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mechanically-ventilated neonates

# Changes in Mean Esophageal Pressure during Early Recovery in Mechanically-Ventilated Neonates—Evidence for Airway-Closure and Gas-Trapping?

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## Summary

**We studied transmission of a constant mean airway pressure through the lungs to the pleural space in nine mechanically-ventilated neonates with low-compliance lung disease. Infants were studied for 3.1 ± 1.6 hr during a period of clinical improvement, but at a time when lung compliance was still markedly reduced. Two of our infants were studied during recovery from fluid overload, while seven infants with hyaline membrane disease were studied at a stage of disease during which maximal diuresis has been found to occur. During the study period, mean esophageal pressure *decreased* in all infants from 5.6 ± 1.3 to 4.2 ± 1.8 cm $H_2O$ ($P < 0.001$) while total compliance increased slightly.**

## Speculation

**Edema of the pulmonary interstitium may contribute to airway-closure and gas-trapping. We propose that a loss of fluid from the interstitium during early recovery from low-compliance lung disease may lead to less gas-trapping and a fall in mean esophageal (pleural) pressure.**

Several studies have demonstrated poor transmission of the applied airway pressure to the pleural space during mechanical ventilation of infants with hyaline membrane disease (HMD) (7, 8, 11). Current recommendations for the ventilatory management of HMD include reduction of ventilator pressure once recovery is under way, thereby preventing excessive pressure transmission, pulmonary overdistension and cardiovascular tamponade (4, 8, 11). Esophageal pressure measurements have, therefore, been used to determine optimal airway pressures (2, 12). The use of esophageal pressure measurement to aid ventilator management in infants with HMD in our neonatal unit unexpectedly revealed that, in the very early recovery phase, clinical improvement appeared to be associated with a *fall* in mean esophageal pressure. The present study was therefore designed to measure changes in transmission of applied airway pressure through the lungs to the pleural space during early recovery from low-compliance lung disease.

## MATERIALS AND METHODS

Nine infants with severe lung disease were included in the study. All were mechanically-ventilated with a time-cycled pressure-limited respirator (Baby Bird Ventilator, Bird Corp., Palm Springs, CA). The study was limited to infants who had been paralyzed with tubocurarine chloride, or who were making no spontaneous respiratory efforts. Seven premature infants with a clinical and radiographic diagnosis of HMD were studied. The clinical details are summarized in Table 1. All but one of these infants had been curarized during the initial phase of disease because of poor gas exchange. They remained paralyzed throughout the study period, and tubocurarine was readministered with any signs of returning muscle activity including a negative deflection on the esophageal pressure tracing. One infant had suffered an intraventricular hemorrhage (Tables 1 and 2; no. 3), and respiration was controlled without muscular paralysis. These infants were studied at 39 ± 12 hr of age (mean ± S.D.) during the early recovery phase of their disease. This was arbitrarily defined as the period during which improving gas exchange had allowed a reduction in inspired oxygen ($F_{IO_2}$) and at least two reductions in ventilator pressure settings from requirements at the peak of disease. In addition, two full-term infants were studied at 3½ and 4 days, respectively, (Tables 1 and 2; nos. 8 and 9), at a time of clinical improvement as determined by arterial blood gas (ABG) analysis. The infant with congenital pneumonia was studied after furosemide had been administered for clinical signs of fluid overload. The infant with congenital ichthyosis, coarctation of the aorta, and ventriculoseptal defect was studied during recovery from severe congestive cardiac failure. Both infants were curarized.

The study period commenced when infants were stable, with $F_{IO_2}$ ventilator pressures set to achieve pH > 7.25, $P_{CO_2}$ <45 torr, and $P_{O_2}$ 50 to 70 torr. Esophageal pressure ($P_{es}$), tidal volume (TV), and airway pressure (AP) were measured until the next change in ventilator pressure settings. By studying infants who were not breathing spontaneously and by making measurements during a period of constant ventilator pressure settings, we were able to assess changes in transmission of a constant mean airway pressure (MAP) to the pleural space. ABG analysis and calculation of total compliance ($C_{tot}$) provided some indicators of pulmonary status during the study period.

