The pulmonary physician in critical care • 1: Pulmonary investigations for acute respiratory failure

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This is the first in a series of reviews of the role of the pulmonary physician in critical care medicine. The investigation of mechanically ventilated patients is discussed, with particular reference to those presenting with acute respiratory failure and diffuse pulmonary infiltrates.

Patients with acute respiratory failure (ARF) commonly require intensive care, either for mechanical ventilatory support or because adequate investigation of the precipitating illness is impossible without endotracheal intubation. Similarly, respiratory complications such as nosocomial infection, pulmonary oedema, and pneumothorax are common in the critically ill. Here we discuss the investigation of patients who are mechanically ventilated with emphasis on those presenting with ARF and diffuse pulmonary infiltrates.

BRONCHOSCOPY

The British Thoracic Society recommends that fiberoptic bronchoscopy (FOB) should be available for use in all intensive care units (ICUs). In patients presenting with ARF of unknown cause, FOB may facilitate the collection of diagnostic material, but alternative indications for the procedure include the relief of endobronchial obstruction, the facilitation of endotracheal tube placement, and the localisation of a site of trauma or of a source of bleeding (reviewed later in this series by Corris).

Practical conduct

The inspired oxygen concentration (FiO2) should be raised to 1.0 before the bronchoscope is introduced through a modified catheter mount incorporating an airtight seal around the suction port of an endotracheal or tracheostomy tube. The resultant increased resistance to expiration results in gas trapping and increased positive end expiratory pressure (PEEP). With an 8 mm endotracheal tube the level of PEEP should remain less than 20 cm H2O, making it the smallest size that can be used safely with an adult instrument. Paediatric bronoscopes may be passed through smaller endotracheal tubes at the cost of a smaller visual field and significantly less suction capability. Complications are few. Malignant cardiac arrhythmia occurred in about 2% of cases in an early series in which FOB was performed in patients soon after cardiopulmonary arrest. In a subsequent series no serious complications were reported. In patients with ARF requiring mechanical ventilation, adequate sedation and paralysis facilitate not only effective oxygenation but also obviate the risk of damage to the instrument should the patient bite the endotracheal tube. Finally, limiting the duration of instrumentation by intermittently withdrawing the bronchoscope during the operation helps to maintain adequate alveolar ventilation and to limit the rise in Paco2, which may be particularly relevant in those with head trauma. When prolonged instrumentation of the airway is expected—for example, during bronchoscopic surveillance of percutaneous tracheostomy—monitoring of end tidal CO2 is recommended.

Specimen retrieval techniques have been reviewed recently elsewhere. In terms of establishing a microbiological diagnosis, there is little difference in sensitivity and specificity between FOB directed bronchoalveolar lavage (BAL) and protected specimen brush (PSB). In order to obtain samples for cellular analysis (table 1), repeated aliquots of 50–60 ml to a total of 250–300 ml should be instilled, of which about 50% should be retrieved. In ventilated patients a lower volume is commonly used to reduce ventilatory disturbance, although there is no standard recommendation. Bacteriological analysis requires collection of only 5 ml fluid, although larger volumes are more commonly used. Blind (non-bronchoscopic) tracheobronchial aspiration is routine practice in all ventilated patients to provide upper airway toilet. Blind sampling of lower respiratory tract secretions (aspiration or mini-BAL using various catheter or brush devices to obtain specimens for quantitative cultures) has been extensively examined as an alternative diagnostic method in cases of suspected ventilator associated pneumonia (VAP). Generally, these have compared favourably with bronchoscope guided methods in trials on critically ill patients.

Transbronchial (TBB) versus open lung (OLB) biopsies

TBB carries a substantial risk of pneumothorax which afflicts 8–14% of ventilated patients. For this reason, TBB is rarely performed in these circumstances except in patients after lung transplantation where the sensitivity for detection of acute or chronic rejection is 70–90%, with a specificity of 90–100% when performed in an appropriate clinical context. The Lung Rejection Study Group recommends collecting at least five pieces of lung parenchyma to get an adequate sample of small bronchioles and to diagnose bronchiolitis obliterans. Widespread pulmonary infiltrates developing within 72 hours of lung transplantation are more likely to represent alveolar oedema caused by ischaemia-reperfusion injury than rejection or infection.
A 10 year retrospective review of 24 mechanically ventilated patients undergoing OLB found that a diagnosis was made histologically in 46%.22 Intraoperative complications were generally well tolerated, although 17% had persistent air leaks and two patients died as a consequence of the procedure. Complication rates in other series have been lower. In a retrospective review of 27 OLBs in patients with ARF, persistent air leak occurred in six but there were no perioperative deaths.21 In a retrospective series of 80 patients,23 many of whom were immunosuppressed, eight had a persistent air leak with one perioperative myocardial infarction.

