Perinatal medicine

**G30 TRANSIENT ADRENOCORTICAL INSUFFICIENCY OF PREMATURITY (TAP) AND SYSTEMIC HYPOTENSION IN VERY LOW BIRTH WEIGHT INFANTS**

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**Aims:** Human corticotrophin releasing hormone (hCRH) stimulation test was used: (i) to determine the relation between pituitary-adrenal responsiveness and systemic hypotension in very low birth weight (VLBW) infants, and (ii) to characterise the endocrinological features of 'Transient Adrenocortical insufficiency of Prematurity' (TAP).

**Study design:** hCRH tests were performed on 137 VLBW infants at day 7 and 14 of life in a tertiary neonatal centre.

**Results:** Basal and peak serum cortisol at day 7 were associated significantly with the lowest blood pressures recorded during the first two weeks of postnatal age (r > 0.38, p < 0.0001 and r > 0.41, p < 0.0001 for basal and peak levels, respectively). These cortisol levels correlated significantly but negatively, with the maximum and total cumulative dose of inotropes (r > −0.22, p < 0.02), total volume of crystalloid (r > −0.22, p < 0.02), and duration of inotropic treatment (r > −0.25, p < 0.006). Although the hypotensive infants (Group 2) were significantly less mature and more sick than infants with normal blood pressure (Group 1), their basal plasma ACTH at day 14 and the peak levels at days 7 and 14 were significantly higher than infants of Group 1 (p = 0.03, p = 0.001 and p = 0.01, respectively). In contrast, both basal and peak serum cortisol at day 7 were significantly lower in Group 2 than in Group 1 infants (p = 0.004 and p = 0.001, respectively). There was, however, no significant difference in serum cortisol between the groups at day 14.

**Conclusions:** This study characterises the fundamental endocrinological features of TAP, namely: (i) normal or exaggerated pituitary-adrenal response, (ii) pituitary-adrenal insufficiency, and (iii) good recovery of adrenal function by day 14 of postnatal life. Neonatal clinicians may consider early corticosteroids replacement in preterm hypotensive infants with low serum cortisol level.

**G31 PROLACTIN PROMOTES THERMOREGULATION IN THE NEONATE**

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**Aims:** The rapid recruitment of nonshivering thermogenesis in response to cold exposure to the extra-uterine environment is critical for neonatal survival. This adaptation is effected by the large increase in abundance and activity of the brown adipose tissue specific mitochondrial protein, uncoupling protein (UCP) 1. We have previously shown a close relationship of prolactin receptor and initial appearance of UCP1 in fetal adipose tissue in late gestation. The present study aimed to establish whether administration of prolactin to neonatal lambs would enhance thermoregulation.

**Methods:** Seven pairs of day old triplet lambs were entered into the study and randomly assigned to prolactin (2mg/ml) or vehicle treatment. All lambs remained with their mother throughout the duration of the study. Prolactin or vehicle treatment was administered to all lambs via the jugular vein. Colonic temperature was measured prior to treatment and then at ten-minute intervals for the next two hours. Blood samples were taken and plasma concentration of non-esterified free fatty acid (NEFA) and glucose concentration determined. Results are means with their standard errors.

**Results:** There was no difference in colonic temperature between groups at the start of the study (vehicle 39.5 ± 0.11 and prolactin treated 39.38 ± 0.12 (°C)). However, there was a significant increase in the colonic temperature of the prolactin treated lambs compared to the control lambs 40 to 60 minutes after treatment. The concentration of NEFA was significantly increased after PRL treatment (vehicle 0.06 ± 0.4 and PRL 0.23 ± 0.4 nmol/litre (p=0.025), which is likely to increase the thermogenic potential of UCP1. Plasma glucose was unaffected by prolactin.

**Conclusion:** Prolactin’s positive effect on thermoregulation was observed in the absence of shivering suggesting, that prolactin acting via its receptor promotes lipolysis and therefore nonshivering thermogenesis in brown adipose tissue.

