Transient Respiratory Distress Syndrome in the Newborn*

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The variable duration and severity of the respiratory distress syndrome (RDS) make it difficult to assess any therapeutic régime. We have observed 12 infants who at age 4 hours had clinical and biochemical findings indicative of moderate to severe respiratory distress syndrome but who improved rapidly with a standard therapeutic régime, their respiratory distress disappearing or becoming minimal during the first day of life. We describe the clinical, acid-base, and blood-gas course of these infants. For comparison, we also studied a group of 19 distressed premature newborns who initially manifested a similar clinical and biochemical picture, but in whom the respiratory distress syndrome persisted beyond age 30 hours despite the same therapeutic régime. For the purposes of comparison, we refer to those infants with minimal or no respiratory distress at age 18 hours as the *transient* respiratory distress syndrome group (TRD), and those whose respiratory distress persisted beyond age 30 hours as the *moderate-severe* respiratory distress syndrome group (RDS). (It happened that there were no infants whose respiratory distress resolved between 18 and 30 hours of age.)

Procedures and Methods

Infants who manifested idiopathic respiratory distress were clinically evaluated on the basis of a scoring system given in Table I. This scoring system, 0 to 10, has significant linear correlation with the alveolar-arterial PO_2 gradient, arterial hydrogen ion concentration, and P_aCO_2 (Downes, Vidyasagar, Morrow, and Boggs, 1967). If, over a 2-hour period, an infant maintained a score of 4 or more, and other causes of respiratory distress were not evident, a presumptive diagnosis of idiopathic respiratory distress syndrome was made. Umbilical artery catheterization was then performed and the catheter inserted 10 to 14 cm., depending on the length of the infant, so that its distal tip was in the thoracic aorta below the ductus arteriosus (Dunn, 1966). After

the infant had been breathing 100% O_2 by mask at 10 l./min. for 15 minutes, the initial arterial sample was obtained. Subsequently, if the infant's condition permitted, arterial PO_2 was measured, with the infant breathing room air for 15 minutes. Blood was analysed for pH and carbon dioxide tension (P_aCO_2) by the interpolation method (Astrup, Jørgensen, Siggaard Andersen, and Engel, 1960) and the base deficit (negative base excess) calculated from a nomogram (Siggaard Andersen, 1962). The base deficit values were corrected for oxygen saturation and the effect of increases in P_aCO_2 (Dell, Engel, and Winters, 1966). The arterial oxygen tension (P_aO_2) was determined with a modified Clark electrode (Radiometer-Beckman) calibrated with tonometred water and maintained at 38° C. All readings were corrected for temperature differences and P_aO_2 for non-linearity of the electrode at oxygen tensions above 200 mm. Hg. Minimum colonic temperature at the time of the initial sample was 36.0° C. Arterial pH values were converted to hydrogen ion concentration for averaging and the mean values reconverted to pH for presentation.

The 12 infants in the TRD group had initial clinical scores between 4 and 7 at age 4 hours. The 19 infants in the RDS group were selected on the basis of a clinical distress score between 4 and 7 at the same age. As can be seen from Table II, the mean birthweight, gestational age, and five-minute Apgar scores of both groups of infants are comparable. Four of the RDS infants subsequently died. None of the infants had clinical findings suggestive of aspiration syndrome (Schaffer, 1960), pneumothorax, or pneumomediastinum (Malan and Heese, 1966).

TABLE I
Clinical Respiratory Distress Scoring System

Score	0	1	2
Respiratory rate (breaths/min.)	60	60-80	80 or apnoea
Cyanosis ..	None	In air	In 40% O_2
Retractions ..	None	Mild	Moderate-severe
Grunting ..	None	Audible with stethoscope	Audible without stethoscope
Air entry (crying) ..	Clear	Delayed or decreased	Barely audible

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TABLE
Clinical and Arterial Blood Data: Transient Respiratory Distress Syndrome