**Bronchoscopy in specific conditions**

**Pneumonia**

The microbiological yield from bronchoscopy is low (13–48%) in ventilated patients with community acquired pneumonia (CAP), possibly because of the frequency of antibiotic administration before admission to the ICU.23–25 By contrast, patients who have been mechanically ventilated for several days generally have extensive colonisation even of the lower respiratory tract. In these patients with suspected VAP, negative microbiological culture predicts the absence of pneumonia but false positives arise frequently. Invasive investigation has not been shown in patients with either CAP or VAP to alter treatment and outcome significantly25–29 and may be reserved for patients failing first line treatment or those from whom specimens are not readily obtainable by blind tracheobronchial aspiration (see later reviews in this series by Baudouin and by Ewig and Torres). Patients with common causes of immunosuppression, such as the acquired immune deficiency syndrome (AIDS) and malignancy, have a poor prognosis when admitted to the ICU with ARF (see review later in this series by Boyton and Kon). For example, bone marrow transplant recipients requiring mechanical ventilation have an inhospital mortality in excess of 95%.20 Although these data have deterred referral of such patients to the ICU, temporary endotracheal intubation may be required for sedation and FOB to be performed safely.

The sensitivity of BAL in the detection of AIDS related pneumocystis pneumonia (PCP) is high (86–97%).30–32 Fewer organisms may be recovered by BAL from patients using nebulised pentamidine prophylaxis33 or with non-AIDS related PCP, but the yield may be increased by taking samples from two lobes and targeting the area of greatest radiological abnormality.34 Cytomegalovirus (CMV) pneumonia is a common cause of death after transplantation, particularly in recipients of allogeneic bone marrow and lung grafts.35 The definitive diagnosis of CMV pneumonia is made by the finding of typical cytomegalic cells with inclusions on BAL or TBB,36 the latter being more sensitive. Detection of early anti-gen fluorescent foci (DEAFF)37 performed on virus cultured from BAL fluid allows a presumptive diagnosis to be made. Invasive pulmonary aspergillosis occurs predominantly in neutropenic patients38 in whom early diagnosis and treatment are essential.39 The incidence of aspergillosis may be rising in this patient group, probably secondary to more aggressive chemotherapy regimens and more widespread use of prophylactic broad spectrum antibiotics and antifungal agents. The sensitivity of BAL is high in the presence of diffuse radiological changes.37 A positive culture has a specificity of 90% but results may take up to 3 weeks.21 The sensitivity of culture alone (23–40%) is greatly increased by the addition of microscopic examination for hyphae (58–64%).23 Galactomannan antigen testing of blood provides an early warning of infection40 and may prove useful in BAL fluid.

**Respiratory failure due to non-infectious lung disease**

Patients presenting with ARF and pulmonary infiltrates are generally assumed to have pneumonia and further investigation is prompted by treatment failure. Analysis of BAL fluid may distinguish the differential diagnoses and/or pulmonary risk factors for the acute respiratory distress syndrome (ARDS), many of which have specific treatments (table 2). The BAL white cell differential provides information that may be diagnostically helpful (table 1).21 A moderate eosinophilia (>15%) implicates a relatively small number of conditions including Churg-Strauss syndrome, AIDS related infection, eosinophilic pneumonia, drug induced lung disease, or helminthic infection.41–43 Apart from helping to uncover a cause or differential diagnosis for ARDS, the BAL fluid cell profile may give prognostic information. In patients with ARDS secondary to sepsis a BAL fluid neutrophilia had adverse prognostic significance while a higher macrophage count was associated with a better outcome.44 The fibroproliferative phase of ARDS may be amenable to treatment with steroids45 and it is recommended that either BAL or PSB is performed before starting treatment to exclude infection.

For patients with suspected or confirmed ARDS a sensitive and specific marker of disease would have several benefits. Firstly, it might improve the ability to predict which patients with risk factors develop ARDS46 so that potentially protective measures could be assessed and developed. Secondly, it may help to quantify the severity of disease and to predict complications such as fibrosis and superadded infection. Most studies have involved assays on plasma samples or BAL fluid.41 Analysis may provide information about soluble inflammatory mediators (see review later in this series by Bellingan) and by-products of inflammation (such as shed adhesion molecules, elastase, peroxynitrite) in the distal airways and air spaces. Analysis of samples from patients at risk has revealed

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**Table 1**  Typical bronchoalveolar lavage differential cell counts in conditions associated with acute respiratory failure and diffuse pulmonary infiltrates

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cell differential counts</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Macrophage</td>
<td>Lymphocyte</td>
</tr>
<tr>
<td>Normal</td>
<td>90%</td>
<td>10%</td>
</tr>
<tr>
<td>Acute interstitial pneumonia</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Alveolar haemorrhage ARDS</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Bacterial pneumonia</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Eosinophilic pneumonia</td>
<td>↑↑</td>
<td></td>
</tr>
</tbody>
</table>