**G32 THE EFFECT OF CYCLOSPORINE ON TAURINE TRANSPORT IN HUMAN CORD BLOOD CELLS**

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Cyclosporine is a potent immunosuppressant used in the field of organ and tissue transplantation for prevention of graft rejection. A number of reports have commented on the increased occurrence of intrauterine growth restriction (IUGR) in mothers on cyclosporine treatment during pregnancy and suggest that this might result from an inhibitory effect of cyclosporine on taurine uptake by the placenta. We investigated taurine transport in cord blood cells, an alternative and easily obtainable foetal tissue, and studied the effects of cyclosporine on taurine transport in these cells.

Cord blood was obtained from placentas from normal term pregnancies in accordance with local ethical approval. Mononuclear cells were preferentially selected by dilution with Hank’s Biological Salt Solution (HBSS) and centrifugation at 400 X g for 30min. [3H] taurine uptake was measured in HBSS with or without 10mM [3H] taurine at 37°C and with or without pre-incubation with cyclosporine (5µM). 37°C for 10min using methods similar to those previously described. Data are expressed as mean ± SEM; n = number of placentas from which cord blood samples were taken.

Uptake of [3H] taurine by cord blood cells was linear over the first 15 min (5.49±0.92 fmol/ 10^6 cells/min, n=6). This uptake was inhibited by [3H] taurine, a substrate for system β amino acid transporter (0.22±0.09 fmol/ 10^6 cells/min, n=6 p<0.05 Student’s t test). Pre-incubation with cyclosporine (5µM) inhibited [3H] taurine uptake by 29.3±5.3% (n=8, p<0.05 Paired Students t test). There was no effect on the uptake of [3H] taurine by methanol, the vehicle used to dissolve cyclosporine. Finally, the β-alanine insensitive component of taurine uptake was not affected by cyclosporine thus ruling out possible cytotoxic effects of the drug.

In conclusion, the effect of β-alanine on taurine uptake into cord blood cells suggests that this was mediated by system β amino acid transporter, although further characterisation is required. The inhibitory effect of cyclosporine on taurine transport in cord blood cells was comparable to that seen in choriocarcinoma cells. Thus the increased incidence of IUGR reported in mothers being treated with cyclosporine A might be due to both the effect of cyclosporine on taurine transport across the placenta and that into other foetal tissues utilising this amino acid.

**G33 COMPARISON OF CEREBRAL PALSY (CP) PREVALENCE IN SPONTANEOUS AND ARTIFICIAL REDUCTION OF TRIPLET GESTATIONS**

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**Background:** CP rates at birth increase with decreasing birthweight. Compared with singletons, triplets are at increased risk of preterm delivery, low birth weight and CP. The surviving infants of multiple gestations where there has been spontaneous loss of a conceptus are at very high risk of CP, selected by dilation with Hanks Biological Salt Solution (HBSS) and centrifugation at 400 X g for 30min. [3H] taurine uptake was measured in HBSS with or without 10mM [3H] taurine at 37°C and with or without pre-incubation with cyclosporine (5µM). 37°C for 10min using methods similar to those previously described. Data are expressed as mean ± SEM; n = number of placentas from which cord blood samples were taken.

**Aims:** To test the null hypothesis that children from triplet gestations with selective termination of one fetus would have similar CP rates to children from triplet gestations with selective reduction or no selective reduction.

**Methods:** Two separate surveys were carried out. Identical questionnaires were sent to the General Practitioner of surviving infants of all registered triplets in England and Wales born 1993–5 where one or two of the triplets were either a stillbirth or a livebirth that died in infancy. Survey 1 involved the survivors of triplets seeking information on the current status of the child specifically for CP or other disability. Survey 2 involved the survivors of triplet pregnancies from a single fetal medicine department, some of which had been reduced to twins by selective termination (term).

**Results:** There was no difference in colonic temperature between groups at the start of the study (vehicle 39.5 ± 0.11 and prolactin treated 39.38 ± 0.12 (°C)). However, there was a significant increase in the colonic temperature of the prolactin treated lambs compared to the control lambs 40 to 60 minutes after treatment. The concentration of NEFA was significantly increased after PRL treatment (vehicle 0.06 ± 0.4 and PRL 0.23 ± 0.4 nmol/litre (p=0.025), which is likely to increase the thermogenic potential of UCP1. Plasma glucose was unaffected by prolactin.

