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Routine Peritoneal Dialysis in Prematures with Respiratory Distress Syndrome

By

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Since 1969 peritoneal dialysis has been applied for the routine treatment of the respiratory distress syndrome. Results are illustrated by statistical figures for the years 1967 and 1969. Mortality rate among the premature patients fell from 42.6% in 1967 to 34.7% in 1969. Improvement was especially marked in perinatal mortality. Mortality rate of the distressed cases was considerably more favourable in 1969 than in 1967, and also conditions respecting restoration of the acid—base balance were much better in 1969. Theories concerning the mode of action of dialytic treatment are offered.

Led by theory that accumulated metabolites are essentially involved in the pathogenesis of the respiratory distress syndrome (RDS), the possibility of controlling the disease by peritoneal dialysis has been studied in this Department since 1966 [6, 7]. Having found that peritoneal dialysis of newborn rabbits and adult mice increased their resistance to hypoxia, the procedure was applied in 50 premature babies with RDS, who had failed to respond to other treatments. Results were compared with controls chosen at random [8].

Since peritoneal dialysis yielded satisfactory results even in advanced cases of RDS, we adopted it in 1969 as a routine method for the treatment of all premature infants suffering from the disease. This paper presents an account of our observations and results; considering that it involved a large material, it may command some interest since only a few papers on single cases treated with dialysis have appeared since our first communication [11, 22].

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Material and Methods

In the following we present statistical data of our premature ward from the years 1967 and 1969.

Rules of admission and conditions of nursing were the same in the two years examined. More than 50% of the premature infants were referred to us by the Department of Obstetrics of Szeged University Medical School, the rest was sent by the obstetric sections of hospitals situated within a radius of 100 km. Babies with a birth weight exceeding 2000 g were admitted only if they displayed some complication. While all infants weighing less than 2000 g were admitted from the

Obstetrics Department, admission of underweight babies from other hospitals was subject to selection. With a view to avoiding unnecessary transportation, these hospitals referred to us mainly babies born with less than 1500 g weight and even among those the grave cases. Transportation occurred in special incubators.

The premature ward of our Department is provided with incubators kept at a temperature between 34.0 and 35.5 °C. For cyanosed cases the oxygen content of the inhaled air was raised to 40—50%. Humidity in the incubators was about 70%.

RDS was diagnosed on the evidence of clinical manifestations (respiratory rate, thoracic retraction, grunting, cyanosis). Besides, acid—base values in arterialized capillary blood were checked at least twice daily by means of the micromethod of ASTRUP et al. (3). In order to avoid systematic catheterizations of the umbilical arteries, arterial pO_2 was not controlled regularly. If the clinical and laboratory findings pointed to the probability of RDS, thoracic X-rays were made to facilitate diagnosis and estimate the gravity of the condition.

In 1967, prematures with RDS were treated with USHER's [33] alcali—glucose—insulin infusion in doses determined by laboratory results. Sodium—bicarbonate was added to the infusion if the acid—base balance failed to normalize. In the case of respiratory arrest, manual resuscitation was resorted to and the manipulation was continued with intermittent positive pressure breathing. The first attempts with peritoneal dialysis were made in 1967; the material of that year included 26 randomly chosen grave cases treated with dialysis.

As from 1969, all cases of RDS were immediately subjected to peritoneal dialysis, and this method of treatment was preferred even in doubtful cases with a birth weight of less than 1500 g. Dialysis was not combined with drug treatment or rehydration. In cases of respiratory failure we proceeded as in 1967.

We are applying continuous peritoneal dialysis. The right abdominal wall is pierced with a cannula and through this a thin polyethylene tube is introduced into the abdominal cavity for the inflow of the dialysing solution. A special tube with numerous holes in its 4 cm terminal portion or a 8—9 F gastric tube perforated at 30 to 40 points serves for outflow. This tube, too, is introduced into the abdominal cavity through the lumen of thick cannula. Sealing and fixation of the tubes were ensured by sutures. After connecting the inflow tube to the dialysing apparatus, treatment was started with 40 to 60 drops/min. The outpouring fluid was conducted into a tank by the outflow tube. By piercing this with a thick needle, an air hole was created which eliminated the sucking effect. The point of puncture determined the pressure of the intraabdominal fluid. We applied a positive pressure of 2 to 3 cm H_2O; if pressure in the abdominal cavity exceeded this value the fluid overflowed and was conducted into the tank. By this technique a continuous fluid exchange at the rate of 120—150 ml/hr was obtained.

