Bronchoalveolar Lavage – Do We Need It?

a report by
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Bronchoalveolar lavage (BAL) has been used as a research and diagnostic tool since Reynolds and Newball introduced its current form of application in the 1980s,1 after the development of fibre optic bronchoscopy by Ikeda at the end of the 1970s.2 The procedure involves wedging a bronchoscope, usually at a subsegmental level of the third and fourth degree of the bronchus, then sterile isotonic saline that has been warmed to body temperature is instilled and immediately retrieved through the instrument. Since then, the technique has prompted numerous studies, scientific and clinical, resulting in a wealth of publications in the field of human and animal pathology and pathophysiology.

In 1989 the first European report on bronchial lavage was published, which discussed the technical aspects of the handling and clinical use of specimens obtained using this method.3 It was revised in 1990,4 after the foundation of the European Society of Pneumology (SEP) Task Group on BAL, and revised again in 1992.5 An exclusive issue of the European Respiratory Review in July 19996 was devoted to a study of the non-cellular components of BAL, and made further recommendations for the standardisation of the technique; this was the result of the combined efforts of 49 authors from 15 different countries and 21 guest reviewers.

Thus, this group has been continuously renewed and reinforced by researchers from different cultural and professional backgrounds, and as a result cannot be considered exclusively European, despite the fact that it is part of the current European Respiratory Society (ERS) (under the auspices of its Clinical Assembly). It has been known by a variety of names: the Bronchoalveolar Lavage Group, the Clinical Pathobiology and Bronchoalveolar Lavage Group, the Clinical Pathobiology Group and, most recently, since September 2004, the Diffuse Parenchymal Lung Disease Group.

Technical Aspects
The introduction of the most recent report into non-cellular components6 and the editorial of the European Respiratory Journal, published at the same time,7 both list reasons for the variability of BAL specimens and make recommendations regarding their interpretation (see Table 1).

In fact, one of the main technical problems related to BAL is the variability of the specimens obtained, which is related not only to the underlying pathological process and personal characteristics of the patient such as smoking or the use of medication, but also other factors, such as the existence of additional pathologies. These can affect the assessment of results and lead to inter-institutional differences.

Other variables are: the volume of fluid instilled (at least 100ml of sterile isotonic saline and ideally between 200 and 240ml); the number of aliquots used; the time interval between instillation and aspiration, otherwise known as the ‘dwell time’, which should be as short as possible; the pressure used during aspiration, which should also be as low as possible (between 25 and 100mmHg); the percentage of fluid withdrawn; the lung location of the lavage (preferably in the middle lobe); and the positioning of the patient during lavage.

All procedures following the performance of the BAL itself are also subject to interpretation, such as the transportation, handling, storage and processing of specimens.

Up-to-date recommendations now exist for all of these factors, which allows a certain degree of flexibility while encouraging centres to be consistent about procedures used and to insist on the need for specification. This enables comparative studies to be conducted between institutions that employ different methodologies.

Utility of Bronchoalveolar Lavage in the Assessment and Diagnosis of Bronchopulmonary Disease
Despite technical considerations, BAL enables the acquisition of data of a varied nature regarding the identification and quantification of immune inflammatory cells, non-cellular soluble components of alveolar origin, micro-organisms, tumour cells and inhalation particles. A total cell count should be performed in a Neubauer chamber –

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Diagnostic Monitoring and Procedure

Table 1: Recommendations for Obtaining and Processing Bronchoalveolar Lavage

<table>
<thead>
<tr>
<th>Causes of Variability</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological process</td>
<td>Specify underlying pathology</td>
</tr>
<tr>
<td>Smoking</td>
<td>Specify if patient is a smoker or ex-smoker</td>
</tr>
<tr>
<td>Treatment</td>
<td>Specify, e.g., anti-inflammatories</td>
</tr>
<tr>
<td>Associated pathology</td>
<td>Specify, e.g., asthma</td>
</tr>
<tr>
<td>Patient position</td>
<td>Specify</td>
</tr>
<tr>
<td>Area lavaged (one or more lobes, middle lobe or other)</td>
<td>Specify</td>
</tr>
<tr>
<td>Volume of fluid instilled</td>
<td>Use &gt;100ml for adults and specify quantity (200–240ml recommended)</td>
</tr>
<tr>
<td>Number of aliquots used</td>
<td>Specify and standardise (four recommended)</td>
</tr>
<tr>
<td>Aspiration pressure</td>
<td>Maintain minimum and specify if extended</td>
</tr>
<tr>
<td>Fluid retrieved</td>
<td>Specify volume and percentage (establish minimum percentage)</td>
</tr>
<tr>
<td>Handling and storage of specimens</td>
<td>Recommendations in specific sections of the report</td>
</tr>
<tr>
<td>Dosage methods and control</td>
<td>Recommendations in specific sections of the report</td>
</tr>
</tbody>
</table>

Adapted from Haslam et al., 1999.7

Figure 1: Normal Bronchoalveolar Lavage Smear

In the figure only macrophages are observed. This is the most frequent cell in baseline situations. May-Grünwald Giemsa stain, 100x amplification, immersion oil.

