken as representing those of the Department of Health.

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AUTHOR'S REPLY I thank Drs Maynard and Waller for their comments on my article, and their clarification of the various guidelines and limits on atmospheric pollution levels. I suspect that I am not alone in finding them a little confusing. The point I wanted to make in the article is that in the study by Sunyer *et al* (their ref 1) everyday variations in usual levels of atmospheric pollution had small but measurable effects on respiratory morbidity. The vast majority of this variation was well within all of the guidelines and limits. We need guidelines for monitoring and enforcing pollution controls, but if there was any doubt before it is surely now evident that pollution that does not contravene existing guidelines still causes respiratory morbidity. The question is whether this degree of morbidity is an acceptable or necessary price to pay for economic development and, if it is, how much society should be prepared to accept.

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Pulmonary function in chronic renal failure: effects of dialysis and transplantation

In their article (June 1991;**46**:424–8) Drs A Bush and R Gabriel referred to decreased carbon monoxide transfer (TLCO) in four groups of patients with chronic renal failure. Apparently, their TLCO values were corrected for haemoglobin, which was low in most of their patients. Thus the decreased TLCO should be attributed to causes other than a low haemoglobin pool. The authors speculated that it was due to interstitial lung fibrosis, caused by chronic subclinical oedema.

These authors' results differ from those of others. TLCO is usually reduced in uraemic patients because of coexisting anaemia; adjusting to a normal haemoglobin concentration therefore produces normal TLCO values.[1 2] In the population they studied, however, the underlying cause could not be determined from their data. Interstitial fibrosis with resulting deterioration of the membrane TLCO component (Dm) is the only possible factor. The authors did not perform chest radiography, which could have helped to resolve the issue. Moreover, there are even more sensitive tools for such evaluation—specifically high resolution computed tomography and a separate determination of Dm and the vascular component of the TLCO: pulmonary capillary blood volume (Vc) and the reaction rate of carbon monoxide with haemoglobin (theta, θ). According to the theory of Roughton and Forster—expressed as $1/TLCO = 1/Dm + 1/\theta Vc$—$\theta$ increases with increased haemoglobin. Without measuring the components of TLCO therefore, even after adjustment for haemoglobin, one cannot determine whether Dm or Vc predominantly affects the overall TLCO. There are also reports that haemodialysis (their group 3) per se affects TLCO,[1] which was not considered by the authors. In the sample that we studied[1] the effect of haemodialysis was a reduction in TLCO of about 10%, due entirely to a decrease in Vc of about 20%, which we attributed to a decrease in blood volume with consequent reduction in Vc.

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1 Dujić Ž, Tocilj J, Ljutić D, Eterović D. Effects of hemodialysis and anemia on pulmonary diffusing capacity, membrane diffusing capacity and capillary blood volume in uremic patients. *Respiration* 1991;**58**:277–81.
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AUTHOR'S REPLY We thank Professor Dujic and colleagues for their interest in our paper and for raising some interesting points. Our findings of a reduced TLCO even after correction for anaemia is in accord with the findings of other workers[1 2] not cited in their own paper.[3] We agree that the pathological cause of the physiological abnormalities could not be determined; we did not think that additional radiography was justified when we designed the study, but agree that in the light of our findings quantitative computed tomography[4] would be of great interest. The issue of the meaning (if any) of attempting to measure Dm and Vc separately has been debated at length elsewhere.[5 6] The theoretical problems include non-uniform DL/VA in the real lung, the dangers of extrapolating back to the intercept beyond the data points, and the profound effects that oxygen itself has on the pulmonary circulation, altering the variable one is trying to measure. There is also experimental evidence that Dm is insignificant.[7] Thus we believe that TLCO does indeed measure the amount of blood (or, strictly, haemoglobin) within the pulmonary capillary bed. We did consider in detail the acute effects of haemodialysis on the lungs[8 9]; the acute fall in TLCO takes place early in the dialysis, and it has reverted almost completely to predialysis values by the end of a six hour dialysis. We studied our patients within 24 hours of dialysis, to try to minimise the effects of accumulation of lung and body water between dialyses. Our final speculations are confirmed to some extent by pathological studies[10]; we agree that a new computed tomography, biopsy, or necropsy study is needed to determine the underlying pathology.

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Haematological effects of inhalation of *N*-formyl-methionyl-leucyl-phenylalanine in man

We read with interest the description by Dr M J Peters and colleagues (April 1992;**47**: 284–7) of temporary peripheral blood leucopenia, in particular neutropenia, immediately following the inhalation of the tripeptide *N*-formyl-methionyl-leucyl-phenylalanine (FMLP) in normal subjects, accompanied by activation of peripheral blood neutrophils as measured by chemiluminescence.

We agree that the likely mechanism is