Case No.	Birthweight (g.)	Gestation (wk.)	Apgar at 5 min.	RDS Score			P _a O ₂ (mm. Hg)		
				2-8 hr.	8-18 hr.	20-30 hr.	F _i O ₂ 21%	F _i O ₂ 100%	F _i O ₂ 21%
TRD									
1	2070	35	8	5	3	2	—	—	76
2	1620	32	7	5	2	3	—	—	69
3	2100	32	5	4	2	1	61	390	67
4	1820	38	10	4	2	0	55	435	68
5	2390	?	10	7	3	2	49	345	—
6	2590	35	9	6	3	3	76	305	—
7	2250	37	8	4	1	1	78	285	80
8	1420	30	?	4	3	3	70	270	—
9	1720	31	?	4	3	2	73	390	51
10	1590	31	9	6	2	2	63	310	63
11	1480	30	5	7	1	0	25	74	—
12	1770	32	8	7	3	0	—	67	74
Mean	1901	33	8	5.4	2.2	1.6	61	287	65
Number	12	11	10	12	12	12	9	10	8
S.E.	11	—	—	—	—	—	5.5	28	3
RDS									
Mean	2017	34	8	5.8	5.3	5.1	46	251	—
Number	19	16	16	19	19	15	17	18	—
S.E.	141	0.8	—	—	—	—	1.3	25	—
TRD vs RDS: p	n.s.	n.s.	—	—	—	—	<0.02	n.s.	—
Controls									
Mean	2080	35	—	0	0	0	79	—	70
Number	18	17	—	—	—	—	9	—	9
S.E.	67	1	—	—	—	—	6.2	—	4
TRD vs Normal: p	—	—	—	—	—	—	n.s.	—	n.s.

* $\Delta P_{aCO_2} = (P_{aCO_2} \text{ at } 2-8 \text{ hr.}) - (P_{aCO_2} \text{ at } 8-15 \text{ hr.})$.

† Base excess at 2-8 hr. before intravenous NaHCO₃.

Both groups of infants received equivalent therapy with high oxygen concentrations, sufficient to maintain the P_aO₂ at 70 to 100 mm. Hg if possible, intravenous NaHCO₃ in a dose calculated to correct the base deficit in order to maintain the arterial pH above 7.30, and an intravenous infusion of 5% glucose. The skin temperature was maintained at 36 ± 0.5° C.

In 17 premature infants, who were otherwise normal and were maintained at the neutral temperature, arterialized capillary blood provided control data for arterial pH, P_aCO₂, and P_aO₂. The mean P_aO₂ values from arterialized blood agreed closely with the umbilical artery data in full-term infants at comparable ages (Prod'hom, Levison, Cherry, Drorbaugh, Hubbell, and Smith, 1964).

Results

The initial clinical score, P_aO₂, and acid-base status for each patient were determined at 2-8 hours, 8-18 hours, and 20-30 hours of age. The results of these serial studies are presented in Table II. The TRD infants had a mean initial score of 5. At an average age of 12 hours this had decreased below 4 in every case with a mean score of 2. By an average age of 24 hours the mean score further decreased to 1.5 (Table II). The infants in the RDS group had an initial mean score of 6 which decreased to 5 by the average age of 12 hours, and all of these infants still had a score of 4 or greater beyond age 30 hours.

The initial P_aO₂ values obtained during inhalation of 100% O₂ had a mean of 287 mm. Hg in the TRD group and 251 mm. Hg in the RDS group. These means were not significantly different. However, after breathing room air for at least 10 minutes, the TRD group had a mean P_aO₂ of 61 mm. Hg, compared to a mean of 46 mm. Hg in the RDS group. These means are significantly different (p < 0.02). The mean P_aO₂ of the TRD group at 2-8 and 20-30 hours during air breathing is not significantly different from that of the control premature infants. Therefore, the P_aO₂ during air breathing may prove to be a useful though not absolute guide in distinguishing these two groups of infants early in their illness.

The TRD infants had an initial mean P_aCO₂ of 62 mm. Hg, hardly different from the mean of 57 mm. Hg in the RDS group. By an average age of 12 hours the mean P_aCO₂ had decreased to 41 mm. Hg in the TRD group, a reduction of 21 mm. Hg in only 8 hours. This P_aCO₂ is significantly lower (p < 0.05) than the mean of 53 mm. Hg in the RDS group. The mean P_aCO₂ remained at 41 mm. Hg in the TRD group at 24 hours of age, a level again significantly lower (p < 0.05) than the mean of 51 mm. Hg in the RDS group, but significantly higher (p < 0.001) than in the controls.

