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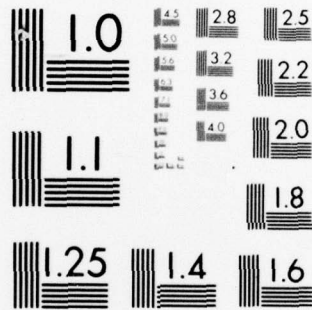
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PULMONARY RESPONSE TO HEMORRHAGIC SHOCK

FINAL REPORT

RESPONSIBLE INVESTIGATOR: HERBERT B. HECHTMAN, M.D.

February 24, 1978

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Summary

Studies have shown that end expiratory pressure may induce a humorally mediated decrease in cardiac output. The agent is secreted as a result of lung stretch and acts on the heart to decrease contractility.

Key Words

LUNG STRETCH - ENDOTHELIUM - DECREASED CONTRACTILITY -
END EXPIRATORY PRESSURE

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PULMONARY RESPONSE TO HEMORRHAGIC SHOCK

This three month period was designed to complete our initial studies on the causes of the decline in cardiac output during PEEP. Three papers have been accepted for publication in Surgery. One of these papers will be presented at the Society of University Surgeons in February 1978.

The mechanism of the decrease in cardiac output (C.O.) observed with the use of positive end expiratory pressure (PEEP) is debated. The literature cites decreased filling pressure of the right and left ventricles, decreased coronary blood flow, or increased afterload to the right ventricle as responsible factors, which act alone or in concert.

Eight dogs on mechanical ventilation underwent complete chest wall excision so that pleural pressure was always atmospheric. Central venous, pulmonary and systemic arterial and left atrial catheters were placed. Application of 15 cm of PEEP caused a significant drop in thermodilution measured C.O. from a mean of 3.03 to 2.06 l/min ($p < .01$) and mean systemic arterial pressure (MAP) from 105 to 69 mm Hg ($p < .001$). Concurrently, there was a rise in mean central venous pressure (CVP) from 18.0 to 23.3 mm Hg ($p < .01$) and mean left atrial pressure (LAP) from 6.3 to 8.0 mm Hg ($p < .03$). Tightening of a pulmonary artery choker to reproduce the elevated pulmonary arterial pressure observed with 15 cm of PEEP failed to cause a drop in C.O. There was also no

significant change in CVP, LAP or MAP.

The data indicate that PEEP may depress the C.O. independent of intrathoracic pressure. This drop in C.O. is accompanied by a rise in both right and left ventricular filling pressures, the criteria for biventricular failure. Furthermore, C.O. does not drop when right ventricular afterload is increased to a level equal to that at which PEEP caused a fall in C.O. The results are consistent with the action of a neural and/or humoral agent on cardiac function and suggest an additional mechanism whereby PEEP may induce hemodynamic abnormalities. (1)

Two additional experimental designs were used to study the mechanism of the decreased cardiac output associated with the use of positive end expiratory pressure (PEEP). In the first study of nine dogs the application of 15 cm H₂O PEEP led to a decrease in cardiac output (CO) from 2.68 L/min \pm 1.05 SD to 2.01 L/min \pm 1.26 SD ($p < .05$) concomitant with an increase in transmural central venous pressure of 5.2 mm Hg \pm 0.9 SD to 8.4 mm Hg \pm 2.7 SD ($p < .05$) and a slight increase in transmural left atrial pressure of 6.8 mm Hg \pm 3.3 SD to 7.3 mm Hg \pm 3.6 SD ($p < .1$). These data are consistent with altered ventricular performance. In a second study, nine pairs of dogs were cross circulated. Application of 15 cm H₂O PEEP to one member of the experimental pair led to a decrease in the CO of the other member from 2.71 L/min \pm 0.98 SD to 2.21 L/min \pm 0.81 SD ($p < .001$). This decrease returned towards baseline with the removal of PEEP ($p < .02$). Results

indicate that one mechanism whereby PEEP reduces the cardiac output is through the action of a humoral agent. (2)

Evidence exists indicating that varied ventilatory patterns will alter pulmonary metabolic activity. This study examines the effects of positive end expiratory pressure (PEEP) on metabolically mediated changes in cardiac contractility. Experiments were conducted in a group of 33 temperature controlled, isolated, paced, canine hearts undergoing coronary perfusion from a support dog, at a fixed rate of 1.3 ml/min·g tissue. A left ventricular balloon was used to construct Starling curves during each period that a new variable was applied to the support dog. Application of 15 cm H₂O PEEP led to a fall in peak systolic pressure (PSP) in the isolated heart. This occurred at each of five diastolic pressures (DP) tested within the range 7.1 to 19.4 mm Hg ($p < .01$). Thus, at a DP of 19.4 mm Hg, PSP fell from 132 to 112 mm Hg after PEEP was applied ($p < .01$). Bleeding the support dog while on 0 cm H₂O PEEP (ZEEP) to reduce cardiac output (CO) to levels observed on PEEP led to an adrenergic response. PSP increased relative to the PSP observed during ZEEP ($p < .01$). PEEP plus blood infusions to restore CO of the support dog to baseline levels, led to myocardial depression ($p < .01$). Finally 15 cm H₂O PEEP was applied while pleural and airway pressures were equal. This condition was achieved by coupling the expiratory port to bilateral thoracostomy tubes. The functional residual capacity was held constant. The isolated heart was not depressed ($p < .01$). Radio-

immune assays of arterial prostaglandin $F_{2\alpha}$ and $F_{2\alpha}$ metabolites were unchanged during PEEP. Results indicate that lung stretch produced by PEEP causes the release of a humoral agent which decreases left ventricular contractility. (3)

PUBLICATIONS

1. Liebman, P.R., Patten, M.T., Manny, J., Shepro, D. and Hechtman, H.B.: The mechanism of depressed cardiac output on PEEP. Surgery (In press).
2. Patten, M.T., Liebman, P.R., Manny, J., Shepro, D. and Hechtman, H.B.: Humorally mediated alterations in cardiac performance as a consequence of positive end expiratory pressure. Surgery (In press).
3. Manny, J., Patten, M.T., Liebman, P.R., Grindlinger, G.A. and Hechtman, H.B.: PEEP, lung stretch and decreased myocardial contractility. Surgery (In press).

Personnel Listing

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