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Neonatal Society

Meeting held on 4 July 1980 in Southampton

Cells in human milk. C J Rolles and L Cussens. General Hospital, Southampton, and Monash University, Queen Victoria Memorial Hospital, Melbourne, Australia.

A cellular element in milk has been recognised for over a century. During the last decade there has been a renewed interest in milk cells but reports present a wide variety of methods of analysis, and the results and interpretation of findings have been inconsistent. We have devised our own techniques of collecting, storing, and analysing milk for its cellular content. Milk samples were taken from 53 healthy women who had been lactating from 4 days to 15 months. From each woman three samples were analysed—pre-, mid-, and postfeed from one breast. In addition 12 women gave similar samples from the other breast at the same feed, and in some of these the procedure was repeated at the next feed.

Leucocytes were found in all samples. The range was $1 \cdot 0$–$33 \cdot 0 \times 10^9$/l. Most samples had counts between $3 \cdot 0$ and $15 \cdot 0 \times 10^9$/l. There was considerable variation in cell numbers during each feed 'profile', with a tendency for the cell count to rise markedly towards the end of the feed. Differential cell counts were as follows: macrophages—40 to 90%, polymorphs—5 to 50%, lymphocytes—0 to 10%.

It is evident that a fully breast-fed baby probably ingests as many viable leucocytes every day as it has circulating at any one time. Evidence of a biological role for these cells in the neonate is beginning to emerge.

Fat content of bank human milk. L Carroll, D Conlan, and D P Davies. Leicester Royal Infirmary Maternity Hospital.

Milk which is collected for human milk banks is heterogeneous in the method ('expressed' or 'drip') and stage in lactation of its collection. In view of considerable physiological variation in the fat content of breast milk in relation to time of the day and stage of lactation, we wished to examine the variability of fat (and therefore of energy content) in human milk as it reaches our milk bank.

In 140 samples of milk (mainly collected by the 'drip' method) arriving in the milk bank of the Leicester Royal Infirmary Maternity Hospital, the fat content was estimated in each by the creamatocrit method. The results are shown in the Table.

	Fat concentration (g/l)				
	<10	*10–19*	*20–29*	*30–40*	*>40*
No of samples (%)	34 (24%)	62 (45%)	28 (20%)	13 (9%)	3 (2%)

There was marked variability in fat content (5·8–67 g/l). The mean value was low at 17 g/l. There was no significant difference in the mean fat content of 'early' and 'late' milk. We believe that the reason for the fat content varying in our samples was contained in the methods of collecting the milk. A widely quoted reference value for fat in breast milk is 40 g/l, and most of the samples in our investigation had a much lower fat content. Reference values for the fat in breast milk are therefore of little value when dealing with individual samples. In assessing the adequacy of bank breast milk for babies, especially for those of low birthweights, as much attention must be paid to the fat content as previously had been accorded to its nitrogen and electrolyte composition.

Excretion of paracetamol in human breast milk. E L Hurden, D R Harvey, and P J Lewis. Queen Charlotte's Maternity Hospital, London.

Paracetamol is one of the most common analgesic drugs prescribed for women after delivery but its passage into breast milk has not been studied. 11 normal women were investigated between 3 and 9 days after delivery. 1 g paracetamol was administered orally, and blood and expressed milk samples were collected at intervals up to 4 hours after the dose. Paracetamol concentrations were measured by gas–liquid chromatography. The mean ($\pm$ SD) concentration of paracetamol in 32 samples of breast milk was $9 \cdot 0 \pm 6 \cdot 9$ μg/ml. The milk-to-plasma ratio varied between $0 \cdot 2$ and $1 \cdot 9$ (mean $1 \cdot 0$) $n = 30$. Even assuming a total milk intake of 1 litre/day the average intake of paracetamol by the infant would

not exceed 10 mg, presumably a subtherapeutic dose. The very variable milk-to-plasma ratios found are difficult to explain. We have confirmed by ultrafiltration that paracetamol is only moderately protein-bound in either plasma or milk, <7%-bound at therapeutic concentrations. On theoretical grounds if the pKa (9·5) were the sole determinant of the milk-to-plasma partition the ratio should be almost one. However, variable milk-to-plasma ratios are reported for a variety of drugs and these theoretical calculations, derived from steady-state kinetic experiments, may not have a direct application when plasma concentrations are rising and falling after single doses of a drug.

