Part II: Respiratory Failure

Chapter 25: Adult Respiratory Distress Syndrome

T E Oh

The adult respiratory distress syndrome is a form of respiratory failure resulting from a variety of direct and indirect pulmonary injuries, all of which present with similar pathophysiological changes. Names which have been used for this syndrome include "wet lung", "shock lung", "post-traumatic pulmonary insufficiency", "adult hyaline membrane disease", "ventilator lung" and "pump lung". The syndrome is characterized by a clinical picture of marked respiratory distress, diffuse pulmonary infiltration on chest radiography, reduced pulmonary compliance and marked increase in alveolar-arterial oxygen difference (A-aDO_2) (Table 1), and is now most commonly known as the adult respiratory distress syndrome (ARDS).

Aetiology

A list of clinical conditions which have been implicated in the causation of this syndrome is shown in Table 2. These may affect the lungs directly (i.e. aspiration) or indirectly (i.e. sepsis). Shock is not a prerequisite for the development of ARDS. Major risk factors appear to be sepsis, aspiration, lung contusion, and multiple fractures. The true incidence is unknown and may be only 7% of at risk patients.

Pathophysiology

A proposed pathophysiological process of ARDS is shown in Figure 1. Pulmonary endothelial injury, "capillary leak", and surfactant abnormalities result in interstitial and alveolar oedema. Attenuated alveolar type I cells are lost and replaced by cuboidal microvillous Type II cells resulting in thickened alveolar walls. The interstitium becomes infiltrated with inflammatory and other cells, while many alveoli are filled with proteinaceous and haemorrhagic fluid debris. Hyaline membrane, focal atelectasis, and capillary micorembolism are common findings. Pulmonary fibrosis appears and progressively obliterates pulmonary architecture, including the microvasculature.

The pathological changes result in reduced functional residual capacity (FRC), increased shunt effect, reduced lung compliance, and gross hypoxaemia. The role of abnormal surfactant is speculative. Bronchoalveolar lavage fluids from ARDS patients have demonstrated abnormally aggregated and inactive surfactant.

Pathogenesis

The mechanism of lung damage is controversial, but the concept of "non-cardiogenic capillary leak" is over-simplified. Post-mortem, clinical and animal studies have suggested certain hypotheses, the two most significant are discussed below. However, no mechanism or common factor has been established as a common pathway to the acute lung injury of ARDS.

1. Complement Activation

ARDS has been suggested to be initiated by complement activation, a common consequences of predisposing events. Complement activation causes leuocyte sequestration in pulmonary capillaries. The aggregated neutrophils injure endothelial cells through unknown mechanisms which liberate toxic oxygen (superoxide) radicals, arachidonic acid metabolites, and proteases. In addition, the proteases destroy structural proteins (such as collagen, elastin, and fibronectin) as well as plasma proteins (thus promoting further local inflammatory changes). Normal pulmonary antiproteases, i.e. alpha1 antitrypsin are inactivated by oxygen radicals, leading to increased injury.

Complement activation has been shown in sheep experiments, and the presence in plasma of a peptide product of activated complement, C5a, has been reported to accurately predict ARDS. Broncho-alveolar lavage (BAL) studies have detected the presence of neutrophils, proteolytic enzymes, chemotactic factors and abnormal antiproteases in lavage washings.

2. Fibrinolysis and Platelet Aggregation

Activation of the clotting system may be a causative mechanism of ARDS from trauma. ARDS may be related to intravascular coagulation and platelet aggregation. Disseminated intravascular coagulation (DIC) is a common finding in ARDS. Platelet-fibrin thrombi have been found in post-mortem lungs of patients with ARDS. The platelet-fibrin micro-emboli release vasoactive substances, such as serotonin and prostaglandins. Fibrinolysis produces fibrinogen degradation products (FDPs) which together with vasoactive substances, may injure endothelium and pulmonary microvasculature. The FDP "D antigen" has been identified in patients who develop ARDS and may be a marker or mediator of injury.