Esophageal pressure was measured in the distal third of the esophagus. Infants were supine and were not disturbed during the study period. After placement of the esophageal catheter and radiologic confirmation of position, movement was prevented by taping the catheter to the face. In four infants a size 4 French transducer-tipped catheter was used (Millar Mikro Tip Catheter Pressure Transducer, Millar Instruments, Inc., Houston, TX). The use of this catheter for direct measurement of pleural pressure has been reported previously (6). Similar catheters have been used in children and adults to measure $P_{es}$ (1, 19). In four infants a water-filled system was used (2, 7) to measure $P_{es}$. A size 5 or 8 French polyvinyl feeding tube was positioned in the esophagus, and the proximal end connected to a 3-way stopcock which was taped to the chest wall in the midaxillary line. Two additional holes were made in the catheter, and the system was flushed prior to measurements to ensure patency of the holes. The transducer catheter was connected to the stopcock via a Luer adapter and used as the external pressure transducer. The two methods of measuring $P_{es}$ were validated in three rabbits during spontaneous and controlled

Table 1. *Clinical details and blood gas measurements*

| | Birth wt (g) | Diagnosis[1] | Age at study (hr) | Duration of study (hr) | Initial and final blood gas measurements over study period | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | pH | $P_{CO_2}$ | $HCO_3$ | $P_{O_2}$ | $F_{IO_2}$ |
| 1 | 1020 | HMD | 21 | 6 | 7.25 | 38 | 16 | 54 | 0.8 |
| | | | | | 7.25 | 38 | 16 | 73 | 0.8 |
| 2 | 1690 | HMD | 28 | 4 | 7.25 | 45 | 18 | 99 | 0.5 |
| | | | | | 7.27 | 46 | 19 | 77 | 0.4 |
| 3 | 540 | HMD | 36 | 2 | 7.27 | 46 | 19 | 46 | 0.9 |
| | | | | | 7.29 | 43 | 20 | 64 | 0.8 |
| 4 | 1100 | HMD | 52 | 2½ | 7.30 | 47 | 22 | 69 | 0.4 |
| | | | | | 7.37 | 36 | 20 | 74 | 0.3 |
| 5 | 1230 | HMD | 45 | 1 | 7.31 | 38 | 18 | 61 | 0.7 |
| | | | | | 7.30 | 37 | 17 | 65 | 0.7 |
| 6 | 4120 | HMD, IDM | 56 | 2 | 7.53 | 25 | 20 | 69 | 0.21 |
| | | | | | 7.53 | 23 | 18 | 53 | 0.21 |
| 7 | 1800 | HMD | 32 | 2 | 7.32 | 34 | 16 | 82 | 0.75 |
| | | | | | 7.32 | 35 | 18 | 75 | 0.70 |
| 8 | 2720 | Congenital ichthyosis, coarctation of aorta, VSD, CHF | 93 | 4 | 7.40 | 32 | 18 | 74 | 0.28 |
| | | | | | 7.32 | 34 | 16 | 97 | 0.28 |
| 9 | 3500 | Congenital pneumonia, fluid overload | 85 | 4 | 7.41 | 44 | 27 | 47 | 0.7 |
| | | | | | 7.50 | 40 | 30 | 51 | 0.7 |

[1] IDM, infant of diabetic mother; VSD, ventriculoseptal defect; CF, congestive heart failure.

Table 2. *Changes in lung mechanics during study period*

| | Ventilator settings | | Data listed are initial and final measurements over study period | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | Transmission | | | Total compliance | |
| Method for $P_{es}$ | Rate (cycles/min) | Pressure[1] (cm $H_2O$) | MAP (cm $H_2O$) | $MP_{es}$ (cm $H_2O$) | ($MP_{es}$/MAP × 100) | Δ Trans | Tidal volume (ml) | (ml/cm $H_2O$) | % Change |
| 1 Intrapleural | 36 | 25/5 | 12.9 | 6.3 | 49% | −10% | 10.6 | 0.53 | +9 |
| Millar | | | 13.7 | 5.3 | 39% | | 11.6 | 0.58 | |
| 2 Millar | 40 | 27/5 | 17.5 | 6.0 | 34% | −6% | 12.5 | 0.57 | +23 |
| | | | 17.6 | 4.9 | 28% | | 15.4 | 0.70 | |
| 3 $H_2O$ cath | 35 | 27/4 | 11.7 | 5.1 | 43% | −11% | 17.2 | 0.75 | +1 |
| | | | 11.7 | 3.8 | 32% | | 17.5 | 0.76 | |
| 4 $H_2O$ cath | 34 | 30/5 | 17.3 | 5.8 | 33% | −5% | 15.0 | 0.60 | +5 |
| | | | 17.4 | 4.9 | 28% | | 15.8 | 0.63 | |
| 5 Millar | 52 | 26/5 | 10.2 | 6.1 | 60% | −8% | 15.4 | 0.70 | +3 |
| | | | 9.9 | 5.1 | 52% | | 15.8 | 0.72 | |
| 6 $H_2O$ cath | 35 | 25/6 | 14.4 | 6.2 | 43% | −14% | | | |
| | | | 15.5 | 4.5 | 29% | | | | |
| 7 Millar | 48 | 29/5 | 13.8 | 2.7 | 20% | −14% | | | |
| | | | 12.6 | 0.7 | 6% | | | | |
| 8 $H_2O$ cath | 26 | 28/5 | 11.4 | 7.4 | 65% | −5% | 34.5 | 1.5 | +13 |
| | | | 11.5 | 6..9 | 60% | | 39.1 | 1.7 | |
| 9 Millar | 32 | 25/5 | 16.5 | 4.8 | 29% | −16% | 33.2 | 1.7 | +24 |
| | | | 16.9 | 2.1 | 13% | | 42.0 | 2.1 | |
| Mean ± S.D. | Initial value: | | 14.0 ± 3 | 5.6 ± 1.3 | 41.8 ± 14 | −9.9 ± 4.2% | 19.8 ± 10 | 0.9 | +11.1 ± 9 |
| | Final value: | | 14.1 ± 3 | 4.2 ± 1.8 | 31.9 ± 17 | | 22.4 ± 13 | 1.0 | |
| $2P$[2] | | | | $P < 0.001$ | $P < 0.001$ | | | | |
| $1P$ | | | NS | | | | 0.03 | 0.03 | |

