Perinatal medicine

G22 MEASURING URINE OUTPUT BY WEIGHING NAPPIES—WHAT IS THE EFFECT OF HUMIDITY?

S.J. Oddie, R. Adappa, J.P. Wyllie. *Neonatal Unit, James Cook University Hospital, Middlesbrough*

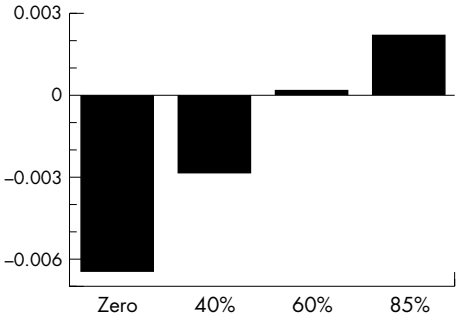
Background: Measurement of urine output by weighing nappies is a validated and widely used technique. However work measuring significant evaporative losses with different nappies and in different environments has led to recommendations that nappies should be weighed very two hours.

Aims: To assess the impact of differing humidity environments on the weight of standard hydrophillic nappies over a six hour period.

Methods: Fifty one premature infant nappies were weighed before and after the addition of a 5ml aliquot of normal saline. They were then placed in Drager 8000 1C incubators with stable (>1 hour) humidity readings of zero, 40, 60 or 85% for 6 hours at 39°C. Weights were recorded at intervals using a precision balance. Statistics were calculated using analysis of variance assuming linear weight gain or loss over time.

Results: At 85% humidity nappies gained weight. Nappies at zero and 40% humidity lost weight. The differences between all groups were statistically significant ($p<0.05$). Infants nursed at 85% humidity might have a 5g urine output overestimated by 0.8g over 6 hours, while those at 40% or zero humidity might have it underestimated by 1.0g or 2.5g respectively in 6 hours.

Conclusions: Measurement of urine output is affected by the use of incubator humidity, but provided humidity is used the clinical effects are small even for the smallest infants, even when nappies are only weighed every six hours.



Abstract G22 Rate of weight change in differing humidity settings (g/min).

G23 DUPLEX KIDNEYS—ANTENATAL DIAGNOSIS, CLINICAL SIGNIFICANCE, AND GENETICS

S.M. Whitten, L.S. Chitty, D.T. Wilcox, S. Malcolm, A.S. Woolf. *Units of Clinical and Molecular Genetics and Nephro-Urology, Institute of Child Health, London; Department of Paediatric Urology, Great Ormond Street Hospital; Fetal Medicine Unit, Elizabeth Garrett Anderson Hospital, London*

Aims: To assess clinical outcome of antenatally diagnosed duplex kidneys to elicit the implications and long-term significance of such a finding, and to identify kindreds where more than one individual has a duplex kidney to assess the potential genetic basis for duplex kidneys.

Methods: Retrospective identification of 62 patients with an antenatal diagnosis of duplex kidney between 1992 and 2001 was made from our computerised databases. Results of postnatal radiological investigations were obtained. The clinical course was ascertained in confirmed cases. Renal sonography was undertaken on parents and siblings of index cases, including the extended family when a history of duplex kidneys was known.

Results: Postnatally, duplex kidneys were confirmed in 46 patients (74%), with a female:male ratio of 2:1. Correct diagnosis was strongly associated with detection of a split renal pelvis (93%) or ureterocoele (90%), and with the presence of two or more prognostic features. Of the 43 liveborn infants with duplex kidneys, 16 have remained asymptomatic with conservative management, whilst two have undergone ureterocoele puncture. The remaining 25 have undergone heminephrectomy at ages varying from 0–6 months (6), 6–12 months (12), 12–18 months (5), with two after 18 months of age.

Families of 21 index cases underwent renal sonography, with a duplex kidney being found in 28% (22/78) of all relatives. A quarter of all first-degree relatives were affected (15/59), comprising 26% of siblings (7/27) and 25% of parents (8/32). In seven families with a prior history of duplex kidneys, 40% of family members were affected (16/40), with 32% of first-degree relatives affected (9/28), compared to 25% of first-degree relatives (4/16) in nine families with no background history of renal disease.

Conclusions: Antenatal detection of duplex kidneys with identification of specific prognostic features can inform antenatal counselling and postnatal management. The case for a genetic basis for duplex kidneys seems clear, given an incidence of 1% in the general population. The exact mode of inheritance has yet to be established.

G24 RANDOMISED CONTROLLED TRIAL OF LOW DOSE ERYTHROMYCIN IN PRETERM NEONATES WITH FEED INTOLERANCE

P.A. Cairns [1], R. Tubman[2], S. Craig[2], R. Roberts[3], B. Schmidt[3]. [1]*Department of Child Health, St Michael's Hospital, Bristol;* [2]*Department of Child Health, The Queens University of Belfast;* [3] *Faculty of Health Sciences, McMaster University, Canada*

Background: Erythromycin is a macrolide antibiotic which has attracted interest as a prokinetic agent in low doses. It has been demonstrated to improve gut motility in intestinal dysmotility in adults.

Aim: The objective of this study was to test the hypothesis that low dose, intravenous erythromycin would improve feed intolerance in infants with gastrointestinal dysmotility of prematurity.

Design: Double blind, randomised controlled trial. Study population: Infants with post-conceptional age <37 weeks who did not tolerate enteral feeds despite receiving minimal enteral nutrition for a minimum of 3 calendar days. At randomisation infants were stratified into post-conceptional age <33 weeks (stratum1) or >32 weeks (stratum 2). Intervention: 3mg/kg/dose erythromycin or placebo 6 hourly intravenously until tolerating full enteral feeds. Primary outcome: Time to full feeds of 150ml/kg/day.

