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ASSISTED VENTILATION IN TERMINAL HYALINE MEMBRANE DISEASE*

BY

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Following the work of Donald (Donald and Young, 1952; Donald and Lord, 1953; Donald, 1954), reports are accumulating in the literature of the use of assisted ventilation in the treatment of the respiratory distress syndrome (RDS) (Donald, Kerr, and Macdonald, 1958; Benson, Celander, Haglund, Nilsson, Paulsen, and Renck, 1958; Benson and Celander, 1959; Stahlman, Young, and Payne, 1962; Heese, Wittmann, and Malan, 1963). Since the clinical and biochemical status immediately before the initiation of assisted ventilation has not been defined in detail, the purpose of this study has been to assess the potential of assisted ventilation in reversing the acidaemia of terminal and apparently hopeless cases of RDS.

Materials and Methods

The 18 infants studied were divided into three groups of 6 on the basis of duration of apnoea, cardiac condition, and type of cyanosis (Table 1). The corresponding blood chemistries are also shown in Table 1. All were continuously monitored electrocardiographically and had been receiving comparable treatment with glucose bicarbonate solution by infusion through a catheter placed in the inferior vena cava via the umbilical vein, since admission. All had failed to respond to generally accepted methods of resuscitation, including positive pressure manual ventilation by endotracheal tube which failed repeatedly to initiate and maintain spontaneous respiration.

The gestational ages and weights of the infants are shown in Table 2. The average weight of the infants in Group III is raised by the presence of two infants of diabetic mothers.

Immediately before intubation a sample of central venous blood was withdrawn. Subsequent central venous samples were taken at intervals until death or recovery.

Ventilation was accomplished using Cole's endotracheal tubes in conjunction with a ventilator† equipped with the minimal dead space (0·28 ml.) infant circle (S. Segal, 1963, personal communication).* Positive pressures used varied from 15 to 35 cm.H_2O. Where assisted ventilation was required for longer than 36-72 hours (Cases Ly. and Ko.) a low tracheostomy was performed (Fearon, 1962) and ventilation continued through Hollinger tubes.

*p*H was measured by glass electrode, and CO_2 content by means of the Kopp-Natelson-gasometer (Natelson, 1951; Holaday and Verosky, 1956), from simultaneous measurements of *p*H and Pco_2 using a Severinghaus and Bradley (1958) type Pco_2 electrode. Blood buffer base was derived from the Singer and Hastings (1948) nomogram using simultaneously measured haematocrits. Measurements were made at 38° C. and no correction was made for the infant's body temperature. However, temperatures at the time blood samples were taken are given in Table 2.

Results

The evolution of the acid-base status in the three groups is shown in Table 2 and Figs. 1 and 2.

Mean survival time on the ventilator was 1 hour for Group I, 10 hours for Group II, and 50 hours for Group III (Fig. 2). One infant (Ly) in Group III was ventilated for seven days and survived.

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† Bird Mark VIII Respirator, Bird Corporation, Richmond, California.

* Designed by Dr Sydney Segal (1963) and manufactured by the Bird Corporation.

TABLE 1

INITIAL CLINICAL AND BIOCHEMICAL STATUS (VENOUS BLOOD) OF 18 INFANTS DIVIDED INTO THREE GROUPS OF 6 PATIENTS ON BASIS OF INCREASING SEVERITY

Clinical Group	I	II	III
Respiratory arrest	> 5'	> 3'	> 1'
Heart	Arrest > 3'	Arrest > 3' or Rate < 20'	Arrest > 1' or Rate < 60'
Cyanosis	Pallid	Mottling	Livid
*p*H	< 6·5	< 6·75	< 6·75
$PvCO_2$ (mm.Hg)	> 100	> 100	< 100
Buffer base (mEq l.)	< 15·0	< 20·0	< 20·0