The congenital small lung. P Helms, D Hatch, and S G Haworth. The Hospital for Sick Children, London.

10 infants with unilateral small lung demonstrated on chest radiography have been studied. Two had no associated anomalies, 2 had cardiovascular anomalies, 1 had skeletal deformities, and 5 were studied after congenital diaphragmatic hernia repair. Thoracic gas volume (TGV) and airways resistance (RAW) were measured in an infant plethysmograph, with static lung compliance estimated by using an intermittent positive pressure technique and rubber respiratory jacket. Results were compared with the 99% confidence limits in normal infants. TGV was reduced in 3 infants, static lung compliance was in the low normal range in all except 1 infant, and in 4 of the 5 infants studied in the first 8 weeks of life RAW was markedly reduced. All the remaining infants were studied between 8 weeks and 16 months of age.

The normal TGV and the tendency to lower lung compliances found in most infants suggests significant compensatory emphysema, and the reduced RAW in those studied in early infancy with an uncomplicated course agrees with the reduction in airway generation number found on lung morphology in similar but more severely affected infants. When assessing the significance of lung function data in infants it is essential to take into account the clinical course in each case, and to consider any relevant anatomical factors.

Quantitative biochemical studies on human fetal lung hypoplasia. J S Wigglesworth and R Desai. Hammersmith Hospital, London. To be published in full in the *Archives*, 1981, **56**, as **Use of DNA estimation for growth assessment in normal and hypoplastic fetal lungs.** J S Wigglesworth and R Desai, and **Fetal lung hypoplasia: biochemical and structural variations and their possible significance.** J S Wigglesworth, R Desai, and P Guerrini.

Immotile cilia syndrome: a new cause of neonatal respiratory distress. A Whitelaw, A Evans, and B Corrin. Northwick Park Hospital, Harrow, Queen Mary's Hospital for Children, Carshalton, and Cardiothoracic Institute, London. To be published in full in the *Archives*, 1981, **56.**

Neonatal mechanical ventilation and 'expired' CO_2. J K Stothers, C A Campbell, and A I Mukhtar. London Hospital Medical College, and London Hospital.

Great interest has been expressed in noninvasive monitoring of $Paco_2$ in sick neonates using transcutaneous sensors. As yet, in practice problems still exist. End-tidal CO_2 closely reflects $Paco_2$; but in infants its measurement requires expensive and sophisticated equipment. The sample flow rate of the analyser should be small (10–20 ml/min) and the response time fast ($\approx$0·1 second). Recently a relatively cheap CO_2 analyser was manufactured (Datex CD 101P), with a minimal sample flow rate of 50 ml/min and a response time of 0·3–0·4 second. At first it appears unsuitable for neonatal monitoring, but the respiratory rate of mechanically-ventilated infants is often less than 30 min and in these circumstances it seems possible that this analyser might record end-tidal CO_2.

Our aims were to compare values obtained using this machine with arterial levels. In infants with compliant lungs the correlation between these values was extremely good. In those with 'stiff' lungs, again the correlation was good, but the excretion 'pattern' was rather more complicated. Preliminary findings suggest that this analyser is of use in recording changes in expired and, within limits, end-tidal CO_2. Further experience of this method of monitoring the $Paco_2$ may enable mechanical ventilation to be controlled more physiologically.

Mechanism of brain volume homeostasis during hyponatraemia in the newborn calf. R M Gardiner and A G Wilkinson. Physiological Laboratory, University of Cambridge.

