**Bronchoalveolar lavage**

Flexible fibreoptic bronchoscopy is increasingly used to study the upper and lower airways of children. Flexible bronchoscopy should take place in a setting in which full monitoring and resuscitation facilities are immediately available. It is also advisable that access to rigid bronchoscopy is readily available in the event of therapeutic procedures being necessary, such as removal of an unexpected foreign body. This may require the establishment of a joint endoscopy service with ear, nose, and throat or thoracic surgeons. It is necessary that the bronchoscopist maintains manual skills and expertise in the interpretation of findings. The latter requires an understanding of pulmonary physiology, developmental anatomy, and pathology and it is likely that these skills will be acquired and maintained by paediatric respiratory physicians working in regional centres.

The diagnostic capabilities of fibreoptic bronchoscopy may be usefully extended by performing bronchoalveolar lavage, which is used to recover epithelial lining fluid (ELF) from the airways and alveoli of the respiratory tract. The recovered bronchoalveolar lavage fluid (BALF) in which ELF is diluted contains both lung cells and ELF solutes including proteins and inflammatory mediators. Examination of BALF constituents has been widely used for diagnosis of a number of pulmonary disorders in adults and for investigations of their basic mechanisms and response to therapy.

Fibreoptic bronchoscopy and bronchoalveolar lavage is technically straightforward in children but the necessary invasiveness of the technique has largely limited its use to diagnosis in specific disease groups. Bronchoalveolar lavage with a paediatric flexible bronchoscope is also limited by the diameter of the instrument in relation to airway size. However, non-bronchoscopic modifications of the technique have recently been used in studies of intubated newborn infants.

### Technical aspects

Although bronchoalveolar lavage is essentially a simple procedure, there are a number of technical considerations that may alter interpretation of results, particularly in the case of ELF solutes which are diluted by BALF.

In principle, the bronchoscope is introduced into a segmental or subsegmental bronchus, often in the right middle lobe, where it is wedged to occlude the airway. Warmed saline is then introduced through the operating channel of the bronchoscope and aspirated into a suitable receptacle. Factors that may influence the nature of fluid obtained include the site of lavage, the volume of saline instilled, sequential lavage with subsequent aliquots, and the time between instillation and aspiration. Fluid return is best from lavage of the right middle lobe. A small volume lavage is believed to sample ELF from proximal airways whereas increased lavage volumes sample more distal airways and alveolar sites. Sequential lavage samples progressively more distal sites with successive aliquots.

Fluid exchange between the airspaces, vascular compartment, and interstitium may occur during lavage and variable dwell times may alter the dilution of ELF within lavage fluid. This leads to errors in measurement of solute concentrations if a correction is not made for ELF volume. Rennard and colleagues proposed that urea passively diffuses into ELF and acts as a dilution marker, but urea influx may occur during the lavage procedure and can also be demonstrated to increase in disease states, leading to overestimation of ELF volume and consequent underestimation of solute concentrations. Given these and other limitations, it is important that techniques are adequately described in reports of BALF findings.

### Bronchoalveolar lavage in children

The major application of bronchoalveolar lavage in children has been the diagnosis of infection, particularly in the immunocompromised host. Perhaps the best recognised indication is the diagnosis of *Pneumocystis carinii* pneumonia in children with immune deficiency. Several studies of bronchoalveolar lavage in immunocompromised children with acute pulmonary symptoms have demonstrated a consistently high diagnostic yield of around 50%, with *P carinii* the commonest organism identified. Although less invasive techniques such as sputum induction with nebulised hypertonic saline may demonstrate a pathogen in symptomatic, immunocompromised children, bronchoalveolar lavage remains an important diagnostic investigation in this situation.

The role of bronchoalveolar lavage in the immunocompetent child with pulmonary infection is less clear. Its use in the diagnosis of primary pulmonary tuberculosis in children is questionable as gastric washings are more sensitive. Bronchoalveolar lavage has been used for the detection of respiratory syncytial virus in infants with severe bronchiolitis before treatment with tribavirin (ribavirin) and also to identify a causative organism in acute pneumonia before commencing antimicrobial treatment. Concerns that contamination of BALF by upper respiratory tract flora might occur during bronchoscopy may be addressed by examination of lavage fluid from an unaffected lobe as well as the site of interest. Enthusiasm for using bronchoalveolar lavage to diagnose primary respiratory infections in otherwise healthy children is variable and the technique might better be reserved for investigation of those with atypical features or lack of response to a primary course of antibiotics.

Inflammatory responses of the lungs to infection in children with cystic fibrosis have been studied using bronchoalveolar lavage. Concentrations of interleukin-1 are raised in association with bacterial pulmonary infections, as with lung infections complicating other diseases. Neutrophil activation can be examined by studying expression of the complement receptors, CR1 and CR3, on polymorphonuclear cells from BALF. In cystic fibrosis, maximal upregulation of these receptors appears to occur in the lungs but subsequent cleavage of CR1 by proteases may interfere with normal phagocytosis.