Image shows dark intracytoplasmic inclusions obtained by bronchoalveolar lavage of a heavy smoker. May-Grünwald Giemsa stain, 100x amplification, immersion oil.

Figure 2: Giant Macrophage with Multilobulated Nucleus

With the highest sensitivity (>90%) and specificity (>95%) in bronchopulmonary infections, from a diagnostic perspective the main role of BAL is identifying Pneumocystis jiroveci oocytes, especially in immunocompromised hosts.8,9 This applies also to situations of an occupational nature, namely the observation and classification of particles and intra- or extra-cellular fibres, such as the identification of a number higher than one asbestos body per millilitre of retrieved BAL, which represents in the appropriate context the confirmation of pulmonary fibrosis caused by labour or environmental exposure.10–13

The value of this methodology is equally important in diagnosing tumours and lymphangitic carcinomatosis,14,15 and is useful in the diagnosis of various interstitial lung diseases associated with specific inflammatory profiles, specifically concerning diffuse pulmonary pathologies of wider prevalence. Such conditions include moderate lymphocytic alveolitis with marked elevation of the CD4/CD8 ratio in sarcoidosis (the figure 3.5 in this ratio represents the separating line enabling the acquisition of higher sensitivities and specificities) and wider-dimension alveolitis with more marked alveolar lymphocytosis in hypersensitivity pneumonitis, which is associated with typical morphological alterations – namely the presence of so-called ‘foamy macrophages’, an increase in neutrophils and an eventual increase in eosinophils in more moderate alveolitis and lymphocytic idiopathic pulmonary fibrosis.16

Other perspectives can be gathered with computer back-up, such as the use of mathematical analysis of logistical regression resorting to diverse variables related to BAL, i.e the percentage of fluid retrieved, total cell count and quantification of macrophages, lymphocytes and neutrophils. This is also true for discrimination of the gender and age of the population under study as a method of high positive forecast of the differential diagnosis of the more frequent pulmonary interstitial...
conditions, i.e. sarcoidosis, hypersensitivity pneumonitis and idiopathic pulmonary fibrosis.17,18

The CD4/CD8 ratio in BAL has been used in the diagnostic back-up of various pathologies, especially its inversion in hypersensitivity pneumonitis and in other fibrosing disorders or associated with immunosupression, as well as its increase in sarcoidosis and other granulomatous conditions. Also, there is the possibility of this determination being used to assist in the differential diagnosis of pneumoconiosis by the reduced values in silicosis and the high values in beryllium disease and asbestosis.13,16 Likewise, taking for granted the fact that the lung as an organ is a preferential target of systemic pathology, the detection of cell alterations in BAL, even without a clinical or functional definition, may represent an indicator of the activity and the prognosis of the respective clinical situations;10 however, by means of these subclinical alveolitis it is not possible to dissociate specific organic involvement of non-pathological local expression of multi-organic disease.

Complementary Techniques

However, there are alternatives to BAL, namely for the study of bronchial disorders, which enable in a less invasive way an equally direct assessment of the airways. Within this pathophysiological scope, as well as to support the diagnosis, clinical assessment and therapeutic monitoring of bronchopulmonary pathology of interstitial origin, there is a more recently developed methodology that pays particular attention to induced sputum techniques and exhaled breath condensate studies.

Conclusion

It can be concluded that BAL is a technique that has provided important support in the understanding and assessment of normal and pathological mechanisms of the functioning of the broncho-pulmonary territory. Together with the clinical assessment, pulmonary function testing, imaging pathology and other laboratory studies, BAL represents a useful, validated support for providing information for the development of pneumological sciences.

European Respiratory Society 18th Annual Congress

The European Respiratory Society (ERS) will hold its 18th Annual Congress in Berlin, Germany from Saturday 4 October to Wednesday 8 October. The ERS Annual Congress is one of the largest events in the respiratory field, and is the best place to present and discuss the most up-to-date scientific opinion and the hottest new topics.

The ERS has received a record number of abstract submissions for the 2008 Annual Congress. Considering the broad spectrum of the scientific and educational activities that will take place, the Congress hopes that not only respiratory health specialists but also internists, general practitioners and specialists from other disciplines will attend.

The Scientific Programme will be one of the most comprehensive ever in the field of lung health and disease. It will address the latest advances in clinical diagnosis and treatment, including:

- 65 symposia, including hot topics and grand rounds;
- free communication sessions, including oral presentations, e-communication sessions and thematic posters;
- 22 post-graduate courses and 18 ‘meet the professor’ seminars; and
- evening symposia organised by industry.

Hot Topics in This Year’s Programme Include:

- Improving pulmonary distribution of combination therapy: implications for asthma treatment.
- New imaging modalities in the staging of lung cancer.
- Lung imaging in critically ill patients.
- Update of long-term oxygen therapy.
- Improved diagnosis and clinical decision-making by integrating information from new biomarkers.

For further information:

Please visit dev.ersnet.org/415-general-information.htm or phone: +41 21 213 01 01.

Source: European Respiratory Society.