**Conclusion:** Prolactin’s positive effect on thermoregulation was observed in the absence of shivering suggesting, that prolactin acting via its receptor promotes lipolysis and therefore nonshivering thermogenesis in brown adipose tissue.
Outcomes in early adulthood for very low birth weight infants

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Background: Follow-up studies of very low birth weight (VLBW) infants without major neuro-disabilities during school years have shown a high prevalence of behavioural and learning difficulties, and poor growth. Now that these infants are adults, it is of interest to know how well they are faring.

Population: A cohort of 137 VLBW infants together with 160 term controls (T) born in 1980-83 and studied longitudinally in mainstream schools since.

Methods: VLBW and T subjects were studied using a postal questionnaire. The questionnaire included the SF-36 Quality of Life (QoL) questionnaire, The Hospital Anxiety and Depression Scale (HADS), a Social Activities Scale, and questions on risk taking, contact with police, relationships, size and self-image, medications, education, qualifications, family and occupation.

Results: 70 (58%) VLBW and 63 (46%) T subjects that could be contacted responded and completed a questionnaire. The SF-36 has 9 domains describing QoL. VLBW scored significantly lower than T on only one domain, physical function. Scores for anxiety and depression on HADS were similar. No differences in the rate of participation in 9 different social activities was noted. VLBW drank alcohol, smoked cannabis, and used heroin and Ectasy significantly less frequently than T. Similar rates for cigarette smoking and frequency of sexual intercourse were seen in both groups. VLBW had more children. No differences in contacts with police were seen. T were significantly taller, and 33% T women thought themselves more attractive than others (2.5% VLBW). VLBW lived significantly more often with their parents. T were twice as likely to have entered higher education, and have significantly higher qualifications.

Conclusions: Educational disadvantages result in significant differences in adult life for VLBW, although their self-perceived QoL is generally good.

Catch-up growth in extremely preterm children

M.A. Bracewell, N. Marlow, D. Wolke D (on behalf of the EPICure Investigators Group). School of Human Development, University of Nottingham, UK; Department of Psychology, University of Hertfordshire, UK

Aims: We observed low growth velocity from birth to 2¹⁄₂y in a population-based study of children born ≤25w gestation in the UK and Ireland between March and December 1995. We have reassessed growth at early school age to determine whether there has been significant catch up.

Methods: 7 paediatricians performed formal developmental and neurological assessments and growth measures using standardised measures in school children without major neuro-disabilities during school years. Index children were smaller, lighter and slimmer than with comparison children. Mean difference for head circumference (OFC) Z scores was 1.31sd (95%CI 1.07–1.55), for weight: 1.24sd (1.09–1.51); for height 0.97sd (0.74–1.19) and for body mass index (BMI) 0.95sd (0.7–1.21) (each: p<.001). Changes in Z scores from 2¹⁄₂ to 6y are shown in the table. Head circumference was lower in children with cerebral palsy (p=47; Z=–2.2) compared to those without (p=192; –1.95; p=0.006); for both groups OFC was weakly correlated with IQ (CP: r=0.15; no CP r=0.04) and visuospatial performance (r=0.20 and 0.04, respectively) but for sensorimotor skills the correlation was only strong for the children with CP (r=–0.41 and <.001, resp).

Conclusions: Extremely preterm children show significant catch up particularly in height and weight over early school years but remain smaller than their peers. Poor head growth is only weakly correlated with cognitive performance for those without cerebral palsy.

Change in prevalence of disability in extremely preterm children between 2½ and 6 years of age

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Aims: Outcome assessment following preterm birth is recommended at 2½y, but the predictive value of this assessment is uncertain. The EPICure study has evaluated disability at 2½y corrected age and 6y chronological age in a study of children born ≤25w gestation in the UK and Ireland in 1995. This study addresses the predictive value of the earlier assessment at 6y.

