LETTERS TO THE EDITOR

Bronchoalveolar lavage as a research tool

I enjoyed the timely review of bronchoalveolar lavage by Drs E H Walters and P V Group (Thorax 1991; 46:613-8) but take exception to several of their conclusions. They referred to their earlier work in which "H2O was incorporated into the blood or airspace fluid and its movement between these compartments was measured. From this they calculated that 39% of the aspirated fluid flowed into the airspaces from the blood. I would argue that exchange of "H2O between these compartments is driven by concentration differences and would occur regardless of whether or not there was any net movement of fluid.

Net movement of fluid from the blood into the airspaces would dilute solutes present in the airspaces and the authors cite decreases in methylene blue concentrations seen by themselves and others to support their hypothesis. They did not, however, rule out diffusion of this small solute out of the airspaces or its reduction to colourless derivatives. Decreases in airway concentrations of 99mTc colloid, which they also observed, may be related to sedimentation or adherence of this indicator to epithelial membranes. When soluble macromolecules (labelled albumin or labelled dextran) have been instilled into the airspaces by several different investigators, no decreases in concentrations were detectable (see, for example, ref 2).

Bulk movement of water across the pulmonary epithelium is constrained by the high reflection coefficients of the epithelium to both small and large solute molecules, and movement of electrolytes and water across the epithelium is too slow to suggest significant movement of fluid between these compartments during lavage. It can be calculated from these reflection coefficients that ultrafiltration of solute free fluid into the airspaces would require extreme pressures, which are not generated during lavage (>5000 mm Hg).

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Ventral fractures in steroid dependent asthma and involutional osteoporosis: a comparative study

We read with some interest the study by Dr M C Penno and colleagues (November 1991; 46:803-6). In this study the authors suggest that, in the presence of corticosteroid associated osteoporosis, bone densitometry is less useful for detecting patients at risk of dorsal C spine peripheral vertebral fracture than in involutional (postmenopausal) osteoporosis. This is contrary to our own experience with dual energy x ray

AUTHOR'S REPLY
I am grateful for the comments on our editorial on bronchoalveolar lavage from Professor Effros. Professor Effros perhaps assumes that the clinical technique of bronchoalveolar lavage is essentially the same as his elegant in vitro model of the fluid filled, perfused animal lung preparation. I don't believe that this is really the case, and calculations and assumptions based on the latter are unlikely to apply to the former. Our data would suggest that bronchoalveolar lavage distorts the epithelial barrier in the bronchopulmonary segment studied, either by more extensive local inflation at the time of injection of fluid or at the time of aspiration, or both, resulting in the opening up of "unphysiological" intercellular pores with much lower reflection coefficients than that found by others. The intrinsic stimuli on relatively undisturbed whole lungs. In our studies of water and solute "fluxes" at bronchoalveolar lavage to which he refers (his ref 1) the large influxes of water into the lavage fluid at aspiration were remarkably similar whether calculated indirectly by dilution of methylene blue or large molecular colloid "markers" or directly measured from bidirectional movements of tritiated water. It is difficult to extol the sorts of potential artefacts which Professor Effros quite reasonably mentions could give such consistency. Our studies with tritiated water were precipitated only by the finding that larger molecular weight markers were diluted to a degree that could not reasonably be explained merely by incorporation of the putative lung epithelial lining fluid.

In addition to the recent work in our laboratory indicates that relatively large influxes of urea as well as water occur into bronchoalveolar lavage fluid at aspiration, even after minimal dwell time. This again emphasises the assumptions that Professor Effros has built up from his studies on relatively stable pulmonary epithelial membranes, and even in his more recent whole lung lavage model in rats (his ref 4), don't seem to apply to the acute and potentially locally disruptive process of bronchoalveolar lavage, which seems to induce some process of filtration across the bronchopulmonary epithelium, as well as movements due to differences in transpulmonary pressure.