CFA = cryptogenic fibrosing alveolitis; ARDS = acute respiratory distress syndrome.
increased alveolar levels of the potent neutrophil chemokine interleukin 8 (IL-8) in those patients who progress to ARDS. 53

The development of established fibrosis conveys a poor prognosis in ARDS. 52 Type III procollagen peptide is present from the day of tracheal intubation in the pulmonary oedema fluid of patients with incipient lung injury, and the concentration correlates with mortality. 53 Less invasive methods of sampling distal lung lining fluid using exhaled breath condensates 54 or exhaled breath condensates 55 are being examined in critically ill patients. The assay of potential biomarkers is currently used exclusively as a research tool.

### Table 2

<table>
<thead>
<tr>
<th>Condition</th>
<th>Specific treatment</th>
</tr>
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| Pneumonia                  | Isolated bronchiolitis, diffuse alveolar haemorrhage, pulmonary oedema, lung contusion, the detection and quantification of pleural fluid by the supine chest radiograph is inaccurate. 57–59

Central venous catheters should be positioned in the superior vena cava (SVC) at the level of or slightly above the aygous vein. Caudal to this, the SVC lies within the pericardium making tamponade likely in the event of vessel perforation. Encroachment of lines into the atrium may cause cardiac arrhythmia. Positioning of left sided lines with their ends abutting the wall of the SVC is a risk factor for perforation. The ideal radiological placement of pulmonary artery catheters has not been studied, and the balloon should be sited in the largest diameter pulmonary artery that will provide a wedge trace on inflation. However, placement should be reviewed constantly and migration of the catheter tip away from the hilum on the chest radiograph is a cause for concern.

### Radiographic appearances in ARF

The radiographic appearance of ARDS is a cornerstone of its diagnosis (see review later in this series by Atabai and Matthay). However, distinguishing between cardiogenic and high permeability pulmonary oedema on radiographic signs alone is unreliable. 51 The cardiac size and vascular pedicle width reflect the haemodynamic state of the patient, 52 but this sign relies on exact and often unachievable patient positioning. Pleural effusions and Kerley’s lines reflecting lymphatic engorgement are not features of ARDS because the high protein content and viscosity of the oedema fluid prevents it from spreading into the peripheral interstitial and pleural spaces. Air bronchograms are seen in up to one third of cases as the airways remain dry in ARDS, thereby contrasting with the surrounding parenchyma.

In contrast to hydrostatic pulmonary oedema, the radiographic signs of ARDS are frequently not visible on the plain chest radiograph for 24 hours after the onset of symptoms. Early changes comprise patchy ill defined densities that become confluent to form ground glass shadowing. In ventilated patients air space shadowing commonly results from pneumonia or atelectasis; other causes are ARDS, haemorrhage, and lung contusion. The detection and quantification of pleural fluid by the supine chest radiograph is inaccurate. 57–59

### Thoracic ultrasound

The presence of fluid within the pleural space has an adverse effect on ventilation-perfusion matching 55; removal improves oxygenation and pulmonary compliance. 56–58 Drainage may be performed safely by ultrasound guided thoracocentesis in the ventilated patient. 57–59

### Thoracic computed tomography (CT)

Transportation to and monitoring of a critically ill patient for CT scanning involves a team effort from medical, nursing, and technical support staff. There are no published data describing the risks and benefits of this investigation in a well defined group of critically ill patients. However, in a retrospective review of 108 thoracic CT scans performed on patients in a general ICU, at least one new clinically significant finding (most commonly abscess, malignancy, unsuspected pneumonia, or pleural effusion) was identified in 30% of cases and in 22% led to a change in management. 59 The normal standards and precautions for transporting critically ill patients apply, 50 including a period of stabilisation on the transport ventilator prior to movement. Despite the added risk of complications such as pneumothorax, haemodynamic instability and lung derecruitment associated with transportation, we routinely scan patients with ARDS if their gas exchange on the transport ventilator is acceptable. Portable CT scanners provide mediastinal images of comparable quality to those obtained in the radiology department, but the images of the lung parenchyma are inferior. 51
Insight into the nature of ARDS has been obtained from CT scanning, for example, by defining the disease distribution and demonstrating ventilator induced lung injury (see review later in this series by Whitehead and Slutsky). CT scans of the lung parenchyma show that the diffuse opacification on the plain radiograph is not homogenous; classically, there is a gradient of decreasing aeration passing from ventral to dorsal dependent regions. Tidal volume is therefore directed exclusively to the overlying anterior regions which are consequently overdistended. This may account for the anterior distribution of reticular damage seen on CT scans in survivors. The improvement in oxygenation of patients with ARDS following prone positioning suggests improved ventilation-perfusion matching. However, microsphere CT studies in animal models of ARDS have failed to demonstrate redirection of perfusion with prone positioning; redirection of ventilation to the consolidated dorsal regions may therefore be the mechanism responsible.

