

**PC.21 HOW INSPIRED OXYGEN CONTROL BEHAVIOURS AFFECT OXYGEN LEVELS ACHIEVED IN VENTILATED PRETERM INFANTS**

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**Introduction:** Hyperoxia has been linked to the risk of bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), necrotising enterocolitis (NEC) and neurological outcome in preterm infants. We aimed to explore the contribution of oxygen adjustment behaviours to the amount of time infants are hyperoxic, after controlling for the intrinsic instability of the infants.

**Methods:** We studied the oxygen adjustment behaviours of 24 trained neonatal nurses while caring for 13 ventilator-dependent infants during 133 shifts. We determined the average time per shift that each individual infant spent hyperoxic. We then compared the oxygen control behaviours of 11 nurses (increased hyperoxia group) in whom for  $\geq 50\%$  of their shifts the infant in their care spent more time with oxygen saturation ( $\text{SpO}_2$ )  $> 94\%$  than the average for that infant with the remaining 13 nurses (decreased hyperoxia group). Behaviours compared were the number of changes in fractional inspired oxygen ( $\text{FiO}_2$ ) per shift, mean size of change in  $\text{FiO}_2$ , mean  $\text{FiO}_2$  variability, mean  $\text{FiO}_2$  administered and mean  $\text{SpO}_2$  maintained. Differences between groups were compared by independent samples t-test.

**Results:** Nurses in the increased hyperoxia group made significantly larger changes in  $\text{FiO}_2$  compared with nurses in the decreased hyperoxia group (9.6% versus 7.7%,  $p = 0.007$ ). There were no other significant differences in control patterns between the groups. When cared for by nurses in the increased hyperoxia group infants had slightly higher mean saturation, although this was not statistically significant. They spent no more time with saturation  $< 86\%$ .

**Conclusions:** After controlling for the intrinsic instability of the infant we found that large changes in  $\text{FiO}_2$  contribute to a greater time spent with hyperoxia.

## BAPM/NNS: Infection and Gut

**PD.01 MANAGEMENT OF CONGENITAL CYTOMEGALOVIRUS INFECTION: AN EVIDENCE-BASED APPROACH**

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**Objective:** To develop an evidence-based structured approach to the management of neonates with congenital cytomegalovirus.

**Materials and Methods:** MEDLINE/OVID database and Cochrane Collaboration Library were searched for related papers and graded for their level of evidence.

**Results:** 39 papers were identified including nine reviews. Neonates with abnormal neurological signs, ie, microcephaly, seizures, abnormal cranial ultrasound, sensorineural hearing loss, chorioretinitis or signs of disseminated infection, ie, intrauterine growth restriction, thrombocytopenia or abnormal liver function tests should be evaluated for congenital cytomegalovirus infection. Asymptomatic neonates: Current evidence does not support the treatment of babies who only have positive cytomegalovirus PCR. Symptomatic neonates: Evidence recommends treatment of all newborns with positive cytomegalovirus PCR and central nervous system (CNS)-related/sensorineural symptoms to prevent further neurological deterioration. Intrauterine growth restricted newborns are thought to have systemic involvement including CNS and could also therefore be considered for treatment. There is evidence to suggest that newborns with no CNS symptoms but other signs of systemic involvement could be treated to avoid neurological

sequelae if their viral load in the peripheral blood is high. Neonates with normal neurology but lower viral loads should be closely followed up for evidence of sensorineural hearing loss. Treatment should be with intravenous ganciclovir. Increasing evidence suggests that oral valganciclovir for 6 weeks as an effective alternative. Close follow-up for evidence of toxicity and neurological deterioration is required.

**Conclusions:** Evidence for neonates who would benefit from treatment is growing. We have tried to formulate this structured protocol in order to treat neonates with signs and symptoms that would affect the long-term prognosis.

**PD.02 PROCALCITONIN IS A USEFUL ADDITIONAL MARKER IN LATE-ONSET NEONATAL SEPSIS**

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**Aim:** To evaluate the usefulness of procalcitonin compared with C-reactive protein (CRP) as a marker for late-onset neonatal sepsis.

**Methods:** Seventy-three infants admitted to two neonatal units over a 2-year period with suspected late-onset neonatal sepsis were included in this prospective study. Infants were categorised to have "sepsis" or "no sepsis" based on clinical and laboratory findings. Serum procalcitonin and CRP were determined at the onset of symptoms. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) with 95% CI were calculated for procalcitonin (cut-off value of 0.5 ng/ml) and CRP (cut-off value of 10 mg/l).

**Results:** A total of 112 septic episodes from 73 infants were included in the study. There were 59 episodes in the sepsis group and 53 episodes in the no sepsis group. The results were as shown in the table. Serum procalcitonin concentrations were significantly higher at the onset of symptoms in the "sepsis group" (2.5 ng/ml) compared with those in the "no sepsis" group (0.5 ng/ml).

