

Effect of Alterations in Mechanical Ventilator Settings on Pulmonary Gas Exchange in Hyaline Membrane Disease

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Reynolds, E. O. R. (1971). *Archives of Disease in Childhood*, **46**, 152. **Effect of alterations in mechanical ventilator settings on pulmonary gas exchange in hyaline membrane disease.** The effect of altering peak airway pressure, respiratory frequency, and inspiration:expiration ratio on arterial blood gas tensions, blood pressure, and calculated right-to-left shunt was investigated in 6 infants undergoing mechanical ventilation for hyaline membrane disease with a Bennet ventilator. The use of a very long inspiratory phase resulted in a large increase in P_aO_2 and fall in right-to-left shunt without affecting mean arterial blood pressure.

The mortality rate of infants with hyaline membrane disease who collapse and need mechanical ventilation is high (Reynolds, 1970b). Even with the use of pure oxygen as the ventilating gas and high airway pressures, many infants die from hypoxia during the first few days of life. Other mechanically ventilated infants may survive into the second week or later, only to succumb with massive lung fibrosis which is probably caused by a combination of mechanical damage to the lungs and oxygen toxicity (Northway, Rosan, and Porter, 1967; Hawker, Reynolds, and Taghizadeh, 1967).

Very few data are available on the effect of alterations in ventilator settings on pulmonary gas exchange in infants with hyaline membrane disease (Owen-Thomas, Ulan, and Swyer, 1968; Smith *et al.*, 1969; Harrison, Heese, and Klein, 1969). This report describes the effect of altering respiratory frequency, airway pressure, and inspiration:expiration ratio in 6 infants during mechanical ventilation

Infants Studied

Some details of the infants studied are set out in Table I. All had the clinical and radiological features of hyaline membrane disease (Reynolds, 1970a) and their general management was as previously described (Reynolds, 1970a; 1970b). The 6 infants were con-

secutively admitted cases who required mechanical ventilation.

Indications for mechanical ventilation. One infant (Case 1) never breathed spontaneously and was mechanically ventilated from birth. Four infants (Cases 3, 4, 5, and 6), who became apnoeic or collapsed with gasping respirations and a heart rate of less than 80/min, failed to respond to endotracheal intubation and manual positive pressure ventilation and were therefore mechanically ventilated. Case 2 was ventilated because, though still breathing spontaneously, she developed profound hypoxaemia, hypercapnia, and acidaemia (see Table II). Oro-endotracheal tubes (Warne No. 12) were used and the ventilator was the Bennett PR2. The technique of management of the infants while undergoing mechanical ventilation has been described elsewhere (Adamson *et al.*, 1968; Reynolds, 1970b).

Methods

Arterial blood gas tensions, pH, and base excess. A No. 5 French gauge Argyle catheter was introduced into the umbilical artery until a free flow of blood was obtained and then advanced a further 2 to 3 cm. The position of the catheter tip was verified radiologically to be in the aorta at the level of the 2nd or 3rd lumbar vertebra in 3 infants. After flushing the dead space, 0.75 ml samples of blood were taken into heparinized syringes and analysed immediately for arterial oxygen tension (P_aO_2), carbon dioxide tension (P_aCO_2), pH, and base excess (BE). The P_aO_2 was measured at 38°C with a Radiometer E5044 Clarke-type oxygen

TABLE I
Clinical Details of Infants Studied

Case No.	Sex	Birthweight (g)	Gestational age (wk)	Age at Which Mechanical Ventilation Began (hr)	Clinical Details and Outcome
1	M	1520	30	Birth	Never breathed spontaneously; died aged 65 hours; necropsy: hyaline membrane disease, intraventricular haemorrhage
2	F	2500	37	27	Mechanically ventilated for 41 hours; survived
3	M	1530	32	23	Mechanically ventilated for 3 days and then intermittently for 3 weeks; operated upon for hypertrophic pyloric stenosis aged 8 weeks; survived
4	F	980	28	7	Died aged 6 days; necropsy: hyaline membrane disease, intraventricular haemorrhage
5	F	1520	32	54	Mechanically ventilated for 3 days; survived
6	F	2150	33	30	Caesarean section for severe Rhesus haemolytic disease; 2 exchange transfusions; mechanically ventilated for 3 days, recovering from hyaline membrane disease but developed massive pulmonary haemorrhage and hypoglycaemia, aged 5 days, mechanically ventilated for a further 2 days, died aged 7 days, necropsy: resolving hyaline membrane disease, massive pulmonary haemorrhage

electrode, a correction being applied for the blood-gas difference of the electrode. pH was measured at 38°C using the Astrup apparatus (Astrup *et al.*, 1960), and P_aCO_2 and BE were derived from the Siggaard-Andersen nomogram after allowing for the amount of unsaturated haemoglobin (Siggaard-Andersen, 1962). Corrections for the rectal temperature of the infant were made (Severinghaus, 1965).