Both hypotheses, however, suffer from sparse clinical evidence. Complement activation is non specific and has no predictive value. ARDS may develop in neutropaenic patients (i.e. without neutrophil activation). BAL findings are non specific, and from the airway endothelium, which may be different from the vascular endothelium. The pathogenesis may be multifactorial, with complement and neutrophil activation, reticular endothelium system dysfunction, and direct toxicity of endotoxin, oxygen and other factors being implicated.

Clinical Presentation

The syndrome usually develops insidiously 24-72 hours following the precipitating event. The usual features are dyspnoea, tachypnoea, cyanosis and fine crepitations in both lung fields. Arterial blood gases reveal severe hypoxaemia and an increased A-aDO_2. Chest radiography shows widespread, diffuse opacification. As the disease progresses, lung compliance decreases and the dead space:tidal volume ratio increases. An increasing minute volume is required to maintain an adequate arterial PaO_2.

ARDS may develop in patients who are already on mechanical ventilation, and is manifested by the deterioration of the above pulmonary function parameters.

Management

Treatment is directed against the precipitating conditions, but is otherwise empirical and supportive.

1. Mechanical Ventilatory Support

The mainstay of treatment is mechanical ventilatory support via na endotracheal tube or a tracheostomy if ventilation is prolonged. Continuous mechanical ventilation (CMV) using intermittent positive pressure ventilation (IPPV) may be used. Alternatively, some spontaneous breathing component, i.e. intermittent mandatory ventilation (IMV) or pressure support may be used. This may help reduce mean airway and intrathoracic pressure and be advantageous in some patients. The optimal mode of ventilation is not known.

If oxygenation cannot be maintained at an adequate level with an inspired oxygen concentration less than 60%, then positive end expiratory pressure (PEEP) should be used. PEEP helps recruit or maintain open lung units that are otherwise collapsed, and partly restores the reduced FRC, thus improving oxygen transport across the lung. PEEP does not, however, decrease lung water and this is not a mechanism for gas exchange improvement. Early "prophylactic" use of PEEP does not prevent the development of subsequent progress of ARDS. A range of 5-15 cm water (0.5-1.5 kPa) of PEEP is usually used. The benefits of PEEP are counterbalanced by the decreased cardiac output and increased risk of barotrauma. Higher levels of PEEP have been advocated, but better results have not been consistently substantiated, despite the increased advantages.

The optimal level of PEEP is controversial. "Best" or "optimal" PEEP has been reported to mean various levels, producing:

(a) the lowest shunt, i.e. venous admixture below 20% cardiac output;

(b) the maximum oxygen delivery to tissues;

(c) adequate arterial oxygenation at the lowest inspired oxygen concentration; and

(d) maximum improvement in lung compliance.

The minimal level of oxygen necessary to achieve adequate oxygenation (i.e. PaO_2 of approximately 60 mmHg, 8.0 kPa) should be supplied. Oxygen in high concentrations is toxic to the lungs. PEEP allows reduction of inspired oxygen, which should if possible, be kept below 50%. Nevertheless in critically hypoxaemic patients, PEEP as well as 100% oxygen may be required. PEEP should thus be adjusted to produce the "optimal" clinical improvement, with monitoring of haemodynamic, respiratory and oxygenation variables.

Recent developments in high frequency ventilation may minimize mean intrathoracic pressure, but do not appear to reduce mortality.

2. Fluid Management

Fluid administration must be carefully controlled to allow improvement of systemic and pulmonary perfusion without aggravating the pulmonary oedema. Central venous pressure monitoring may be adequate, but a more reliable guide to fluid management is the measurement of pulmonary capillary wedge pressure (PCWP) using a Swan-Ganz catheter. Indeed, it is necessary to measure PCWP to properly diagnose ARDS. The choice of fluid replacement remains controversial. Colloid replacement to restore the Starling relationship (Table 3) between hydrostatic and colloid osmotic pressure is commonly used.

The use of concentrated salt-poor albumin with concomitant diuretic (frusemide) therapy is believed to be benficial. Plasma colloid osmotic pressure is elevated, which may aid in removing extravascular lung water. Concentrated albumin infusion also allows fluid and salt restriction without significant haemodynamic deterioration. However, it has also been suggested that extravascular lung water may be increased with the use of colloid compared with crystalloid infusions. Clinically, there appears no advantage in the of colloid or crystalloid.

