THE RESPIRATORY DISTRESS SYNDROME OF THE NEWBORN

A REPORT OF 135 CASES TREATED CONSERVATIVELY

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The respiratory distress syndrome is the term most commonly used to describe the clinical picture of respiratory difficulty which occurs in some newborn infants. It occurs most frequently in prematurely-born infants, in neonates born to diabetic mothers,[1,2] and frequently in infants delivered by caesarean section[3]—or when the pregnancy is complicated by antepartum haemorrhage or toxaemia.[4] Less frequently, the syndrome occurs in full-term infants delivered normally. In those infants who die and come to autopsy, the histological picture of pulmonary hyaline membrane is found.[5] The syndrome is now the most common single cause of neonatal deaths,[6] and presents the major problem in the care of the premature infant. The diagnostic features of the syndrome are chest retraction with inspiration, expiratory grunting, cyanosis and decreased air entry on auscultation of the lungs, present during, and persisting beyond the first 3 hours of life, in the absence of coexisting disease.[7,8]

The aim of this paper is to present the mortality rate from the respiratory distress syndrome as reported in a recent series of cases, and to discuss the various methods of treatment. I will then present a series of 135 cases treated in private practice in Johannesburg during the past 6 years. The treatment of these cases is described, and the results compared with those reported in recent series.

TREATMENT AND PROGNOSIS OF THE RESPIRATORY DISTRESS SYNDROME

The conventional method of treatment of the respiratory distress syndrome involves no specific therapy. In the delivery of premature infants and those neonates potentially liable to develop respiratory distress one obviously minimizes the trauma, asphyxia and exposure to cold after birth. Positive-pressure resuscitation is essential in those infants who remain apnoeic. The infants are usually nursed in incubators with temperatures of 88 - 94°F, with a high humidity. Oxygen is essential to overcome the cyanosis, and the risk of retrolental fibroplasia with an oxygen concentration of more than 40%, is negligible in the presence of cyanosis. Antibiotics are used by some investigators, the commonest being chloramphenicol, while others withhold all antibiotics until there are overt signs of infection.[9] Apnoeic spells are common, so that constant supervision is essential, and immediate resuscitation measures instituted. With the above conventional therapy, it has been estimated that the mortality rate from the disease has ranged from 40% to 50%.[5,10]

Metabolic Changes

In 1959 and 1960 Usher,[11,12] in Montreal, first stressed the importance of the metabolic changes which occur in infants suffering from respiratory distress. The infants invariably first develop an uncompensated respiratory acidosis, which becomes complicated within 12 hours, by a metabolic acidosis and hyperkalaemia. He presented preliminary results of treatment with intravenous glucose and bicarbonate, the quantities required being controlled by frequent estimations of the blood pH, pCO_2, and plasma bicarbonate. His preliminary report suggested that the expected mortality rate of 50% could be reduced to 25%. In subsequent investigations, Usher has confirmed the lowering of the mortality rate, and in 1963[13] he reported the results of a controlled trial of 70 premature infants with the respiratory distress syndrome. In the 35 control

infants, in whom conservative treatment was used, the mortality rate was 37%, but in the group of 35 neonates given intravenous therapy, the mortality rate was only 17%. However, only in the group of premature infants weighing more than 1,750 G at birth, was there a statistically significant difference in the 2 methods of treatment.

Other workers, adopting Usher's method of treatment, have also reported a reduction in the mortality rate from the disease. In 1962 Hutchison *et al.*,[9] from Glasgow, reported a fall in mortality rate from 66% to 41%. In 1964 these workers[14] again reported a mortality rate of 46% in a group of 100 infants treated with intravenous glucose and bicarbonate. Among the 46 infants who died, a large number had complicating problems, especially cerebral haemorrhage, which caused their deaths. Hyperbaric oxygen was used in a small number of patients, but although cyanosis was quickly abolished, there appeared to be no improvement in the prognosis.