The inspired oxygen concentration ($F_{I}O_2$) was measured with a Beckman D2 paramagnetic oxygen analyser. Hb concentration was measured by the cyanmethaemoglobin method.

Calculation of right-to-left shunt. Right-to-left shunt (\dot{Q}_s/\dot{Q}_T) was calculated from the shunt equation (Berggren, 1942; Comroe *et al.*, 1955).

$$\dot{Q}_s/\dot{Q}_T = (C_aO_2 - C_eO_2)/(C_{\bar{v}}O_2 - C_eO_2)$$

where C_aO_2 = arterial oxygen content (ml/100 ml), C_eO_2 = end-pulmonary capillary O_2 content (ml/100 ml), and $C_{\bar{v}}O_2$ = mixed venous O_2 content (ml/100 ml).

'Ideal' alveolar oxygen tension was derived from the alveolar air equation (Riley and Courmand, 1949), assuming a respiratory exchange ratio of 0.8 (Adams, *et al.*, 1964) and was taken to be identical with pulmonary end-capillary oxygen tension. Hb saturations in arterial and pulmonary end-capillary blood were obtained from the oxygen dissociation curve for fetal blood (Oh, Arcilla, and Lind, 1965), after applying a correction for pH (Severinghaus, 1965). In one infant (Case 6) who had had an exchange transfusion, the adult oxygen dissociation curve was used. The saturation of mixed venous blood was assumed to be 15% lower than in arterial blood (Rudolph *et al.*, 1961). Oxygen capacity in ml per 100 ml blood was obtained as $Hb (g) \times 1.34$. Oxygen content in arterial, pulmonary end-capillary, and mixed venous blood was

derived from O_2 capacity, O_2 saturation, and the solubility of O_2 in blood (0.003 ml/mmHg per 100 ml).

The validity of this method of calculation and the possible errors involved have been discussed by Strang and MacLeish (1961), Nelson *et al.* (1963) and Chu *et al.* (1967).

Arterial blood pressure. Arterial blood pressure was measured by attaching the arterial catheter directly to a Type 267BC Sanborn strain-gauge transducer connected to a Type 350-2700 Sanborn carrier pre-amplifier and direct writing oscillograph.

Airway pressure. Airway pressure was recorded by inserting a wide-bore needle into the ventilator tubing just proximal to the endotracheal tube and connecting it by means of a stiff plastic catheter to the pressure transducer.

Variation of ventilator settings. The ventilator was set as a pressure generator with minimal internal resistance (Mushin *et al.*, 1969). 80-100% oxygen, fully humidified at body temperature, was used as the ventilating gas and the following control settings were employed: peak flow—maximum; negative pressure—off; terminal flow—off; nebulization—off. The rate, sensitivity, and expiration time controls were arranged to produce a respiratory frequency of 30 a minute at a peak airway pressure of 25 cm H_2O (30 cm H_2O in Case 2) with an inspiration/expiration ratio (I : E) of 1 : 1. After stabilization for at least 2 hours a series of between 6 and 8 predetermined alterations in respiratory frequency, peak airway pressure, and I : E ratio were carried out. The order in which the alterations were made was different in each infant. Respiratory frequencies of 30 and 80 breaths a minute, peak airway pressures of 25 and 30 cm H_2O , I : E ratios of between

TABLE II

Effects of Varying Peak Airway Pressure, Respiratory Frequency, and Inspiration : Expiration (I : E) Ratio on Arterial Blood Gas Tensions, Right-to-Left Shunt (\dot{Q}_s/\dot{Q}_T), and Mean Arterial Blood Pressure