The stock solution for the dialysing fluid was composed of Na^+, 100; Ca^{++}, 4; K^+, 4; Mg^+, 2; Cl^-, 110 mEq/litre, and 1.5% glucose. To this solution were added 40 to 50 ml mol $NaHCO_3$, 100 U heparin and 100,000 U penicillin per litre.

When dialysis lasted more than 36 hrs, plasma was infused in order to replace the lost amount of protein. Oral feeding in the form of sugar water and human milk, administered by a gastric tube, was started after or sometimes already during, dialysis.

All data of every case treated in 1967 and 1969 were marked on punch cards, coded and suitably arranged.

The gravity of the disease at admission was graded according to WEISSER's [34] classification: O = no RDS; I = mild symptoms of RDS; II = marked, grave

symptoms of RDS; III = desperate condition. Another method we used for indicating the gravity of the disease was the so-called Fulham score [15] which is based on birth weight, temperature, pulse rate, respiratory rate, cyanosis, respiratory phenomena, laboratory results, and X-ray records but in our present study the arterial pO_2 was estimated on the basis of clinical signs. The gravest condition observed during the first 14 postnatal hours determined the degree of the disease.

Acid—base disturbances were likewise graded by means of the Fulham score: pH: 7.2—7.29 2; pH: <7.2 4; 5—15 base deficit: 2; >15:4; 54—60 pCO_2:1; > 60:2

Since we had to rely on the statements of others as regards time of pregnancy, this parameter was disregarded in evaluation, in order to eliminate a source of error.

Statistical significance was computed by the four-field Chi square test.

Results

Sex ratio, birth weight, gravity of the disease at admission, according to Weisser [34] and to the Fulham, score, comparative data regarding traumatization and vital diseases not connected with prematurity, are presented in Table I. It can be seen that conditions regarding birth weight were unfavourable in both years. Most of the babies were gravely ill when admitted or, else, developed

Table I

Data regarding the material of premature infants

Year	1967	1969
Number of premature babies	291	311
Male	142	162
Female	149	149
Birth weight (g)		
Less than 1500	118	107
More than 1500	173	204
Degree of the disease on entry (according to Weisser (34)]		
0	115	115
I	87	71
II	58	91
III	32	34
Fulham score (15)*		
Less than 15	115	134
15—20	30	24
21—30	62	61
More than 30	61	51
Signs of traumatization	26	39
Other vital disease	10	10

* Data not indicated in the Table were not available.

serious clinical symptoms shortly thereafter. Prognosis was unpromising in many cases because of traumatization or some other primary disease. In 1969, the proportion of male babies was larger, more infants displayed grave symptoms on arrival and there were more traumatized infants; on the other hand, conditions were more favourable in respect of weight distribution and the Fulham score. These differences were, however, negligible.

Table II shows the mortality rate. The incidence of fatalities amounted to 34.7% in 1969 against 42.6% in 1967. Improvement of life expectation was further shown by the fact that in 1969, death ensued later than in 1967; figures regarding death in the perinatal period revealed a still more marked improvement.

Table III presents data on cases in which death was due some complication other than RDS. It can be seen that in both years more prematures died of later complications (usually infection) after the first symptomless postnatal days or after having survived RDS.

As to the incidence of fatal haemorrhagic complications, intracranial haemorrhage from the terminal vein is considered to be chiefly of hypoxic and not of traumatic origin; it is a partial phenomenon of haemorrhagic disease [21, 26]. The incidence of this complication was considerably less in 1969 than in 1967, especially in the cases of simultaneous RDS. Intracranial haemorrhage, a phenomenon accompanied by sudden stupor, circulatory and respiratory failure, occurred also in babies who had displayed no previous symptoms. The rate of pulmonary haemorrhage, an invariably fatal complication observable in the course of resuscitation at exposure of the trachea, was similar in both years.

The other fatalities were mainly due to RDS and to a lesser extent

TABLE II

Mortility data of premature infants

Year	1967	1969
Number of treated prematures	291	311
Recovered	157	203
Died	124 ←→	108
Time of death		
Within 12 hrs	33	24
Between 12 and 36 hrs	30	24
Between 26 hrs and 3 days	30	17
Between 3 and 7 days	20	25
After more than 7 days	11	18

←→ Statistically significant ($p < 0.05$).

to traumatization; most of these cases showed a desperate condition at admission.

Data in respect of all cases diagnosed as RDS are assembled in Table IV. The number of cases was almost identical in the two examined years with a considerably more favourable mortality rate in 1969. The Table shows further the postnatal hour at which the first symptoms of RDS appeared.

