

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 Gardiner (September 1991;46:613-8) but take exception to several of their conclusions. They referred to their earlier work¹ in which ³H₂O 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 ³H₂O 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 ^{99m}Tc 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,³ and movement of electrolytes and ¹⁴C urea across the epithelium is too slow to suggest significant movement of fluid between these compartments during lavage.⁴ 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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- 1 Kelly CA, Fenwick JD, Corris CA, Fleetwood A, Hendrick DJ, Walters EH. Fluid dynamics during bronchoalveolar lavage. *J Appl Pathol* 1983;55:1262-8.
- 2 Effros RM, Mason GR, Hukkanen J, Silverman P. New evidence for active fluid transport in edematous rat lungs. *J Appl Pathol* 1989;66:906-19.
- 3 Effros RM, Mason GR, Sietsema K, Hukkanen J, Silverman P. Pulmonary epithelial sieving of small solutes in rat lungs. *J Appl Pathol* 1988;65:640-8.
- 4 Effros RM, Feng D, Mason G, Sietsema K, Silverman P, Hukkanen J. Solute concentrations of the epithelial lining fluid in anesthetized rats. *J Appl Pathol* 1990;68:275-81.

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 the excessive 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 are found by applying osmotic 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 see how 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, more 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 that 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 procedure of bronchoalveolar lavage, which seems to induce some process of filtration across the bronchopulmonary epithelium, as well as movements due to diffusion alone.

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 presumptions about the dilution and calculation of epithelial lining fluid are likely to be highly oversimplistic.

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BOOP and COP

I read with interest the editorial on obliterative bronchiolitis organising pneumonia and cryptogenic organising pneumonitis (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 eigenthümliche Erkrankung der kleinen Bronchien und Bronchiolen (Bronchitis et Bronchiolitis obliterans)" (*Dtsch Arch Klin Med* 1901;70:342-64). He reported on two patients who presented with a pneumonic illness with fever, cough, increasing dyspnoea, and crackles on auscultation. The postmortem findings were described by 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 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 fairly clear from this 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/idiopathic BOOP is the cryptogenic/idiopathic 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 alveoli affected extend out 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 walls.

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

We read with some interest the study by Dr M Luengo 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 developing vertebral fracture than in involutional (postmenopausal) osteoporosis. This is contrary to our own experience with dual energy x ray