Results: Thirty two babies were randomised to erythromycin and 28 to placebo. The mean (SD) gestational ages at randomisation were 27.8(1.9) and 27.5(1.8) weeks respectively. Two infants in each group were greater than 32 weeks postconceptual age (stratum 2). The mean (SD) times since first feeds were attempted were 8.0(4.7) and 8.6(6.6) days. Twenty six (81%) and 25 (89%) were fed with expressed breast milk.

The mean (SD) times to full feeds in stratum 1 were 13.7(10.1)and 15.7(7.1) days in the erythromycin and placebo groups respectively. In stratum 2 the time to full feeds were 13.0 (14.1) and 26.5 (20.5) days.

The adjusted difference was (mean (95%confidence limits) -2.7(-7.5 to 2.2) days, p=0.27.

Conclusions: Low dose intravenous erythromycin does not significantly reduce the length of time to full feeds in infants with gastrointestinal dysmotility of prematurity. In infants over 32 weeks gestation there may be a beneficial effect. However the number of infants in this stratum was small.

G25 IDENTIFICATION OF THE TIP OF THE LONG LINE IN PRETERM BABIES USING THE INVERSION OF IMAGE TECHNIQUE ON PACS (PICTURE ARCHIVING AND COMMUNICATION SYSTEM)

N.B. Soni, M. Becker , H. Dixon, R. Miles. *Department of Paediatrics, Hinchingbrooke Hospital, Huntingdon, UK*

Background: Positioning of long lines into the heart has serious consequences including death due to cardiac tamponade.[1] The tip of long lines is accurately visible in only 50% of plain radiographs.[2] Identification of the line using radio opaque contrast media requires caution. The use of an insufficient volume of contrast will falsely identify the tip in an apparently more proximal position, whereas a film taken during active injection may cause the line to appear longer due to a jet of contrast issuing from the tip of the line. Ultrasound may be of value but it requires expertise to perform and interpret[1].

Aims & Methods: We conducted a retrospective study comparing visibility of the tip of long lines on plain radiographs versus inverted images on PACS. Three independent observers assessed the images.

Abstract G25

Observer	Tip visible on ***plain X ray***	Tip visible on ***inverted image***	Improvement	Statistics *(paired t test)*
A	06/24 **(25%)**	15/24 **(63%)**	**38%**	P= 0.001
B	12/23 **(52%)**	17/23 **(74%)**	**22%**	P= 0.02
C	40/69 **(58%)**	65/69 **(94%)**	**36%**	P= 0.000
Reece et al[2]	31/62 **(50%)**	29/31 **(94%)** ***contrast study***	**44%**	

Results: see table above.

Conclusions: Inversion of image on PACS is better than plain radiograph in identifying the tip of the long lines and results comparable to contrast studies can be achieved using this technique.

1. Review of four neonatal deaths due to cardiac tamponade associated with the presence of a central venous catheter. Recommendations and department of health response, June 2001.
2. A Reece, *et al.* positioning long lines: contrast versus plain radiography. *Arch Dis Child Fetal Neonatal Ed* 2001;**84**:F129–30.

G26 MECHANICAL VIBRATION IN NEONATAL TRANSPORT

N.E.Edi-Osagie[1], P. Gaydecki[2], C. Jackson[1], M.J. Robinson[1]. [1]*NICU, Hope Hospital Salford M6 8HD UK,* [2]*Dept of Instrumentation and Analytical Science, University of Manchester Institute of Science and Technology, Manchester UK*

Background: Levels of vibration in excess of 2g are extremely uncomfortable for healthy adults. Space travel will subject astronauts to forces of between 4 and 7g.

Aim: To quantify the level of vibration in ambulance transport.

Methods: A system comprising two triaxial (*xyz*) accelerometers connected to two three-channel programmable amplifiers was connected to an analogue-to-digital converter (ADC) system and linked to a notebook PC. This was mounted on a standard neonatal transport incubator in which a mannequin restrained with "bubble wrap" was placed. One accelerometer was attached to the mannequins forehead while the other was attached to the top of the incubator. Emergency and non-emergency journeys were then made to simulate actual transport runs.

Results: Acceleration was measured in the *xyz* planes on both the mannequins head and the incubator. The x-axis represents left to right movement, y-axis represents forward-backward movement and the z-axis represents up-down movement. The *xyz* acceleration vector (vibration) recorded on the mannequin during an emergency run (average speed 55mph) was a maximum of 5.22g (51.21ms^{-2}) while on the incubator the maximum was 2.81g (27.57ms^{-2}). The *xyz* acceleration vector recorded on the mannequin during a non-emergency run (average speed 35mph) was a maximum of 7.30g (71.6ms^{-2}), while on the incubator the maximum was 4.5g (44.15ms^{-2}).

Conclusion: Vibration in neonatal transport can exceed levels tolerable for healthy adults. In immature compromised infants who are less able to cope, this is a cause for concern. Modification of equipment is necessary but as there are significant differences between vibration in incubators and that experienced by patients, this should be taken into account. g is equivalent to 9.81ms^{-2}.

G27 CENSUS OF NEONATAL TRANSFERS DURING A 3-MONTH PERIOD IN LONDON AND THE SOUTH-EAST OF ENGLAND

S.T. Kempley, A.K. Sinha on behalf of the Thames Regional Perinatal Group (TRPG) *Neonatal Unit, Royal London Hospital, Whitechapel, London*

Aims: To determine the number and characteristics of neonatal ex-utero transfers to or from hospitals within the former Thames Regions.

Methods: Data were requested from 53 TRPG units for the period 1st Jan to 31st March 2001. Transfers were recorded prospectively and classified as urgent, elective, or short-term. A dual-logging system was used with transfers recorded by both source and destination units. No personal details were collected; transfers were matched on date, gestation, weight, and birth date.