**Conclusions:** Procalcitonin is more sensitive but less specific than CRP in predicting late-onset neonatal sepsis. Procalcitonin would be a useful additional tool along with other laboratory parameters in the evaluation of late-onset neonatal sepsis.

**Abstract PD.02 Sepsis versus no sepsis**

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
PCT	74 (61 to 85)	70 (54 to 80)	73 (60 to 83)	71 (57 to 82)
CRP	64 (50 to 76)	83 (70 to 91)	80 (66 to 90)	68 (55 to 78)

CRP, C-reactive protein; NPV, negative predictive value; PCT, procalcitonin; PPV, positive predictive value.

**PD.03 VITAMIN K: MAKING IT NICE**

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**Background:** Vitamin K prophylaxis prevents vitamin K deficiency bleeding. Several studies have reported a resurgence of late vitamin K deficiency bleeding coincident with policies using oral vitamin K. NICE recommends giving all babies intramuscular vitamin K.

**Objectives:** (1) To assess parents' preferred route of vitamin K administration; (2) to review policies of vitamin K prophylaxis in maternity units in the United Kingdom; (3) to audit compliance of oral vitamin K prophylaxis in Swansea.

**Methodology:** Parents attending an antenatal clinic were asked to complete a questionnaire. Maternity units in the United Kingdom were telephoned regarding their current practice. 200 sets of notes of babies born in the Singleton Hospital were reviewed.

**Results:** 100 questionnaires were completed. 62% preferred the intramuscular route, 24% the oral route and 14% had no preference. All 100 formula-fed babies received two full doses of Konakion MM 2 mg as per policy. Of the breastfed babies 92 received three doses as per policy, two received no vitamin K, two received one dose only and four received two doses only. Out of 227 units surveyed, information was received from 226. 132 (56%) maternity units recommend the intramuscular route, 30 (13%) recommend oral and 74 (31%) advocate parental choice. The preparation and the dose of oral vitamin K varied in different units.

**Conclusions:** The method of vitamin K prophylaxis is not uniform in the United Kingdom. Among breastfed babies, compliance with oral prophylaxis is not adequate. Most parents would prefer their baby to have vitamin K by intramuscular injection.

# PD.04 USING BENCHMARKING AND QUALITY IMPROVEMENT TECHNIQUES TO REDUCE NOSOCOMIAL INFECTION IN VERY LOW BIRTHWEIGHT INFANTS

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**Introduction:** Nosocomial infection is a common cause of morbidity and mortality in preterm infants. When we joined the international benchmarking organisation, Vermont–Oxford Network (VON), in 2001 we discovered our incidence of late-onset sepsis was >97th centile and aimed to improve.

**Methods:** Data items are submitted to VON on all babies with birthweights <1501 g at 28 days and at discharge. Forty data items are routinely collected, including aspects of antenatal and intrapartum care and diagnoses, outcomes and interventions in the neonatal unit. A manual of operations gives clear definitions to ensure valid comparisons. Reports are published quarterly and are available on-line at any time. VON also runs a quality improvement programme, NIC/Q, providing education and support. Between 2002 and 2006 we implemented several changes, guided by an Internet-based NIC/Q course, using techniques shown to reduce infection.<sup>1</sup> Our target was to reduce “any late infection” and “coagulase-negative staphylococcal infection” rates by 50%.

**Results:** Over the 5 years we admitted mean 83 babies <1501 g per year—75% inborn. Gestation and birthweight profiles were similar to those of the network overall. Through a combination of evidence-based guidelines, audit, education and team-building activities, we reduced our incidence of any late infections (beyond 3 days) from 44% to 25% and of coagulase-negative staphylococcal infection from 37% to 15%.

**Conclusions:** Our 5-year focus on reducing nosocomial infection has demonstrated how vigilance, multidisciplinary teamwork and clear guidelines can improve outcome. These techniques can be adapted to many other aspects of neonatal intensive care unit care.

1. Horbar J, Rogowski J, Plsek P, et al. Collaborative quality improvement for neonatal intensive care. *Pediatrics* 2001;**107**:14–22.

# PD.05 WITHDRAWN

# PD.06 FEEDING GROWTH-RESTRICTED INFANTS: INTERNATIONAL DIFFERENCES

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**Introduction:** Intrauterine growth restriction (IUGR) is associated with an increased risk of necrotising enterocolitis. It has been suggested that enteral feeds should be advanced cautiously in IUGR (birthweight <10th centile).<sup>1</sup> This survey examines approaches to feeding in UK and Canadian neonatal units.