It was mainly in cases of RDS that we expected favourable results from dialysis. It seemed therefore necessary to compare the figures of the two years in respect of cases in which the prematures were suffering from uncomplicated RDS. From all the cases of RDS we selected those in which the patients died in the first 4 postnatal hours as well as those in which RDS was associated with complications. Figures so obtained are

TABLE III

Causes of death other than RDS and traumatization

Year	1967		1969	
	Combined with RDS	Without RDS	Combined with RDS	Without RDS
Infection	9	5	9	9
Late complication	5	5	8	10
Intestinal atresia	—	3	—	4
Congenital defect	—	3	—	1
Chromosomal anomaly	—	—	—	1
Spina bifida	—	—	—	2
Intracranial haemorrhage	23	3	9	6
Pulmonary haemorrhage	5	3	6	7

TABLE IV

Data regarding prematures with RDS

Year	1967		1969	
	Total	Recovered	Total	Recovered
Number of RDS cases	150	47	147	71
Onset of RDS				
Less than 2 hrs	95	23	90	38
Between 2 and 6 hrs	28	10	32	19
Between 6 and 12 hrs	20	9	13	6
Between 12 and 24 hrs	7	5	12	8

TABLE V

Perinatal mortality of patients suffering from uncomplicated RDS

Year	1967		1969	
	Total	Recovered	Total	Recovered
Number of cases	102	39	100	65
Fulham score 20—30	40	20	35	20
Fulham score over 30	47	4	32	10

↑ ↑ statistically significant ($p \ll 0.01$).

TABLE VI

Changes in acid—base balance in prematures treated with infusion (1967) and in those treated with peritoneal dialysis (1969)

	1967			1969		
Acid—base imbalance according to Fulham score	0—4	5—6	7—10	0—4	5—6	7—10
Number of examinations	36	17	65	49	31	52
Considerable improvement of acid—base values	18	11	25	29	24	30
Deterioration	15	4	30	7	∅	1

listed in Table V which shows that the number of such cases was practically the same in both examined years with a significantly more favourable survival rate in 1969. It is evident from the Table that, although GOMEZ et al. [15] classified cases with a Fulham score above 30 as hopeless, several babies of this group had survided; moreover, the survival rate in the group with a Fulham score between 20 and 30 was more favourable in 1969 than in 1967.

Figures in Table VI reveal another favourable effect of peritoneal dialysis: acid—base values improved quite considerably in the majority of cases, even in the group with a score between 7 and 10, *i.e.* among the most serious, and even in fatally terminating cases. In contrast, alkali infusion administered in 1967 often failed to restore the acid—base equilibrium, and conditions became sometimes even worse.

Table VII illustrates the correlation between the duration of dialysis and life expectancy. A therapeutic effect can be expected only if dialysis lasts more than 24 hours; prospects are most promising if the symptoms improve so much that the intervention can be discontinued after 48 hours.

TABLE VII

Duration of dialysis and number of recoveries in the year 1969

Duration of treatment	Total	Recovered
0— 4 hrs	10	∅
4—24 hrs	27	2
1— 2 days	53	37
2— 3 days	40	27
beyond 3 days	9	5

TABLE VIII

Number and complications of peritoneal dialysis, number of recoveries in the year 1969

	Total	Recovered
Number of dialysed patients	139	71
Technical complication	7	4
Oedema	7	5
Meteorism	6	4
Biliary regurgitation	3	1
Total number of complications	23	14

Statistical data regarding complications in connection with dialysis are presented in Table VIII. It can be seen that in 16.6% of the cases complications occurred which, however, did not impair the patients' life expectation. Technical complications usually consisted in an obstruction of the outflow tube which could be remedied by a readjustment or, exceptionally, by the exchange of the tube. In 7 cases abdominal and scrotal oedema appeared, it invariably disappeared 24 hours later after the termination of dialysis. In some cases there appeared disturbances of intestinal passage accompanied by the presence of bile in the stomach or by meteorism; these were remedied in 24 hours by continued fasting during which the necessary volume of fluids was supplied by infusions. Late disturbances of evacuation, haemorrhage or peritonitis did not occur.

In order to demonstrate the favourable result of peritoneal dialysis by another parameter, we present the premature mortality rate for the first week of life registered in our Department (Table IX) and that for the entire population of Szeged (Table X).

TABLE IX

Death in the first week of life of premature infants treated at our Department

	1967	1969
Number of prematures	241	272
Died in the first 7 days	61	45

↔ statistically significant ($p < 0.05$).