Finally, however, I need to point out that our emphasis has not really been on trying to define the mechanisms by which water and solutes move between blood stream and lavage fluid during the procedure, which are likely to be complex and multifactorial. Without better data on the surface area-volume-pressure relationships these are likely to remain somewhat speculative. We have been more interested in merely pointing out that relatively large movements of water and solutes between blood and lavage fluid do seem to be occurring at bronchoalveolar lavage and that conventional assumptions about the dilution and calculation of epithelial lining fluid are likely to be highly oversimplistic.

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REPLY
We disagree that Lange was describing COP because in his two cases the disease evidently was affecting all orders of bronchioli and reached as far proximally as to take in small bronchi. It is simply fair to say that Lange's patients would have had an obstructive pattern of disease whereas COP/BOOP is characterised by a restrictive defect, being largely limited to alveoli, alveolar ducts, and only the smaller bronchioli. We are quite sure, however, that German pathologists before Lange described all the pathological features of COP in patients dying with resolving bacterial pneumonia. The feature that distinguishes COP/idipathic BOOP is the cryptogenic/idipathic nature of the condition. It appears that an error occurred in the final draft of the article as the name Lange was omitted from reference 2 and the word "anonymous" inserted in error.

With regard to the site at which the granulation tissue plugs attach to the interstitium in COP/BOOP, the alveolar plug is attached to the periphery of the acinus, well away from the supplying bronchiole. It therefore seems unlikely that they would not have an alveolar attachment. Review of our cases confirms that they do indeed attach to alveolar wall.

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BOOP and COP

I read with interest the editorial on obliterative bronchiolitis organisating pneumonia and cryptogenic organisating pneumonia (BOOP and COP) by Dr D M Geddes (August 1991; 46:545-7) and agree with his conclusion that BOOP and COP are essentially the same condition. I would like to point out one error in his references. Reference 2 in Dr Geddes's editorial was not "anonymous" but by the German pathologist W Lange, who described the pathological lesion of BOOP or COP as early as 1901 in his paper entitled 'Über eine eigentümliche Erkrankung der kleinen Bronchien und Bronchiolen (Bronchitits et Bronchiolitis obliterans)' ('Dtsch Arch Klin Med 1901;70:342-64'. He reported on two patients who presented with a pulmonary illness with fever, cough, increasing dyspnoea, and crackles on auscultation. The postmortem findings were described by Dr Lange in detail, and he found organising exudates with plugs of granulation and young connective tissue that were located within small bronchi, bronchioli, and alveoli. These were exactly the features of the lesion now called BOOP or COP. Lange already recognised that the plugs always extend from the walls of bronchioles into the alveolar lumen, and never grow from the alveolar wall itself.

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REPLY
The letters to the editor on the topic of bronchoalveolar lavage (BAL) and its implications for the understanding of COP have been informative and insightful. It is clear from the responses that the mechanisms of fluid movement during BAL are complex and not fully understood. The debate highlights the importance of careful experimental design and data interpretation in pulmonary research.

The author of the letter to the editor raises concerns about the assumptions made regarding fluid movement during BAL. The author emphasizes the difficulty in applying data from animal models to human BAL, given the complex relationships between blood and alveolar surfactant. The author suggests that the calculated influxes of water and solutes during BAL may be more accurate than previously thought, due to the unique local conditions at lavage.

The editor responds to these concerns by highlighting the limitations of the animal model used for studying BAL. The editor notes that Lange's work on patients with obliterative bronchiolitis and COP is relevant for understanding the complex nature of BAL-induced fluid movement. The editor points out the importance of considering the unique pathological features of COP, which differ from those of BOOP.

The reply from the author of the original editorial acknowledges the error in the reference to Lange's work and corrects the citation. The author confirms that Lange's work was indeed cited, and provides further details on Lange's description of the pathological lesion of COP.

The letters to the editor and the editor's response contribute to the ongoing discussion on the implications of BAL for the understanding of COP. The exchange of ideas and clarification of methodologies is essential for advancing our knowledge in this field.