# Abstract PD.06

	IUGR (n = 52)	AGA (n = 319)	p Value
First feed (days)	4.1 (2.7)	3.5 (1.9)	0.226
First to full feeds (days)	13.6 (7.9)	12.8 (10.8)	0.052
AGA	UK (n = 202)	CAN (n = 117)	p Value
First feed (days)	3.2 (1.7)	3.9 (2.3)	0.025
First to full feeds (days)	10.6 (7.4)	16.7 (14.1)	<0.001
IUGR	UK (n = 37)	CAN (n = 15)	
First feed (days)	4.1 (2.7)	4.0 (2.7)	0.967
First to full feeds (days)	11.5 (5.5)	18.7 (10.6)	0.005

AGA, appropriate for gestational age; CAN, Canada; IUGR, intrauterine growth restriction.

**Methods:** Records of babies 23–29 weeks’ gestation, admitted to 15 UK and three Canadian units were examined. Data were collected for time to first feed and time to reach feeds of 150 ml/kg per day.

**Results:** 465 babies were included; mean (SD) gestation 27.5 weeks (1.5); birthweight 1024 g (254). 65 (14%) were IUGR. 37 (five IUGR) died before being fed and 18 before reaching full feeds. 371 babies had complete feeding data. Results are summarised in the table with data presented as mean (SD). There was a trend to slower feeding in IUGR. Progression to full feeds was significantly different between the United Kingdom and Canada in both IUGR and appropriate for gestational age groups.

**Conclusions:** Both UK and Canada advanced feeds more slowly in IUGR; however, UK appropriate for gestational age babies were fed more rapidly than Canadian IUGR babies. Such variation may influence important outcomes in high-risk babies.

1. Yu YH, Upadhyay A. *Semin Fetal Neonatal Med* 2004;**9**:403–9.

# PD.07 A REVIEW OF POSITIVE BLOOD CULTURE RATES AT THREE LEVEL 3 NEONATAL UNITS IN NORTH-WEST ENGLAND: A BENCHMARKING EXERCISE

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**Background:** Infection is a relatively common complication of preterm birth resulting in significant morbidity and mortality in very low birthweight (VLBW) babies. There is a lack of standardised data enabling comparison of infection rates between different centres. We aimed to describe and compare bacteraemia/fungaemia rates in VLBW babies between level 3 neonatal units in North-West England.

**Methods:** Using microbiology databases and neonatal unit patient information systems we collected data on positive blood cultures in each unit over a 5-year period, from January 2002 to December 2006. A pure growth of any organism in a blood culture was considered to be a significant isolate. These data were cross-referenced against each unit’s database of VLBW admissions. Crude bacteraemia/fungaemia rates were adjusted according to the number of VLBW admissions and intensive care unit plus high dependency unit activity in each centre.

**Results:** See table.

**Conclusions:** Considerable variation exists in bacteraemia/fungaemia rates between similar centres within the same region. Standardising for the number of admissions and intensive care unit plus high dependency unit activity allows more meaningful comparisons of these rates. There is no correlation between rates of bacteraemia and fungaemia between units. Differences in identification of cases, case-mix and clinical or laboratory practices may help to explain variations in bacteraemia/fungaemia rates.

## Abstract PD.07

	Centre A	Centre B	Centre C
VLBW admissions	463	1023	872
Bacterial			
Positive BC/month	3.4	11.2	5.4
Positive BC/100 VLBW admissions	44.5	65.5	31.7
Positive BC/1000 ICU + HDU days	16.3	21.8	12.2
Fungal			
Positive BC/year	1.0	3.4	6.4
Positive BC/100 VLBW admissions	1.1	1.8	3.1
Positive BC/1000 ICU + HDU days	0.4	0.6	1.2

BC, blood culture; HDU, high dependency unit; ICU, intensive care unit; VLBW, very low birthweight.

#### PD.08 LOW RATES OF *CHLAMYDIA TRACHOMATIS* CONJUNCTIVITIS IN THE NEWBORN: POSSIBLE EFFECTS OF CHANGING BIRTH DEMOGRAPHICS

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**Aims:** To study the incidence of neonatal conjunctivitis in a defined geographical area, with particular reference to disease caused by *Chlamydia trachomatis*.

**Methods:** In a prospective population-based study, taking place from 1 August 2004 to 30 September 2005, the eyes of infants aged 3–28 days with evidence of neonatal conjunctivitis were swabbed. Isolation and characterisation of bacteria were performed using conventional microbiological methods. Immunofluorescence and strand displacement amplification were used to detect *C. trachomatis*.

**Results:** There were 1117 deliveries in the study period. The mean maternal age at booking was 31.8 years. The rate of Caesarean section delivery was 34.5%. Eighty one babies with conjunctivitis were identified (7.2% of all live births). Bacteria were cultured in 62 patients (76.5%). Only one case of *C. trachomatis* was detected. The other organisms were *Staphylococcus epidermidis* in 35 cases (43.2%), *Streptococcus viridans* in 13 cases (16.0%) and *Staphylococcus aureus* in eight (9.9%).