II

Respiratory Distress Syndrome, and Control Premature Newborns

P _a CO ₂ (mm. Hg)			ΔP _a CO ₂ *	pH			Base Excess (mEq/l.)†		
2-8 hr.	8-18 hr.	20-30 hr.	8-18 hr.	2-8 hr.	8-18 hr.	20-30 hr.	2-8 hr.	8-18 hr.	20-30 hr.
48	33	42	-15	7.26	7.39	7.41	-3.4	-4.0	+2.8
77	37	43	-40	7.17	7.43	7.44	+1.5	+1.5	+5.5
47	38	40	-9	7.25	7.32	7.34	-5.7	-5.5	-3.4
61	44	42	-17	7.22	7.36	7.40	-1.8	+1.2	+1.8
61	49	45	-12	7.16	7.34	7.36	-5.3	+1.7	+1.5
53	42	39	-11	7.25	7.39	7.42	-2.9	+1.8	+1.6
52	32	39	-20	7.26	7.35	7.40	-2.0	-7.0	+0.6
48	45	36	-3	7.19	7.36	7.43	-10.9	+0.2	+0.3
46	40	34	-6	7.28	7.34	7.36	-4.2	-3.3	-5.0
60	38	38	-22	7.26	7.35	7.38	-0.3	-3.5	-1.5
92	56	48	-36	6.99	7.25	7.41	-6.4	-2.7	+6.5
99	41	47	-58	7.08	7.39	7.35	-4.1	+0.8	+0.5
62	41	41	-21	7.20	7.36	7.39	-3.8	-1.6	+0.9
12	12	12	12	12	12	12	12	12	12
5.0	2.0	1.0	4.7	0.03	0.01	0.01	0.9	0.9	1.0
57	53	51	-4.5	7.19	7.30	7.31	-5.9	-1.3	-0.2
19	19	16	19	19	19	16	19	19	16
5.5	4.8	4.8	4.6	0.02	0.02	0.02	0.6	0.9	1.2
n.s.	<0.05	<0.05	<0.02	n.s.	<0.02	<0.01	n.s.	n.s.	n.s.
38	33	32		7.32	7.36	7.37	-6.4	-6.0	-5.7
17	6	17		17	6	17	17	6	17
1.6	2.8	1.0		0.01	0.02	0.01	0.4	0.4	0.5
<0.001	<0.05	<0.001		<0.001	n.s.	n.s.	<0.02	<0.001	<0.001

Values corrected for effect of raised P_aCO₂ (Dell *et al.*, 1966).

n.s. = non-significant.

The initial mean arterial pH of 7.20 in the TRD group was essentially the same as that of 7.19 in the RDS group. By mean age 12 hours, the pH of the TRD group had risen to 7.36 following intravenous NaHCO₃. This level was equal to that of the control premature infants at this age, and significantly higher ($p < 0.02$) than the mean of 7.30 in the RDS group. The persistence of a lower pH in the RDS group was attributable to the high P_aCO₂. At age 24 hours the TRD group had a mean pH of 7.39, a value again equal to that of control infants, and significantly higher ($p < 0.01$) than the mean of 7.31 in the RDS group.

The mean initial base deficit (or negative base excess) of the TRD group was 3.8 mEq/l., a value not significantly less than the mean of 5.9 mEq/l. in the RDS group. After the initial sample, the TRD and RDS infants received a single intravenous injection or rapid infusion of NaHCO₃ in a dose calculated to correct completely the base deficit, and to raise the arterial pH above 7.30. Subsequently, both groups received intermittent injections of NaHCO₃ calculated to keep the arterial pH above 7.30. This therapy resulted in a negligible average base deficit in both groups of patients at 8-15 and 20-30 hours of age. The mean base deficit of about 6 mEq/l. in our control premature infants

throughout the period 0-30 hours compares with a value of about 4 mEq/l. found by Bucci, Scalamandrè, Savignoni, and Mendicini (1965) and of about 2 mEq/l. found by Malan, Evans, and Heese (1965).

Chest x-ray films obtained in 6 of the TRD infants showed hyperaeration and, in 2 cases, the reticulo-granular pattern usually associated with RDS.

As can be seen from Table II, Cases 11 and 12 in the TRD group had initial clinical scores of 7, a P_aO₂ less than 100 mm. Hg in 100% O₂, and an arterial pH value of 7.08 and 6.99. The following description of one of these exceptional cases illustrates how rapidly recovery can occur when the infant receives the therapy outlined above.