Various other forms of treatment have been suggested, but no large series of patients has been reported, and no striking results claimed. These treatments include electrophrenic respiration[15] and augmented respiration,[16] intermittent positive-pressure respiration,[17,18] sternal traction,[19] phlebotomy,[20] digitalization,[21] fibrinolytic agents,[22,23] and transfusion and perfusion with oxygenated, heparinized blood.[24]

THE PRESENT SERIES

The present series comprises all neonates with the respiratory distress syndrome whom I have treated in private practice in Johannesburg between June 1958 and June 1964. These infants were all born in private maternity homes in Johannesburg. In all, a total of 135 cases was seen in the period specified.

Clinical Features

All infants diagnosed as suffering from the respiratory distress syndrome exhibited expiratory grunting, tachypnoea with respiratory rates above 70 per minute—a number of infants had respiratory rates above 120 per minute—marked and persistent sternal, subcostal and intercostal recession during inspiration, and cyanosis without oxygen. All the infants had subcutaneous oedema in varying degree, and the majority became jaundiced. It is interesting to note that a transient continuous heart murmur of a patent ductus arteriosus was heard in only 2 of the infants, and a transient systolic heart murmur in another 4 patients.[25-27] Thirty-three of the cases were considered to be of mild or moderate severity. In these, expiratory grunting and tachypnoea were present, but either chest retraction was not severe or cyanosis was not a feature. Sixteen of these infants were considered to be mildly affected, and given no specific treatment, while the other 17 were classified as moderately severe, and treated as were the severely affected infants. None of these 33 infants died.

Method of Treatment

All the infants were nursed in incubators with environmental temperatures of 90 - 92°F, and a humidity of 80 - 90%. Oxygen was administered in sufficient quantities to eliminate cyanosis, and then the lowest concentration required to keep the infant pink was given. Frequently a concentration above 40% was necessary, but I am not aware of any case of retrolental fibroplasia having occurred. Prophylactic intramuscular injections of 300,000 units of procaine penicillin was administered daily to all infants. In addition, all the infants with severe or moderately severe respiratory distress were given 25 - 50 mg. of cortisone acetate intramuscularly every 6 hours, until there were signs of recovery, when the dosage was gradually reduced and eventually stopped. All infants in whom liver enlargement occurred during the course of the disease were digitalized, usually with oral digoxin, but occasionally intramuscular digitalis was required when vomiting prevented oral administration. Digitalis was thus given to all infants in whom the liver became palpable when previously it could not be felt, or when an originally palpable liver became obviously larger.

ANALYSIS OF THE TOTAL NUMBER OF 135 CASES

Details of the 135 cases treated are summarized in Table I. It is seen that there is a slight preponderance of males over females. There were 32 deaths, and of those who died, the same proportion of males to females is maintained. The mean weight of 2,045 G is rather high compared with other reported series, and is explained by the number of infants weighing more than 2,500 G at birth. Of these 49 infants weighing more than 2,500 G at birth, 20 were delivered by caesarean section, and a further 6 were delivered *per vaginam* to diabetic mothers. In a further 10 the delivery was considered to be difficult, necessitating forceps extraction. Twenty-one of the infants were apnoeic for sufficiently long periods to necessitate intratracheal intubation for resuscitation, and 11 of these infants died.

TABLE I. ANALYSIS OF 135 CASES OF RESPIRATORY DISTRESS SYNDROME

Sex	
Males	78 = 58%
Females	57 = 42%
Mean weight	4 lb. 8 oz. — 2,045 G
Mean gestational age	34 weeks
Asphyxia neonatorum (requiring resuscitation)	21 = 15·5%
Deaths	32
Males	18 = 56%
Females	14 = 44%

TABLE II. DAY OF DEATH OF 32 INFANTS WITH RESPIRATORY DISTRESS SYNDROME

Day	*1*	*2*	*3*	*4*	*5*
No. of deaths	15	11	4	1	1

Results of Treatment

There were 32 deaths in the series. The day on which these infants died is shown in Table II. As in all other reports, it is clear that the majority of deaths occurred in the first 72 hours after birth. Postmortem examinations were performed on 8 of these infants, and in each case, the classical features of pulmonary hyaline membrane disease were found.

The mortality rate in the whole series has been calculated in the various birthweight groups (Table III). It is seen that the over-all mortality rate is 23·7%. There are too few infants in the birthweight groups of below 1,500 G to allow for much comment, but it should be stressed that a

fair proportion of these very small sick prematures do survive, often with no sequelae related to the respiratory difficulty or to cerebral anoxia.