Results: Completed census returns were provided by 42 (78%) of units, but the dual-logging system ensured that transfers were recorded in or out of 52 (98%) of participating units. A total of 620 transfers were recorded. Numbers and maturity in each category of transfer are shown in the table below, with the mean number of staff hours spent on transfers each day.

A maximum of 8 urgent transfers took place in any one day. There was a weekly variation with less urgent transfers on Sundays. It took over 4 hours for 90% of ambulances to arrive at retrieving units and over 6 hours for 90% of teams to arrive at source units. Of the urgent transfers, 62% took place for the baby to obtain specialist services such as surgery or cardiac services.

Conclusions: Although three dedicated teams could meet the demand identified in this census, more than 50 units are currently forced to maintain a transfer capability. Despite this, present arrangements provide a sub-optimal service, with long delays in reaching vulnerable patients.

Abstract G27

Category of transfer	Numbers of transfers: Jan-Mar 2001	Daily equivalent	Annual equivalent	Number (%) premature	Average staff hours per day
Urgent	242	2.7	968	130 (54%)	11.2
Elective	314	3.5	1256	270 (86%)	7.8
Short term	64	0.7	256	38 (59%)	2.9
TOTAL	620	6.9	2480	438 (71%)	21.4

G28 FAECAL CALPROTECTIN AS A MARKER OF GUT INFLAMMATION IN NEONATES

D. Carroll[1], R.D.Spicer[1], P.A Cairns[2]. [1]*Department of Paediatric Surgery, Bristol Royal Hospital for Sick Children, upper Maudlin St, Bristol, BS2 8BJ;* [2]*Consultant Neonatologist, Department of Child Health, St. Michael's Hospital, St. Michael's Hill, Bristol, BS2 8BJ*

Aims: Necrotizing enterocolitis (NEC) can be difficult to diagnose as early clinical, radiological and laboratory findings may be nonspecific. Infants with possible NEC are often deprived of enteral nutrition and treated with broad-spectrum antibiotics for 7–10 days. The aim of this study was to assess faecal calprotectin levels as a marker of bowel inflammation in neonates with suspected NEC. Calprotectin is an abundant neutrophil protein, which is extremely stable

in faeces. Faecal calprotectin levels have been used to demonstrate disease activity in inflammatory bowel disease in children[1].

Methods: Faecal calprotectin was measured using a simple enzyme-linked immunosorbent assay in spot stool samples from 7 neonates with definite NEC and 7 age, gestational age and sex-matched controls.

Results: Compared with age-matched controls there is a statistically significant difference in faecal calprotectin levels in infants with definite or advanced NEC (p<0.001). A calprotectin level of >68mg/L gave a sensitivity and specificity of 100%.

Conclusions: We hypothesize that faecal calprotectin levels may be a useful marker of intestinal inflammation in neonates. Further examination of its usefulness in cases of suspected NEC is required

1. Bunn SK, Bisset WM, Main MJ, *et al*. Fecal calprotectin: validation as a noninvasive measure of bowel inflammation in childhood inflammatory bowel disease. *J Pediatr Gastroenterol Nutr* 2001;**33**:14–22.

G29 CARDIAC TROPONIN T (CTNT) AND CARDIAC FUNCTION IN RESPIRATORY DISTRESS SYNDROME (RDS)

S.J.Clark[1], P. Newland[2], C.W. Yoxall CW, N.V. Subhedar[3]. [1]*University of Liverpool;* [2]*Royal Liverpool Children's Hospital;* [3]*Liverpool Women's Hospital*

Background: cTnT is a highly sensitive and specific marker of myocardial injury in adults. Cord blood cTnT is raised in neonates who develop RDS, an association that is independent of demographic variables.

Aims: To investigate (1) postnatal blood levels of cTnT and (2) the relationship between cTnT and cardiac function in infants with RDS.

Methods: Blood samples were taken for cTnT levels and echocardiographic examination performed in term and preterm neonates with RDS during the first 3 days of life. Cardiac function was assessed by calculating fractional shortening (FS) and cardiac output (CO). A subgroup of infants had serial daily cTnT levels and/or serial echocardiographic examinations.

Results: Values are given as median (interquartile range). 46 infants with RDS were studied, gestation was 29 (27–31) weeks, birth weight was 1.13 (0.91–1.93) Kg and cTnT was 156 (73–286) pg/mL. Serial samples were obtained in 22 infants on days 1, 2 and 3. cTnT levels were higher in infants with RDS compared with samples taken from 68 healthy infants divided into the same time points (table). In infants with RDS cTnT did not change with time. Echocardiographic examination and cTnT levels were performed in 18 infants and here was a correlation between cTnT and FS (rho= -0.73, p=0.001) and CO (rho=0.47, p=0.05).

Abstract G29

cTnT (pg/mL)	Healthy Infants	Infants with RDS
Day 1	10 (10–19)	98 (60–136) *
Day 2	24 (10–55)	102 (45–231) *
Day 3	45 (10–87)	130 (61–265) *

*p<0.001 compared with infants with no RDS at respective time points.

Conclusion: cTnT levels are elevated over the first 3 days in infants with RDS compared with healthy infants. Infants with RDS had a significant negative correlation between cTnT and echocardiographic markers of cardiac performance. We speculate that cTnT may be a useful marker of cardiac dysfunction in the neonate.

G30 DOES IL6-174 GENOTYPE PREDICT THE DEVELOPMENT OF SEPTICAEMIA IN PRETERM INFANTS?