The potassium (K) content of brain tissue is reduced after prolonged hyponatraemia, and it has been suggested that this loss of intracellular electrolyte represents the means by which brain swelling is mitigated under hyposmolar conditions. The present experiments were undertaken to quantify net transfer of K to the circulation from brain tissue drained by the sagittal sinus during sustained dilutional hyposmolar and isosmolar hyponatraemia. Cerebral blood

flow was measured using an H_2 clearance technique, and metabolism and cation transfer quantified by simultaneous determination of arterio-cerebral venous concentration differences.

During hyposmolar hyponatraemia (arterial plasma sodium, 117·1 ± 0·5 mmol/l; plasma osmolality, 232 ± 1 mosmol/kg) cerebral blood flow decreased from 67 ± 3 to 55 ± 2 ml/100 g per min ($P<0·01$), and the net transfer of potassium to the circulation increased from −0·51 ± 0·14 to −1·51 ± 0·07 μmol/100 g per min ($P<0·001$). CSF sodium concentration and osmolality were both decreased. No change in these variables was observed during isosmolar hyponatraemia (plasma sodium, 119·9 ± 0·2 mmol/l; plasma osmolality, 284 ± 2 mosmol/kg). It is suggested that a reduction in sodium concentration of brain extracellular fluid potentiates pumping of potassium to the circulation by a Na^+–K^+ activated ATP-ase located at the abluminal surface of brain capillaries.

Controlled trial of pancuronium during mechanical ventilation for hyaline membrane disease. M J Pollitzer, E O R Reynolds, and D G Shaw. University College Hospital and Medical School, London.

Spontaneous breathing during mechanical ventilation may traumatise the lung. To find out whether the incidence of lung damage could be reduced by muscle-relaxation during ventilation, 50 infants of at least 28 weeks' gestation who required mechanical ventilation for hyaline membrane disease were randomly assigned to a treated or a control group. The treated infants were kept muscle-relaxed on pancuronium until their inspired O_2 requirement had fallen to 40% or less. The mean birthweight, gestational age, duration of ventilation, inspired oxygen concentration during the acute phase of the illness, and ventilator pressures were closely comparable in the two groups. Two of 26 treated infants and one of 24 control infants died; the control infant had bronchopulmonary dysplasia. Four treated and 5 control infants developed pneumothoraces or interstitial emphysema. The length of time that the treated infants required added oxygen was less than in the control infants (Mann-Whitney U test, $P < 0·01$). All treated infants were breathing air spontaneously by one month of age, whereas 7 control infants were still oxygen-dependent ($\chi^2 = 6·56$, $P<0·02$). These 7 infants required additional oxygen until they were 5–18 (mean 10) weeks old.

We conclude that muscle-relaxation during mechanical ventilation for hyaline membrane disease reduces the incidence of chronic oxygen-dependency. We suggest that this effect is due to diminution of traumatic damage to the lung.

Transfer of free palmitic and linoleic acids across the perfused human placenta. C Booth, M Elphick, W Hendrickse, and D Hull. University of Nottingham Medical School, Queen's Medical Centre, Nottingham.

Maternal circulating free fatty acids are available to the fetus for incorporation into fat stores or into structural lipids. Although in the latter case essential long-chain fatty acids are required, results of investigations at elective caesarean section suggest that free fatty acids cross the placenta unselectively and at rates which depend on maternal concentrations. The exception is arachidonic acid which appears in fetal blood in fairly large amounts. To investigate this further we performed some experiments in which we simultaneously measured the transfer of an essential (linoleic) and a non-essential (palmitic) fatty acid, using the technique of Schneider *et al.*, in which a small placental lobe is perfused. Maternal and fetal perfusate, containing 2% albumin, was recycled from small reservoirs. Transfer rates were measured using radio–gas chromatography. Labelled antipyrine was used to assess perfusion efficiency and labelled dextran was added to test integrity of placental membranes. Mean transfer rates of 150, 0·0326, and 0·0433 μmol/min were obtained for antipyrine, palmitic, and linoleic acids respectively. The transfer of dextran was negligible. There was no conversion of linoleic acid to arachidonic acid although this appeared in large amounts into the perfusate. It is concluded that linoleic and palmitic acid across the placenta non-selectively and that the arachidonic acid was derived from placental lipids other than linoleic acid.