**Conclusions:** Neonatal conjunctivitis is common. However, only one case was attributable to *C. trachomatis* (1.2%). Possible explanations may include the high maternal age and Caesarean section rate in the population studied.

#### PD.09 IMPACT OF SEASONAL FLUCONAZOLE PROPHYLAXIS ON INCIDENCE OF INVASIVE CANDIDA INFECTION IN NEONATES

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**Introduction:** Following a previous review that demonstrated an increased incidence of invasive candidiasis between September and February, fluconazole prophylaxis between September and February was introduced in 2002. This review examines the effect of this policy.

**Methods:** A retrospective review of the neonatal and microbiology databases from 2002 to 2007 identifying patients with invasive candidiasis.

**Results:** The table shows the demographic data for babies admitted between 1 August 2002 and 31 July 2007. The annual incidence of invasive candidiasis between 2002 and 2007 of 3.2% compares with an incidence of 3.7% before the introduction of prophylaxis. 55% (15 of 27) occurred between September and February, compared with 73% between September and February before prophylaxis was introduced. Following the introduction of seasonal fluconazole prophylaxis, there was no significant difference in the annual incidence of invasive candidiasis (odds ratio (OR) 0.624, 95% CI

## Abstract PD.09

	Infants <32 weeks with invasive <i>Candida</i> (n = 27)	Infants <32 weeks without <i>Candida</i> (n = 852)
Birthweight	651 g (590–749)*	964 g (732–1301)*
Gestation	24 weeks (24–25)*	28 weeks (25–30)*
Male sex	14 (52%)	487 (57%)
Mortality	9 (33%)	124 (14.6%)

\*Median and interquartile ranges.

0.34 to 1.15) or in the incidence of invasive candidiasis over the months of September to February (OR 0.822, 95% CI 0.51 to 1.32).

**Conclusions:** Although there is evidence to support the use of fluconazole prophylaxis, our review does not support the introduction of targeted fluconazole prophylaxis over the months of September to February.

#### PD.10 COMPARISON OF SENSITIVITY AND SPECIFICITY OF PROCALCITONIN AND IL-6 IN EARLY DETECTION OF NEONATAL SEPSIS

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**Introduction:** In recent years the measurement of serum markers such as CD11b, procalcitonin, IL-6 and IL-8 have been used for the early detection of neonatal sepsis. In this study the sensitivity and specificity of IL-6 and procalcitonin were compared.

**Materials and Methods:** This study is descriptive and cross-sectional and was carried out on 69 newborns admitted to the neonatal intensive care unit of two university affiliated hospitals due to suspected sepsis and 18 controls (healthy newborns referred for the measurement of serum bilirubin). Blood samples of newborns were obtained for culture and other tests. Serum samples were frozen to detect IL-6 and procalcitonin levels. With regard to the results of blood cultures and clinical symptoms, the newborns were classified as: group 1, confirmed sepsis (n = 20) with clinical symptoms and positive blood culture; group 2, suspected sepsis (n = 49) with clinical symptoms and negative blood culture; group 3, control group (n = 18) without clinical symptoms and negative blood culture. IL-6 was measured by ELISA and procalcitonin by immunoluminometry. Data analysis was done by SPSS and the  $\chi^2$  test. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were performed on the basis of a gold standard table.

**Results:** The mean levels of IL-6 were 119.26, 53.74 and 6.62 pg/ml in confirmed, suspected and control groups, respectively (p<0.005) with 85% sensitivity, 100% specificity, 87% NPV and 100% PPV. The mean levels of procalcitonin were 5.7, 3.03 and 0.69 ng/ml in groups 1, 2 and 3, respectively (p<0.05) with 70% sensitivity, 80% specificity, 75% NPV and 80% PPV.

**Conclusions:** The sensitivity and specificity of IL-6 is significantly higher than procalcitonin with high PPV (100%) in the early detection of neonatal sepsis.

#### PD.11 WITHDRAWN

#### PD.12 NEONATAL INFECTIONS IN THE UNITED KINGDOM: THE NEONATAL INFECTION SURVEILLANCE NETWORK (NEONIN) DATABASE

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**Aims:** The Neonatal Infection Surveillance Network (NeonIN) is the first UK-based active neonatal infection surveillance network;



Abstract PD.12

Birthweight	EOS	LOS	Total (%)	GA	EOS	LOS	Total (%)
<1499	14	98	112/718 (15)	<32	16	99	115/1027 (11)
≥1500	23	26	49/2501 (2)	≥32	21	25	46/2202 (2)

standardised data from culture-confirmed infections are collected by clinicians and entered into a web-based database. We describe the incidence, common pathogens and their antibiotic susceptibilities for 2006.