[1] Ventilator pressure-peak inspiratory/end expiratory pressure. Transmission, % MAP transmitted to pleural space/esophagus; Δ-Trans, change in transmission over study period.

[2] $2P$, two-tailed paired $t$ test; $1P$, one-tailed paired $t$ test.

ventilation (Figs. 1*A* and *B*). One infant developed a pneumothorax. Direct pleural pressure measurements were obtained in this infant by connecting the transducer catheter and Luer adapter to an 18-gauge needle inserted into the thoracostomy tubing at the beginning and end of the study period. In the other infants, pressure was measured continuously throughout the study period. Esophageal and pleural pressures may be regarded as being similar (7, 16; Fig 1*C*) and will be referred to as $P_{es}$. The transducer was calibrated against a water column, and calibration was checked at the beginning and end of each study period. Pressure was recorded on a 6-channel recorder (Electronics for Medicine VR6—Electronics for Medicine, Inc., White Plains, NY). Mean $P_{es}$ ($MP_{es}$) was determined from the area under the pressure curve at a time when all recordings ($P_{es}$, TV, AP) were completely stable. A representative recording strip is shown in Figure 2. The mean value of three measurements was taken at the beginning and end of each study period.

Airway pressure was recorded continuously using a Statham PM 131 transducer (Gould Statham, Inc., Hato Rey, Puerto Rico) connected to the ventilator pressure line. Mean AP was determined

from the area under the AP curve at the time of $MP_{es}$ determinations. Transmission of pressure from the airway to the esophagus/pleural space was indexed as the ratio of $MP_{es}$/MAP and expressed as a percentage.

TV was measured by means of a heated screen pneumotachograph (Hans Rudolph, Inc., Kansas City, MO) and a Statham PM-5 differential pressure transducer (Gould Statham, Inc.) The flow signal obtained was integrated by a Pulmonary Function Analyzer (Electronics for Medicine, Inc., White Plains, NY). The pneumotachograph was calibrated against known volumes of gas before and after each study period. TV was measured at the beginning and end of each study period. Measurements were made when the TV recording was stable as described above. The mean value of three TV measurements was taken to calculate $C_{tot}$ according to the formula $C_{tot} = \Delta V/\Delta P$ where $\Delta V$ = TV, $\Delta P$ = change in AP.

Arterial blood was drawn from an umbilical catheter in the abdominal aorta for blood gas measurements at the beginning and end of each study period.

Initial *versus* final values for MAP and $MP_{es}$ were analyzed using the two-tailed paired *t* test. Changes in TV and $C_{tot}$ were analyzed by the one-tailed paired *t* test. As a condition for entry into the study was evidence for improving gas exchange (as demonstrated by a reduction in $F_{IO_2}$ and at least two reductions in ventilator pressure settings), there were *a priori* reasons for expecting an improvement in TV (while ventilator settings remained constant) and $C_{tot}$ during the study period. Under these circumstances, a one-tailed analysis is appropriate. The study protocol was approved by the Clinical Investigation Committee, and parental consent was obtained.

