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Hyaline Membrane Disease

The idiopathic respiratory distress syndrome of the newborn, or hyaline membrane disease, is the commonest cause of death in liveborn premature infants. Its incidence increases sharply with increasing prematurity, and it is rare in infants born at term.[1 2]

The clinical features are apparent at or shortly after birth, and include severe retraction of the chest wall with every breath, cyanosis, an increased respiratory rate, and an expiratory grunting noise. About half the affected infants die, though if they survive beyond the third day recovery is almost certain.[3] Radiographs of the chest show a "ground glass" appearance of the lung fields,[4] while pathologically the lungs are grossly atelectatic, and histologically nearly all the alveoli are found to be collapsed. The terminal bronchioles and alveolar ducts are lined with an eosinophilic hyaline membrane, which has been shown to be composed of fibrin and other materials derived from the plasma.[5]

In 1959 M. E. Avery and J. Mead[6] found that pulmonary surfactant—a lipoprotein that normally lines the alveoli and is essential to the function of the lung[7 8]—is absent in infants dying of the respiratory distress syndrome. This finding has subsequently been confirmed.[9 10] If surfactant is absent from the lung the alveoli will have a strong tendency to collapse. Moreover, uniform distribution of gas within the lung will be impossible, and it is likely that fluid will be sucked from the pulmonary capillaries into the airspaces.[9-11] Hence a deficiency of surfactant can explain the observed clinical and pathological features of the respiratory distress syndrome, and it seems to be the most important abnormality present in these infants.

The newborn infant is extremely vulnerable to the severe disruption of gas exchange caused by atelectasis and pulmonary instability, because the pulmonary arterioles at this stage of life are very sensitive to local changes in the tensions of both oxygen and carbon dioxide and *p*H.[12] In the presence of hypoxaemia and hypercapnia pulmonary vasoconstriction occurs, and the blood, instead of going through the lungs, is diverted through the foramen ovale and ductus arteriosus.[13 14] In other words, the circulation reverts to the foetal distribution, thereby aggravating the hypoxaemia.

The most important reason for the deficiency of surfactant is prematurity.[6 10] It has been shown that the lamb, delivered at a stage before surfactant appears in the lung, develops all the features of the respiratory distress syndrome.[15] In the human foetus surfactant first appears in very small amounts at about 23 weeks of gestation,[10] and is not easy to detect until the 30th week.[10 11] Since surfactant cannot be found by similar techniques in infants dying of the respiratory distress syndrome as late as the 37th week, it appears that some factor, or factors, must operate to destroy the material in at least some infants.[10] The most likely factor capable of doing so is asphyxia before, during, or immediately after birth,[16] and asphyxia appears to enhance the risk of the development of the respiratory distress syndrome in animals.[15] Asphyxia may operate

in two ways to affect the lining layer of the alveoli. Firstly, it may damage the alveolar cells which synthesize surfactant. Secondly, it may allow the exudation of fibrinogen—which has been shown to inactivate surfactant[19]—into the alveoli. Insults of this type might be expected to produce more damage in the smaller premature infants, who have little surfactant present in their lungs to start with.[10] A further possibility to account for absence of surfactant is that the material is lost during breathing, and the mechanism responsible for its synthesis is too immature to replace the deficit. Such an explanation would account for the progressive decrease in lung compliance and increase in right to left shunting of blood so often seen in these infants.[10 14 15]

The treatment of the respiratory distress syndrome is difficult. Every effort should be made to avoid premature delivery. Rapid resuscitation of the premature infant at birth, if necessary by endotracheal intubation and positive-pressure inflation of the lungs,[18] should be performed. The infant should be nursed in an incubator at a temperature which minimizes his oxygen consumption (about 95° F. (35° C.) in the smaller infant).[19] High humidity prevents loss of heat by evaporation. Disturbance should be the minimum consistent with proper observation. Careful monitoring of blood gases and *p*H is mandatory, and every premature-baby unit should be equipped with the means for doing it. An inspired oxygen concentration should be chosen which gives as nearly as possible a normal arterial oxygen tension, and the metabolic acidosis which these infants develop should be corrected with alkali. Intravenous sodium bicarbonate is usually adequate for this purpose and can be made up in a dextrose solution to control hypoglycaemia.[20] Pulmonary vasodilator drugs have been tried, but their effect remains to be proved. Feeding by stomach tube can usually be started on the second or third day.

If respiratory failure supervenes a respirator may be used,[21] and positive-pressure machines are more suitable than negative-pressure ones for this purpose. Very high pressures often have to be applied to open the alveoli, and these interfere with the venous return to the heart; hence survival after respirator treatment is relatively unusual. Infants with the greatest chance are those above 1,800 g. in weight who do not become apnoeic until the second or third day.

Further improvements in the management of this devastating disease of infancy must await practical means of preventing or overcoming the deficiency of surfactant, or of supporting the child, possibly by means of extracorporeal circulation, until the lungs recover.

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Infectious Diseases as a Specialty

It would be unfortunate if advances in immunization and chemotherapy bred complacency in dealing with infectious diseases or the fallacy that specialist physicians are no longer required in infectious-diseases units. The pattern of infectious disease has throughout history been one of constant change, a recent case in point being whooping-cough.[1] Yet two years ago A. Melvin Ramsay and colleagues[2] considered that the reduction in beds in infectious-diseases units had been carried to such dangerous limits that a sudden epidemic might find us unprepared to provide essential services. It should be noted too that the scope of the larger units has, with advantage, been greatly extended since 1948, when they ceased to be restricted to the admission of patients with statutorily notifiable diseases. The greater part they now play is an indication of the increase in frequency of some virus infections, the hazards of antibiotic therapy, and the growing number of resistant staphylococcal infections from the wards of general hospitals.

Despite the reduction in mortality from many of the killing diseases, prompt diagnosis and skilled treatment remain of paramount importance. No one can rest content in the face of 98 deaths from acute meningococcal disease in England and Wales in 1964 and 112 in 1965, for it is usually curable if detected in its early stages. Diphtheria is not always diagnosed as early as it should be, and antibiotics are not always wisely prescribed. Adequate training of undergraduates in the principles of investigation and treatment of infections and a recognized system of training for the intending specialist are still needed.

But there is a danger that trainees in infectious diseases will cease to come forward unless a policy for the preservation of the specialty is adopted. In Scotland it has been. The standing committee on training for consultant physicians, representing the Royal Colleges of Edinburgh and Glasgow and the Scottish representatives of the Royal College of Obstetricians and Gynaecologists, has made important recommendations.[3] The first is that during the period of senior registrar training it is essential that experience be gained in one of the major infectious-diseases hospitals or units. The duration of this should be two years. Secondly, the committee states that experience of a practical nature is desirable in microbiology. This period could be coincidental with the period of clinical training. Thirdly, since clinical work in infectious diseases is concerned with patients of all ages and with complications in different systems of the body, there would be an advantage in spending some of the training in special units for cardiology, neurology, and paediatrics. Likewise it would be valuable to acquire experience in epidemiology. Fourthly, because of increasing interchange between this country and continents such as India and Africa, considerable advantage would be gained from clinical experience abroad—perhaps for six months to a year. Fifthly, the committee states that the training required for the

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