**Methods:** The analyses include data from seven participating units that completed data quality cross-checking with their microbiology laboratories. The results describe episodes of clinical sepsis (positive cultures from a normally sterile site treated with antibiotics for ≥5 days). Coagulase-negative staphylococci were excluded.

**Results:** The incidence of neonatal sepsis was 5/1000 live births (162/32 340) and 50/1000 neonatal admissions (162/3224). Early-onset sepsis (<48 h) represented 23% of infections. Most infections occurred in smaller babies (see table). Gram-positive organisms were found in 49% of episodes: group B streptococcus (32%), *Staphylococcus aureus* (32%, one methicillin-resistant *S. aureus*), *Listeria* (12%). Among Gram-negative organisms (43%) the most common were *Escherichia coli* (26%), *Enterobacter* (23%), *Klebsiella* and *Pseudomonas* (17% each). *Candida* caused 8% of infections. All organisms causing early-onset sepsis tested for antibiotic susceptibility were sensitive to penicillin or gentamicin.

**Conclusions:** The 2006 NeonIN data are consistent with published data on incidence, demographics and pathogen profile. The database gathers antibiotic resistance data to inform rational antimicrobial policies and supports empirical treatment of early-onset infections with penicillin and gentamicin. It monitors changes in infection rates, pathogen distribution and antibiotic susceptibility in real-time.

PD.13 FREQUENCY AND MECHANISM OF ANTIBIOTIC RESISTANCE IN BACTERIA ASSOCIATED WITH PREMATURE BIRTH AND DEVELOPMENT OF CHRONIC LUNG DISEASE OF PREMATURITY

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We screened 55 *Ureaplasma* spp isolates from the lungs of preterm and term infants using a new 96-well method to assess antibiotic resistance.

We identified one tetracycline, one ciprofloxacin and one erythromycin-resistant *Ureaplasma* strains. Tetracycline resistance is mediated by a well-characterised transferable bacterial genetic element (*tetM*), although we also identified a *tetM*-positive isolate from a neonate who lacked tetracycline resistance due to mutation of the gene. Erythromycin resistance was mediated by a non-lethal mutation in the bacterial ribosome complex: deletion of two adjacent amino acids in the L4 protein, whereas the associated L22 protein and 23S ribosomal RNA molecules were identical to sensitive bacteria. This mutation is speculated to alter the ribosome shape to deny erythromycin binding and bacteriostatic activity. Ciprofloxacin resistance was found to correspond to a single amino acid change from aspartic acid at position 82 in the *parC* portion of the bacterial topoisomerase protein to asparagine. More importantly, we found that most of the mutations in bacterial topoisomerase (*parC* and *parE*) or gyrase (*gyrA* and *gyrB*) previously speculated to mediate ciprofloxacin resistance may simply be conserved species-specific differences between the genes for *Ureaplasma urealyticum* and *Ureaplasma parvum* biovars.

Molecular species determination identified 80% as *U. parvum* and 20% *U. urealyticum* and 12/14 *Ureaplasma*-infected premature

neonates developed chronic lung disease. Therefore, treatment and antibiotic resistance screening should be considered for the premature infant group. Hopefully, future studies will enable the development of a rapid PCR-based screening system for antibiotic resistance.

PD.14 QUANTITATIVE DETERMINATION OF BACTERIAL LOAD AND SPECIES IN GASTRIC ASPIRATES BY MOLECULAR METHODS

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**Aims:** To compare culture with molecular methods for the identification of micro-organisms in routinely collected gastric aspirate samples taken shortly after birth. To correlate DNA load with conventional culture results.

**Methods:** Gastric aspirate samples routinely collected as part of the neonatal service protocol were processed by the microbiology department standard operating procedures and by 16s rDNA quantitation and sequencing. Results of culture were compared with molecular methods and correlated with clinical findings.

**Results:** Specimens sufficient to allow both culture and molecular analyses were obtained from 47 infants over a 3-month period in 2007. Of these, 11 (23%) samples were culture-positive and bacterial identification was made in 32 (68%). Median bacterial DNA load was 0.44 pg/μl (range <0.01 to >400). All culture-positive samples had a DNA load of >0.75 pg/μl (see table). In a number of cases established pathogens including group B streptococcus, *Haemophilus influenzae*, *Klebsiella* and *Serratia* species were detected by molecular methods but not by culture. The newly identified pathogen *Leptotrichia amnionii* was also detected.

**Discussion:** This is the first description of the use of quantitative DNA load in neonatal gastric aspirates. The clinical implications of these results are currently under investigation. Molecular methods offer the prospect of improved bacterial detection in these sample types.