Case No.	Age (hr)	Airway Pressure (cm H ₂ O)	Resp. Frequency (breaths/min)	I : E Ratio	F _I O ₂	P _a O ₂ (mmHg)	P _a CO ₂ (mmHg)	pH	BE (mEq/l)	\dot{Q}_s/\dot{Q}_T	Mean Arterial Blood Pressure (mmHg)			
1	12	25	30	1 : 1	0.80	92	39	7.28	-8	0.35	28			
		25	30	4 : 1	0.80	220	40	7.28	-8	0.26	27			
		25	80	1 : 2	0.80	35	32	7.31	-9	0.74	26			
		30	30	4 : 1	0.80	310	37	7.28	-9	0.17	31			
		25	30	2 : 1	0.80	185	37	7.30	-8	0.30	31			
		25	30	1 : 2	0.80	88	37	7.28	-9	0.34	29			
		30	30	1 : 1	0.80	117	35	7.31	-9	0.33	29			
		2	27 30	Spont. breathing				0.95	13	140	6.98	-9		30
30	30			2 : 1	0.96	112	46	7.37	0	0.36	31			
30	30			1 : 2	0.96	56	51	7.36	0	0.59	32			
30	80			1 : 2	0.96	52	37	7.42	-1	0.60	33			
30	30			4 : 1	0.96	183	57	7.33	0	0.26	32			
35	30			4 : 1	0.96	222	53	7.34	0	0.25	33			
25	30			1 : 1	0.96	47	51	7.35	0	0.66	34			
30	30			3 : 1	0.96	130	48	7.37	0	0.32	34			
30	30			1 : 1	0.96	62	43	7.38	0	0.55	34			
3	23 32			Spont. breathing*				0.98	23	150	6.81	-13	0.76	—
				25	80	1 : 2	0.96	44	76	7.23	-1	0.67	37	
		25	30	1 : 1	0.96	54	72	7.23	-2	0.58	39			
		25	30	4 : 1	0.96	86	82	7.22	-1	0.41	40			
		30	30	4 : 1	0.96	106	84	7.22	0	0.39	40			
		25	30	1 : 2	0.96	60	85	7.23	-2	0.53	38			
		25	30	2 : 1	0.96	81	85	7.21	0	0.43	38			
		30	30	1 : 1	0.97	85	84	7.23	+1	0.41	38			
4	6 21	Spont. breathing*				0.90	36	50	7.07	-9	0.68	—		
		25	30	1 : 1	1.00	121	38	7.53	+9	0.43	33			
		25	80	1 : 2	0.99	49	32	7.56	+8	0.74	32			
		25	30	4 : 1	1.00	215	37	7.52	+8	0.37	34			
		25	30	1 : 2	0.99	107	35	7.53	+8	0.47	35			
		30	30	1 : 1	1.00	142	33	7.56	+9	0.42	36			
		30	30	4 : 1	1.00	278	40	7.52	+9	0.33	35			
5	54 58	Spont. breathing*				0.96	55	150	6.96	-2	0.46	—		
		30	30	1 : 1	0.97	114	71	7.28	+1	0.40	41			
		25	30	4 : 1	0.96	126	75	7.27	+2	0.39	40			
		25	30	1 : 2	0.96	65	72	7.28	+2	0.52	38			
		30	30	4 : 1	0.97	194	77	7.25	+1	0.34	38			
		25	80	1 : 2	0.97	61	65	7.29	+1	0.55	36			
		25	30	2 : 1	0.97	143	73	7.26	+1	0.39	36			
		25	30	1 : 1	0.97	91	74	7.26	+2	0.41	36			
6	29 32	Spont. breathing*				0.92	31	134	7.07	-1	0.72	—		
		25	80	1 : 2	0.96	50	57	7.34	+2	0.66	46			
		25	30	1 : 1	0.97	81	69	7.31	+3	0.49	45			
		30	30	4 : 1	0.96	285	69	7.31	+3	0.27	49			
		25	30	1 : 2	0.96	105	69	7.32	+3	0.42	47			
		30	30	1 : 1	0.96	145	60	7.33	+2	0.39	46			
		25	30	2 : 1	0.95	193	71	7.31	+2	0.38	48			
		25	30	4 : 1	0.96	244	65	7.32	+2	0.31	49			

*Last values obtained while the infants were still breathing spontaneously.