Methods: Independent paediatricians assessed children at both ages. Data were encoded using similar record sheets. At 6y disability was graded as severe (non-ambulant; IQ <–3SD; blind; profound SNHL) or moderate (ambulant CP; IQ –2 to –3SD; other functional visual or hearing loss; autism). Cognitive function at 6y was measured by one of 8 psychologists using the Kaufman-ABC. Other areas of impairment were recorded.

Results: 236 children were assessed at each age, 24% of these had moderate or severe disability at 6y. Of 50 children classified as ‘severe disability’ at 2½y, 42 (84%) were disabled at 6y (PPV: 86%; NPV 95%; Likelihood ratio 18.7); seven of the other 8 had a total of 13 impairments (4 motor, 3 cognitive, 3 vision, 3 behaviour). Sixty-five children (35%) had ‘other disability’ at 2½y of whom only 9 (14%) had disability at 6y (PPV: 4%; NPV 90%; Likelihood ratio 0.42); of these 9, 3 had single severe disability (motor 1, cognitive 2) and 6 moderate (2 motor, 3 cognitive, 1 hearing, 2 behaviour). Of the six children without disability at 2½y classed with disability at 6y, 4 developed cognitive disability (1 severe, 3 moderate) and 2 with hearing loss and 5 had other impairments.

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<table>
<thead>
<tr>
<th>No. of pairs</th>
<th>2 ¹⁄₂ years Mean (sd)</th>
<th>6 years Mean (sd)</th>
<th>Difference Mean (95%CI)</th>
<th>p</th>
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<tr>
<td>Head (OFC)</td>
<td>231</td>
<td>–1.76 (1.42)</td>
<td>–1.63 (3.10)</td>
<td>0.13 (0.00, 0.25)</td>
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<tr>
<td>Weight</td>
<td>226</td>
<td>–1.58 (1.32)</td>
<td>–2.21 (3.02)</td>
<td>0.37 (0.23, 0.50)</td>
</tr>
<tr>
<td>Height</td>
<td>216</td>
<td>–1.39 (1.14)</td>
<td>–0.07 (1.10)</td>
<td>0.42 (0.31, 0.52)</td>
</tr>
<tr>
<td>BMI</td>
<td>212</td>
<td>–0.88 (1.34)</td>
<td>–0.88 (3.10)</td>
<td>0.0 (–0.18, 0.18)</td>
</tr>
</tbody>
</table>
Conclusions: The severe disability classification at 2½y was highly predictive of significant problems at 6y but the ‘other’ disability category had a low positive predictive value for disability at 6y. Care is required in counselling parents as to outcomes based on early assessments in extremely preterm populations.


G37 EVALUATION OF BILICHECK AS A SCREENING TOOL FOR NEONATAL JAUNDICE IN TERM AND NEAR TERM BABIES
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Introduction: Using transcutaneous bilirubinometry to screen for significant jaundice has been shown to reduce the need for measurements of serum bilirubin SBR by 34%. 1 “Bilicheck” (Spectrex Inc) is a new transcutaneous bilirubinometer.

Aim: To determine the accuracy of BC as a measure of SBR and to evaluate the effectiveness of BC in screening for significant neonatal jaundice (SBR>250µmol/l).

Study population: All babies >33 weeks gestation with clinically detectable jaundice requiring measurement of SBR. Babies who had received phototherapy prior to the measurement were excluded.

Methods: SBR was measured in a capillary blood sample. BC measurements were made simultaneously from the forehead.

Results: 300 babies were recruited. Male: Female ratio was 1:1. There was a strong correlation between BC and SBR (n=300, r= 0.77, p<0.0001). The mean difference between the two methods (SBR - BC) was 10.7 µmol/l, the limits of agreement were -79.6 µmol/l to 58.1 µmol/l. The area under the ROC curve to detect a significant jaundice was 0.85 (0.79-0.91). Measuring SBR only in babies with BC>150 would have detected significant jaundice with a sensitivity of 91% and specificity of 66%. This would have prevented 166 blood tests (55%). There would have been 5 false negatives, all of these with SBR>300 µmol/l.

Conclusions: Bilicheck cannot be used to measure SBR. It can be used as a screening tool to detect babies who require blood tests. In our practice this could reduce blood tests by 55% without missing any babies with potentially neurotoxic level of SBR.