TABLE

CLINICAL AND BIOCHEMICAL DATA (VENOUS

Name	Sex	Birth Weight (kg.)	Gestation (wk.)	Admission Age (hr.)	Immediately Before Ventilation: Rectal Temp (°C.)	pH	$Pv(CO_2)$ (mm.Hg)	B.B. (b) (mEq/L.)	CO_2 (b) (mM/L.)	20% Ventilator Life Span*: Rectal Temp. (°C.)	pH	$Pv(CO_2)$ (mm.Hg)	B.B. (b) (mEq/L.)	CO_2 (b) (mM/L.)	40% Ventilator Life Span*: Rectal Temp. (°C.)	pH	$Pv(CO_2)$ (mm.Hg)
Group II																	
Ma.	♂	2·9	39	12	36·5	6·75	120	17·0	15·0	36·5	7·05	35	26·0	18·8	—	—	—
Mo.	♂	1·3	28	6	34·9	6·74	125	17·5	16·0	34·8	6·91	70	26·0	14·0	35·0	7·08	48
Fi.	♂	2·0	36	10	35·4	6·69	110	14·0	11·0	35·2	6·88	54	22·0	10·0	35·6	7·07	55
Gi.	♂	1·3	32	7	33·5	6·62	140	15·0	12·5	33·5	6·67	88	14·0	9·0	34·5	6·73	84
Br.	♂	1·6	32	45	35·4	6·58	138	13·0	9·5	35·4	7·07	36	27·0	10·4	35·6	7·22	19
De.	♂	1·2	29	10	35·0	6·66	135	14·0	12·5	34·5	7·08	35	27·5	9·8	34·0	7·10	35
Group III																	
Ch.	♂	3·9	40	8	35·5	6·93	98	31·0	20·0	37·5	7·26	34	38·0	14·2	37·5	7·29	38
La.	♂	1·7	35	12	35·0	6·91	100	31·0	19·5	36·1	7·34	52	48·0	25·0	37·0	6·37	51
Ca.	♂	3·1	37	24	35·4	6·93	100	31·0	20·8	36·9	7·34	42	44·0	20·0	36·8	7·32	51
Wi.	♂	3·1	37	1	35·0	6·99	95	32·0	21·2	36·5	7·36	40	46·0	19·0	37·2	7·41	38
Ko.	♂	1·4	30	8	34·8	7·00	96	33·0	22·0	36·8	7·36	40	43·0	20·8	38·2	7·36	45
Ly.	♀	1·8	32	12	34·9	6·77	110	22·0	16·0	36·2	7·34	46	47·0	21·0	37·2	7·40	42

*Ventilator life span (as detailed in the column before last) has been proportioned to 100 to facilitate tabulation and comparison of the widely differing life
B.B. (b) = blood buffer base. CO_2 (b) = blood CO_2 content. H.M. = hyaline membrane. P.M. = post-mortem.

Case Report

Case Ly. This female infant was the third born of a 22-year-old mother. The gestation was 34 weeks and the birth weight 1·8 kg. Within half an hour respirations became indrawing and grunting; these symptoms worsened over the next 17 hours when she was transferred to the Hospital for Sick Children. A radiograph at 18 hours showed a reticulo-granular pattern. Her condition then stabilized with 50% oxygen, at the neutral temperature, until at 35 hours she had a series of apnoeic spells

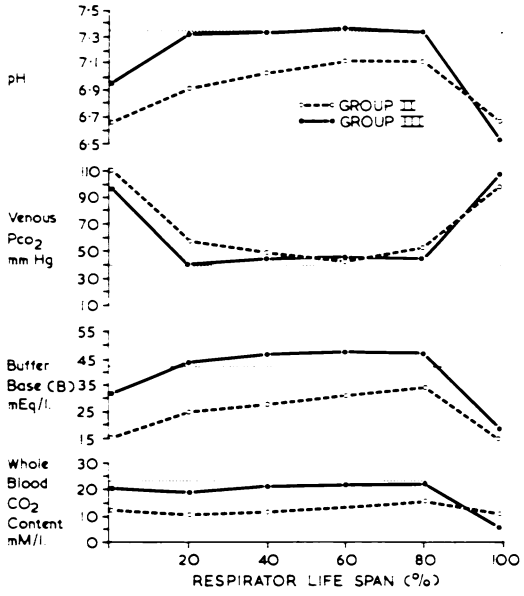

FIG. 1.—Average changes in acid-base measurements (venous blood) during positive pressure ventilation in Groups II and III. Patient Ly. is excluded from the calculations for Group III because she survived with normal figures during her ventilator life span.