1 : 2 and 4 : 1, and the effect of a 5 cm H₂O increment of peak airway pressure at an I : E ratio of 4 : 1 were investigated. The pressure, rate, expiration time, and sensitivity controls were used to produce the alterations, the other controls remaining untouched. Two airway pressure recordings are illustrated in Fig. 1. After each alteration in ventilator settings the lungs were held statically inflated for 3 to 4 seconds, and 15 minutes were then allowed to elapse before readings of arterial blood

pressure, and samples of arterial blood for analysis, were taken.

No steps were taken to control the attempts which were occasionally made by the infants to breathe against the ventilator.

Statistical methods. Student's t test was used to determine whether, between each pair of ventilator settings, the mean of the differences between readings

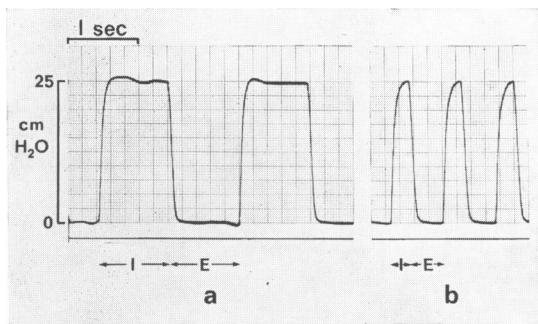


FIG. 1.—Airway pressure recordings in Case 5. (a) Frequency 30/min, I : E ratio 1 : 1. (b) Frequency 80/min, I : E ratio 1 : 2.

of P_{aO_2} , P_{aCO_2} , \dot{Q}_s/\dot{Q}_T , and mean arterial blood pressure was significantly different from zero.

Results

Table II shows the age after birth at which the study was performed and the results obtained in

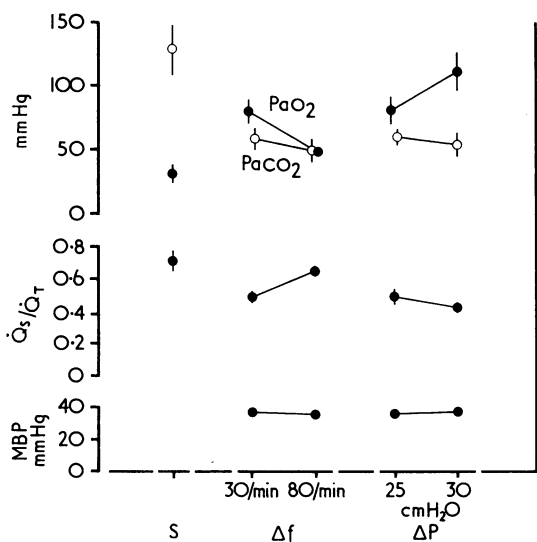


FIG. 2.—Effect of varying respiratory frequency, and peak airway pressure on arterial oxygen tension (P_{aO_2}), carbon dioxide tension (P_{aCO_2}), calculated right-to-left shunt (\dot{Q}_s/\dot{Q}_T), and mean arterial blood pressure (MBP). In the uppermost part of the diagram ● = P_{aO_2} and ○ = P_{aCO_2} . Mean values ± 1 SEM are shown (for actual data see Table II). S = the last values obtained during spontaneous breathing. Δf = values at respiratory frequencies of 30/min and 80/min; peak airway pressure constant at 25 cm H_2O , I : E ratio constant at 1 : 2. ΔP = values at peak airway pressures of 25 cm H_2O and 30 cm H_2O ; respiratory frequency constant at 30/min, I : E ratio constant at 1 : 2.

each infant for peak airway pressure, respiratory frequency, I : E ratio, F_{iO_2} , P_{aO_2} , P_{aCO_2} , pH , BE, \dot{Q}_s/\dot{Q}_T , and mean arterial blood pressure (MBP), arranged in the order in which the observations were made.

Fig. 2 and 3 show data obtained from the last blood sample taken while the infant was still breathing spontaneously, and data obtained during mechanical ventilation showing the effect of altering respiratory frequency, peak airway pressure, and I : E ratio on P_{aO_2} , P_{aCO_2} , \dot{Q}_s/\dot{Q}_T , and MBP.