Recovery from ARDS is commonly complicated by pneumothoraces which are often loculated. If a pneumothorax does not extend to the lateral thoracic wall, it will not be readily apparent on a chest radiograph. Its presence may be inferred from a range of indirect signs such as a vague radiolucency or undue clarity of the diaphragm, but this gives no information as to whether the collection of air is located anteriorly or posteriorly. Similarly,
empyema and abscess formation may cause treatment failure in patients with pneumonia and ARDS and are not uncommonly obvious on the CT scan (fig 1) when not seen on the plain radiograph. CT guided percutaneous drainage may be required for loculated pneumothoraces and may be an alternative to surgery for lung abscesses.

Pulmonary embolus
Massive pulmonary embolus is a treatable cause of rapid cardiorespiratory deterioration which is frequently not diagnosed before death (see review later in this series by Morrell and McNeil). Radionuclide scanning has a long image acquisition time and assays for detecting D-dimers are unduly sensitive in this setting, making both unsuitable for the critically ill patient. CT pulmonary angiography is the investigation of choice and may provide an alternative diagnosis to account for this setting, making both unsuitable for the critically ill patient.

Trauma
Routine CT scanning of all victims of serious trauma uncovers lesions (pneumothorax, haemothorax, pulmonary contusion) not detected on clinical examination and plain radiography. However, there is no evidence to suggest that a better patient outcome follows routine scanning. Different trauma centres favour aggressive and conservative management of small pneumothoraces in the ventilated patient.

LUNG FUNCTION
Formal assessment of lung function is most commonly required for patients who experience difficulty in weaning where measurements of peak flow, vital capacity, and respiratory muscle strength may be useful (see reviews later in this series by Goldman and by Hart and Simonds). An airway connection between the endotracheal tube and a hand held spirometer can give accurate and reproducible results. A vital capacity of 10 ml/kg is usually required to sustain spontaneous ventilation. If respiratory muscle weakness is suspected, measurements should be performed sitting and supine. A supine reduction of 25% or more indicates diaphragmatic weakness. Direct measurement of diaphragm strength is useful where borderline results are obtained from spirometric testing, in uncooperative patients, or in those with lung disease that impairs spirometric measurements. Transdiaphragmatic pressure, an index of the strength of diaphragmatic contractility, is measured by peroral passage of balloon manometers into the oesophagus and stomach. A volitional measurement is made by asking the patient to sniff forcefully against manometers into the oesophagus and stomach. A volitional measure-ment is made by asking the patient to sniff forcefully against manometers into the oesophagus and stomach. A volitional measure-

ARF and diffuse pulmonary infiltrates

Pneumonia likely

Yes

No

First line antibiotic regimen

Treatment failure

Pulmonary artery catheter

Echocardiogram

CT thorax

Bronchoscopy and BAL

Open lung biopsy

Cardiac cause

Pulmonary embolism

see Table 1

Figure 2 Suggested respiratory investigations in patients with acute respiratory failure (ARF) and diffuse pulmonary infiltrates. BAL = bronchoalveolar lavage.

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INVESTIGATION OF THE PATIENT WITH ARF AND DIFFUSE PULMONARY INFILTRATES

The syndrome of ARF and diffuse pulmonary infiltrates consistent with pulmonary oedema excluding haemodynamic causes is termed lung injury and can be defined as ALI or ARDS if the oxygenation defect is sufficiently severe. Identifying the conditions that precipitate ARDS or which cause a pulmonary disease with a different pathology but a similar clinical presentation is crucial to management because many have specific treatments or prognostic significance (table 2). A simple scheme for investigating ARF and diffuse pulmonary infiltrates is shown in fig 2, although investigations not specifically targeting the lung may be equally important—for example, serological tests in the diagnosis of diffuse alveolar haemorrhage (see review by Griffith and Brett later in this series).

Many patients develop respiratory failure while being treated for presumed pneumonia. The diagnosis of high permeability pulmonary oedema is made by excluding cardiac and haemodynamic causes because there is no simple and reproducible bedside method for assessing permeability of the alveolar-capillary membrane. Where possible we perform thoracic CT, bronchoscopy, and lavage in patients with lung injury in order to diagnose underlying pulmonary conditions and their complications such as abscess, empyema, and pneumothorax (fig 1). Repeating these investigations should be considered at any time it is felt that the patient is not recovering as predicted. Occasionally, OLB may be required. In our practice this has revealed a variety of pulmonary diseases including herpetic pneumonia, organising pneumonia, bronchoalveolar cell carcinoma, and disseminated malignancy.

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REFERENCES


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