PERINATAL

G96 NEONATAL INTENSIVE CARE WAITING LISTS? THE RESULTS OF A UK CENSUS

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A previous BAPM survey confirmed that requests for neonatal transfer were frequently refused. Recently there has been a suggestion that the problem was increasing. This was plausible since: provision was largely static, increased numbers of preterm babies have been offered intensive care and survival has improved. In attempt to quantify the situation a 3 month prospective census was carried out under the auspices of the BAPM with funding from NHS R&D.

We chose to focus on a particular aspect of sub optimal care resulting directly from service pressure i.e. transfers out of tertiary units (either in utero or after delivery) occurring because the unit was "full" and not because the hospital was incapable of providing the care needed. Transfers of this kind had previously been highlighted as poor practice by the Clinical Standards Advisory Group (CSAG). A panel of experts, representing each of the English regions as well as Wales, Scotland and Northern Ireland, identified the largest perinatal centres across the UK. Individual contacts were then identified in each of the units, one obstetric and one neonatal, who were asked to complete a simple data sheet in relation to any such transfers. The study ran from 1/4/99 to 30/6/99.

37 units were identified by the expert group and all provided data. The number of intensive care cots in each unit was between 5 and 16. 309 transfers occurred during the 3 months (equivalent to 1236 per year) of which 264 were in utero and 45 post natal. 65 in utero transfers involved multiple births hence the census related to 382 babies (1528 per year). There was significant regional variation. The reason for transfer in the large majority of cases was "lack of neonatal beds".

Currently most major perinatal centres in the UK are regularly unable to meet demand.

G97 A COMPARISON OF TWO STYLES OF NIC: SCANDINAVIAN AND UK

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It is clear from the literature that neonatal intensive care practice varies between countries but there are few reports that examine the impact of these differences. The aim of this study was to compare two styles of neonatal intensive care: those of Scandinavia and the UK. The former system relies heavily on minimal handling and early use of nasal CPAP. By comparison the UK has traditionally used ventilation as the primary means of life support.

The entire Danish national cohort of babies born in 1993 and 1994 was used to represent "Scandinavian NIC". The Trent Health Region was used to represent "UK NIC". In both geographically defined populations data were collected on all babies born < 28 weeks gestation and or < 1000 grammes birth weight. In both settings the data were collected prospectively as part of another study.

Population size was similar in both localities (Trent 4.6 million Denmark 5.2 million). However there were important demographic differences eg: babies born < 28 weeks gestation and or < 1000 grammes per 1000 livebirths 4.18 vs 3.3 respectively. The pattern of care in the neonatal units was very different:

	Trent	Dk		Trent	Dk
Number	491	461	LSCS	47%	54%
BW (mean)	831g	852g	Surfactant	62%	38%
Gest (mean)	26.4	26.7	Ventilation	88%	37%
Steroids	68%	53%	CPAP	23%	76%

Despite these differences in medical and nursing care short term outcome measures were similar: survival to discharge Tr 58% Dk 59%; mean length of stay Tr 86.3 days Dk 74.4 days. The attitude towards the most immature infants (whether or not to offer intensive care) did not seem responsible for the observed disparities.

Conclusion: Further study of these, and other, approaches to NIC are merited to see if there are associated differences in cost and long term morbidity.

G98 SNAPII, A SIMPLIFIED NEWBORN ILLNESS SEVERITY AND MORTALITY RISK SCORE

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Aims: We developed and validated a neonatal illness severity and mortality risk score. The primary outcome was in-hospital mortality.

Methods: Three independent neonatal research networks collected data on all (n=25,429) admissions from 30 neonatal intensive care units (NICU) for 22-32 months during the mid-1990s. We employed the data elements from the Score for Neonatal Acute Physiology (SNAP) during the first 12 hours in the NICU. We derived the most parsimonious logistic model using 10,819 randomly selected records from the Canadian cohort. This model (SNAP-II) consisted of 6 physiologic items. We then added birth weight, low Apgar score, small for gestational age status to create a 9 item SNAP-Perinatal Extension-II (SNAPPE-II). We validated SNAPPE-II on the remaining Canadian cohort, the Kaiser Permanente cohort, and the New England cohort and optimized the calibration using the same data elements.