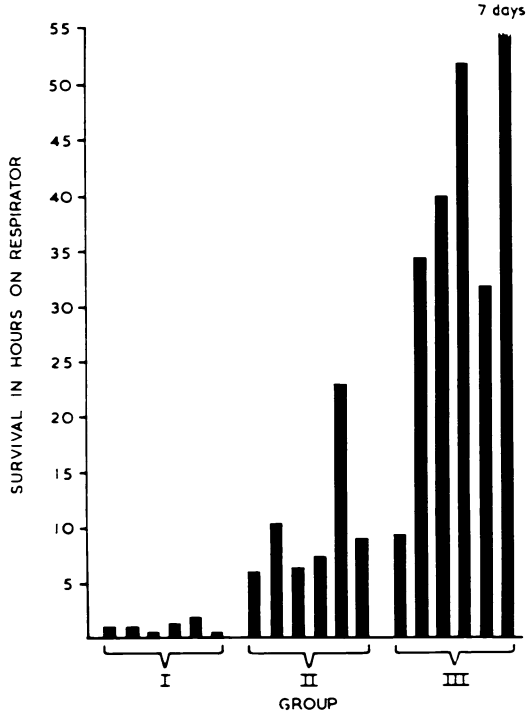

FIG. 2.—Survival in the three groups. Patient Ly. in Group III was weaned from the respirator at 7 days and survived.

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BLOOD) OF INFANTS IN GROUPS II AND III

60% Ventilator Life Span*							80% Ventilator Life Span*					Terminal Stage on Ventilator					Total Hours on Ventilator	P.M.
B.B. (b) (mEq/l.)	CO_2 (b) (mM/l.)	Rectal Temp. (°C.)	pH	$PvCO_2$ (mm.Hg)	B.B. (b) (mEq/l.)	CO_2 (b) (mM/l.)	Rectal Temp. (°C.)	pH	$PvCO_2$ (mm.Hg)	B.B. (b) (mEq/l.)	CO_2 (b) (mM/l.)	Rectal Temp. (°C.)	pH	$PvCO_2$ (mm.Hg)	B.B. (b) (mEq/l.)	CO_2 (b) (mM/l.)		
—	—	36·8	7·09	57	31·5	16·0	36·0	7·10	58	32·0	17·0	38·0	6·70	118	13	12·2	6·0	H.M.
30	13·4	38·2	7·24	29	31·0	11·0	—	—	—	—	—	37·3	4·80	98	22	15·0	10·5	H.M.
31	15·0	36·0	7·17	36	31·0	12·0	—	—	—	—	—	34·6	6·60	110	12	8·0	6·5	H.M.
18	11·5	34·6	6·78	72	19·0	11·0	34·0	7·00	45	26·0	10·5	34·0	6·87	100	18	18·0	7·5	H.M.
28	7·0	36·0	7·29	25	32·0	11·0	36·8	7·20	35	31·5	12·4	35·8	6·60	120	10	7·8	23·0	H.M.
28	10·0	—	—	—	—	—	—	—	—	—	—	33·0	6·73	100	15	11·0	9·0	H.M.
40	16·5	38·0	7·32	42	43·0	19·8	38·0	7·34	45	45·0	20·8	37·0	6·69	115	15	12·0	9·5	H.M.
50	26·0	37·0	7·39	50	52·0	25·4	36·5	7·37	50	50·0	24·0	36·4	6·70	120	15	12·5	34·5	H.M.
46	23·0	37·5	7·46	42	53·0	24·8	36·6	7·34	50	49·0	24·0	37·0	6·58	140	10	11·0	26·0	H.M.
49	20·0	37·1	7·45	36	46·0	19·5	37·3	7·40	42	49·0	22·0	33·6	6·70	110	13	10·5	52·0	H.M.
47	22·5	37·5	7·28	48	42·0	18·1	36·8	7·36	43	45·0	21·2	34·5	6·64	110	12	10·0	32·0	H.M.
46	22·5	37·0	7·34	46	43·0	21·5	37·4	7·40	42	48·0	22·5	37·8	7·36	44	46	21·5	146·0	Survived

spans in real time.