TABLE X

Death in the first week of life of premature infants born in Szeged

	1967	1969
Number of prematures	138	166
Died in the first 7 days	36	34

↔ statistically *not* significant ($p > 0.05$).

DISCUSSION

The fact that figures for 1969 are compared in this study with those for 1967 and that the differences were evaluated statistically does not mean that the year 1967 should be regarded as a control period. All we wanted was to have a basis for comparison. Results obtained from a simultaneously randomized control group are more convincing; examinations of this nature, confined to the gravest cases have been reported earlier [8]; they revealed a statistically significant difference in favour of dialysed patients. The data quoted in the present paper had only the purpose to demonstrate the improvement obtainable by routine peritoneal dialysis, especially if it is started soon enough. Early dialysis leaves the possibility open that in some cases other methods of treatment might also have been beneficial. Yet, in view of the simplicity of the method applied by us and the small number of complications this risk may safely be incurred. Our experience collected in the course of 290 peritoneal dialyses has made it clear that the intervention is surprisingly well tolerated by premature babies.

Figures regarding our premature material for 1969 alone make it evident that the results were promising, a fact mainly attributable to peritoneal dialysis. Of course, owing to congenital anomalies, vital complications, traumatization and susceptibility to infections, prematurity still carries a high mortality rate, but peritoneal dialysis presumably improves conditions despite these fac-

tors. The best results were achieved in cases of RDS unaccompanied by other disorders. That results were not still more favourable in 1969 was due to the advanced stage of the disease and the loss of time caused by transportation. Other limiting factors were pulmonary and intracranial haemorrhage, complications which may suddenly arise in patients after having recovered from the primary disease.

As to the presumable mechanism of the effect of dialysis on RDS, we assume that a disturbance of intermediary metabolism caused by the insufficiency of oxidative processes lies in the background of the disease. Accumulation of metabolites interferes with intracellular processes, and it seems that peritoneal dialysis ensures the observed therapeutic result by the elimination of metabolites.

Disturbances of the acid—base balance is an essential pathogenic factor of RDS [10, 17, 27, 33]. Peritoneal dialysis is an efficient method for the restoration of homoeostasis, without burdening the organism with superfluous electrolytes.

The changes in blood chemistry in cases of RDS are not as severe as in uraemia. This notwithstanding, a grave impairment of renal function has been demonstrated to occur with RDS [13, 22, 26]. Peritoneal dialysis eliminates this source of danger.

Constriction of the pulmonary vessels and the resulting pulmonary hypoperfusion syndrome seem to be likewise important pathogenic factors of RDS. The role of humoral mediators has repeatedly been demonstrated [10, 1, 18, 19, 20, 35]. Dialysis ensures good results also in this respect.

Several authors have observed an accumulation of vasoactive substances which gives rise to microcirculatory disturbances [9, 17, 18, 35]. The sudden increase in the circulation of brown adipose tissue observed under conditions of hypoxia [20] is brought about by the mediation of catecholamines, a further phenomenon favourably influenced by dialysis.

There are numerous experiments to prove that an apparently important factor in the pathology of RDS, disturbances in blood coagulation, especially in fibrinolytic activity [25], is likewise brought about by humoral mediation. This, too, may respond to dialysis.

Lack of surface-active material coating the alveoli [4] is undoubtedly a decisive pathogenic factor in RDS. Several experimental observations [29] justify the supposition that this, too, is a result of metabolic disorders since after vagotomy the lack of surfactant can be counteracted by sympatholytic drugs [19].

There is an increasing number of data to show the pathogenic importance of the obstruction of pulmonary lymph flow [2, 14, 28, 32]. Owing to its vast surface the peritoneal cavity is in close contact with the lymphatic system. The peritoneum may be regarded in this respect not merely as a dialysing surface, for it is through the lymph vessels that not only fluids but also macromolecules and even cells are absorbed from the ab-

dominal cavity. Peritoneal dialysis must affect a certain degree of lymph drainage, a supposition supported by the observation that body weight of our patients was found to have diminished by the termination of treatment.

Other presumably favourable therapeutic effects of peritoneal dialysis are its local action on splanchnic microcirculation and its indirect action on hepatic activity *via* the portal vessels.

A further advantage of the method consists in the high glucose concentration of the dialysing fluid which counteracts hypoglycaemia, a frequent concomitant of RDS; besides, the glucose serves as a calorie source. The fact that the outflowing fluid contains a considerable amount of bilirubin must also be regarded as a beneficial effect of dialysis.

