LETTERS TO THE EDITOR

Fetal familial surfactant protein B deficiency

EDITOR.—In 1993 a sibship of three infants who died of hyaline membrane disease had an absence of surfactant protein B (SP-B) and its mRNA in lung tissue.1 The gene coding for SP-B has been located and a frameshift mutation in this gene has been identified in this family.2,3 This adds to the evidence that the family relationship is significant.2 A further six cases of SP-B deficiency with varying clinical and genetic findings have been described.3 We describe the first British cases in two siblings.

Case 1

This first girl of healthy, non-consanguineous, caucasian parents was born in 1991, at term, weighing 3.5 kg. Apgar scores were nine and 10 at one and five minutes respectively. At 5 hours of age she developed respiratory distress and was mechanically ventilated. She received maximal ventilation and failed to respond to artificial surfactant, Thrombin or propranolol. She died at 26 hours of age. The clinical diagnosis at death was persistent fetal circulation. Postmortem examination found extensive hyaline membrane with no evidence of pulmonary artery hypertension. Occasional alveoli contained granular eosinophilic material.

Case 2

This boy, the index case, was born at term, weighing 3.2 kg after a normal pregnancy, labour, and delivery. Apgar scores were nine and 10 at one and five minutes, respectively. Respiratory distress was evident from 1 hour of age and mechanical ventilation was started at 16 hours. He remained ventilator dependent until death. Chest x ray pictures showed severe hyaline membrane disease and remained unchanged throughout the course of his illness. There was only a transient response to artificial surfactant, Dexamethasone, and high frequency oscillation. No microbial pathogens were identified and echocardiography was normal. Open lung biopsy on day 21 showed alveoli filled with granular eosinophilic material staining positive with periodic acid Schiff. Degenerating foamy and granular macrophages were present. Immunohistochemistry showed undetectable concentrations of SP-B in lung tissues. SP-B was undetectable by enzyme linked immunosorbent assay (ELISA) in tracheal aspirates, and accumulation of a pro-SP-C fragment, typical of SP-B deficiency, was present (personal communication, J Whitsett, Cincinnati). DNA studies identified the known mutation in one allele (personal communication, L Nogee, Baltimore). Following informed consent from both parents, ventilation was electively discontinued on day 32.

Comment

These two infants illustrate the clinical presentation of this newly diagnosable condition. The histological findings are identical with those seen in pulmonary alveolar proteinosis, a rare alveolar disease described in older children and adults. The aetiology of this condition is unknown but in babies presenting from birth it is likely to be due to surfactant B protein deficiency. This diagnosis should be considered in all term babies dying of respiratory distress. As further mutations are identified antenatal diagnosis will be possible and in the future gene therapy may be effective. We have subsequently identified two further cases in Asian babies. We urgently need data on the prevalence of this condition in Britain and we have contacted the British Paediatric Surveillance Unit with a view to establishing this.

John RALL
P A J CHECTU
Department of Child Health,
Leeds General Infirmary, 
‘Strandown Wing’
Leeds LS2 9NN

D BEVERLEY
Department of Paediatrics,
York District Hospital,
York YO1 7HE


Application of measured spontaneous inspiratory and expiratory times to improve infant ventilation

EDITOR.—We read with interest the two papers from Addenbrooke’s Hospital.1 These two studies measured spontaneous inspiratory times (Ti) by a method unaffected by ventilator settings, and confirm our impressions based on endotracheal flow information in practice. However, the obvious application of the method remains to facilitate true synchronised ventilation to spontaneous inspiratory and expiratory efforts.

We have attempted to synchronise both phases of respiration using VIP Bird Infant Ventilator. We ventilated 12 neonates during their disease. When the infant triggers ventilator breaths with preset inspiratory times during periods of high respiratory rate, there is a danger of reversed ratios, and the inspiratory time exceeds the expiratory time (Tc). Moreover, using a graphical interface, which displays breath to breath measurements of endotracheal flow and pressure, we have also demonstrated that endotracheal inspiratory flow may decay to zero or minimum flow (generated by continuous gas leak around the tube) well before the ellipse of a preset inspiratory time. Thus alveolar ventilation does not occur throughout the fixed inspiration cycle.

In weaning babies not dependent on a high mean airways pressure for oxygenation, fixed inspiratory time can be reduced without adverse effects on blood gases. On the VIP, the ventilator will then use an algorithm to reduce the delivered inspiratory time during fast breathing and increase it during slower breathing, known as ‘termination sensitivity’. This uses the detection of inspiratory flow decay to signal termination of ventilator inspiration. Thus ventilation becomes pressure limited, and flow cycled into both inspiration and expiration, allowing the infant to select its own inspiratory time. We use this ‘termination sensitivity’, to calculate the allowed inspiratory time in weaning infants 0.2 to 0.25 seconds. We have confirmed previously reported observed improvements in oxygenation and tidal volumes.8—9 Inspiratory flow decay is subject to lung volume and time constant, and may be founded by altered peak ventilator pressure and changes in pulmonary dynamics.

In the use of the ‘termination sensitivity’, the display of pressure-volume loops in real time allows us to optimise ventilator pressure to minimise these effects. In addition, as with all ventilator settings, termination sensitivity is subject to rigorous review and adjustment on a frequent basis, which minimises variation induced by the compliance of changing lung pathology.

Graham DERRICK
SUNIL SINHA
Neonatal Services,
South Cleveland Hospital,
Marton Road,
Middlesbrough TS4 3BW


Drs Mockridge and Morley comment: 
We would like to address the obvious problem that neonatologists, in our experience, may not always be able to synchronise the ventilator with the patient's breathing. The obvious solution, in our experience, is to reduce the inspiratory time, if the ventilator is not triggered, to zero or minimum flow. This allows the infant to take spontaneous breaths during periods of reduced respiratory drive. However, we would like to address some points arising from their letter.

We believe triggering has inherent problems. Neonatologists need to be aware that spontaneous breathing may not be identical to ventilator triggering. Therefore, we suggest that ventilators should be designed so that they do not deliver breaths when the patient is not triggering. However, we believe this would be unrealistic for reasons of safety and practicality.

In conclusion, the use of ‘termination sensitivity’ is a useful technique to improve ventilation in weaning infants. However, we believe that it should be used in conjunction with other measures to improve ventilation in these infants.