Discussion

In the original article by Dubowitz et al. (1970) and in the subsequent studies there were few infants of very low weight or gestational age: there were only 3 infants at 32 weeks, one at 31, and 2 at 28 weeks. The line for the lower gestations is an extrapolation of the correlation found nearer term. Singer et al. (1973) added a further 16 scores below 32 weeks. It is therefore gratifying to have found a satisfactory correlation between the scored and calculated ages in the present study. The correlation could probably be improved if detailed antenatal findings were also used to calculate the duration of gestation. But it is in communities where such antenatal care is minimal that the highest incidence of very premature deliveries occurs. Mothers from less sophisticated backgrounds are, however, surprisingly accurate with their dates.

Summary

The accuracy of gestational age assessment (Dubowitz et al., 1970) was tested for infants weighing 1500 g or less. There was good correlation with known dates. This system is applicable to and accurate for infants delivered very prematurely.

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Short reports

Desquamative fibrosing alveolitis unresponsive to steroid or cytotoxic therapy

Fibrosing alveolitis is not uncommon in adults but is rare in infancy, though cases have been reported with predominantly a fibrosing pattern (Hilton and Rendle-Short, 1961) and with a desquamative pattern (Liebow 1972; Howatt et al., 1973). We describe a further case diagnosed by needle lung biopsy which showed a number of important differences from the usual adult pattern.

Case report

The patient was a male infant delivered by forceps at 39 weeks' gestation, weighing 3·6 kg, to a 40-year-old mother whose pregnancy had been complicated by mild hypertension for which she received diazepam and nitrazepam. 2 previous children, aged 10 and 14 years, and both parents were healthy. Though his immediate neonatal progress was uncomplicated and he was discharged home on the 5th day, he was readmitted to the Churchill Hospital aged 2 months because of persistent tachypnoea and failure to thrive. He had an occasional dry cough and was very irritable. There were no abnormal physical signs apart from his obvious growth failure. At this stage a number of investigations were carried out which failed to reveal any cause for his problems. Cystic fibrosis and immunodeficiency disorders were excluded and no pathogens were isolated. He was treated with high calorie feeds but did not gain weight.

Over the next 2 months the infant became obviously cyanosed at rest and pink when given O2. Despite persistent tachypnoea there were still no abnormal signs in his chest and chest x-rays were thought to be normal. Arterial blood gases showed hypoxia breathing air with a PO2 of 27 torr, PCO2 of 35 torr, and pH 7·3. When given 90% O2 the PO2 rose to 287 torr, suggesting severe ventilation-perfusion imbalance and excluding atelectasis or cardiac causes of right to left shunting. He was transferred to Brompton Hospital for further investigations. His chest was now clinically hyperinflated and this was confirmed by x-rays. Lung mechanics were studied in the whole body infant plethysmograph (Dr. M. Radford). Thoracic gas volume was 240 ml (expected 135 ml) confirming the hyperinflation, and airways resistance was 16 cm H2O/l per s (expected: 12 to 14 cm H2O/l per s).

A needle aspiration biopsy of the left lung was carried out under radiological control (Dr. I. Kerr). This was reported (Dr. K. W. Hinson) as showing thickening of alveolar walls with mononuclear cell infiltrations. Other large mononuclear cells lined the alveolar spaces and were present free in the lumen. There was no apparent increase in fibrous tissue. Examination for Pneumocystis carinii was negative, as was screening for a range of autoantibodies. Because of the histological
FIG. 1.—Whole lung sections from each lung to show the diffuse nature of the disease process. (H. and E. normal size.)

FIG. 2.—Thickening of walls, a cuboidal or low columnar lining to air spaces containing many desquamated cells. (H. and E. × 66.)
picture treatment was begun with prednisolone which was increased to a maximum of 20 mg/day with no improvement. He developed signs of heart failure and was digitalized. At the age of 7 months treatment was begun with azathioprine up to a dose of 25 mg/day but this made no difference to his clinical condition, blood gases, or lung mechanics. His chest remained clear to auscultation and he did not develop clubbing but slowly deteriorated and died at the age of 9 months.