## RESULTS

The mean duration of each study period was 3.1 ± 1.6 hr (± S.D.). ABG analysis at the onset and conclusion of each study period showed that gas exchange was stable or improving in all infants while lung mechanics also improved. TV and $C_{tot}$ increased by 11.5 ± 8.1% and 11.1 ± 9%, respectively (mean ± S.D.), in 7

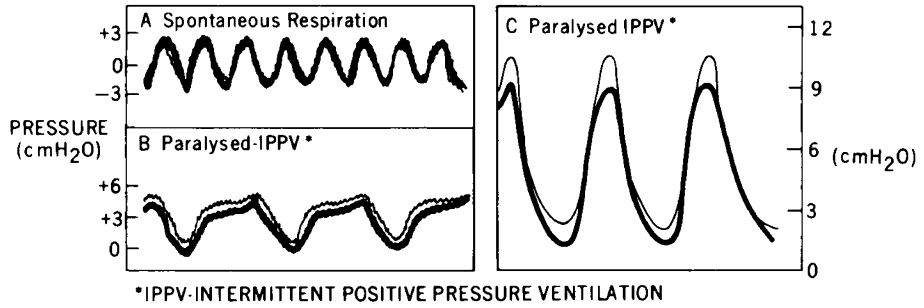


Fig. 1. Pleural and esophageal pressure measurements in rabbits. *A* and *B*, esophageal pressure during spontaneous and controlled respiration using water-filled (▬) and transducer (−) catheters. *C*, direct intrapleural (▬) and esophageal (−) pressure measured with two transducer catheters.

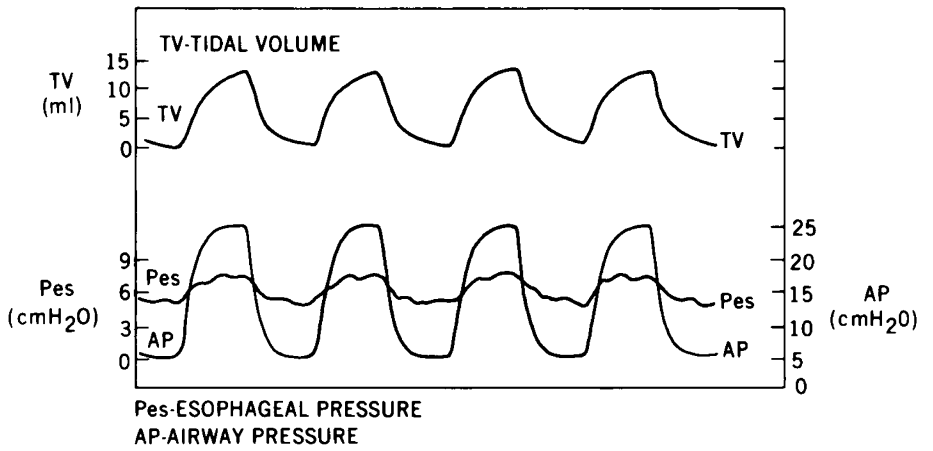


Fig. 2. Sample recording of AP, $P_{es}$, TV at time of measurement.

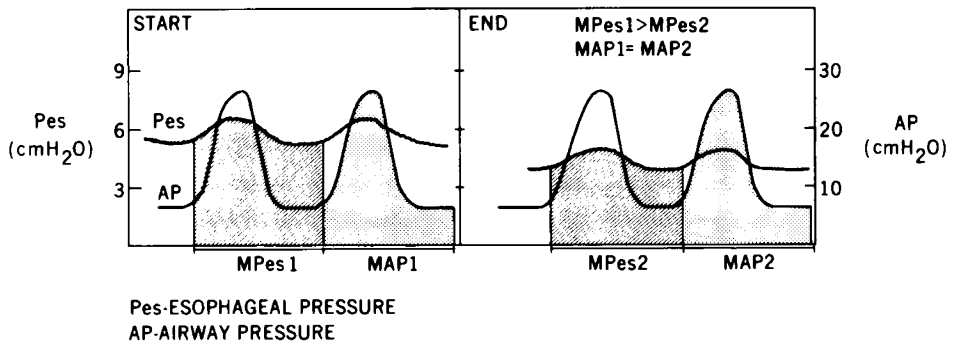


Fig. 3. Esophageal pressure changes during study period. Note decrease in $MP_{es}$ while MAP remains constant.