G38 ENTEROVIRUS MYOCARDITIS IS A CAUSE OF NEONATAL COLLAPSE
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Aim: To describe the presentation and natural history of neonatal enterovirus myocarditis.

Methods: Retrospective review of seven cases of neonatal enterovirus myocarditis presenting to our institution between 1996–2002.

Results: The infants presented at a median of 9 days of age (range 5–18 days) with cardiorespiratory collapse. Median base deficit on presentation was –10.7 (range –1 to –24) and lactate was 4.3 (range 1.8 to 20). All had ischaemic electrocardiograms and an echocardiography had dilated left ventricles with very poor contractility. Median creatine kinase on presentation was 427 (range 222–1344) with an MB fraction of 13% (range 11–25). Diagnosis of enterovirus infection was by isolation of enterovirus DNA by PCR of blood (n=6) or cerebrospinal fluid (n=1) or by demonstration of enterovirus IgM (n=1). 3 infants had duct dependent systemic circulation from a relatively well preserved right ventricle. These infants were treated as having single ventricle physiology analogous to that seen in the hypoplastic left heart syndrome, with prostaglandin E1 to maintain ductal patency and avoidance of both hyperoxygenation and lactic acidosis. 4 infants were supported with extracorporeal membrane oxygenation and 2 of these died. The remaining 5 infants are long term survivors but all have reduced left ventricular function and are on medical treatment for cardiac failure.

Conclusions: Neonatal enterovirus myocarditis may be an underrecognised cause of neonatal collapse. The diagnosis is suggested by an ischaemic electrocardiogram, raised cardiac enzymes and demonstration of left ventricular dysfunction on echocardiography. Infants with reduced post ductal saturations are likely to have a duct dependent systemic circulation, requiring measures to ensure ductal patency and to maintain the systemic circulation.

G39 PREVALENCE OF MATERNAL DRUG MISUSE BY MECONIUM ANALYSIS
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Aims: To establish the prevalence of maternal drug misuse during the second and third trimesters of pregnancy utilising the technique of analysis of meconium for metabolites of drugs.

Methods: Anonymous randomly collected samples of meconium were analysed by immunoassay for eight drugs of misuse in 400 neonates over a 3 month period. Positive samples were confirmed by gas chromatography / mass spectrometry. The frequency of detection of each drug was determined.

Results: 184 (46%) samples yielded opiates (subgroups; morphine 183 (45.75%), codeine 162 (40.5%), methadone 15 (3.75%). 71 (17.75%) yielded benzodiazepines (subgroups; diazepam 70(17.5%), temazepam 49 (12.25%). 63 (15.75%) yielded cannabinoids. 2 (0.5%) yielded cocaine, and 9 (2.25%) yielded amphetamines. Multiple drug detection correlated with the presence of methadone; 80% of samples containing methadone had a total of 4 or more of the 8 drugs present. This was true of only 6.5% (26) of the remaining sample. The presence of illicit drugs, benzodiazepines or morphine at concentrations >20mg/ml also correlated with multiple drug detection.

Conclusion: Meconium analysis can be applied to this population to determine rates of foetal exposure to various drugs. This method will not differentiate between illicit ‘street’ drugs and legally prescribed drugs, although future developments in the analysis may make this possible. Fetuses exposed to methadone are usually exposed to several other drugs, including illicit drugs. It therefore appears that pregnant women taking methadone are also misusing other drugs.

G40 PARENTERAL NUTRITION IN PRETERM BABIES: STANDARDISED OR CUSTOMISED?
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Background: Parenteral Nutrition (PN) is an integral part of nutritional provision in preterm neonates. However, there is no consensus as to whether “Standardised” or “Customised” PN should be used.

Aim: To evaluate clinical and economical aspects of Standardised and Customised PN use in stable preterm neonates of less than 29 weeks gestation.

Methods: Review of all the hospital records of fifty surviving babies, of less than 29 weeks gestation and cared for in two tertiary NICUs using different PN strategies. Babies with congenital malformations and surgical problems including necrotising enterocolitis were excluded.