Abstract PD.14

DNA load (pg/μl)	n	Sequence positive (%)	Culture positive
<0.25	17	2 (12)	0
0.25–0.75	8	8 (100)	0
>0.75	22	22 (100)	11 (50%)

PD.15 SERUM THYROID FUNCTION TESTS IN BABIES OF MOTHERS WITH THYROID DISEASE: EXPERIENCE IN THE NORTH WEST

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In a retrospective study, all serum thyroid function tests of babies born to mothers with thyroid disease performed over a 3-year period (2004–6) at our institution were correlated with the result of the Guthrie test and clinical outcome of the baby.

The study showed that serum thyroid function tests (65 samples from 44 babies) were generally abnormal (TSH >5.5 mmol/l) and thus not interpretable if done early (less than 6 days of life). Serum thyroid function tests tended to normalise to within accepted reference ranges in the second week of life. When done, Guthrie tests were normal. All these babies were euthyroid with a normal clinical outcome.

The Guthrie screening test may be enough to screen/detect problems in this population of babies, especially if a 100% uptake is guaranteed. This is recommended in a new local guideline, which also suggests that thyroid function testing in this group of babies could be considered after 7 days of life. In addition, the guideline also describes an at-risk population of babies in which clinical examination is sensitive in identifying neonatal thyrotoxicosis

and will determine the necessity for earlier thyroid function testing.

A survey of current practice within northwest neonatal units is also presented.

**PD.16** IS SPONTANEOUS INTESTINAL PERFORATION OF NEWBORN DIFFERENT FROM NECROTISING ENTEROCOLITIS: A RETROSPECTIVE DESCRIPTIVE STUDY

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**Background:** Awareness and diagnosis of spontaneous intestinal perforation (SIP) in newborns are increasing and the need to differentiate it from necrotising enterocolitis (NEC) is a much-debated subject. Although the aetiology and pathology of NEC are well described in the literature, more work is needed with regards to SIP.

**Aims:** To compare the clinical findings in SIP with NEC in newborns.

**Methods:** Clinical information was obtained retrospectively from case records of newborns who underwent laparotomy over 2 years. Newborns with intestinal perforation were classified into NEC and SIP based on histological findings. Clinical information collected included relevant antenatal problems, clinical presentation, interventions, investigations and outcome.

**Results:** 110 neonates underwent laparotomy. 31 out of 110 were found to have intestinal perforation. Out of these 31, 21 neonates had NEC and 10 had SIP. Neonates with NEC were found to have lower platelet counts compared with those with SIP. Early commencement of enteral feeding was directly associated with pathogenesis of NEC when compared with SIP. There was no significant difference between the groups with regard to gestational age, birthweight, delivery status, resuscitation, mode of ventilation, type of feeds, time of presentation and known risk factors, clinical features, radiological features and outcome.

**Conclusions:** Our study showed that NEC and SIP are difficult to differentiate on the basis of clinical parameters. The difference between the groups was in the platelet count and feeding policy (early commencement of feed). We hypothesised that there may be some element of underdiagnosis of SIP due to lack of awareness.

**PD.17** SURVEY ON THE USE OF EXPRESSED DONOR BREAST MILK AMONG NEONATAL HEALTHCARE PROFESSIONALS

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The use of donor-expressed breast milk (EBM) in neonatal practice has been controversial and there are varying views about the benefits and cost-effectiveness of its use.

**Aim:** To identify the varying practices, differences in usage and the underlying reasons.

**Methods:** An e-mail-based survey questionnaire including details of the usage, reasons for usage and non-usage was formulated and e-mailed to all neonatologists based on tertiary centres in the United Kingdom and to all antenatal nurse practitioners.

**Results:** 116 of 340 responded (60 consultants and 56 antenatal nurse practitioners) to the questionnaire. Donor breast milk is used by 62% of them, the common indications being prematurity, intrauterine growth restriction and absent end-diastolic flow. Donor EBM is being used by 16% in the case of non-availability of breast milk in mothers, the perceived advantages being better feed tolerance and prevention of necrotising enterocolitis. There was a written policy for the use of donor EBM in 50% of units. One fifth have audited their practice and half of them had perceived benefits from the use of donor EBM. There were no added benefits perceived in 10% but none of them have discontinued the use. The commonest reason for non-usage is non-availability (33%) followed

by cost and risk of infection. Overall, 50% of respondents felt that more evidence is needed for the use of donor EBM and 38% felt that it is being used less frequently than it should be.

**PD.18** ANTENATAL BETAMETHASONE EXERTS SEXUALLY DIMORPHIC EFFECTS ON PLACENTAL GLUCOCORTICOID METABOLISM AND FETAL AND NEONATAL ADRENAL FUNCTION FOLLOWING PRETERM BIRTH

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**Aim:** Female infants exhibit greater response to antenatal betamethasone, the mechanisms of which remain unknown. We have shown that betamethasone exposure results in a sexually dimorphic placental 11  $\beta$ -hydroxysteroid dehydrogenase 2 (11 $\beta$ HSD2) response. We investigated whether sex-specific placental, fetal and neonatal adrenal responses to betamethasone contributed to physiological stability after preterm birth.

