LETTERS TO
THE EDITOR

“Dewatering” the lungs

Editor,—In response to the commentary by Professor Walters,1 we must first correct him in referring to our model for the normal alveolus as “dry” when, in fact, it is based on many classic morphological studies2 demonstrating fluid layers—just enough to “wet” the septal corners. In proposing that an oligolamellar lining of surface-active phospholipid (SAPL) adsorbed to epithelium “pushes water aside” from the gas-exchange surface, we agree that it is difficult to prove direct binding conclusively. However, any intervening aqueous layer is no more than that normally sandwiched between adjacent planes of polar groups in such structures (fig 1). Moreover, this physiological milieu contains mobile cations3 which can neutralise the negative phosphate ions in the SAPL molecules to render them cationic, facilitating their tight binding into a very effective molecular barrier.4 Hence SAPL is pseudocaptonic.

In citing evidence to support the conventional concept of a continuous liquid layer separating the surfactant lining from alveolar epithelium, Professor Walters refers to the recent study by Bastacky, Clements, and others,5 who, do indeed, demonstrate such a liquid layer. However, they have created a totally artefactual situation by pre-inflating the liquid layer. Hence SAPL is pseudocaptonic.

Surely, the oligolamellar SAPL lining shown in fig 1, SAPL layers not only act as a protective, elastic molecular barrier. Note how it forms a continuous barrier spanning an intercellular junction (arrowed). The bar represents 50 nm.


Cognitive, educational, and behavioural outcomes at 7 to 8 years

Editors,—In our study1 we referred to research conducted by the Scottish Low Birthweight Study Group on developmental outcomes among a birth cohort of Scottish very low birthweight (VLBW) infants born in 1984. We stated that the Scottish study had yet to publish data on school aged outcomes among this cohort, and further that the study lacked comparative data on outcomes among a general child population sample.

It has been pointed out to us that both of these claims are, in fact, incorrect. The Scottish Group has published findings on the school attainment, cognitive ability, and motor function of their cohort at age 8 years,2 and included, as part of their analyses, comparative outcome data for a general child sample matched for age and gender with the VLBW cohort and selected from the same school classes in which the VLBW cohort members were enrolled. Our own findings, based on a New Zealand birth cohort, show strong parallels with the Scottish study, particularly in relation to the higher rates of educational problems and poorer cognitive functioning experienced by VLBW children in comparison to their peers. It would have been useful to draw these comparisons in the discussion of our own findings. We very much regret this oversight on our part and apologise to the Scottish Group for our error.

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Diagnostic tests for bacterial infections

Editors,—Fowlie and Schmidt reviewed numerous publications on haematological parameters and C reactive protein for the diagnosis of bacterial infections and tried to select these publications according to well chosen criteria.3 However, they omitted to...
examine the publications for two criteria that substantially influence the study results.

Eight studies on band counts or immature to total neutrophil ratios were reviewed. But only the authors of two studies actually defined how an immature neutrophil was differentiated from a segmented neutrophil—that is, morphological criteria, including the width of the connection between the nuclear segments. Segmented neutrophils are defined variably in published studies; most authors require an indentation of the nucleus of less than a third of the maximal nuclear diameter, but others require an indentation to 50% or that the connections between nuclear segments are filiform. Discrepancies in the definition of bands and segmented neutrophils may be one of the reasons that the results for sensitivity and specificity vary largely between studies.

Diagnostic parameters and especially C-reactive protein have characteristic kinetics in the course of a bacterial infection: C-reactive protein has a low sensitivity at the onset of the course of a bacterial infection: C reactive protein have characteristic kinetics in various tests were carried out may explain differences in how the definitions are filiform. Discrepancies in the definition of bands and segmented neutrophils may be one of the reasons that the results for sensitivity and specificity vary largely between studies.

Diagnostic parameters and especially C-reactive protein have characteristic kinetics in the course of a bacterial infection: C-reactive protein has a low sensitivity at the onset of the course of infection but the sensitivity improves with the course of infection. Unfortunately, Fowlie and Schmidt included two studies in which the timing of blood sampling was not precisely defined.

**Alpha-coma in an infant with hypoxic-ischaemic encephalopathy**

**Editor,—**Alpha coma (AC) is the combination of coma and an electroencephalographic (EEG) pattern of synchronous, rhythmic 8–13 Hz activity which has been described in certain severe neurological conditions such as post anoxic or ischaemic encephalopathy, head trauma, brain stem infants and drug overdoses. In neonates AC has been associated with chromosomal abnormalities and inborn errors of metabolism and rhythms have been described transiently during seizure activity. Most reported cases have been associated with a poor outcome

**Case report**

A boy weighing 4080 g was born by vaginal delivery following prolonged fetal distress and meconium stained amniotic fluid to non-consanguineous parents. Cesarean section had been refused. Apgar scores were 1, 6, and 7 at 1, 5, and 10 minutes, respectively. At one hour, arterial pH was 7.29, bicarbonate 20 mmol/l, and base deficit 6 mmol/l. The infant developed mild meconium aspiration syndrome that required mechanical ventilation. Increased tone, fisting of both hands, and blank staring were noted shortly after birth. When 6 hours old, coma and convulsions appeared. Treatment with phenobarbital and subsequently phenytoin was partially effective, with serum concentrations in the therapeutic range. The convulsions diminished and the coma resolved over several days. Blood count, blood glucose, serum electrolytes, calcium and magnesium and urinary amino and organic acids were normal. Metabolic acidosis was not detected throughout the hospital course. Karyotype was normal.