Table 3. The Starling Equation

$$F = K ((P_c - P_i) - (II_c - II_i))$$

F = Fluid flux favouring extravasation of fluid
K = Membrane permeability coefficient
P_c = Pulmonary capillary pressure
P_i = Interstitial space hydrostatic pressure
II_c = Capillary colloid osmotic pressure
II_i = Interstitial space colloid osmotic pressure

3. Cardiac Support

Optimal preload is achieved with fluid administration according to the PCWP. Inotropic agents such as adrenaline, dopamine or dobutamine are necessary in circulatory failure. Vasodilators are used by some to decrease afterload. There has been recent interest in pulmonary hypertension in ARDS, which signifies a poor prognosis, and attempts to reduce the pulmonary arterial pressures have not met with significant success.

Since many treatment variables are involved, serial cardiac output and shunt fraction estimations, and continuous mixed venous oxygen saturation monitoring are useful to derive optimal fluid and inotrope delivery as well as ventilation settings, especially PEEP. It is important that oxygen transport is optimized, as oxygen consumption in ARDS appears to be *dependent* on oxygen delivery. Hb should be kept at 12-13 g/dL, and hypophosphataemia (for 2,3-DPG) and systemic alkalosis avoided.

4. Nutrition

Adequate nutrition should be supplied to minimize muscle wasting and immune deficiency.

5. Physiotherapy

Physiotherapy, adequate removal of secretions and frequent posture changes of the patient are important. Self-sealing endotracheal tube adaptors are necessary for tracheal suctioning of patients ventilated on PEEP.

6. Other Therapeutic Consideration

(a) *Corticosteroids*

The use of corticosteroids is controversial. Steroids may reduce lung injury by inhibiting complement-induced leucocyte aggregation, and reduce capillary permeability if used early for a short period (i.e. 1-2 g methylprednisolone/day for 24-48 H). There is however, the potential effect of reducing host defences with increased mortality, and the role of steroids in ARDS awaits further confirmation.

(b) *Positive airway pressure*

Continuous positive pressure breathing with spontaneous ventilation (i.e. continuous positive airway pressure) has been used in the management of ARDS. However, many patients in severe respiratory distress cannot tolerate this mode of ventilatory support.

(c) *Antibiotics*

The specific antibiotic should be used for organisms cultured, including anaerobic organisms. Blind use of prophylactic broad spectrum antibiotic cover should be avoided.

(d) *Heparinization*

This will depend on criteria for the diagnosis of DIC and not for ARDS.

(e) *Extracorporeal membrane oxygenators (ECMO)*

The use of ECMO for prolonged periods has been disappointing, resulting in the same mortality as that of conventional treatment. A combination of ECMO (for CO_2 removal) and low frequency ventilation to provide oxygen uptake has also been reported (LFPPV an ECCO2R).

(f) *Ultrafiltration*

The use of ultrafiltration (with or without renal dialysis) to remove interstitial water, may be indicated in patients less responsive to diuretics. It has been reported to be useful in septic patients with ARDS, postulated to be due to the removal of harmful vasoactive peptides. More clinical evaluation is however, required.

(g) *Experimental agents*

There is interest in using various pharmacological agents to inhibit postulated pathogenetic pathways of ARDS or vasoactive mediators. Hence vasodilators, prostacyclin, prostaglandins, ketanserin, fibronectin, free radical scavengers, non-steroidal antiinflammatory drugs, and damazol have been tried with no real clinical success. Many therapeutic mechanisms are speculative and, at best, warrant clinical trials.

Outcome

Patients with ARDS may recover. Otherwise progressive deterioration, commonly accompanied by sepsis, coagulopathy, and multi-organ failure, lead to death within 3-4 weeks. Death is attributed to multi-organ failure via septic mechanisms, rather than hypoxaemia per se. The mortality rate of over 50-60% has remained unchanged over the last decade despite advances in treatment modalities. Present poor figures may be a result of the stringent diagnostic criteria of ARDS today. Most survivors have normal lung function although abnormalities in gas transfer persist. Other survivors have a reduction in vital capacity and obstruction of air flow.