**Methods:** Infants born at 24–36 weeks ( $n = 60$ ), grouped into those delivered <72 h and those delivered >72 h after betamethasone exposure, were studied. 11 $\beta$ HSD2 activity was measured by radiometric conversion assay. Umbilical arterial cortisol and 24-h urinary cortisol (days 1, 3, and 5) were determined.

**Results:** 11 $\beta$ HSD2 activity was greater in female infants ( $p = 0.006$ ) born <72 h after betamethasone exposure. A similar interaction between sex and betamethasone exposure was observed for umbilical arterial cortisol ( $p = 0.011$ ), being higher in female infants if born <72 h after steroid exposure ( $p = 0.01$ ). In infants born <72 h after maternal betamethasone with evidence of perinatal distress, day 1 urinary cortisol was higher in female infants ( $p = 0.003$ ). Urinary cortisol was greater in female infants on day 1, but not days 3 or 5 in those infants born >72 h after betamethasone administration ( $p = 0.01$ ). 11 $\beta$ HSD2 activity alone exhibited a negative correlation with clinical illness severity ( $p = 0.01$ ) and a positive correlation with blood pressure ( $p = 0.043$ ) only in those infants born >72 h after maternal steroids.

**Conclusions:** Adrenal insufficiency after preterm birth is associated with morbidity and mortality. Sex-specific placental responses to betamethasone may influence fetal hypothalamic-pituitary axis maturation and adrenal response to preterm birth explaining male excesses in morbidity and mortality.

**PD.19** WITHDRAWN

**PD.20** INTRAVENOUS IBUPROFEN DOES NOT REDUCE SUPERIOR MESENTERIC ARTERY BLOOD FLOW VELOCITY IN VERY LOW BIRTHWEIGHT INFANTS

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**Background:** Published data from a small number of babies studied after intravenous ibuprofen administration describe an increase in superior mesenteric artery (SMA) blood flow velocity (BFV) between 30 and 120 minutes after treatment. These data demonstrate no significant change between baseline to 120 minutes and suggest an initial drop in SMA BFV.

**Hypothesis:** Intravenous ibuprofen significantly decreases SMA BFV in very low birthweight (VLBW) infants.

**Design/Methods:** Doppler BFV of the SMA were performed before and at 15, 30, 45 and 60 minutes after a 10 mg/kg dose of intravenous ibuprofen for the treatment of a symptomatic patent ductus arteriosus. Average velocity, end-diastolic velocity and pulsatility index were calculated from the Doppler waveform. Arterial mean and diastolic blood pressure were measured

concurrently with Doppler studies. Changes were analyzed using repeated measures ANOVA.

**Results:** 25 infants, median (range) birthweight 710 g (490–1320), gestational age 25.7 weeks (23.7–29.1) and age 7 days (3–26) were studied. SMA average velocity significantly increased ( $p < 0.05$ ) and pulsatility index decreased ( $p < 0.05$ ) by 45 minutes after treatment. A significant rise in mean blood pressure was seen by 45 minutes ( $p < 0.05$ ) and in diastolic blood pressure by 60 minutes ( $p < 0.05$ ). There was a non-significant trend ( $p = 0.07$ ) towards and increase in end-diastolic velocity.

**Conclusions:** SMA average velocity significantly increases and pulsatility index falls following treatment with intravenous ibuprofen and in contrast to our hypothesis there was no evidence of an initial reduction in SMA flow. SMA BFV improves within an hour of intravenous ibuprofen treatment in VLBW babies with a significant patent ductus arteriosus. The changes seen in blood pressure and BFV measurements are in keeping with acute ductal constriction and a reduction in ductal steal.

# PD.21 GUT BLOOD FLOW VELOCITY RESPONSES TO ENTERAL FEEDS IN BABIES WITH CONGENITAL HEART DISEASE

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**Background:** In term babies gut blood flow increases with postnatal age and enteral feeds. Abnormalities in gut blood flow increase the risk of necrotising enterocolitis (NEC). In term babies NEC is associated with underlying cardiac lesions.

**Aims:** To describe gut blood flow velocity (BFV) responses to a 5 ml/kg bolus enteral feed in babies with congenital heart disease (CHD) and in controls.

**Methods:** Doppler BFV measurements from the coeliac artery and superior mesenteric artery (SMA) were performed before and at 15-minute intervals after a bolus feed. Average velocity was calculated from the Doppler waveform.