Respiratory frequency. (Fig. 2, Δf). At an I : E ratio of 1 : 2 and a peak airway pressure of 25 cm H_2O , P_{aO_2} was lower at a respiratory frequency of 80 breaths a minute than at 30 breaths a minute (mean difference between paired readings 31.5 mmHg ± 10.7 SEM, N = 6, $P < 0.025$). P_{aCO_2} was also lower at the faster frequency (mean diff. 8.3 ± 1.7 mmHg, N = 6, $P < 0.0025$). \dot{Q}_s/\dot{Q}_T was less at the slower frequency (mean diff. 0.18 ± 0.06 , N = 6, $P < 0.025$).

Peak airway pressure. At a respiratory frequency of 30 breaths a minute and an I : E ratio of 1 : 1 (Fig. 2, ΔP), P_{aO_2} was higher at an

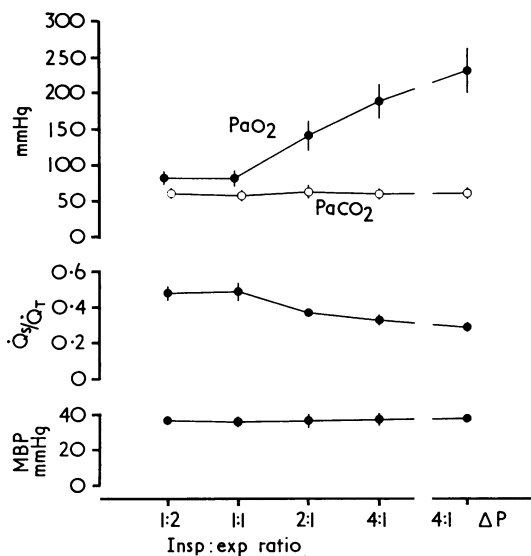


FIG. 3.—Effect of altering I : E ratio on arterial blood gas tensions, right-to-left shunt, and mean arterial blood pressure (abbreviations as in Fig. 1). Peak airway pressure constant at 25 cm H_2O in 5 infants and 30 cm H_2O in one. Respiratory frequency constant at 30/min. 4 : 1, ΔP shows the effect of a 5 cm increment in airway pressure at an I : E ratio of 4 : 1.

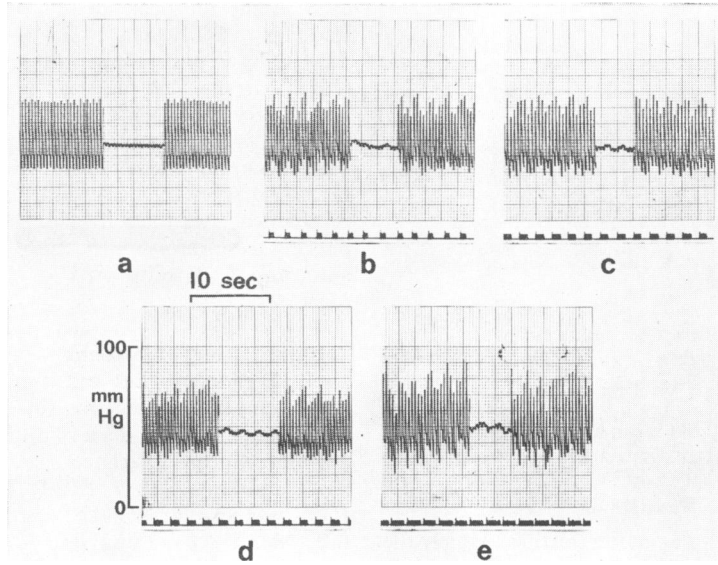


FIG. 4.—Arterial blood pressure recordings from Case 6. (a) Peak airway pressure (PAP) 25 cm H₂O, respiratory frequency (*f*) 80/min, I : E ratio 1 : 2. (b) PAP 25 cm H₂O, *f* 30/min, I : E 1 : 2. (c) PAP 25 cm H₂O, *f* 30/min, I : E 1 : 1. (d) PAP 30 cm H₂O, *f* 30/min, I : E 1 : 1. (e) PAP 30 cm H₂O, *f* 30/min, I : E 4 : 1. The length of inspiration is marked as a black bar at the bottom of b—e. Mean arterial pressure was unaffected by increasing peak airway pressure and I : E ratio, though oscillations of pressure were somewhat greater when long inspiratory phrases were used.

airway pressure of 30 cm H₂O than at 25 cm H₂O (mean diff. 29.8 ± 7.1 mmHg, N = 6, P < 0.005); \dot{Q}_a/\dot{Q}_T was less at the higher pressure (mean diff. 0.07 ± 0.03, N = 6, P < 0.05).