Results: In all birth weights and in birth weight groupings below and above 1500 grams, SNAPPE-II had excellent discrimination and calibration, and good correlation with the older SNAP-PE score. Areas under ROC curves ranged from 0.84 $\pm$ 0.03 to 0.93 $\pm$ 0.01, and the overall calibration (Hosmer-Lemeshow goodness of fit) was 0.97.

Conclusions: SNAP-II and SNAPPE-II are valid, empirically-weighted illness severity scores which perform well across many populations and be incorporated into routine use for performance review and benchmarking.

G99 COMPARISON OF TWO METHODS FOR DEFINING DEPENDENCY LEVEL OF PATIENTS ON THE NEONATAL UNIT

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Background: Monitoring activity on the neonatal unit (NNU) is important for planning service provision and as part of monitoring quality of care. It is important to determine the dependency level of the patients cared for as well as the numbers. Two methods for determining the level of dependency in the neonatal period are defined by the British Association for Perinatal Medicine (BAPM) and by the Northern Neonatal Network (NNN).

Aim: To compare the BAPM and NNN definitions of dependency level.

Setting: Regional Neonatal Intensive Care Unit and a District General Hospital Special Care Baby Unit.

Method: 40 details relating to current clinical status and treatment being given were recorded daily for each patient on the two NNUs over a 17 month period. These details were recorded in a computer database and dependency levels were calculated for each patient day using both systems.

Results: 21,537 patient days were recorded for 1,444 patients. Using the BAPM system, 3877 (18%) days were Level 1, 2850 (13%) were Level 2 and 14810 (69%) were Level 3. Using the NNN method, 3537 (16.5%) were category A days, 3527 (16.4%) were category B, 12049 (56%) were category C and 2424 (11.3%) category D. A comparison of the methods is shown.

	Level 1	Level 2	Level 3
Cat A	3537	0	0
Cat B	204	1286	2037
Cat C	132	1557	10360
Cat D	4	7	2413

Conclusions: There two systems agree about what constitutes the highest level of intensive care. BAPM Level 3 is a very broad group containing a disparate group of patient days. The NNN criteria subdivide these patient days into smaller groups providing more meaningful information about each. The NNN criteria are also simpler to apply.

G100 PREMEDICATION FOR NEONATAL INTUBATION—CURRENT PRACTICE IN AUSTRALIA AND THE UK

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Aims: The routine administration of drugs to facilitate non-emergency tracheal intubation (TI) on neonatal intensive care units is becoming established practice in Australia. We were interested to define routine use of premedication (PM) in term and pre-term neonates in the UK and make comparisons with current practice in Australia.

Methods: A survey was conducted of practice in UK units with 6 or more intensive care cots (52) and Australian level 3 units (21). The format was a semi-structured telephone interview of the nurse in charge of the shift when the call was made. All interviews were conducted by one of two of the authors.

Results: There was a 100% response rate. Results were:

	UK		Australia	
Routine premedication (%)	Term 22 (42)	Pre-term 18 (34)	Term 15 (71)	Pre-term 14 (67)
Opiate	13	11	2	4
Benzodiazepine (BDZ)	1	0	2	1
Opiate+BDZ	1	1	0	0
Opiate+Muscle relaxant + Atropine	6	6	11	9
BDZ+Muscle relaxant + Atropine	1	0	0	0

Seven different combinations of PM drugs were in routine use in Australia compared with 14 different combinations in the UK.

Conclusions: In Australian units the routine administration of PM for non-emergency TI of term and pre-term neonates is common practice and there is

some uniformity in the combinations of drugs used. We were surprised at the relatively frequent use of PM in the UK but note that there is more diversity of prescribing. There is a growing body of evidence that PM for TI reduces traumatic injury to the upper airway and improves physiological stability. Further research is needed to determine the ideal combination of drugs to use.

