Bronchoalveolar lavage: a standardized procedure or a technical dilemma?

U. Costabel*

Bronchoalveolar lavage (BAL) is widely used for analysis of cells and soluble components of the lower respiratory tract. In its infancy, this simple and safe method has been applied as a pure research tool. Meanwhile, "the child has grown up", and its clinical usefulness for routine diagnostic purposes has been recognized worldwide in the various interstitial lung diseases and particularly in opportunistic infections of the immunocompromised patient [1]. However, even though this valuable tool has by now "almost reached adulthood" having been developed by Reynolds and Newball in 1974 [2], there is still considerable criticism of it for not being a standardized technique. Clearly, the technique of performing BAL and processing the material in the laboratory is not done under identical, carefully controlled conditions in the many centers using this method. But is this really necessary? Recently the European Society of Pneumology (SEP) task group on BAL published technical recommendations and guidelines for BAL in this journal [3]. These guidelines were based on the principle of the so-called smallest common denominator, hence allowing great technical variations for the different steps of the BAL procedure. It is not possible in this short editorial to discuss all of the different steps in detail, but several aspects are exemplified below and stand for the whole.

For example, the correct information about cell differentials is important for clinical purposes. In this regard, the volume of fluid infused can range from 100-250 ml without affecting the cell differentials. This has been shown for normal volunteers [4] and for patients with interstitial lung diseases [5]. For routine purposes, therefore, a small 100 ml volume seems to be sufficient for reliable analysis of cell differentials. A larger 200-300 ml volume may be a disadvantage, because of increased patient morbidity due to the more pronounced drop in oxygen saturation during the BAL procedure [6], and increased incidence of post-lavage side-effects such as fever [5, 7].

Another parameter which may influence the BAL results is the bronchopulmonary segment in which the lavage is performed. In this context, segments of the middle lobe or the lingula are recommended as the standard sites in patients with diffuse shadowings on the chest roentgenogram for two reasons: 1) their easy accessibility with the bronchoscope; and 2) the better recovery of fluid and cells which is 20% greater than from the lower lobes [8]. Are the results obtained from BAL at one location representative for the whole lung? Or should BAL be routinely performed at several locations in order to minimize the sampling error? Several studies have addressed the interlobar variation of BAL cell differentials [9, 10], lymphocyte subpopulations [11], and asbestos body counts [12] by performing a BAL on the right side and on the left side in the same patient and analysing the two sites independently. In general, these studies have shown a good interlobar correlation in patients with nonfocal disease on the chest roentgenogram. Patients with sarcoidosis and uneven distribution of infiltrates may have widely varying percentages of cells, however [9], and one third of patients with idiopathic pulmonary fibrosis may show discrepancies greater than 10% regarding the percentage of neutrophils between the two different sites [10].

In this issue of the Journal, Schmeker et al. [13] shed further light on the problems related to the interlobar variability of lavage components. In 12 healthy subjects, they looked for the interlobar variation of neutrophils and eosinophils and their secretory products myeloperoxidase and eosinophil cationic protein, respectively. They analysed separately the first 50 ml aliquot (bronchial wash) and the following two pooled 50 ml aliquots (bronchoalveolar lavage). In both compartments, they observed a significant interlobar correlation for the number and concentration of neutrophils and eosinophils, but not for the solutes. This inconsistency of solute recoveries between different lobes has to be considered when investigating patients with interstitial lung diseases. Up to now, studies looking for interlobar variations of soluble components in patients with interstitial lung diseases are lacking, to my knowledge, and should urgently be performed.

In contrast to the analyses of the cell profiles in BAL, which are used for clinical purposes, the quantitation of soluble components has mainly remained a research tool. One reason for this may be that a reliable method to assess the true epithelial lining fluid (ELF) does not exist. The problem is that the saline used for lavage significantly dilutes the ELF that is sampled. Several reference substances have

been proposed, such as albumin or potassium, but both have limitations, albumin because of its possible leakage from plasma due to increased permeability of the epithelial capillary membrane in inflammatory disease processes, and potassium because of its potential release from lysed cells in the BAL fluid [3]. Methylene blue has been suggested as an external marker of dilution [14] and urea as an internal marker [15]. Both markers are not ideal. Methylene blue may be lost by passing into the circulation or by binding to cells of the lower respiratory tract, and urea may diffuse from the plasma during the lavage procedure, thereby leading to an overestimation of the ELF volume [16]. A recent study compared albumin and urea as reference markers in BAL fluid from patients with interstitial lung diseases [17]. Urea showed less variability between groups than did albumin, and hence was concluded to be the better available marker, if dwell time is kept to a minimum. In this report, the mean dwell time was only 3.2±0.4 min, because the authors excluded all lavages exceeding 4 min in order to reduce passive diffusion of urea into the BAL. This selection criterion may have caused a significant bias in favour of urea and against albumin. Such a bias would make it difficult to extrapolate the results of this study to routine analyses of soluble components, since in daily routine lavages it would be impossible to keep the dwell time below 4 min in every patient.

The fluid dynamics during BAL are complex and not well understood. A recent study demonstrated a bidirectional flux of water across the alveolar membrane during BAL, the net result being an influx of fluid from the circulation into the lung [18]. These fluid kinetics may depend on a number of factors including BAL volume, site of lung segment, and suction pressure applied. The fluid movements during BAL may dilute the solutes which are to be measured to an unpredictable degree.

Thus, the findings to date indicate that BAL is sufficiently standardized for clinical routine purposes with respect to the enumeration of cell differentials including lymphocyte subpopulations. The quantitation of soluble components, however, is still hindered by the variable and unpredictable dilutional effects occurring during the BAL procedure. In this regard, BAL still represents a technical dilemma. Further work is needed to develop methods allowing correct determinations of solutes in the fluid of the lower respiratory tract.

References