CPAP and PEEP—A Perspective

The treatment of severe, progressive arterial hypoxemia in patients who have intrapulmonary veno-arterial shunting has undergone a remarkable evolution during the past 15 years. The intermittent “deep breath” was introduced in the early 1960’s. Subsequently, patients requiring intermittent positive-pressure ventilation (IPPV) received repeated “deep breaths” with the use of automatic intermittent “sighs” or with large tidal volumes and a slow respiratory frequency. In the late 1960’s, the concept of positive end-expiratory pressure (PEEP) was reintroduced as an adjunct to therapy of patients who had progressive and potentially fatal hypoxemia. Subsequently, this concept was applied to the newborn with idiopathic respiratory distress syndrome both in conjunction with IPPV and during spontaneous, unassisted ventilation (CPAP). When all of these techniques have failed, selected adult patients have survived with the use of a membrane oxygenator and extracorporeal circulation.

The application of CPAP and PEEP in the treatment of arterial hypoxemia proved to be one of the most important advances in the history of respiratory therapy. However, the mechanisms by which elevated end-expiratory pressures increase arterial oxygen tension remain unclear. Indications and contraindications in various cardiopulmonary disorders and the relationships between the magnitude of end-expiratory pressure, arterial oxygen tension, and effects on vital systems await precise definition. The ultimate effects of various end-expiratory pressures in the normal and the diseased lung, and the incidences of serious complications in different disease states, must be determined before these techniques can be used with maximum benefit and minimum risk. It is appropriate at this time to establish a perspective on CPAP and PEEP in clinical medicine.

Historical Development

The use of intermittent and continuous positive airway pressure in spontaneously ventilating patients with pulmonary disease was described in 1878 by Oertel. It remained for Barach and associates to reintroduce this concept for the relief of hypoxia associated with acute pulmonary edema in 1938. Subsequently, Gagge in 1945, demonstrated the improvement in arterial oxygen saturation achieved with CPAP in normal man at high altitude. Over the next 25 years, CPAP was advocated by many clinicians as a valuable adjunct to the treatment of pulmonary edema and chronic obstructive pulmonary disease. However, pressures to 15 torr above atmospheric were shown to decrease cardiac output significantly in subjects with normal lungs and in some, but not all, patients with cardiopulmonary disease. This undesirable effect of CPAP retarded its ex-
tended use during anesthesia and in treatment of arterial hypoxemia in patients with pulmonary disease.

In 1959, Frumin and co-workers quantified the relation between increases in arterial oxygen tension, functional residual capacity (FRC), and positive end-expiratory pressure during mechanical ventilation in anesthetized, paralyzed normal man. Yet another decade passed before Uzawa and Ashbaugh\(^6\) proved that in dogs with extensive pulmonary damage PEEP resulted in significantly improved arterial oxygen tensions that more than offset the depression of cardiac output. The treated animals had improved compliance and lower ventilation requirements than dogs receiving IPPV at zero end-expiratory pressure. Concomitantly, Ashbaugh and his group applied PEEP to the treatment of patients with the adult respiratory distress syndrome,\(^7\) resulting in striking improvements in arterial oxygen tension and survival. Shortly thereafter, McIntyre\(^8\) showed that 4 torr PEEP in patients who had pneumonia or adult respiratory distress syndrome increased \(P_aO_2\) and FRC without detrimental effect on cardiac output. These reports, and the subsequent paper by Gregory on the use of CPAP in the idiopathic respiratory distress syndrome of the newborn,\(^9\) initiated renewed, vigorous interest in the use of elevated end-expiratory pressures for the treatment of patients of all ages who had arterial hypoxemia resulting from cardiopulmonary disease.

**CPAP in Newborn Respiratory Distress Syndrome**

Interest in the use of increased end-expiratory pressure for the treatment of the newborn with idiopathic respiratory distress syndrome (IRDS) and other cardiopulmonary disorders stems not only from the work cited above but also from the observation of Harrison\(^10\) in 1968 on the importance of grunting as a mechanism by which the newborn can increase arterial oxygen tension. He found that orotracheal intubation and zero end-expiratory pressure with spontaneous ventilation in infants with RDS significantly depressed \(P_aO_2\). In 1970, Lewellyn and Swyer\(^*\) first reported the efficacy of PEEP in association with IPPV in the treatment of newborns with respiratory failure due to IRDS. The following year, the classic paper of Gregory and co-workers,\(^6\) describing the improvements in \(P_aO_2\) and survival associated with CPAP, appeared. These infants were breathing spontaneously through an orotracheal tube, mechanical ventilation being added only if severe hypercapnia or apnea occurred. Shortly thereafter, Cherwick and Vidyasagar\(^11\) described similar improvement in arterial oxygen tensions with continuous negative chest-wall pressure in newborns with IRDS using a cuirass type of ventilator. This technique did not necessitate tracheal intubation of the infant with adequate alveolar ventilation, but access to the baby was cumbersome and leaks around the neck seal common. The attempt of Gregory *et al.* to achieve CPAP without tracheal intubation using a headbox\(^9\) met with limited success because of problems with the neck seal and limited access to the infant's head. By using nasal prongs and CPAP, Kattwinkel and associates\(^12\) achieved improved arterial oxygenation without tracheal intubation in infants weighing more than 1,200 g at birth who had moderate hypoxemia resulting from IRDS. Since the newborn is an obligate nose breather, the increased airway pressure is transmitted to the trachea and lungs. This technique is now being used throughout the United States and Canada for early treatment of the less severely ill newborns with IRDS.