G101 SOCIAL DEPRIVATION AND THE CAUSES OF STILLBIRTH AND INFANT MORTALITY

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Aim: To investigate whether causes of stillbirth and infant death are linked to the level of social deprivation in the area of maternal residence.

Methods: Data on 209842 live births, 1147 stillbirths and 1223 infant deaths in Wales between 1993 and 1998 were obtained using the Child Health System and All Wales Perinatal Survey. A postcode linkage file enabled us to allocate births and deaths to electoral wards based on the postcode of maternal residence. Social deprivation was measured using the Townsend score which is derived for each ward and calculated from 1991 census data. Statistical analysis was by Poisson regression.

Results: The Townsend score was significantly related to the number of stillbirths and infant deaths in an electoral ward ($p<0.01$). The stillbirth and infant mortality rate increased by 4% for each unit increase in Townsend score, with a 114% increase over the whole range of deprivation. A similar relationship existed for the following causes of death:

Cause of death	Number of deaths	p value	Increase over whole deprivation range (%)
Unexplained stillbirth	699	0.0001	150
Infection	142	0.0012	177
Specific conditions	134	0.0019	231
Sudden infant death syndrome	166	0.0001	776

Conclusions:

- The number of stillbirths and infant deaths in a locality is related to the level of social deprivation
- Unexplained stillbirth, infection, and SIDS are most strongly linked to social deprivation
- Resources need to be directed towards deprived communities.

G102 FORMULA SUPPLEMENTS GIVEN TO HEALTHY BREASTFED PRETERM BABIES INHIBIT POSTNATAL METABOLIC ADAPTATION: RESULTS OF A RANDOMISED CONTROLLED TRIAL

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Breastfeeding preterm infants are commonly given routine supplements of infant formula. We hypothesized that this practice impairs normal postnatal metabolic changes, explaining previously observed differences between term and preterm infants[1].

46 healthy neonates of 34-36 weeks gestation, whose mothers wished to breastfeed, were randomised to be breastfed exclusively (unsupplemented, US, group) or to receive reducing volumes of formula supplements over the first 72 postnatal hours (supplemented, S, group). Prefeed blood samples were taken for concentrations of glucose (BG) and ketone bodies (KB) at intervals on days 0-5.

Significantly more babies in the US group had two consecutive BG levels <2.0mmol/l than in the S group (56% vs 18%, p=0.008). However, the median peak KB concentration achieved by the US group was significantly greater than that of the S group (1.037 vs 0.330mmol/l, p=0.002), and comparable to that previously documented in healthy term infants[1]. After adjustment for postnatal age, cumulative formula intake was significantly negatively related to peak KB (p=0.002). In the US, but not the S group, there was a significant inverse relationship between BG and peak KB concentrations (p=0.009). There was no significant difference between the groups in proportions breastfed during the first 6 months.

Low blood glucose levels are found in healthy, moderately preterm breastfed infants but are associated with adaptive metabolic responses which will ensure cerebral fuel supply. This could influence ability to respond to metabolic challenges in the longer term.

1. Hawdon JM et al. *Arch Dis Child* 1992;**67**:357-65.

G103 HYPOSTOP GEL IN THE TREATMENT OF NEONATAL HYPOGLYCAEMIA: A RANDOMISED CONTROLLED TRIAL

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Aim: To establish the efficacy of hypostop (40% dextrose gel) in treatment of neonatal hypoglycaemia.

Methods: 75 day 1 neonates admitted to the neonatal intensive care of $\geq$36 weeks gestation with hypoglycaemia (capillary blood glucose $\leq$2.5 mmol/l) were enrolled. Each was randomised to hypostop 1 ml/kg buccally plus feed (H, n=39) or control of feed alone (C, n=36). Infants with intravenous fluids already in situ were excluded. HemoCue evaluation of capillary blood glucose (H/cu) was measured at baseline, 15 and 30 minutes. Primary outcomes were the change in H/cu at 15 (ΔH/cu 15) and 30 minutes (ΔH/cu 30) compared to baseline. Secondary outcomes were the subsequent requirement for intravenous dextrose and the volume of next feed taken following randomisation (bottle-fed neonates).