As regards the drawbacks of peritoneal dialysis, it involves the loss of proteins, aminoacids and vitamins; it may even wash out therapeutically administered drugs. All these disadvantages are readily corrigible.

Complications are negligible if compared to the risk of the primary disease; the method, as applied by us, is technically simple and does not interfere with respiration.

Peritoneal dialysis is not incompatible with other methods of treatment, *e.g.* with intermittent positive pressure breathing and this the less as this intervention is applied only in advanced stages of the disease [12, 31]. We resort to it only after resuscitation following prolonged apnoea if spontaneous respiration cannot otherwise be restored. The use of respirators was rarely successful in cases of this kind; it yielded better results in the treatment of grave pulmonary complications appearing after the fourth day of life. Viewed from this angle, peritoneal dialysis may be expected to reduce the necessity of IPPB; if it is nevertheless unavoidable, dialysis improves the chances of survival.

In the last analysis, the mechanism of the therapeutic action of peritoneal dialysis is still obscure. It seems logical to suppose that as a number of factors are involved in the pathogenesis of RDS, the therapeutic action of dialysis is also of a complex nature. The fact that the disease responds to peritoneal dialysis will in any case facilitate the search for the decisive pathogenic factor of the respiratory distress syndrome.

References

1. Adams, F. H.: Fetal and neonatal cardiovascular and pulmonary function. Ann. rev. Physiol. **27**, 257 (1965).
2. Aherne, W., Dawkins, M. J. R.: The removal of fluid from pulmonary airways after birth in the rabbit and the effect on this of prematurity and prenatal hypoxia. Biol. Neonat. **7**, 214 (1964).
3. Astrup, P., Siggaard-Andersen, O., Jorgensen, K., Engel, K.: The acid—base metabolism. A new approach. Lancet **1**, 1035 (1960).
4. Avery, M. E., Mead, J.: Surface properties in relation to atelectasis and hyaline membrane disease. Amer. J. Dis. Child. **97**, 517 (1959).
5. Bannon, A. E., Lindley, A., Rosenblut, E., Matorell, R., Lubchenco, L. O.: Fibrinolytic activity in prema-

ture infants. Relationship of the enzyme system to the respiratory distress syndrome. Amer. J. Dis. Child. **113,** 312 (1967).

6. Boda, D., Murányi, L., Bélay, M., Ébrey, P., Eck, E.: Demonstration of the accumulation of metabolites in hypoxic conditions of premature infants to indicate the gravity of the disease. Therapeutic trials with peritoneal dialysis. Pediat. Res. **1,** 411 (1967).
7. Boda, D., Murányi, L., Bélay, M., Veress, I., Eck, E.: The treatment of hypoxia in newborn infants by peritoneal dialysis. In: P. J. Huntingford, K. A. Hüter, E. Saling (eds): Perinatal medicine. Thieme Stuttgart 1969.
8. Boda, D., Murányi, L., Altorjay, I.: Peritonealis dialysis, a gyermekkori homoeostasis, különösen a koraszülöttek distress syndromájának kezelésében. Orv. Hetil. **111,** 132 (1970).

8/a. Boda, D., Murányi, L., Altorjay, J., Veress, J.: Peritoneal dialysis in the treatment of hyaline membrane disease of newborn premature infants. Results of a controlled trial. Acta paediat. scand. (Stockh.) **70.** 1971. In press.