Gregory *et al.*\(^9\) also found that some infants with irregular breathing and periods of apnea developed a regular ventilatory pattern and frequency with application of CPAP. Spiedel and Dunn\(^13\) recently studied and confirmed this observation in infants with IRDS using a Gregory headbox. The mechanism for this effect of CPAP remains unclear. During discontinuation of CPAP in intubated infants,

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arterial oxygen tension often decreases when end-expiratory pressure is reduced to zero. This retards tracheal extubation and often results in prolonged use of low levels of CPAP. Berman and colleagues have shown in infants recovering from IRDS that zero end-expiratory pressure decreased arterial oxygen tension and FRC in infants who had acceptable PaO₂ levels at CPAP of 1.5 torr. Following extubation, PaO₂ and FRC returned to levels equivalent to those at 1.5 torr CPAP. Whether this occurs in other cardiopulmonary disorders of infancy and childhood has not been determined, but it would seem reasonable to extubate infants' tracheas directly from 1.5 torr CPAP rather than subject them to a trial at zero end-expiratory pressure.

**CPAP in Congenital Heart Disease**

In 1987, Eisenmenger described the apparent stiffness of the lungs of children who had ventricular septal defects. This astute observation has been confirmed recently by Griffin et al., who found decreases in total pulmonary compliance in infants with ventricular septal defects and pulmonary arteries hypertension, as well as in infants who had other cardiovascular lesions associated with excessive pulmonary blood flow and pulmonary vascular engorgement. Abnormally low ventilation-perfusion ratios are known to exist in these patients and must contribute to their arterial hypoxemia. Although specific proof is lacking, it appears likely that the small airways of such infants may close prematurely as a result of edema of surrounding tissues, thus further reducing the normally smaller closing volume of the infant or small child. Gregory et al. recently described an alarming decrease in FRC to levels approximately a third of normal following thoracotomy in infants with congenital heart disease. This must cause closing volume to exceed FRC and engorg

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have been accomplished without superb medical and nursing care.

**Sequelae of CPAP**

As with all techniques in medicine, CPAP and PEEP are not free of adverse effects and complications. The decrease in cardiac output with CPAP in normal man has long been appreciated and underlies the depression of renal plasma flow and urine flow described by Drury in 1947. The decrease in urinary output also may be partly mediated by the release of antidiuretic hormone.

Although the addition of PEEP to IPPV in adults has not been associated with an increased incidence of pneumothorax or pneumomediastinum, CPAP and PEEP in the newborn who has IRDS result in an incidence of lung rupture of approximately 20 percent, double that observed at zero end-expiratory pressure. Unequal distribution of gas with overdistention of the more compliant areas of the lung may be responsible. However, in these infants CPAP and PEEP have been associated with a decrease in bronchopulmonary dysplasia, a condition characterized by chronic diffuse fibrosis and emphysema that may be a manifestation of pulmonary oxygen toxicity. This reduction in the incidence of bronchopulmonary dysplasia could reflect the ability to achieve a satisfactory Pao2 at lower inspired oxygen concentrations in infants receiving elevated end-expiratory pressure.

**Future of CPAP**

Limited numbers of adult patients who have acute respiratory failure and progressive hypoxemia due to diffuse alveolar disease refractory to conventional therapy with IPPV and PEEP have responded favorably and recovered with levels of PEEP as high as 32 torr. These extreme pressures in this group of patients did not decrease cardiac output or increase the incidence of pneumothorax. Application of such levels of PEEP in infants with similar pulmonary involvement has not been evaluated, but would probably produce an unacceptable incidence of lung rupture.

As Pang and Mellins recently stated, the responses of different patients to CPAP or PEEP will depend not only on the pulmonary disease and its effect on lung volume and compliance, but also on the amount of pressure applied, airway resistance, the volume and distribution of circulating blood, and the function of the right ventricle. The optimal end-expiratory pressure must be defined in terms of oxygen transport (arterial oxygen content x cardiac output) to the tissues, as recently done by Suter and coworkers in adult patients. Determination of this best level of CPAP or PEEP and its physiologic effects in various conditions of infancy and childhood has become a major goal of clinical research in pediatric pulmonary disease.

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