A 5 cm H₂O increment in peak airway pressure at an I : E ratio of 4 : 1 (Fig. 3, ΔP) also caused an increase in P_aO₂ (mean diff. 53.3 ± 10.2 mmHg, N = 6, P < 0.025) and a fall in \dot{Q}_a/\dot{Q}_T (mean diff. 0.04 ± 0.01, N = 6, P < 0.025).

Inspiration : expiration ratio. (Fig. 3). The peak airway pressure was constant at 25 cm H₂O in Cases 1, 3, 4, 5, and 6 and constant at 30 cm H₂O in Case 2; the respiratory frequency was always 30 breaths a minute. No significant differences were found between an I : E ratio of 1 : 2 and one of 1 : 1, but as I : E increased from 1 : 1 to 2 : 1 and 4 : 1, a significant increase in P_aO₂ occurred (mean diff. 1 : 1 vs. 2 : 1, 69.2 ± 14.6 mmHg, N = 5, P < 0.005; 1 : 1 vs. 4 : 1, 97.3 ± 21.9 mmHg, N = 6, P < 0.005; the increase in P_aO₂ between 2 : 1 and 4 : 1 did not reach statistical significance—mean difference 28.8 ± 15.7 mmHg, N = 5, 0.05 < P < 0.1).

As I : E increased from 1 : 1 to 4 : 1, \dot{Q}_a/\dot{Q}_T progressively fell (mean diff. 1 : 1 vs. 2 : 1, 0.13

± 0.05, N = 5, P < 0.05; 1 : 1 vs. 4 : 1, 0.15 ± 0.05, N = 6, P < 0.025; 2 : 1 vs. 4 : 1, 0.04 ± 0.02, N = 5, P < 0.025).

No other significant differences were found; in particular the mean arterial blood pressure did not alter during the investigation, and P_aCO₂ did not change except with respiratory frequency.

Fig. 4 shows blood pressure recordings obtained in Case 6.

Discussion

When mechanical ventilation was first used in our unit for the treatment of infants with hyaline membrane disease, fast respiratory frequencies of up to 80 breaths/min were employed (Adamson *et al.*, 1968). The reasons for choosing a fast frequency were twofold: firstly, the infants had been breathing spontaneously at least as fast as 80 breaths/min before collapsing, and it was found that fighting against the machine was less likely to occur when mechanical ventilation was initiated at a fast frequency than when a slow frequency was used. Secondly, since lung compliance is grossly reduced in hyaline membrane disease, it was thought that adequate gas exchange should be attainable at a lower peak airway pressure if a fast frequency

was selected. With this type of ventilation (Fig. 1b) little difficulty was experienced in keeping the P_aCO_2 at a normal level but adequate arterial oxygenation was often impossible to achieve.

With further experience we found that an increase in P_aO_2 followed slowing the respiratory frequency, or increasing peak airway pressure. In 1969, Smith *et al.*, using methods similar to ours proved that slow respiratory frequencies and high peak airway pressures caused an improvement in P_aO_2 . The data presented in Fig. 2 confirm their conclusions and also show that the P_aCO_2 , as well as the P_aO_2 , is higher at a frequency of 30/min than at a frequency of 80/min.

Inspiration : expiration ratio. Several lines of reasoning suggested that the use of a long inspiratory phase on the ventilator might improve arterial oxygenation. Firstly, because the air-liquid interface in the alveoli is deficient in pulmonary surfactant during the acute phase of hyaline membrane disease (Avery and Mead, 1959), the alveoli will probably collapse completely during expiration and only reopen during inspiration when a transpulmonary pressure greater than about 15–20 cm H_2O has been generated (Clements, 1962; Reynolds and Strang, 1966). Secondly, observing the exposed visceral pleural surface of the lungs of immature, surfactant deficient lambs with hyaline membrane diseases showed that the alveoli were open only during peak inspiration (Normand *et al.*, 1968). Thirdly, it appeared possible that the improvement in P_aO_2 , caused in infants with hyaline membrane disease by slowing the respiratory frequency and increasing peak airway pressure, was due to improved alveolar inflation. It was therefore reasoned that if the alveoli could be held open for a longer proportion of each breath, oxygen uptake might be improved. There are two possible ways in which the alveoli could be held open, by applying an end-expiratory pressure with the ventilator, or by increasing the inspiration : expiration ratio. The latter alternative was chosen because it would be difficult to apply an end-expiratory pressure with a Bennett ventilator, and also because interference with venous return to the heart should be less if intrathoracic pressure is allowed to return to zero for at least part of the ventilatory cycle.