Results: There was no significant improvement in H/cu in the Hypostop group compared to controls; ΔH/cu 15: 1.3 +/- 0.2 mmol/l SEM in H group v 0.9 +/- 0.2 mmol/l in C group (p=0.1) and ΔH/cu 30: 1.8 +/- 0.2 mmol/l in H v 1.4 +/- 0.2 mmol/l in C (p=0.2). There was no significant difference in the requirement for intravenous dextrose (33% of H group, 26% of C group, p=0.7). Volume of the next oral feed taken spontaneously was significantly less in the hypostop group (H: 7.6 +/- 1.0 ml/kg SEM v C: 13.1 1.1 ml/kg, p=0.001).

Conclusions: Hypostop combined with feed had no beneficial effect on recovery from hypoglycaemia at 15 and 30 minutes compared to feed alone. In bottle-fed infants the volume of next feed was significantly lower in the Hypostop group compared to controls. If Hypostop is used in neonates one needs to be aware of the potential depressant effect on the subsequent feed.

G104 LEPTIN AND METABOLIC HORMONES IN INFANTS OF DIABETIC MOTHERS

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Aim: To compare the relationship between leptin and other metabolic hormones (insulin, ACTH, cortisol, TSH and FT_4) in normal term infants and infants of diabetic mothers. The change of the hormonal pattern in the first week of life was also determined.

Methods: One hundred and sixteen term newborns were prospectively enrolled and categorised into 3 groups: 44 were normal infants (Group C); 41 were infants born to mothers with gestational diabetes on dietary treatment (Group D), and; 31 were infants born to mothers with gestational or pre-gestational diabetes on insulin treatment (Group I). Blood samples were obtained on day 1 and day 4-5 of life.

Results: No significant difference in serum leptin on day 1 was observed between the 3 groups. Thus, the results were pooled and analysed. Serum leptin was found to correlate positively with serum insulin ($p<0.035$, $r=0.20$), insulin/glucose ratio ($p<0.001$, $r=0.57$), HBA1c ($p<0.001$, $r=0.40$; Group D and I), birth weight ($p<0.001$, $r=0.31$), and body mass index (BMI) ($p<0.002$, $r=0.28$); but negatively correlated with plasma glucose ($p<0.05$, $r=-0.19$). Significant changes in the pattern of metabolic hormones were observed in the first week of life. Serum insulin ($p<0.002$), plasma glucose ($p<0.002$) and insulin/glucose ratio ($p<0.02$) were significantly increased, whereas plasma ACTH ($p<0.005$), serum leptin ($p<0.05$), cortisol ($p<0.002$) and FT_4 ($p<0.05$) were significantly decreased, between day 1 and day 4-5. There was also a significant association between HBA1c and the decrement of serum leptin concentration during this period ($p<0.001$, $r=-0.62$).

Conclusion: This study provides evidence that the adipoinsular axis is active *inutero* and maternal insulin/glucose homeostasis may affect the functioning of the fetal adipoinsular pathway. A decline in the circulating levels of leptin within the first week of life may be of distinct physiologic advantage to the growing infant, as low leptin and catabolic hormone concentrations can reduce the total body energy expenditure and assists in maintaining a positive energy balance for growth and development.

G105 OCULAR GROWTH IN PREMATURE INFANTS WITH & WITHOUT RETINOPATHY OF PREMATURITY

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Aims: To monitor the change in ocular growth in eyes with and without Retinopathy of Prematurity (RoP).

Methods: Babies screened for RoP were examined at 32, 36 and 40 weeks post-conceptional age, then 1 and 3 months corrected age: Axial length (AXL), anterior chamber depth (ACD), and lens thickness (LT) were measured using ultrasound biometry. Babies were then refracted, and the stage of RoP was noted.