Changing blood culture isolates in a referral neonatal intensive care unit. O Battisti, R Mitchison, and A Oto. Hammersmith Hospital, London.

All cases of bacteraemia occurring in the neonatal intensive care unit at Hammersmith Hospital over a 4-year period, 1976–9 inclusive, have been analysed. During that time 113 infants were found to be bacteraemic; 27 were inborn (a rate of 5·6/1000 hospital live births), and 86 outborn (a rate of 160/1000 outborn admissions to the neonatal unit). 33 of the infants became bacteraemic early, in the first 48 hours of life. When the present results were compared with those in a previous survey from this unit certain differences were found. Gram-positive isolates outnumbered Gram-negative isolates by more than 2:1, whereas the opposite was the case in the years 1967–75. This difference was due solely to the increasing frequency of *Staphylococcus epidermidis* isolates (a proportion of them showing multiple

antibiotic resistance), both in early infections in outborn infants and in later infections among inborn and outborn infants; this organism had been encountered only rarely previously. As the relative frequency of Gram-negative infections has remained largely unchanged, bacteraemia is now more common in this unit. Although group B beta-haemolytic streptococcus was isolated early from several outborn infants, no case of early infection occurred among inborn infants in the 4-year period, whereas in the 9 years previously it had been the organism most often responsible for early infection in such babies. A neonatal unit population of decreasing birthweight and maturity, and certain changes in obstetric practices may be at least partially responsible for these changes.

Growth and body composition in preterm infants fed donor breast milk. A A Jackson, J C L Shaw, A Barber, and M H N Golden. Tropical Metabolism Research Unit, University of the West Indies, and University College Hospital Medical School, London.

Eight studies were carried out in 3 preterm infants between 8 and 30 days of age. The infants, born between 31 and 33 weeks' gestational age, were all small for gestational age. They were fed on pasteurised human breast milk. Nitrogen balance was measured every 7 to 10 days for periods of 72 hours during which intermittent tracer doses of ^{15}N glycine were given. The composition of the milk varied widely. The mean energy content was 289 kJ/100 ml (260–316) and mean protein content 1·44 g/100 ml (1·16 to 1·97). The intakes for energy and protein were 485 to 694 kJ/kg per day (mean 583) and 1·95 to 4·08 g/kg per day (mean 2·79) respectively. Each child gained weight at a rate appropriate for gestational age, but inadequate to allow for catch-up growth. The average weight gain was 15·6 g/kg per day and the protein equivalent of the retained nitrogen ranged from 1·11 to 2·52 g/kg per day. Thus the component of weight gain attributable to lean tissue deposition (20% protein) varied from 34 to 89%. The rate of nitrogen accumulation was very much less than that calculated for a fetus of equivalent gestation or equivalent weight. In 6 of 8 studies urinary urea was not enriched with ^{15}N.

The data show that growth in preterm infants fed donor breast milk is inadequate, in terms of weight gain and nitrogen retention when growth of the fetus is used as a reference standard. The requirements for glycine vastly exceed the dietary intake, and endogenous synthesis may be limited. In this situation glycerine may be acting as a limiting nutrient and thus become a semi-essential amino-acid.

British Paediatric Association

Annual meetings

1981	7–11 April	York University
1982	20–24 April	Aviemore Centre, Scotland
1983	12–16 April	York University
1984	10–14 April	York University
1985	16–20 April	York University