**Results:** We recruited 15 babies with CHD and 12 controls. There were no differences in birthweight, gestational age or the proportion receiving maternal milk between the groups. Age at study was lower ( $p < 0.01$ ) in controls. Coeliac artery average velocity increased from baseline in controls ( $p < 0.05$ ) but not in CHD. SMA average velocity increased in both groups. The magnitude of rise in SMA average velocity differed between groups, with controls having higher SMA average velocity by 15 minutes post-feed persisting to 60 minutes,  $p < 0.01$ . The subgroup of babies with hypoplastic left heart syndrome ( $n = 8$ ) showed no increase in their SMA average velocity and a drop in coeliac artery average velocity ( $p < 0.05$ ) after the bolus feed.

**Conclusions:** Gut BFV response to a bolus enteral feed is significantly blunted in stable postoperative babies with CHD. In babies with hypoplastic left heart syndrome there was no increase in SMA average velocity and coeliac artery BFV was lower post-feed, indicating a risk of gut ischaemia in these babies with the introduction of enteral feeds.

# PD.22 BOWEL APPEARANCE AS A PREDICTOR OF OUTCOME IN GASTROSCHISIS: A 7-YEAR REVIEW

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**Introduction:** During ante and postnatal counselling it is difficult to predict outcome for neonates with gastroschisis. A retrospective review of all liveborn neonates with gastroschisis over a 7-year period (2000–6) was undertaken to assess whether ante and postnatal bowel appearance could be prognostic indicators.

**Methods:** Discharge and theatre databases were used to identify patients. Maternal and neonatal case notes were used to collect

demographic data, antenatal ultrasound findings, postnatal bowel appearance, feeding details and duration of hospitalisation.

**Results:** 60 neonates were identified with 55 case notes available for analysis. Median gestation was 36 weeks (24–39), birthweight 2408 g (470–3220). Five patients died before discharge. 58 were diagnosed antenatally of which 38 had bowel appearance recorded. Of these 22 had abnormal bowel appearance. Postnatally, seven of these had abnormal bowel (matted, peel, thickened, ischaemic), six had atresias, six were normal and in three no comment was made. 16 were normal antenatally, of these seven were abnormal and one atretic. Sensitivity for abnormal bowel 81%, specificity 43%. Median duration of parenteral nutrition was 171 days (20–411) for neonates with atresia, 28 (9–553) with abnormal bowel and 19 (11–84) with normal bowel and time to full enteral feeding was 135 days (21–413), 34 (15–470) and 20 (11–87), respectively. Median time to discharge was 62 days (10–314), 47 (22–865), 45 (22–222).

**Conclusions:** Antenatal ultrasound correlates poorly with postnatal bowel appearance. The postnatal bowel findings are highly predictive of duration of parenteral nutrition, time to establish full enteral feeding and duration of hospital stay.

# PD.23 WITHDRAWN

## BMFMS: Fetal Medicine

# PFM.01 LONG-TERM EXPRESSION OF HUMAN FACTOR IX AFTER ULTRASOUND-GUIDED DELIVERY OF AAV8 hFIX TO FETAL SHEEP IN UTERO

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**Introduction:** Haemophilia B is a life-threatening coagulopathy caused by human factor IX (hFIX) deficiency. In 15% of patients hFIX antibodies prevent adequate hFIX replacement therapy. Adult gene therapy trials with adeno-associated virus (AAV) show only short-term hFIX expression. We hypothesised that fetal delivery of AAV would give long-term hFIX expression, without stimulating an immune response to the transgenic hFIX protein.

**Methods:** We injected AAV8 hFIX vector ( $1-9 \times 10^{12}$  p/kg) into the peritoneal cavity of fetal sheep under ultrasound guidance in early ( $n = 3$ ) or late ( $n = 4$ ) gestation. Fetal and lamb blood was tested for hFIX expression, antibody responses and liver damage up to a year after birth. Lambs received subcuticular injection of hFIX protein with Freund's complete adjuvant at 6 months ( $n = 2$ ) or 1 year ( $n = 2$ ) after birth to test for immune tolerance.

**Results:** High-level hFIX was detected 3–21 days after early (8.7%) and late (44% and 28%) gestation injection, but hFIX levels dropped rapidly as fetal liver and lamb weights increased. Low level hFIX (0.7%) was detectable 1 year after birth in early and 4 months after birth in late gestation injected lambs. There was no evidence of liver pathology or functional antibodies to the hFIX protein. After injection of hFIX protein, lambs mounted an antibody response.

**Conclusions:** Long-term hFIX expression is possible after AAV fetal gene therapy in a large animal, but immune tolerance was not demonstrated.

# PFM.02 A STEREOLOGICAL STUDY OF CHRONIC UTEROPLACENTAL INSUFFICIENCY ASSOCIATED WITH NORMAL BIRTHWEIGHT: A DISTINCT ENTITY

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**Objectives:** Chronic uteroplacental insufficiency (CUPI) causes accelerated villous maturation. Of 800 low-risk pregnancies, 79