Necropsy. This revealed a thin infant weighing 5·23 kg. There was pronounced right ventricular hypertrophy and dilatation. The lungs were enlarged and showed a diffuse, fine cystic pattern with clear lobular demarcation. The bronchial tree was normal. Histologically there were diffuse changes throughout both lungs (Fig. 1) which were essentially the same as those seen earlier in the needle biopsy. Apart from the mononuclear inflammatory cell infiltration of alveolar walls and desquamation of cells into the lumen (Fig. 2), there was also some eosinophilic, PAS-positive material present, sometimes spilling into the bronchioles. This material was apparently derived from breakdown of the desquamated large mononuclear cells; it did not react for fibrin and no iron was present. Both the mononuclear cells and the derived material reacted positively with Alcian Blue and Sudan Black, suggesting the presence of acid mucopolysaccharides and lipids—possibly phospholipid. A prominent feature was smooth muscle hyperplasia around bronchiolar walls and particularly at the necks of alveolar ducts. Further smooth muscle hyperplasia was identified around arterioles indicating pulmonary hypertension. The rest of the necropsy findings were unremarkable.

Discussion

This infant suffered a severe progressive pulmonary disease which did not respond to steroids or immunosuppressive agents. The histological appearance of the lungs, with preservation of the architecture, minimal fibrosis, and infiltration, and an extensive alveolar exudate composed of cells of PAS-positive cytoplasm, is that characterized by Leibow, Steer, and Billingsley, (1965) as desquamative interstitial pneumonia. Though Leibow (1972) makes a clear distinction between desquamative interstitial pneumonitis and fibrosing alveolitis both in adults and children, other authorities (Scadding and Hinson, 1967; Brown and Turner-Warwick, 1971; Patchefsky, Fraimow, and Hoch, 1973) believe that the two conditions are at different ends of the spectrum of diffuse fibrosing alveolitis.

Although the infant received oxygen for the last 6 months of life, pulmonary disease developed before oxygen therapy was started and pulmonary histology at biopsy and at necropsy showed changes quite distinct from those attributed to pulmonary oxygen toxicity.

In adults this is one of the group of restrictive lung diseases characterized by breathlessness, hypoxia, fine basal crepitations, clubbing, mottling on the chest x-ray, and small stiff lungs. In adults with desquamative type of histology the response to steroid therapy or immunosuppressive agents is usually good (Brown and Turner-Warwick, 1971). Infants usually have a rapidly progressive disease with tachypnoea, hypoxia reversed by oxygen, and hyperinflation of the lungs, though the present case is the only one known to us in which this was confirmed physiologically in life. The disease is rare, only 8 cases have been described in infants; the prognosis is poor. Cases with a fibrosing histology described by Feinerman and Harris (1957), Mann (1959), and Hilton and Rendle-Short (1961) have all died, though 2 of the cases in infancy reviewed by Leibow (1972) with the desquamative histology did respond as expected (Brown and Turner-Warwick, 1971) to steroids. Our case and the one described by Howatt et al. (1973) did not. The case described here is the only one in infancy in which both steroids and immunosuppressive agents have been tried and proved unhelpful.

Summary

A case of desquamative fibrosing alveolitis beginning in early infancy is described. The disease was characterized by tachypnoea, hypoxia relieved by $O_2$, absence of signs in the chest or clubbing, and radiological and physiological evidence of hyperinflation. The diagnosis was made by needle biopsy of the lung. Treatment with steroids and immunosuppression was without effect and the infant died at 9 months. The disease has a high mortality in infancy, only 2 out of 9 reported cases having survived. The difference from the usual course in adults and older children is noted.

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References


Short reports

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Isosorbide in treatment of infantile hydrocephalus. J. Lorber.


Thymic dysplasia, persistence of measles virus, and unexpected infant death. P. F. Roberts.
Desquamative fibrosing alveolitis unresponsive to steroid or cytotoxic therapy.

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