D. Harding [1] ,H. Montgomery[2], S. Dhamrait[2], A. Millar[3], S. Humphries[2] , N. Marlow[4], A. Whitelaw[1]. *University of Bristol* [1]*Dept of Child Health,* [3]*Lung Research Group; Southmead Hospital;* [4]*University of Nottingham School of Human Development;* [2]*University College London Cardiovascular Genetics*

Aims: Preterm infants have an immature immune system and are vulnerable to infection. Defence from infection is in part mediated by the cytokine interleukin 6 (IL6). Variation in the IL6 gene (the –174G allele) is associated with reduced IL6 levels in neonates. The objective was to determine whether the IL6-174 G allele or GG genotype is associated with the development of septicaemia.

Methods: The study group comprised 157 infants born at <32 weeks gestation who had participated in a prospective neonatal outcome study. IL6 genotype was determined from DNA extracted from Guthrie blood spots. Septicaemia was defined as clinical deterioration with a positive blood culture.

Results: Genotype distribution was 54 (34.4%) GG, 72 (45.9%) GC, 31 19.7% CC. The G allele was not associated with systemic infection (p.07). Infants who were GG genotype had 44.4% risk of septicaemia (24/54) whereas infants who were CG or CC had a 26% infection rate (27/103), p.021, OR 2.3, 95% CI 1.1 – 4.5. Multiple binary logistic regression modelling of other significant predictors of the development of sepsis (gestation, days of initial ventilation, duration of hospitalisation) confirmed this association, GG genotype and septicaemia, p.019, OR 2.7, 95% CI 1.2 – 6.3.

Conclusion: The IL6-174 GG genotype is associated with the development of septicaemia after preterm birth.

G31 GLUCAGON STIMULATION IN PRE-TERM INFANTS: MARKERS OF INSULIN RESISTANCE PREDICT RESPONSE

L. Jackson, A. McGeechan, A. Burchell, R. Hume. Tayside Institute of Child Health, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY

Background: Glucose-6-phosphatase (G6Pase) determines the rate of hepatic gluconeogenesis and glycogenolysis. Genetic deficiency of hepatic G6Pase is characterised by fasting hypoglycaemia and an attenuated hepatic response to glucagons (type 1 glycogen storage disease). Many preterm infants do not attain adult levels of G6Pase activity in the post-natal period resulting in relative G6Pase deficiency, and a potential vulnerability to repeated hypoglycaemia.

Aims: To evaluate the post-natal maturation of hepatic glucose production in preterm infants in response to intravenous glucagon (100mcg/kg).

Methods: Seventy-eight infants participated in a two-phase study. Day one: infants were fasted for up to 8-hours, or less if hypoglycaemic with a hormonal and metabolic profile at study completion. Day two: a standard milk feed was replaced by a glucagon bolus, and blood glucose and lactate concentrations were obtained quarter-hourly for a period of two-hours via an in-dwelling cannula.

Results: An adequate response to glucagon was arbitrarily defined to be a rise in glucose level of >1mmol/l (55 infants). An inadequate response was < 1mmol/l (23 infants). The group with a lesser glycaemic response had a negative glycaemic excursion 60 minutes post-glucagon, a higher lactate excursion and several abnormalities in carbohydrate metabolism: relative fasting hyperglycaemia (3.7mmol/l *v* 3.3mmol/l, p=0.008); fasting hyperinsulinaemia (4.3mU/l *v* 2.6mU/l p=0.014); an increased insulin : glucagon ratio (0.19 *v* 0.11, p=0.014) and an increased frequency of early neonatal hypoglycaemia (7.76 *v* 4.02 episodes, p=0.017) on a retrospective case-record review.

Conclusions: Post-natal development of glucose homeostasis is abnormal in many preterm infants. We have previously shown some infants have abnormal metabolic responses to a fast and now have identified a sub-group of preterm infants who are relatively insulin-resistant with an attenuated response to glucagon, and who are more prone to hypoglycaemia in the early neonatal period.

G32 BACTERIA IN PRETERM FETAL MEMBRANES DETECTED, USING FLUORESCENCE IN SITU HYBRIDISATION, WITH AND WITHOUT INFLAMMATION

N.L Kennea, J.H. Steel, S.R. Sooranna, M.H.F. Sullivan, P. Duggan, P.R. Reynolds, E.W. Adams, A.D. Edwards. *Imperial College School of Medicine; MRC Clinical Sciences Centre, Hammersmith Hospital, London, UK*

Aims: We have developed a novel and sensitive method for detection and characterisation of bacteria within the fetal membranes in order to determine the relationship of bacteria in fetal membranes and the presence of histological chorioamnionitis, and cytokine evidence of inflammation in the cord blood.

Methods: Bacteria in the fetal membranes from a cohort of preterm infants born <32 weeks (n=50) and term controls (n=52) were detected using a fluorescence *in situ* hybridisation (FISH) approach. Paraffin sections were hybridised with FITC-labelled antisense or sense oligonucleotides to detect 16S ribosomal RNA. Results were

compared with histological chorioamnionitis and evidence of fetal inflammation from IL-6, IL-1β, TNFα levels in cord blood, measured using specific ELISAs.

Results: Using FISH, bacteria were clearly demonstrated in the chorion and/or amnion in 75% of preterm infants. The results ranged from negative to heavily infected and different morphological types were seen. Chorioamnionitis was present in 48% of preterm samples, and 86% of these had positive FISH. In those samples without chorioamnionitis, 65% had bacteria present. 78.6% of preterm infants born by caesarian section had positive FISH. In term control group, 58% had positive FISH, although chorioamnionitis was present in <10%. In the preterm infants chorioamnionitis, but not the presence of bacteria, was associated with high IL-1β and TNFα levels in cord blood ($p<0.05$).

Conclusions: The presence of bacteria is more common in the fetal membranes than other methods have demonstrated. Bacteria are evident without inflammation in many term and preterm infants suggesting a possible difference in the host response to infection.