TABLE III. FATALITY RATES ACCORDING TO BIRTHWEIGHTS OF ALL CASES OF RESPIRATORY DISTRESS

Birthweight	*No. of infants*	*Deaths*	*% mortality*
< 1,000 G (2 lb. 3 oz.)	4	2	50
1,000–1,500 G (2 lb. 3 oz.–3 lb. 4 oz.)	8	2	25
1,500–2,000 G (3 lb. 4 oz.–4 lb. 6 oz.)	30	12	40
2,000–2,500 G (4 lb. 6 oz.–5 lb. 8 oz.)	44	10	22·7
> 2,500 G (5½ lb.)	49	6	12·2
Total	135	32	23·7

The mild and moderately severe cases have been eliminated in the further analysis of the results of therapy, and the mortality rate in the severely affected infants is seen to be 31·4% (Table IV). If the 17 moderately severe cases who were treated with cortisone are included, then the mortality rate is 26·9%. It is clear that the mortality rate is inversely related to the birthweight of each group. Of those infants weighing less than 2,000 G at birth, there were 40 cases with 16 deaths—a mortality rate of 40%. If the group weighing more than 2,500 G at birth is excluded, then the total mortality rate in those infants weighing less than 5½ lb. with severe respiratory distress is 36%, i.e. 26 deaths out of 72 infants treated.

TABLE IV. FATALITY RATES ACCORDING TO BIRTHWEIGHTS OF SEVERE CASES OF RESPIRATORY DISTRESS

Birthweight	*No. of infants*	*Deaths*	*% mortality*
< 1,000 G (2 lb. 3 oz.)	4	2	50
1,000–1,500 G (2 lb. 3 oz.–3 lb. 4 oz.)	8	2	25
1,500–2,000 G (3 lb. 4 oz.–4 lb. 6 oz.)	28	12	42·8
2,000–2,500 G (4 lb. 6 oz.–5 lb. 8 oz.)	32	10	31·3
> 2,500 G (5½ lb.)	30	6	20
Total	102	32	31·4

TABLE V. MORTALITY RATE IN RESPIRATORY DISTRESS SYNDROME

Author	*No. of cases*	*Deaths*	*% mortality rate*
Usher, R. (1960)	49	12	24·5
Driscoll and Smith (1962)	44	20	45
Usher, R. (1963) (treated conventionally)	94	38	42
Usher, R. (1963) (IV therapy)	118	24	20
Miller, H. C. (1963)	181	81	44·7
Hutchison *et al.* (1964)	100	46	46
Present series (1964)	135	32	23·7
Severe cases only	102	32	31·4

In Table V, the mortality rates in various recently reported series are presented. From this it appears that the mortality rate in the conventionally treated series, is in the region of 40 - 45%. Only Usher reports a marked reduction of the fatality rate to 20 - 25%.

COMMENT AND CONCLUSIONS

In the present series of infants suffering from the respiratory distress syndrome, treated with cortisone, penicillin and digitalis when indicated, the mortality rate seems to be within the extremes claimed by Usher and by those using conventional methods. Before complicated forms of therapy are embarked upon, it must be borne in mind that a recovery rate of about 70% can be achieved with the simple method of treatment as described above.

To assess whether cortisone has any specific role in promoting the recovery of infants suffering from respiratory distress syndrome, is difficult without using the steroid in an organized double-blind trial. Perhaps the adrenal steroids serve as a non-specific life-promoting hormone, and thus permit the distressed infant to live longer, and so reach the stage of the disease at which spontaneous recovery can be expected, i.e. the 3rd or 4th day of life.

SUMMARY

The treatment of the respiratory distress syndrome of the newborn is discussed, and the reported mortality rates are presented.

A group of 135 cases treated conservatively in private practice in Johannesburg is presented, the method of treatment outlined, and the mortality rate compared with reported series in the recent literature.

It is shown that with the treatment as described, there is a recovery rate of at least 70%, which compares favourably with the results claimed by most other workers in treating the syndrome in the neonate.

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