Results: The two study groups were comparable in terms of mean gestation (27.3 v 26.6 weeks), mean birth weight (990 v 969 grams) and mean weight for gestation (+ 0.19 v +0.07 z score). Duration of PN and proportion of prescribed PN received were also similar in both groups. Babies who received Customised PN had more blood samples as compared to the other group (207 v 138). However there was no difference in either the proportion of babies who had abnormal biochemical (48%) or the frequency of documented abnormal results (23%) in each group. Weight gain was not better in Customised group; with 64% losing weight whilst on PN, compared to 48% in Standardised group. The change of mean weight for gestation between birth and discharge was similar in two groups (–0.82 v –0.81 z score). Medical and Pharmacy time were almost double in Customised group, and there was 50% more laboratory resources used by this group whilst the babies were on PN.

Conclusion: Use of Customised PN did not offer any added advantages in terms of biochemical stability and weight gain in stable preterm babies, but involved more workload on medical, laboratory and pharmacy teams.
WHAT CAUSES CONGENITAL ANOMALIES?

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Background: Many congenital anomalies are consistent with having been caused by an ischaemic insult. We hypothesise that atresias and stenoses of the cardiac valves and the gut atresias have an ischaemic origin due to twin-to-twin transfusion. This may be associated with early loss of one twin.

Aim: To compare prevalence of atresias and stenoses of the cardiac valves and the gut atresias in like and unlike twins.

Methods: Covering E&W, data were obtained from: all stillbirth and death certificates from twin registrations 1993–2000; a questionnaire to the general practitioners of all surviving twins 1993–5, where the co-twin had been a fetal or infant death; notifications of congenital anomalies in surviving twins born 1997–2000. Comparison of prevalence in like and unlike sex twins.

Results: See table. Among all twins in E & W 1993–2000, the ratio of like to unlike pairs is 2:1. The observed ratio of 4:2:1 for these congenital anomalies shows a highly significant excess (p=0.02).

Conclusion: The data sources used do not allow the separation between mono- and di-zygotic twins. As all monozygotic twins are of like sex, these results support the hypothesis that zygosity is important in the pathogenesis of the congenital anomalies. Within monozygotic-like sex, these results support the hypothesis that zygosity is important.

How common are violations of good prescribing practice in the neonatal unit?

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Background: The UK department of health is committed to reducing by 40% the number of serious errors in the use of prescribed drugs by 2005. Although drug errors in neonates feature prominently in lay and medico-legial litigation, little is known of the baseline rates of errors in drug prescription in this population in the UK.

Aims: To define the rate of prescribing errors and their severity in a neonatal intensive care unit using a structured Neonatal Formulary.

Methods: Elements of good prescribing practice were derived from the British National Formulary, Neonatal Formulary and Medicines for Children. A clinically significant error was defined as per the definition of Dean et al. I analysed the drug charts of 429 consecutive infants in whom there was involvement of the neonatal service. There were 1432 prescriptions written for 229 infants with median (range) of 4 (1–71). Deviations from good prescribing practice occurred in 752 (52%) of these prescriptions (0.3 errors/day of neonatal unit stay). There were 26 different types of violations, the common being non-use of block letters (72%), impossibly accurate dose (12%), unacceptable abbreviation of micro- and nano-grams (6%), illegible prescriptions (5%), and wrong preparation (5%). None of these errors resulted in actual harm but 2% and 18% of those with errors were considered to be capable of potentially major impact, and significant but non-serious impact on patient care, respectively.

Conclusions: Deviations from good prescribing practice are common in neonatal intensive care. Although actual injury was prevented by the vigilance of neonatal nurses and pharmacists, there remains substantial potential for harm should these safeguards fail. Education on good prescribing is essential to prevent most of such errors.

The Protein C Activation Pathway in Necrotising Enterocolitis

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Aims: Protein C is activated by thrombin bound to thrombomodulin (TM), catalysed by endothelial protein C receptor (EPCR). Activated protein C (APC) has anti-coagulant, pro-fibrinolytic and anti-inflammatory properties. In severe sepsis, there is evidence of an acquired activation defect and low protein C levels correlate with poor outcome. APC therapy improves survival. Necrotising Enterocolitis (NEC) is associated with multiple organ failure and coagulopathy. The PC/APC pathway may therefore be of pathophysiological and therapeutic importance. We aimed to characterise TM and EPCR expression in neonatal control and NEC gut specimens.