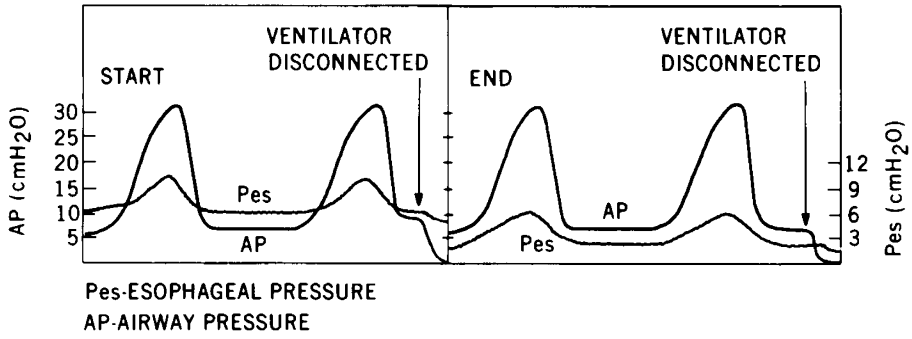


Fig. 4. Resting esophageal pressure after interruption of positive pressure ventilation. Note drop in AP to 0 while $P_{es}$ decreases only slightly from end-expiratory $P_{es}$.

infants. These increments were statistically significant ($1P = 0.03$), although the final $C_{tot}$ values were still extremely low (3, 10). TV data from two infants were discarded as a result of excessive drift which rendered the recordings uninterpretable.

In all the infants studied there was a fall in $MP_{es}$ over the study period while MAP remained constant (Table 1). Figure 3 illustrates these changes in one infant. The decline in $MP_{es}$ from an initial value of 5.6 ± 1.3 cm $H_2O$ to a final value of 4.2 ± 1.8 cm $H_2O$ (mean ± S.D.) was highly significant ($2P < 0.001$). This represented a 9.9 ± 4.2% (mean ± S.D.) reduction in transmission of the constant MAP to the pleural space over the study period.

When the ventilator was disconnected for several seconds for connection of the pneumotachograph at the beginning and end of each study period, we observed an immediate drop in AP to zero while $P_{es}$ remained above the base line. The "resting" $P_{es}$ was higher at the beginning than at the end of the study period, and in each case approximated the end-expiratory $P_{es}$ observed during ventilation (Fig. 4). Transducer drift was excluded as a cause for the reduction in resting $P_{es}$ by calibration of the transducer to zero before the measurement.

## DISCUSSION

Our data are consistent with previous studies demonstrating poor transmission of the applied AP to the pleural space in infants with low-compliance lung disease (7, 8, 11). However, we have demonstrated that during the early recovery phase, when compliance is still markedly reduced (3, 10), an improvement in clinical condition may be associated with a *fall* in $MP_{es}$. We believe this may be explained by a progressive decrease in intrathoracic gas-trapping during the early recovery phase.

Airway closure may occur within the tidal volume range in healthy adults during spontaneous ventilation and under anesthesia (15). Positive pleural pressure at the resting expiratory level was documented in a study of anesthetized paralyzed adults with normal lungs (13). Airway closure against positive intra-alveolar pressure, *i.e.*, gas-trapping, was considered to be responsible for the findings. We documented similar positive $P_{es}$ at the resting expiratory level, and a fall in the resting $P_{es}$ over the study period (Fig 4). Infants and children may also collapse airways within the tidal volume range (14). Corbet and coworkers (5, 9) have documented the existence of an underventilated pulmonary compartment with a low ventilation:perfusion ratio in infants with HMD, and envisage this compartment as having high terminal conducting airway resistance due to the small calibre airways and excessive interstitial water (4). Thus, airway closure and gas-trapping may occur in this compartment during expiration (5). The generalized capillary permeability and accumulation of interstitial fluid have been well described in infants with HMD (17, 20), and furosemide-induced diuresis has been show to improve gas exchange (17), presumably by decreasing edema of the pulmonary interstitium. It is of interest that the changes in $MP_{es}$ observed in our infants with HMD occurred at a stage of disease during which maximal diuresis has been found to occur (18). The fact that the two full-term infants studied during recovery from fluid overload showed the same changes in $MP_{es}$ over the study period lends further weight to our contention that, during early recovery, loss of pulmonary interstitial fluid may lead to a progressive decrease in gas-trapping. This mechanism would account for the changes seen in Figure 3 and 4.

Longitudinal studies in our patients would possibly have detected the change from "paradoxical" to normal pressure transmission as recovery continued. Perhaps, while maintaining constant ventilator settings, further improvement in pulmonary status and lung compliance would have resulted in an increase in TV and greater pressure transmission to the pleural space (7). This was not studied, since infants were not curarized beyond the early recovery phase. When $P_{es}$ measurements are used in the ventilator management of infants with low-compliance lung disease, the finding of a falling $MP_{es}$ value could be interpreted as signifying a deterioration in compliance. While this may be so, we have observed a phase of the disease when $C_{tot}$ is still markedly reduced and $MP_{es}$ falls during a period of clinical improvement. We believe this may reflect a progressive decrease in gas-trapping as water is lost from the pulmonary interstitium.

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