G33 RECOMBINANT HUMAN SURFACTANT PROTEIN D (RHSP-D) MODULATES LUNG INFLAMMATION IN MICE PREDISPOSED TO CHRONIC LUNG DISEASE AND EMPHYSEMA

H. Clark[1,2], P. Strong[1], S. Hawgood[3], K.B.M. Reid[1]. *[1]MRC Immunochemistry Unit, Department of Biochemistry, University of Oxford; [2]Department of Paediatrics, John Radcliffe Hospital, University of Oxford; [3]Department of Pediatrics, University of California, San Francisco, USA*

Pulmonary surfactant therapy has successfully reduced mortality from neonatal respiratory distress syndrome, but up to 40% of those surviving after birth at less than 28 weeks gestation develop neonatal chronic lung disease (CLD). Infective episodes, oxidative lung injury due to prolonged ventilation in high concentrations of inspired oxygen and defective alveolar remodelling in response to these insults are all considered to increase the risk of developing CLD. Surfactant protein D (SP-D), a natural component of the lung innate immune system, is not present in surfactant formulations currently in use. SP-D deficient knock-out mice develop chronic inflammation in the lungs with increased numbers of abnormal alveolar macrophages, excess alveolar phospholipid, increased matrix metalloproteinase expression, a susceptibility to oxidative lung injury, defective alveolar remodeling and the development of pulmonary fibrosis and emphysema. To assess if this process could be modulated by replacement of SP-D, SP-D knock-out mice were treated intranasally with multiple doses of recombinant human SP-D (rhSP-D) for 3 to 6 weeks. After 3 weeks of rhSP-D replacement therapy, the excessive number of alveolar macrophages in bronchoalveolar lavage (BAL) from knock-out mice was 50% lower than untreated controls ($p<0.05$, n=6 mice each group). Excess alveolar phospholipid levels were also significantly lower in treated groups after 6 weeks of rhSP-D replacement ($p< 0.05$, n= 6 mice each group). Levels of GMCSF in BAL were increased in SP-D knock-out mice compared to wild-type ($p<0.01$) but decreased after rhSP-D treatment ($p< 0.05$), as were levels of expression of mRNA for the proinflammatory chemokines MCP-1 and MIP-1α. The results show that rhSP-D modulates macrophage mediated inflammation in mice susceptible to emphysematous change because of SP-D deficiency, and suggest that replacement of SP-D in surfactant deficient preterm babies could help reduce the risk of CLD.

Abbreviations: GMCSF: granulocyte monocyte colony stimulating factor.
MIP: macrophage inflammatory protein. MCP: monocyte chemoattractant protein.

G34 ACTIVITY OF MONOCARBOXYLATE TRANSPORTERS (MCTS) IN SYNCTIPTROPHOBLAST MICROVILLOUS PLASMA MEMBRANES OF HUMAN PLACENTAS, AND LOCALISATION OF MCTS 1 AND 4

P. Settle*, J. Glazier, C. Sibley, I. Doughty, T. Johnston, S. D'Souza. *Academic Unit of Child Health, St. Mary's Hospital, University of Manchester, UK*

The lactic acidosis often seen in intrauterine growth restriction (IUGR) is associated with increased morbidity and mortality. As lactic acid is transported out of the fetus by the placenta, a reduction in transport in IUGR might contribute to the severity of the acidosis in this condition. In this study, we investigated the role of monocarboxylate transporters (co-transporters of lactate and H^+) in the syncytiotrophoblast microvillous (MVM) and basal plasma membranes (BM) of placentas from appropriately grown infants.

Methods and results: Uptake of ^{14}C L-lactate (5μM) into purified MVM vesicles was studied in the presence or absence of a pH gradient (pH_i 7.6, pH_o 5.6 or 7.6 respectively). The data confirm uptake of lactate ions driven by a pH gradient. 5mM 4,4'-diisothiocyanatostilbene-2,2'-disulfonic acid (DIDS), an inhibitor of certain MCTs, significantly inhibited uptake (6.8 ± 1.5 vs 18.5 ± 2.9 pmol/mg protein/20 secs, mean ± S.E.M., $p<0.01$). Unlabelled L- or D-lactate inhibited ^{14}C L-lactate uptake in a concentration dependent manner, with the inhibition curves for L- and D-lactate being significantly different ($p<0.0001$), suggesting stereospecificity. Western blot studies on purified MVM and BM suggested that MCT1 was expressed on both membranes whereas MCT4 was predominantly localised to MVM.

Conclusions: These data confirm movement of lactate ions across the MVM of the syncytiotrophoblast. The DIDS sensitivity and stereospecificity confirm involvement of a transporter. Western blot studies suggest that this is likely to be a member of the MCT family. However, MVT4 is not DIDS sensitive, which suggests that another isoform, possibly MCT1, is functionally more important in this membrane. (Supported by Tommy's Campaign.)

G35 INCREASED LUNG COLLAGENASE LEVELS IN A SHEEP MODEL OF CHORIOAMMIONITIS—IMPLICATIONS FOR THE PATHOGENESIS OF NEONATAL CHRONIC LUNG DISEASE

D.G. Sweet[1], M.T. Huggett[2], T.J Moss[3], I. Nitsos[3], J.A. Warner[2], H.L.Halliday[1], J.P. Newnham[3], M. Ikegami[4], A.H. Jobe[4]. *[1]Dept. of Child Health, The Queen's University of Belfast, Northern Ireland; [2]School of Biological Sciences, University of Southampton, Southampton; [3]Women & Infants Research Foundation, Perth, Western Australia; [4]Div. of Pulmonary Biology, Univ. of Cincinnati Medical Centre, Ohio, USA*

Background & Aims: Inflammation plays a key role in the pathogenesis of chronic lung disease (CLD) but the exact mechanisms of inflammatory lung injury are not fully understood. Chorioamnionitis increases the risk of CLD even in the absence of mechanical ventilation and oxygen toxicity. Matrix metalloproteinases (MMPs) 9 and 2 are type- 4 collagenases that can disrupt alveolar basement membranes, leading to airways remodelling. We studied the effects of chorioamnionitis and corticosteroid therapy on levels of MMP-9 and 2 in fetal lung fluid taken from premature lambs at birth.