which responded to stimulation and 100% oxygen by face-mask. At 49 hours she ceased to breathe and the heart rate fell to 50 a minute. She failed to respond to positive pressure respiration by face mask. An endotracheal tube was therefore inserted and assisted ventilation begun at 35 cm. H_2O positive pressure. While the electrocardiogram was monitored 10 mEq $NaHCO_3$ (half the calculated buffer base deficit) was injected slowly through the umbilical vein. There was an immediate and sustained improvement in clinical status, coincidental with correction in both respiratory and metabolic components of the acidosis. A low tracheostomy was performed (Dr Blair Fearon) at 73 hours and following a gradual reduction in pressure from 40 to 25 cm. H_2O, assisted ventilation was discontinued at 9 days. The tracheostomy tube was removed on the 14th day. Progress was complicated by an intercurrent pneumonic infection which responded to antibiotic treatment. The infant was discharged home on the 47th day with minimal perihilar infiltration radiologically, no abnormal symptoms or physical signs, and weighing 2,800 g. Examination at 6 months of age disclosed no neurological or other abnormality, and the chest radiograph was normal. More prolonged follow-up will be required to assess her development.

Necropsy in Group I showed hyaline membrane disease with superimposed massive pulmonary haemorrhage. The fatal cases in Groups II and III showed uncomplicated hyaline membrane disease only.

Discussion

The results show a clear-cut difference in survival times in the three groups which can be correlated with the initial clinical and biochemical status and with the type and degree of biochemical correction.

Infants in the worst condition (Group I) evinced no appreciable clinical or biochemical response. The necropsy finding of massive pulmonary haemorrhage associated with hyaline membranes explains the failure of assisted ventilation to achieve gas exchange.

Infants whose initial condition was somewhat better (Group II) made a rapid correction of their respiratory acidosis but buffer-base levels were relatively unchanged, in fact mean *p*H levels did not rise above 7·11 (Fig. 1). In contrast infants in Group III corrected both the respiratory and the metabolic components of their acidaemia so that *p*H reached normal levels usually within three hours of starting assisted ventilation.

In 5 out of the 6 infants who achieved complete correction, clinical and biochemical deterioration eventually took place after a varying period during which a normal acid-base status was maintained. This final deterioration was relatively rapid, occurring usually over a three-hour period.

It seems that if the stage of clinical death is not too far advanced the condition is potentially reversible. Thus patients in Groups I and II were in late and irreversible stages of clinical death. This is self-evident for Group I patients. In Group II infants, failure to correct metabolic acidosis in spite of a satisfactory lowering of (venous) P_{CO_2} in 5 of the 6 patients suggests the possibility of an irreversible degree of biological cellular damage with metabolic failure.

On the other hand the complete correction maintained on assisted ventilation for many hours in Group III suggests that death before ventilation results from neuromuscular respiratory failure in the presence of sufficient gas exchange surface to support life. This, then, provides the rationale for assisted ventilation.

Our results suggest that the best hope of success with this treatment lies in its application in the preterminal rather than in the terminal state.

Summary

Eighteen apnoeic infants dying from the respiratory distress syndrome have been treated by positive pressure assisted ventilation. The infants were divided into three groups of increasingly advanced clinical death on the basis of duration of respiratory arrest, cardiac status, and type of cyanosis. Initial acid-base state and its changes during treatment were recorded. The duration of survival was related to the severity of the clinical and biochemical condition when ventilation was begun. Only in the least advanced group was significant prolongation of life (average 50 hours) and complete correction of metabolic and respiratory acidosis achieved. One infant in this group survived apparently undamaged.

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