Case Report (Case 12)

This 1770 g. infant was the product of an apparently normal pregnancy, except for premature rupture of the membranes at 32 weeks' gestation, followed within 60 hours by an uncomplicated vaginal delivery. The amniotic fluid was normal and no resuscitation was required. The 1- and 5-minute Apgar scores were 8. At 1 hour, the baby had a clinical respiratory distress score of 6, despite an inspired O₂ concentration of 50% and restoration of skin temperature to 35.5° C. By

3 hours, the clinical score had risen to 7. Analysis of arterial blood at that time gave a P_{aCO_2} of 99 mm. Hg, a pH of 7.08, and a base deficit of 4 mEq/l. The P_{aO_2} was 67 mm. Hg during 100% O_2 breathing. A P_{aO_2} during air breathing was not obtained because of the clinical condition.

The inspired oxygen concentration was subsequently maintained above 90%. At age 3½ hours, an intravenous infusion of 5% glucose was started, with the immediate injection of 5 mEq $NaHCO_3$, followed by the slow infusion of a further 2 mEq over the next 6 hours.

There was rapid improvement, and at age 8 hours the inspired oxygen concentration could be reduced to 60%. At age 10 hours the clinical score had fallen to 3, associated with a decrease in P_{aCO_2} to 41 mm. Hg, a reduction of 58 mm. Hg over 7 hours. Concomitantly, the arterial pH rose to 7.39 and the base deficit was completely corrected. The P_{aO_2} increased to a level of 290 mm. Hg in 60% O_2 .

At age 20 hours the infant had a clinical score of 0, and the P_{aO_2} during air breathing was 74 mm. Hg, normal for this age, and the subsequent course was uneventful.

Comments

Boston, Geller, and Smith (1966), in a study of 51 infants with RDS, divided their patients at about 4 hours of age into a 'high risk' group (mortality 74-81%) and a 'low risk' group, on the basis of an arterial pH above (and equal to) or below 7.20, or a P_{aO_2} above (and equal to) or below 100 mm. Hg during 100% O_2 breathing. Using the arterial pH criterion, one-half of our TRD infants would have been classified in the 'high risk' group, whereas only two (Cases 11 and 12) would have been so designated on the basis of the P_{aO_2} . This experience casts doubt on the arterial pH as a reliable early criterion for the assignment of risk.

Only 2 infants in the TRD group had 5-minute Apgar scores below 7, and though this does not eliminate intrauterine asphyxia during labour as a cause of transient respiratory distress, it seems unlikely that the asphyxia was extreme at the time of delivery. A low birthweight for gestational age occurred in only 2 of the TRD infants (Cases 4 and 7), making this an improbable predisposing factor. The infants with transient tachypnoea, described recently by Avery, Gatewood, and Bramley (1966), are not comparable to our patients.

We conclude that there are some infants who initially manifest the clinical and biochemical picture of moderate or severe respiratory distress, but who recover within the first 18 hours of life after therapy with oxygen, sodium bicarbonate, and intravenous fluids. In any investigation of a new form of therapy to be used early in the respiratory distress syndrome, failure to recognize this group

of patients could lead to misinterpretation of their dramatic improvement as an effect of the new therapy.

Summary

Twelve premature newborns at age 4 hours had respiratory distress syndrome which, though clinically and biochemically of moderate to severe degree, had practically disappeared by 18 hours. Infants with this transient form of respiratory distress (TRD) could not be distinguished at age 4 hours from a group comparable in weight and gestational age with typical respiratory distress syndrome (RDS) persisting beyond age 30 hours, and sometimes proving fatal. Arterial PO_2 during air breathing tended to be somewhat higher in the TRD group, but arterial pH, PCO_2 , and base deficit initially showed changes of similar degree in both TRD and RDS groups. Both groups received equivalent therapy, including oxygen and intravenous sodium bicarbonate. Whereas in the TRD group by age 18 hours the average arterial PCO_2 had fallen by 21 mm. Hg and pH had risen to control levels, in the RDS group, a moderately severe respiratory acidosis persisted throughout the first 30 hours.

The existence of a transient form of respiratory distress should be taken into account when any new therapy for RDS is to be evaluated.

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