Methods: 29 pregnant ewes were randomly assigned to 4 treatment groups at 110 d gestation:[1] Intra-amniotic injection of 10mg endotoxin (ENDO) [2] Intra-muscular injection of 0.5 mg/kg betamethasone (BETA) [3] Both of these (ENDO+BETA) [4] Intra-amniotic saline (CONTROL). Lambs were born by caesarean section at 125 d (term = 150d) and tracheotomised on delivery of the head. Fetal lung fluid (FLF) was aspirated and snap frozen. MMPs in FLF were measured by gelatin zymography and densitometry. Values expressed in ng/mL.

Results: Median (Interquartile Range) shown.

Abstract G35

Group	n	MMP-9	P*	MMP-2	P*
CONTROL	7	0 (0–0)		23 (15–31)	
ENDO	7	7 (1–40)	0.016	71 (39–114)	0.008
BETA	7	0 (0–1)	0.87	31 (21–55)	0.4
ENDO+BETA	8	7 (1–20)	0.01	19 (8–50)	0.64

* Mann-Whitney U test study group vs. control

Conclusions: Endotoxin-induced chorioamnionitis increases fetal lung MMP-2 and MMP-9 levels. Concomitant corticosteroid therapy negates this effect in the case of connective tissue-derived MMP-2, but not neutrophil-derived MMP-9. Neutrophil type-4 collagenase activity may contribute to the lung damage that occurs during the pulmonary inflammation preceding the development of CLD.

G36 VARIATION IN GENETIC POLYMORPHISMS & CHRONIC LUNG DISEASE

M.W. Beresford, J.A. Drury, R. Mountford, R.W.I. Cooke, N.J. Shaw. *Neonatal Unit, Liverpool Women's Hospital, Liverpool, L8 7SS*

Introduction: Inflammation and oxidative damage appear fundamental to the pathogenesis of chronic lung disease of prematurity

Abstract G36

Gene polymorphism	Genotype	Local population	Infants with CLD	Preterm controls	p value*
G-308A TNF-α, n (%)	G / G	32 (64)	21 (66)	23 (58)	
	G / A	14 (28)	8 (25)	17 (42)	
	A / A	4 (8)	3 (9)	0 (0)	**0.08**
C-509T TGF-β, n (%)	C / C	21 (43)	15 (47)	19 (49)	
	C / T	23 (47)	13 (41)	20 (51)	
	T / T	5 (10)	4 (12)	0 (0)	**0.04**
Ile-105val GSTP1, n (%)	Ile / Ile	30 (60)	13 (37)	21 (54)	
	Ile / Val	15 (30)	15(43)	18 (46)	
	Val / Val	5 (10)	7 (20)	0 (0)	**0.004**

* p value: CLD infants versus preterm controls (Fisher's exact test)

(CLD). Genetic polymorphisms of inflammatory cytokines (e.g. TNF-α, TGF-β_1) are associated with up-regulation of their production. Polymorphisms of anti-oxidant enzymes (e.g. GSTP1) result in reduced in enzyme activity.

Aims: To determine whether infants with CLD have a higher incidence of these polymorphisms when compared to a preterm control population.

Methods: Buccal swabs were collected from infants <32 weeks gestation, with and without a diagnosis of CLD. Distribution of polymorphisms G-308A and C-509T of the promoter regions of TNF-α and TGF-β_1 respectively, and isoleucine-105valine in exon 5 of the GSTP1 gene were determined using standard molecular genetic techniques. Comparisons were also made with the incidence of polymorphisms in the local population.

Results: Outcome data are presented in the table.

Conclusions: We have demonstrated a significantly increased incidence of a TGF-β_1 polymorphism, and a trend towards increased TNF-α polymorphism, associated with increased transcriptional production in infants who developed CLD. In addition, we have shown significant difference in the incidence of a polymorphism associated with lower activity of GSTP1, an anti-oxidant enzyme.

G37 CHRONIC LUNG DISEASE OF PREMATURITY AND INTRAUTERINE GROWTH RETARDATION: A POPULATION BASED STUDY

M.K. Lal*, B.N. Manktelow[1], E.S. Draper[1], D.J. Field[2]. [1]*University Hospitals of Leicester;* [2]*Department of Epidemiology, University of Leicester University Hospitals of Leicester*

Objective: To determine the risk of chronic lung disease (CLD) in small for gestation (SGA) preterm infants.

Methods: Observational study derived from a geographically defined population (Trent Health Region, UK). All preterm infants of ⩽32 completed weeks gestation born to Trent resident mothers admitted to neonatal units between 1995 and 1999 (inclusive) were included. Birth weight percentiles were determined for small for gestation (SGA) infants (<10th percentile), reference group infants (between 25th and 75th percentiles) and large for gestation (LGA) infants (⩾90th percentile). Both mortality and CLD rates (28 days and 36 weeks postconceptual age) were determined for these groups of infants. We estimated the effect of increased risk of antenatal infection on mortality and CLD by investigating the influence of the following on the observed rates: a) spontaneous prelabour rupture of membranes b) proven fetal / maternal infection and c) antibiotic treatment to mother prior to birth.