9. Buckingham, S., Sommers, Sh. C., McNary, W. F.: Experimental respiratory distress syndrome. I. Central autonomic and humoral pathogenetic factors in pulmonary injury of rats induced with hyperbaric oxygen and the protective effects of barbiturates and Trasylol. Biol. Neonat. **12,** 261 (1968).
10. Chu, J., Clements, J. A., Colton, E. X., Klaus, M. H., Sweet, A. Y., Tooley, W. H.: Neonatal pulmonary ischemia. Part I. Clinical and physiological studies. Pediatrics **40,** 1709 (1967).
11. Collip, P. J., Meadow, E.: Peritoneal dialysis for the respiratory distress syndrome. J. Amer. med. Ass. **203,** 169 (1968).
12. Cooke, R., Lunding, M., Lomholt, N. F., Yssing, M., Zachan-Christiansen, B., Friis-Hansen, B.: Respiratory failure in the newborn. The techniques and results of intermittent positive pressure ventilation. Acta paediat. scand. (Stockh.) **56,** 498 (1967).
13. Cort, R. L.: Renal function in the distress syndrome. Acta paediat. scand. (Stockh.) **51,** 131 (1962).
14. Deleersnyder, M., Boussaw, L.: The body lymphatics in neonatal hyaline membrane disease. Pediatrics **44,** 126 (1969).
15. Gomez, P. C. W., Noakes, M., Barrie, H.: A prognostic score for use in the respiratory distress syndrome. Lancet **1,** 808 (1969).
16. Gupta, J. M., Dahlenberg, G. W., Davis, J. A.: Changes in blood gas tensions following administration of amine buffer THAM to infants with respiratory distress syndrome. Arch. Dis. Childh. **42,** 416 (1967).
17. Haddy, F. J.: Metabolically linked vasoactive chemicals in local regulation of blood flow. Physiol. Rev. **48,** 4 (1968).
18. Hange, A., Staub, N. C.: Prevention of hypoxic vasoconstriction in cat lung by histamine-releasing agent 48/80. J. appl. Physiol. **26,** 693 (1969).
19. Heim, I., Hull, D.: Blood flow in brown adipose tissue. J. Physiol. (Lond.) **181,** 60 (1965).
20. Imre, S.: Personal communication.
21. Kabus, K., Schenk, W., Künzer, W.: Atemnotsyndrom und Blutgerinnungsaktivität. Untersuchungen über Beziehungen zwischen Säurebasenhaushalt, Blutgerinnungsfaktoren und Hirnblutungen. Versuch einer Therapie mit Plasmafraktion I und ACC76. Z. Kinderheilk. **105,** 55 (1969).
22. Kellner, R., Heine, W.: Möglichkeit zur Behandlung postnataler Azidosen. Int. Symp. zur Senkung der Säuglingssterblichkeit, Berlin 1967.
23. Kerpel-Fronius, E., Varga, F., Bata, S.: Blood gas and metabolic studies in plasma cell pneumonia and in newborn prematures with respiratory distress syndrome. Arch. Dis. Childh. **39,** 473 (1969).
24. Keuth, V., Waiblinger, H. G.: Untersuchungen zum pulmonal-vasculären Soforteffekt von Natriumbicarbonat beim Membransyndrom der Früh- und Neugeborenen. Z. Kinderheilk. **106,** 89 (1969).
25. Lieberman, J.: Pulmonary plasminogen-activator activity in hyaline membrane disease. Pediat. Res. **3,** 11 (1969).
26. Ludwig, H.: Mikrozirkulationsstörungen und Diapedeseblutungen im fetalen Gehirn bei Hypoxie. Fortschr. Geburtsh. Gynäk. **33,** 171 (1968).
27. Nicolopoulos, D. A., Smith, A.: Metabolic aspects of respiratory distress syndrome. Pediatrics **28,** 206 (1961).
28. Normand, I. C. S., Reynolds, E. O. R., Strang, L. B., Wigglesworth, J. S.: Flow and protein concentration of lymph from lungs of lambs developing hyaline membrane disease. Arch. Dis. Childh. **43,** 334 (1968).

29. Scarpelli, E. M.: Lung surfactant: dynamic properties, metabolic pathways, and possible significance in the pathogenesis of the respiratory distress syndrome. Bull. N. Y. Acad. Med. **44,** 431 (1968).
30. Schröter, W.: Grundlagen der intracellulären Stoffwechselregulation in der Perinatalperiode. Mschr. Kinderheilk, **116,** 162 (1968).
31. Silverman, W. A., Sinclair, J. C., Gandy, S. M., Finster, M., Baumann, W. A., Agate, F. J. jr.: A controlled trial of management of respiratory distress syndrome in a body-enclosing respirator. I. Evaluation of safety. Pediatrics **39,** 740 (1967).
32. Strang, L. B.: Uptake of liquid from the lungs at the start of breathing. In: Ciba Foundation Symposium on Development of the lung Churchill, London 1967.
33. Usher, R.: The respiratory distress syndrome of prematurity. I. Changes in potassium in the serum and the electrocardioagram and effects of therapy. Pediatrics **24,** 562 (1959).
34. Weisser, K.: Zur Pathophysiologie des "Respiratory Distress Syndrome". Ann. paediat. (Basel), **200,** 81 (1963).
35. Whitaker, A. N., McKay, D. G., Csavossy, I.: Studies of catecholamine shock. I. Disseminated intravascular coagulation. Amer. J. Path. **56,** 153 (1969).
36. Zweifach, B.: Functional behaviour of the microcirculation. Thomas, Springfield 1961.

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