Methods: Immunohistochemical staining for TM and EPCR in archived bowel specimens resected from 25 NEC patients and 10 patients with ileal atresia (controls). Severely affected bowel and the surgical margins (mild) were examined. The severity of inflammation was described and the intensity of staining (strong, moderate or weak) was assessed compared to controls.

Results: In control intestine, TM is strongly expressed by arterioles, veins and lymph vessels of all calibre, including capillaries of the lamina propria. EPCR marks the larger arterioles of the submucosa. In 25/25 sections of NEC intestine, the expression of TM remained strong in the submucosa, even in severe cases. There is progressive, patchy loss of TM staining in the lamina propria as the severity of NEC advances and the mucosa becomes increasingly damaged. Intestine affected with NEC continued to express EPCR on the endothelium of large arteries.

Conclusions: We have characterised the distribution of TM and EPCR in normal neonatal intestine. TM is widely expressed by arterioles, veins and lymph vessels throughout the tissue layers of the gut. EPCR is found on arterial endothelium, a finding consistent with previously published results. In NEC, we have demonstrated that TM and EPCR continue to be expressed by the intestinal vascular bed, but that where extensive mucosal damage occurs, there is loss of TM expression in the mucosal capillaries. The functional ability of this apparatus to activate protein C is the focus of ongoing studies.

Changing trends in the respiratory care of preterm infants: does it matter?


Aims: To compare the trends in respiratory care and outcome of two cohorts of extremely preterm babies, born ten years apart, in the same geographically defined area.

Methods: Data was prospectively collected from babies who were born between 24 and 27 6/7 weeks of gestation in 1989–1990 (cohort 1) and in 1999–2000 (cohort 2) and admitted to the four tertiary centres within the network. These included demographic details, duration and type of respiratory support given, mortality, oxygen dependency at 36 weeks and estimated cost of care.

Results: There were 812 babies in the study: 409 in cohort 1 and 403 in cohort 2. Their median gestational age and birth weight were similar (28 v 28 wks and 1140 v 1092 g respectively). There was a significant improvement in survival of babies in cohort 2 (74.9% compared to 68.4% in cohort 1; p=0.048). This was most marked in the subgroup of babies born between 26 and 27 weeks (cohort 1, 60% v cohort 2, 73%; p=0.04). Amongst survivors, the median duration of intubation was significantly lower in cohort 2 (5 days) compared to earlier cohort (8 days): p=0.0079, 95% CI for difference = 3. How- ever, there was a parallel increase in the use of nasal CPAP. Total
duration of respiratory support (intubation plus nasal CPAP) was appreciably longer in cohort 2 (median 11 days vs 8 days, p = 0.0001; 95% CI for difference 2 to 5). The proportion of babies dependent on oxygen at 36 weeks, however, was similar in both groups (24% vs 27.5%, p=0.5).

Conclusions: Our study confirms the improved survival of babies born between 24–29 weeks gestation but these babies required significantly longer duration of intensive care therapy. These findings have implications for service management and strongly support the BAPM recommendation for increase in intensive care capacity and resource allocation.

G45 PULMONARY FUNCTION AT FOLLOW-UP OF VERY PRETERM INFANTS FROM THE UNITED KINGDOM OSCILLATION STUDY (UKOS)

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Background: Prematurely born infants supported by conventional ventilation (CV) frequently have abnormal lung function when seen at follow-up. We have performed a randomised controlled trial (UKOS) comparing the outcome of infants supported by either CV or high frequency oscillation (HFO).

Aim: To test the hypothesis that infants who had been randomised to HFO would have superior lung function at follow-up to those who received CV.

Methods: Infants from 10 UKOS centres were recruited for pulmonary function testing at King’s College Hospital. Following sedation with chloral hydrate, lung volume was measured by body plethysmography (FRC) and helium dilution (FRCHe), and airway resistance (Raw) by body plethysmography. Tidal breathing was also analysed, including ratio of time to peak expiratory flow : expiratory time (tPTEF : tE) and respiratory rate.

