

## Introduction

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Respiratory physicians have traditionally been concerned with diseases that restrict the exchange of oxygen and carbon dioxide across the alveolar-capillary membrane. Research into effective therapeutic interventions in pulmonary medicine has been aimed for the most part at improving bronchial and alveolar patency, or supporting respiratory muscle function. In countries other than the United Kingdom, however, pulmonary physicians have for many years been concerned with the care of the critically ill. This seems entirely appropriate, as in these circumstances the uptake of oxygen within and beyond the lung assumes considerable therapeutic importance. The movement of oxygen, the regulation of its distribution between and within tissues, and the monitoring of cell metabolism are now the subjects of major research programmes. In North America and, to a lesser extent, in continental Europe these issues are rightly seen as the legitimate concern of pulmonary physicians; but in the UK anaesthetists have tended to dominate clinical intensive care. The current series of articles aims to highlight clinical problems within the intensive care unit to which respiratory medicine can make a unique contribution. Appropriately, the series starts with a review of the incidence and management of nosocomial pneumonia, increasingly recognised as an important cause of morbidity in the critically ill. Nosocomial infection of the respiratory tract may be due either to translocation of bacteria through the gut wall into the portal circulation or to upward migration and contamination of the bronchial tree via the endotracheal tube. Selective gut decontamination with non-absorbable antibiotics is now known to reduce the incidence of nosocomial infection in ventilated patients, though a significant reduction in mortality has not yet been found.<sup>1</sup>

Two reviews deal with the injured lung, assessing prospects for new pharmacological interventions in the adult respiratory distress syndrome (ARDS) and discussing current and future approaches to mechanical ventilatory support. The prognosis in established ARDS remains poor and has stimulated clinical trials of a wide variety of anti-inflammatory agents. Although corticosteroids have beneficial effects in animal models this success has not been reproduced clinically.<sup>2</sup> Nevertheless, the possibility that certain subgroups of patients may benefit from steroid treatment has not been excluded, particularly among the few patients

who remain ventilator dependent in the rarely seen chronic fibrotic phase.<sup>3</sup> The pharmacological manipulation of the immunoinflammatory cascades thought to precipitate the endothelial injury associated with sepsis is therapeutically attractive and human monoclonal endotoxin antibody has been shown recently to reduce mortality significantly when given to patients with Gram negative bacteraemia.<sup>4</sup> The adult respiratory distress syndrome is associated with abnormalities of surfactant function and early anecdotal reports suggest that surfactant replacement therapy may have a role. The availability of synthetic surfactants will result in some clinical trials—although, as the surfactant abnormality in ARDS appears to be a secondary phenomenon, such treatment is unlikely to have as profound an effect as has been observed in neonates.<sup>5</sup>

Several alternatives to conventional ventilation in ARDS are now available and have been investigated to varying degrees. The assessment of all such techniques is limited by difficulties in designing proper comparative studies and by the time required to recruit a large number of pathologically similar patients. The maintenance of lung volume combined with treatments designed to limit the extent of ventilator induced lung injury is now emerging as the most favoured strategy. Clearly, the extent to which the newer modes of mechanical ventilation are successful in achieving this end will determine the extent to which techniques such as extracorporeal gas exchange (ECGE) are developed further.<sup>6</sup> Although theoretically attractive as a means of “resting” the injured lung and avoiding the damaging effects of mechanical ventilation, ECGE is costly and fraught with complications and has not yet been shown to be effective in controlled trials.<sup>7</sup> Nevertheless, current improvements in ventilatory techniques and our increasing awareness of advances in microbiological and pharmacological treatment suggest that means of improving the persistently disappointing survival figures in ARDS are not far away.

A fourth paper considers pulmonary vascular control mechanisms in modulating ventilation: perfusion mismatch and the clinical effects of lung injury. The phenomenon of hypoxic pulmonary vasoconstriction was first described in 1946, but its underlying mechanism remains unknown. Nevertheless, the importance of hypoxic pulmonary vasocon-

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striction in the regulation of pulmonary blood flow and its role in diverting blood away from areas of unventilated lung is clinically significant. Thus, although increased pulmonary vascular resistance as a consequence of hypoxic pulmonary vasoconstriction may occur in patients with acute or chronic hypoxia secondary to parenchymal lung disease, leading to undesirable pulmonary hypertension, the loss of hypoxic pulmonary vasoconstriction in pneumonia or ARDS may lead to shunting of blood through poorly ventilated areas of lung with equally serious clinical consequences. The therapeutic manipulation of hypoxic pulmonary vasoconstriction according to clinical circumstances might therefore be considered highly desirable.<sup>8</sup>

The consequences and clinical management of pulmonary thromboembolic disease are reviewed in a fifth paper, which includes an evaluation of the impact of thrombolytic treatment on this problem and the re-emergence of surgery as a therapeutic option in chronic venous thromboembolism.<sup>9</sup>

A thorough understanding of the constraints on oxygen transport from the lungs to the tissues is necessary for the appropriate management of patients in respiratory failure and is the subject of the final review in the series. Most of the research effort on improving the prognosis of patients in acute respiratory failure has been aimed at improving the means of supporting the injured lung. The distribution of oxygen between different tissues and the monitoring of cell metabolism and vitality are now major concerns of researchers in the area, particularly as investigators have recognised that the endothelium is an important regulatory body in pulmonary<sup>10</sup> and systemic<sup>11</sup> vascular control and that endothelial damage and loss of integrity have important implications for the development of

both ARDS and the syndrome of multiple organ failure.

The body of knowledge now required to manage patients within the intensive care unit is enormous and training in critical care is still in its infancy in the UK.<sup>12</sup> We hope that this series of articles will point out the important part that respiratory medicine should play in developing appropriate and effective investigations and therapeutic interventions for the critically ill patient with inadequate oxygenation.

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