The data presented in Fig. 3 show a striking and progressive increase in P_aO_2 and fall in calculated right-to-left shunt with increasing I : E ratio beyond 1 : 1. Shunting, which is the principal cause of hypoxaemia during the acute phase of hyaline membrane disease, is thought to occur

mainly because interference with pulmonary gas exchange and atelectasis cause constriction of pulmonary blood vessels and an increase in pulmonary vascular resistance: as P_aO_2 falls and pulmonary vascular resistance rises the foramen ovale and ductus arteriosus reopen and blood passes from the right side of the heart to the aorta without traversing the lungs (Cook *et al.*, 1963; Reynolds and Strang, 1966; Strang, 1966). Intrapulmonary shunts, in which blood flows past atelectatic air-spaces, may also be present (Wallgren *et al.*, 1967; Murdock *et al.*, 1970). The increasing P_aO_2 and decreasing right-to-left shunt found in this investigation caused by increasing the I : E ratio can be ascribed to the release of pulmonary vasoconstrictor tone, to the mechanical effects of alveolar inflation in dilating pulmonary blood vessels (Howell *et al.*, 1961; Cassin *et al.*, 1964), and to the oxygenation of blood passing through intrapulmonary shunts.

No alterations in mean arterial blood pressure occurred during the investigation, even with peak airway pressures of 30–35 cm H_2O and an I : E ratio of 4 : 1, though oscillations of blood pressure became somewhat greater when very long inspiratory phases were used (Fig. 4). With normal lungs a ventilator pressure wave of this type would probably produce impairment of venous return to the heart and a fall in arterial blood pressure (Morgan *et al.*, 1966; Mushin *et al.*, 1969). In hyaline membrane disease the retractile force of the surfactant-deficient air liquid interface should prevent comparatively high intra-alveolar pressures from being transmitted to the intrapleural space.

Implications for ventilator management of hyaline membrane disease. This study was performed with a positive pressure-generating flow (or time) cycled ventilator with minimal internal resistance, capable of holding a plateau of peak airway pressure (Fig. 1a). The results of the investigation cannot be applied to other ventilators, particularly constant flow generators. Using a flow generator, which does not produce a plateau of pressure, Harrison *et al.* (1969) found that the P_aO_2 improved when fast respiratory frequencies were used, presumably because the alveoli were only open briefly during peak inspiration.

With a ventilator producing pressure waves similar to those used in this study some tentative conclusions can be drawn about the settings to be employed during the acute phase of the illness. It seems reasonable initially to use 100% O_2 as the ventilating gas, a respiratory frequency of about 30 breaths/min, a peak airway pressure of 25 cm

H₂O and an inspiration : expiration ratio of 1 : 1.

If the P_aCO₂ is too high it can be reduced by increasing the respiratory frequency, but this will also reduce the P_aO₂.

If adequate arterial oxygenation is not achieved, the P_aO₂ can be improved either by increasing peak airway pressure or by increasing inspiration : expiration ratio. Because high airway pressures may be partly responsible for initiating fibrotic lesions in the lungs (Hawker *et al.*, 1967) and may cause a pneumothorax, it might be safer to increase inspiration : expiration ratio. It must be emphasized that infants have not yet been ventilated with very long inspiratory phases for longer than the brief periods employed in this investigation; if this approach is used arterial, and ideally central venous and intraoesophageal, pressure should be measured. If mechanical ventilation with a long inspiratory phase proves safe for long-term ventilation, it might be possible to reduce the inspired oxygen concentration to a level where pulmonary oxygen toxicity becomes unlikely.

It would probably be dangerous to use long inspiratory phases once recovery has started, on about the 3rd to 5th day. Pulmonary surfactant is found in the lungs of infants dying from hyaline membrane disease if they have survived longer than 5 days (Hawker *et al.*, 1967); and widespread uneven airways obstruction is present (Adamson *et al.*, 1969). A long inspiratory phase during recovery would almost certainly cause circulatory embarrassment and also favour air trapping. At this stage of the illness it would probably be preferable to use an inspiration : expiration ratio of about 1 : 2.

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