Patients: 76 infants (42 HFOV; 34 CV), mean gestational age 26.3 weeks, were studied at a mean corrected age of 12.6 months.

Results: There were no statistically significant differences between the mean pulmonary function test results of the two groups (see table).

Conclusions: In the situation of a randomised controlled trial, initial treatment with HFO appears to offer no advantage over CV regarding pulmonary function at follow-up.

G46 DO CONVALESCENT PRETERM INFANTS SLEEP BETTER PRONE?

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Background: Prematurely born infants are at an increased risk of sudden infant death syndrome (SIDS), particularly if slept prone, the odds ratio being 48.8. Reduced arousals in the prone position have been suggested to be a contributory factor to SIDS in healthy term infants.

Aims: To determine the effect of position on the sleep pattern and arousals of premature infants about to be discharged home from the NICU.

Methods: Video polysomnographic recordings were performed on two successive days. On each day, the infants were studied both supine and prone, each position maintained for 3 hours. The order in which the sleeping positions were examined was randomised between infants. Simultaneous online recordings of 2-channel EEG, 2-channel EOG, nasal airflow, chest and abdominal wall movements, limb movements, EEG, and oxygen saturation were made. Sleep was staged into active, quiet or indeterminate sleep or wakeful state in each 30 second epoch and calculated as the percentage time asleep. Sleep efficiency in each position was calculated by dividing the time spent in sleep by the recording time. Arousal was defined as spontaneous body movements lasting longer than 10 seconds and an arousal index (number of arousals per hour of sleep) calculated. Awakening was an arousal response = 60 seconds or crying.

Patients: Six preterm infants (median GA 27 weeks) were studied at a median post conceptional age of 37 weeks.

Results: Infants had better sleep efficiency (87.8% vs 72.7%, p=0.01) and spent longer time in quiet sleep (26% vs 20.7%, p=0.028) in the prone position. They had significantly more awakenings (16 vs 10, p=0.032) and arousals (arousal index 13.6 vs 11 p=0.008) when supine.

Conclusions: The lower arousability in the prone position further emphasises the importance of recommending supine sleeping for preterm infants following NICU discharge.

G47 EARLY PITUITARY-ADRENAL RESPONSE AND RESPIRATORY OUTCOMES IN PRETERM INFANTS

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Aims: To investigate the relation between early pituitary-adrenal response and respiratory outcomes, in particular, the development of chronic lung disease (CLD) and duration of oxygen supplementation in preterm, very low birth weight (VLBW) infants.

Methods: Human corticotropin release hormone (hCRH) stimulation tests were performed on 137 VLBW infants at day 7 and 14 in a tertiary neonatal centre.

Results: The basal, peak and incremental rise in serum cortisol (ΔCort) at day 7 were negatively associated with the Clinical Risk Index for Babies (CRIB) score (r = −0.19, p < 0.04), alveolar-arterial oxygen gradients (r = −0.21, p < 0.04), duration of mechanical ventilation (r = −0.21, p < 0.02) and oxygen supplementation (r = −0.19, p < 0.04; peak and ΔCort), and maximum mean airway pressure (r = −0.18, p < 0.05). In contrast, peak serum cortisol at day 14 became positively associated with the aforementioned pulmonary indices and outcomes, including duration of mechanical ventilation (r = 0.21, p = 0.04) and oxygen supplementation (r = 0.27, p < 0.008; basal and peak levels). Multivariate regression analysis revealed similar findings between peak serum cortisol and duration of oxygen supplementation at day 7 and 14 (p = 0.05 and 0.02, respectively).

Conclusions: Our findings support the phenomenon of ‘Transient Adrenocortical insufficiency of Prematurity (TAP)’ with adrenal function showing signs of good recovery by the end of the second week. Low serum cortisol at day 7 was associated with prolonged oxygen dependence. This observation supports the hypothesis that an inability to secrete adequate amounts of cortisol may contribute to insufficient dampening of lung inflammation resulting in chronic lung injury.