Results: There were total of 4051 preterm infants ⩽32 weeks gestation during the study period. SGA infants showed higher mortality before 28 days postnatal age and 36 weeks corrected age as compared to the reference group of infants; odds ratio = 2.01, [95% CI = 1.49 to 2.72] and 2.0 [95% CI 1.49 to 2.69] respectively. There was no significant change in the mortality risk before 28 days and 36 weeks corrected age in SGA infants after adjustment for risk of exposure to infection. SGA infants were at greater risk of developing CLD, both at 28 days and 36 weeks corrected age, as compared to the reference group of infants but this was only significant for the latter definition; OR = 1.29 [95% CI 0.99 to 1.68] and 1.78 [95% CI 1.32 to 2.39] respectively. Again adjusting for infection risk had no effect.

Conclusion: SGA preterm infants are at higher risk of death before 28 days and 36 weeks corrected age. They are also more likely to have morbidity associated with CLD. This risk, however, does not appear to increase further with evidence of fetal/maternal infection in our population.

G38 PRETERM MECONIUM STAINING OF THE AMNIOTIC FLUID—ASSOCIATED FINDINGS AND RISK OF ADVERSE CLINICAL OUTCOME

A. Tybulewicz, S. Clegg, G. Fonfe, B. Stenson. *Simpson Memorial Maternity Pavilion, Edinburgh*

Introduction: Preterm meconium staining of the amniotic fluid (PMSAF) is widely held to suggest possible listeriosis. It is unclear how commonly PMSAF occurs or whether it is a risk factor for adverse neonatal outcome.

Aims: To investigate the incidence of PMSAF, the frequency of associated maternal and neonatal infection and the outcomes at discharge of the infants.

Methods: All infants <33 weeks gestation with PMSAF born alive in the Simpson Memorial Maternity Pavilion, Edinburgh between 1/1/94–2/1/01 were identified. Cases were matched to the next inborn infant of the same gender and gestation with clear liquor. Maternal and infant characteristics, culture results, placental histology, and clinical outcomes were compared. Odds ratios and 95% confidence intervals were calculated. Groups were compared with Mann-Whitney-U and Student's-t tests.

Results: 1054 infants <33 weeks gestation were delivered. PMSAF was observed in 45 cases (4.3%). No maternal or infant listeriosis was identified. Birth weight, Apgar scores and pH on admission were not significantly different between cases and controls. PMSAF was associated with preterm prolonged rupture of the membranes (odds ratio 3.41, 95%CI 1.37–8.53) and maternal smoking (odds ratio 3.34, 95%CI 1.07–10.49), but not maternal hypertension, sepsis or chorioamnionitis. Early-onset neonatal sepsis was identified in 2 cases and 3 controls.

Abstract G38

	Cases n=45	Controls n=41	Odds ratio	95%CI
Death	10	4	2.64	0.76–9.21
CLD36	8	4	2.00	0.55–7.22
IVH 3/4	5	0	2.03	1.62–2.53
PVL	1	1	0.91	0.06–15.02

Conclusions: No association between preterm meconium staining of the amniotic fluid and maternal or neonatal infection or perinatal asphyxia was identified. Significantly more infants with PMSAF developed severe intraventricular haemorrhage. PMSAF may be associated with increased risk of adverse outcome.

G39 ANTENATAL STEROIDS ARE ASSOCIATED WITH A REDUCTION IN THE INCIDENCE OF CEREBRAL WHITE MATTER LESIONS IN VLBW INFANTS

R. Agarwal, M.L. Chiswick, G.M. Taylor, R.J.Q. McNally, R.D. Alston, S. Rimmer, S.W. D'Souza. *Neonatal Medical Unit, Immunogenetics Laboratory, Dept of Radiology; Academic Unit of Child Health, St Mary's Hospital, Manchester*

Aims: To investigate whether antenatal steroid treatment reduces the incidence of cerebral white matter lesions in very low birthweight (VLBW) infants.

Methods: All neonates born at St Mary's Hospital between Jan 1998 and Jun 2000, weighing <1500 gm and <31 weeks gestation (n=224) were studied. Infants were divided into two groups; *Group 1* infants were born to mothers who had no antenatal steroids (betamethasone) or within 24 hrs of mother receiving the first dose of steroid (None/Incomplete course). *Group 2* infants were born to mothers who had one or more course(s) of antenatal steroids and delivered >24 hours after having first dose (Complete course). Cranial USS were assessed by a radiologist blinded to infants' clinical details.

Results: Infants born after a complete course of antenatal steroids (Group 2) had a significantly lower incidence of cerebral white matter lesions, compared with those whose mothers received none or an incomplete course (group 1).

Stepwise logistic regression analysis showed that gestational age (p=0.0002) and a complete course of antenatal steroids (p=0.02) had independent effects on cerebral white matter lesions.

Conclusion: A complete course of antenatal steroids may have a protective effect against cerebral white matter lesions in VLBW infants.

Abstract G39

Characteristic	Group 1 (n=71)	Group 2 (n=153)	P value
Male infants	35 (49%)	81 (53%)	NS
Mean (SD) Ges age, wk	27.6 (2.4)	27.2 (2.1)	NS
Mean (SD) B wt, g	1025 (331)	961 (305)	NS
Mortality	20 (28%)	30 (19.6%)	NS
Cranial USS			
Normal/SEH/IVH	49 (69%)	123 (80%)	NS
Ventriculomegaly	4 (5.6%)	9 (6%)	NS
White matter lesions	18 (25.4%)	20 (13%)	<0.05

G40 QUANTATIVE ANALYSIS OF CEREBRAL WHITE MATTER IN PRETERM INFANTS USING DIFFUSION WEIGHTED IMAGING

S.J. Counsell,[1] J.M. Allsop[1], M.C. Harrison[2], D.J. Larkman[1], N.L. Kennea[2], A.D. Edwards[1,2] M.A. Rutherford [1,2]. *[1]Robert Steiner MR Unit, Imaging Sciences Department; [2]Department of Paediatrics, Faculty of Medicine, Imperial College, Hammersmith Campus, Du Cane Road, London, W12 0HS UK*