The EEG on day 3 showed continuous 10–11 Hertz activity with amplitude of 15–40 uV localised over the left parasagittal and temporal regions, with sporadic generalised short bursts of mixed frequencies and sharp waves not associated with clinical correlates. Marked suppression of cortical activity was recorded over the right hemisphere with occasional 10–11 Hertz activity of 10 uV amplitude. (fig 1). The EEG showed burst-suppression pattern on day 4 (fig 2) and prolonged

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polymorphic delta activity of low to medium amplitude when the child was 3 months old. A computed tomography scan showed severe bilateral cortical atrophy, basal ganglia infarcts, and periventricular cystic leukomalacia. At 3 years of age, the child had severe spastic quadriplegic cerebral palsy, pseudobulbar palsy, and psychomotor retardation. In spite of the relatively mild evidence of asphyxia at birth, the intrapartum history, the course of the encephalopathy and the absence of appropriate abnormalities on metabolic or imaging studies make any diagnosis other than HIE unlikely.

The rhythm in this infant was consistent, non-reactive, and not associated with a clinical seizure correlate, as described in AC in other settings. This description of AC in HIE adds to the usual EEG findings of initial voltage suppression pattern. This description of AC in HIE is of ominous clinical significance. The burst-suppression pattern in HIE is of ominous clinical significance. Although we have presented only one case of AC in HIE with poor neurodevelopmental outcome, this may represent an additional poor prognostic indicator.

The cardiac effects of a short course of dexamethasone have been reported before, by Brozanski et al, in their trial of a three day repeatable pulsed course. They also found significant hypertrophy which regressed by discharge. Definition of myocardial hypertrophy by statistical comparison with the “control” group in the study of Skelton et al is of doubtful value. Controls were very different babies, being a median of 3 weeks older and 400 g heavier at birth. Their echocardiograms were performed at different gestational and postnatal ages. Furthermore, the increases in interventricular septal and left ventricular posterior wall thicknesses are described for a 21 day period in the control group and for a variable period (to maximal hypertrophy) in the treatment group. Inspection of the data provided in the figures suggests that comparison between groups after 21 days may not have shown a significant difference.

Which course of dexamethasone?

Editor,—Skelton et al state that “most units start [dexamethasone] by the second week of life, weaning over 2–3 weeks rather than 6” and that such a regimen “has been shown to be comparable in effectiveness with a six week course.” The reference cited is a review paper that provides no evidence for the first statement, and discusses studies that showed a benefit in time to extubation but not in the duration of oxygen treatment. Time of extubation is irrelevant if the incidence of chronic lung disease has not been reduced, and, to our knowledge, a three week course has not shown to have this beneficial effect. Indeed, Cummings et al, in the study in which he reported beneficial effects of the 6 week course, found that an 18 day course was not effective at reducing time in oxygen. There are now at least four dexamethasone regimens described which do reduce the incidence of chronic lung disease. In these days of evidence based medicine, should we not be using one of these?++

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++ Due to the nature of infants receiving dexamethasone, well matched controls were not possible. However, the changes on real time echocardiography were very clear cut. Our controls, as well matched as possible, were included to provide comparison and emphasis of the severity of the left ventricular haemorrhage, rather than prove that it had occurred. In trying to compare groups at 21 days, Bloomfield et al seem to have misunderstood. Twenty eight day old controls was chosen to try to coincide with maximum hypertrophy, at around 10 days after starting dexamethasone. Two time points were felt sufficient, as we found no left ventricular haemorrhage in a normal preterm population of a similar age.++

Brozanski’s study is not comparable. The study population and dexamethasone use differed: repeated doses 3 days every 10 days up to 36 weeks is hardly “short course.” The ethics of placebo is of concern and a low incidence of left ventricular haemorrhage (24%) suggests different natural history or inappropriate reference ranges. Our study is the first to examine in depth left ventricular haemorrhage using current dexamethasone practice.

Finally, these studies emphasise our poor knowledge of dexamethasone and left ventricular haemorrhage. Greater emphasis on the mechanism of action of dexamethasone rather than differing regimens may improve use in small susceptible infants.

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Drs Skelton, Parsons, and Gill reply:

Editor,—We feel that Bloomfield et al may have missed the main purpose of our study. Evans’ recommended screening for left ventricular haemorrhage for infants receiving dexamethasone. We examined the safety of current prevailing practice. In the UK dexamethasone courses have been reduced in length due to concerns about side effects. Pulsed dexamethasone is not often used. Whatever its merits and despite many studies of different regimens, ours reflects current use. Although we hope to prevent chronic lung disease, in practice, early extubation and the stabilisation short courses produce are not “irrelevant.”

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