The role of inflammatory mediators in the diagnosis of pulmonary disease after lung transplantation has recently been studied. Donor specific proliferative responses of BALF lymphocytes are observed in acute and chronic rejection and obliterator bronchiolitis but not in acute infection in transplanted lungs. Increased concentrations of platelet derived growth factor (PDGF) have been demonstrated in BALF from patients with obliterator bronchiolitis. Prospective studies have shown the rise in PDGF to precede the onset of irreversible airway obstruction suggesting a role for PDGF in the fibroproliferative
changes observed in obliterative bronchiolitis after lung transplantation.22

These studies have provided fascinating insights into cellular mechanisms underlying a variety of pulmonary inflammatory diseases and suggest that some BALF constituents may have a role as disease activity markers. In adults with asthma a large number of studies have used bronchoalveolar lavage to examine inflammatory cells and mediators in association with other markers of the disease.23 A relatively small number of studies have been reported in children. Ferguson and colleagues have demonstrated the role of macrophages24 and mast cells25 in bronchial hyperreactivity in children with moderately severe asthma. Platelet activating factor has been demonstrated in BALF from an infant with asthma but not from those with laryngeal stenosis or respiratory distress syndrome.26 The association of right middle lobe collapse with infection in children with asthma has also been demonstrated using bronchoalveolar lavage.27

Bronchoalveolar lavage in intubated neonates

Interest in the mechanism of neonatal lung diseases, notably bronchopulmonary dysplasia, has prompted several workers to adapt methods of bronchoalveolar lavage for intubated infants using non-bronchoscopic techniques. These range from instillation of fluid down the endotracheal tube and suction just distal to the tube tip,28-30 through blind wedging of a standard suction catheter into the right lower lobe bronchus and fluid exchange as for the bronchoscopic method,31 to a bronchial occlusion technique using a balloon catheter.32

It is likely that the same caveats that apply to bronchoscopic lavage will operate in these situations and care should be taken when interpreting results arising from different techniques. This aside, there have been a number of studies that have greatly facilitated our understanding of the pathophysiology of chronic lung disease in the newborn.

During respiratory distress syndrome there is a pulmonary inflammatory infiltrate which consists largely of neutrophils. Later the proportion of neutrophils falls but in infants who develop chronic lung disease the neutrophil infiltration persists for up to six weeks.33 This is associated with increased concentrations of neutrophil elastase activity and a decrease in antiprotease activity, presumed due to oxidation of α1-protease inhibitors, in infants with bronchopulmonary dysplasia compared with controls.34 Grigg and colleagues have demonstrated a possible mechanism for reduction of tissue injury in respiratory distress syndrome by neutrophil apoptosis, or programmed cell death, and removal by alveolar macrophages.35 Increased concentrations of albumin and fibronectin have been demonstrated in lung lavage fluid from infants with bronchopulmonary dysplasia compared with controls36 and tumour necrosis factor-α, a potent inflammatory mediator, has been demonstrated in the airways of infants with prolonged supplemental oxygen dependence.30 The administration of exogenous surfactant to infants with respiratory distress syndrome has not been shown to enhance the inflammatory process compared with the effects of ventilation alone.39

Treatment with dexamethasone of infants who have developed or are at risk for bronchopulmonary dysplasia has demonstrated a reduction in the ability of alveolar macrophages to produce hydrogen peroxide.36 reduced concentrations of neutrophil elastase, fibronectin and albumin in BALF37 with no change or an increase in α1-protease inhibitor concentrations38 associated with improvement in oxygen requirement and respiratory mechanics. Dexamethasone has also been shown to reduce the chemotactic response of polymorphonuclear cells in association with a reduction in leukotriene B4 concentrations in BALF.39

Other applications for bronchoalveolar lavage in neonatal respiratory disease have been the study of surfactant protein A in response to high frequency oscillatory ventilation,30 the study of the pathophysiology of airway inflammation evidenced by increased inflammatory cells and concentrations of interleukin-6 after prolonged membrane rupture.40

Summary

Bronchoalveolar lavage has a well established role in the diagnosis of pulmonary infections, particularly those due to opportunistic organisms in an immunocompromised host. Recent studies of infants and adults with inflammatory lung disease have helped our understanding of the mechanisms underlying these disorders and their responses to treatment. With increasing recognition that pulmonary events in utero and in early infancy are important in the pathogenesis of lung diseases such as asthma,41-43 has the role of the lung's responses to various environmental insults in this population might guide us to developing effective preventative and therapeutic strategies. Bronchoalveolar lavage is one method for accessing a number of pulmonary components and may be useful in this regard, particularly if combined with new methods for examining inflammatory responses, such as those utilising the polymerase chain reaction to assess cellular expression for inflammatory cytokines and growth factors.44

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