The authors then state that "it has also been observed that HIV-1 detection in BAL fluid samples is significantly associated with progression to death but not to reduction of pulmonary function tests." Again our results were from patients with AIDS and the reason for the lack of correlation between these two parameters could be due to a masking by the concomitant opportunistic respiratory infection. It is well established that PCP has a profound effect on the carbon monoxide transfer factor (TLCO) in HIV-1 seropositive individuals.[11] We reiterate that all our patients underwent bronchoscopy because they had a respiratory episode. It should be pointed out that in our study the mean TLCO value in patients was 46·3 regardless of whether HIV could or could not be cultured from the BAL cells of these individuals.[12] Conversely, direct damage to lung physiology by HIV-1 may occur during the asymptomatic phase, in which case any viral-associated reductions would have occurred in these patients prior to our investigations. Perhaps patients with AIDS should have undergone bronchoscopic examination before and in between respiratory episodes to determine what direct effect HIV-1 may be having on pulmonary function, but this was ethically unacceptable at the time of our studies.

Drs Agostini and Semenzato continue by stating that "detailed analyses are needed to characterise HIV-1 strains completing reverse transcription in the lung in vivo. These data are central to verifying whether the emergence of retroviral variants represents an important factor affecting the pulmonary manifestations of HIV-1 infection." We have already shown that the biological phenotypes isolated from BAL cells of patients with AIDS can be distinguished in all instances so far tested from the corresponding phenotype isolated from a matched peripheral blood sample.[13] Furthermore, the emergence of more virulent syncytium-inducing HIV-1 variants does occur in BAL cells of some individuals in the terminal stages of AIDS.[14] Genotypic characterisation of these strains is already underway.

They conclude their editorial by stating that "longitudinal studies of BAL fluid findings in a large number of HIV-1 infected patients followed from an asymptomatic stage until the diagnosis of AIDS are necessary to define clearly the natural course of the respiratory illness in HIV-1 infection." As we have recently shown, dramatic longitudinal changes do occur,[14] and now that ethical approval has been obtained, studies with HIV infected, asymptomatic individuals are already underway at St Mary's Hospital in London. Finally, Drs Agostini and Semenzato point out the necessity to establish a cooperative study to investigate the prognostic impact of BAL analysis in a large cohort of patients being drawn from centres in nine European countries. We agree such studies are vital to the understanding of the role of HIV in lung infection.

J R CLARKE
J D WILLIAMSON
Research Virology, Department of Medical Microbiology, St Mary's Hospital Medical School, London W2 1PG
D M MITCHELL
Department of Respiratory Medicine, St Mary's Hospital, London W2 1NY

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AUTHORS' REPLY We are perplexed by the comments of Dr Clarke and associates regarding our recently published editorial. They state that our review contains "a number of omissions and inaccuracies", complaining that we ignored important studies on the pathogenetic mechanisms of HIV disease in the lung. First of all, Dr Clarke and coauthors may not have realised that our paper was not a review but an editorial and, as such, was not intended to include a detailed analysis and quotation of the complete literature published in the field. In this regard, the ultimate goal of our editorial was to encourage cooperative studies to investigate the prognostic impact of BAL analysis in a large cohort of patients.

Apart from this, most of the concepts raised by Dr Clarke and colleagues had already been taken into account in our recent state of the art review published in the *American Review of Respiratory Diseases*.[1] As an example, they state that we omitted an important pathway through which HIV-1 may enter the lung – namely, cell-free virus that is carried to the lung by the microcirculation – not to mention the possibility that other pulmonary cells, including lung fibroblasts, may be an important reservoir of HIV-1. Both of these concepts and other hypothetical mechanisms of HIV infection of the lung can be found in that review or in another recently published paper.[2]

Dr Clarke and associates continue by stating that we suggest that "their results are inconsistent, even incompatible". This is not so, and these concerns are not easily comprehensible. We obviously respect their work and the proof is that we quoted (appropriately!) four papers from their group (in a total of 29 references) in our editorial. As the reader can readily check, most of the phrases that we report in our editorial were taken from Dr Clarke's manuscripts.[3-8] Naturally, we did not cite his abstract or the letter which appeared in the *Lancet* on 3 September 1994 which was published after our editorial went to press. For the same reason, we did not quote interesting data recently produced by our group on the HIV-1 infection of lung CD8+ cells recovered from the BAL fluid of patients with AIDS.[9]

To conclude, we have taken the letter by Dr Clarke and coworkers to be a provocative challenge to face new issues in the field. In the past we have read with great pleasure and interest their data in several international referenced journals. In the future we look forward to reading other results from their team with undiminished enthusiasm.

GIANPIETRO SEMENZATO
CARLO AGOSTINI
Department of Clinical Medicine Padua University School of Medicine, 1st Medical Clinic and Clinical Immunology Branch, Padua, Italy

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