Background: Magnet ic resonance imaging (MRI) studies of preterm infants at term equivalent age have demonstrated diffuse excessive high signal intensity (DEHSI) in the cerebral white matter on T2 weighted imaging. DEHSI may be associated with diffuse white matter disease. Diffusion weighted imaging (DWI) is a magnetic resonance technique, which provides a quantitative measure of water diffusion in tissue and, therefore, has the potential to objectively assess cerebral white matter in these infants

Aim: The aim of this study was to quantify apparent diffusion coefficient (ADC) values in the cerebral white matter of preterm infants at term equivalent age in order to determine whether there was any difference between infants with normal appearing white matter, infants with white matter pathology demonstrated on MRI and infants with DEHSI.

Methods: MRI was performed on 28 preterm infants at term equivalent age. Transverse T1 and T2 and sagittal T1 weighted images were obtained. Echo planar DWI was obtained in 3 orthogonal directions of sensitization with a b value of 1000s/mm^2. ADC values were calculated from the diffusion weighted images. The infants were divided into 3 groups on the basis of their MRI results: i.Infants with normal appearing white matter on MRI (n = 15) ii.Infants with evidence of white matter pathology on MRI (n = 7). iii.Infants with DEHSI on MRI (n = 6).

Results: ADC values in the cerebral white matter were significantly greater in infants with DEHSI (p = 0.003) and infants with cerebral pathology (p = 0.004) than infants with normal appearing white matter on MRI. There was no significant difference between the infants with DEHSI and those with evidence of white matter pathology (p = 0.57).

Discussion: This study suggests that DEHSI represents diffuse white matter disease. Possible explanations for the elevation in ADC values in DEHSI are diminished axonal diameter, oligodendrocyte immaturity or an increased extracellular space.

G41 LONG TERM OUTCOME FOR BABIES WITH ENCEPHALOPATHY OF EARLY ONSET. A POPULATION BASED STUDY

L. Gillespie[1], J. Madar[2], S. Sinha[1]. *[1]James Cook University Hospital, Middlesbrough, UK; [2]Derriford Hospital, Plymouth, UK*

Aims: To determine long term outcome for babies who had moderate to severe encephalopathy of early onset and received artificial respiratory support.

Methods: A population-based study carried out in a defined geographical area in the North of England. Infants born to mothers resident in the area between 1990–1992, who were greater than 33 completed weeks gestation (>237 days) and had received ventilation for encephalopathy, were included. All infants were identified through multiple data sources and were traced. All survivors from this cohort were followed up to the age of 8–10 years.

Results: 107 babies received respiratory support for encephalopathy during this period [1.0/1000 live births; 95% CI 0.8–1.2]. Of the 53 discharged home alive, 27 (52%) developed cerebral palsy and half of these children subsequently died. Only 38/107 (35%) survived to 8-10 years of age and outcome was known for all. Median score for cognitive assessment (WISC) was 95 (IQ range 82–105). The Vineland assessment on survivors [communication, socialisation and daily living skills] showed severe difficulties in 16/37 (43%) as described in the table.

Abstract G41

	Survivors able to complete WISC	Survivors unable to complete WISC	Total
Number	21	16	37
Number with Cerebral Palsy	2	12	14
Median Vineland Score	92	33	66
(interquartile range)	(78–97)	(25–39)	(35–93)

Conclusion: Despite improvements in neonatal care, the outcome for children with moderate to severe neonatal encephalopathy remains poor. The majority either die or have severe difficulties.

G42 CEREBAL PALSY RATES AMONG VERY LOW BIRTHWEIGHT BABIES FELL IN THE EARLY 1990S

G. Surman, H. Newdick, M. Marques, A. Johnson. *Oxford Register of Early Childhood Impairment Management Group. National Perinatal Epidemiology Unit, Institute of Health Sciences, Oxford*

Aims: Cerebral palsy rates rose among very low birthweight (VLBW: <1500g) babies born in the late 1970s and 1980s. The aim of this study was to ascertain whether this continued into the 1990s.

Methods: Using multiple sources of ascertainment, a population register has been compiled of children with cerebral palsy (CP) born since 1984 to mothers resident in the counties of Berkshire, Buckinghamshire, Northamptonshire and Oxfordshire at the time of delivery. The register includes information on the characteristics of the impairment, the level of motor function and additional impairments. Birthweight specific rates of cerebral palsy in four three year periods: 1984–86, 1987–89, 1990–92, and 1993–95 are described.

Results: In the twelve year period, 898 children were included on the CP register (2.2/1000 live births). 194 (22%) weighed less than

1500g at birth. Neonatal death rates per 1000 live births (NND) and CP rates per 1000 neonatal survivors among VLBW babies fell in the early 1990s.

The *proportion* of children with CP who weighed <1000g at birth has doubled in the 12 year period (3.8% to 7.3%) as has the proportion of CP children who were of a multiple birth (6.5% to 13%).

Conclusions: It is plausible that perinatal care in the early 1990s resulted in a reduction in both mortality and morbidity among very low birthweight babies. It is essential to evaluate elements of perinatal care using randomised controlled trials and to monitor long term outcome in children exposed to interventions in the perinatal period.

Abstract G42

	<1000g		1000–1499g		1500–2499g	
BW	NND	CP	NND	CP	NND	CP
1984–86	441	60	107	64	18.5	11.1
1987–89	471	90	120	77	12.1	10.9
1990–92	404	78	80	65	10.3	9.7
1993–95	368	57	65	40	7.5	8.5