Results: AXL increases linearly up to term, then slows down from term to 3 months in all stages of RoP. However, eyes treated for stage 3 RoP show a slower growth rate, resulting in shorter AXL at 3 months (stage 0 mean AXL=18.71mm,s.d.=.55, stage 3 treated mean AXL=18.19, s.d.=1.58). ACD increases up to 3 months of age in eyes with no RoP (mean ACD at 3 months =2.81,s.d.=.25). In eyes treated with laser for stage 3 RoP, the AC fails to deepen from term to 3 months (mean ACD at 3 months =2.51, s.d.=.39).LT reaches a plateau between term and 3 months in eyes without R.O.P (mean LT at 3 months = 3.88mm,s.d.=.18). In eyes treated for stage 3 RoP, LT continues to increase, (mean LT at 3 months =4.17, s.d.=.38). At present, small numbers in the stage 3 treated group do not reach statistical significance, (N=6) and data collection continues. However, graphical representation of the data does show a visible separation in growth curves.

Conclusions: Compared with eyes unaffected by RoP, eyes requiring treatment for stage 3 RoP develop a shorter AXL, comprised of a thicker lens, and shallower AC. This supports the theory of anterior segment growth arrest, previously not demonstrated at such an early stage of ocular development.

G106 LONGITUDINAL ASSESSMENT OF GRANULOCYTE COLONY STIMULATING FACTOR [G-CSF] IN NEONATES

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Introduction: Longitudinal [G-CSF] were measured in neonates to determine the serum kinetics and to investigate whether persistently elevated or depressed concentrations were related to clinical condition. Samples were taken following chorioamnionitis, pregnancy induced hypertension (PIH), sepsis and NEC.

Method: 328 blood samples were obtained during 6 time periods from birth to >28 d of age in 44 neonates (gestation 25-41wk, mean 32wk). There were 35 episodes meeting specific clinical criteria for sepsis (16 with positive blood cultures) and 4 cases of NEC. Samples were taken within 48h of birth from 25 newborns of which 7 mothers had chorioamnionitis and 9 had PIH. [G-CSF] were measured by ELISA.

Results: Range of [G-CSF] was <10–36000pg/ml. Baseline concentrations (pg/ml), excluding birth and sepsis data, ranged <10–296, median 34, (84% <100 pg/ml). Only during NEC were [G-CSF] persistently elevated and [G-CSF] were unrelated to mortality. 10 of 16 episodes of confirmed sepsis had [G-CSF] >100 (median=119, IQR=63-316) This is significantly different to baseline (p=0.003). 6 of 15 babies with culture negative sepsis had [G-CSF] >100 (median=69, IQR=25-106) (p=0.09). All 4 babies with NEC had [G-CSF] >100 (median=2056, IQR=1500-4450) (p=0.0005). Median (IQR) [G-CSF] following normal delivery, chorioamnionitis and PIH were102 (34-152), 2300 (155-4480) (p<0.001) and 181 (130-668) (p=0.047) respectively. No gestational differences were found and [G-CSF] were similar to those reported in adults.

Conclusions: Neonates show normal serum G-CSF kinetics, irrespective of gestation. [G-CSF] rose transiently during sepsis and following chorioamnionitis and PIH. However, moderate increases also occurred in babies without infection. As a marker of infection [G-CSF] should be interpreted with caution.

G107 SEPSIS RATES AND EFFICACY OF DELIVERY OF TPN USING PERCUTANEOUS LONGLINE OR PERIPHERAL CANNULAE IN NEONATES

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Background: Neonatal total parenteral nutrition (TPN) is administered using either peripheral cannulae or percutaneously inserted longlines. Longlines are perceived as being a risk factor for sepsis. Standard teaching is that sepsis cannot be eradicated unless the catheter is removed. A retrospective audit suggested a catheter-related sepsis rate of 43.0% on our unit; longlines were removed at an average of 7 days post-insertion because of suspected sepsis.

Method: Forty-nine infants receiving TPN were randomised to either a longline or peripheral cannula. Longlines were inserted aseptically by medical staff. Data were collected prospectively regarding suspected or proven sepsis, amounts of TPN prescribed versus amounts received and other complications of TPN/longlines.

Results: Groups were comparable at entry for gestation and birthweight. There was a non-significant excess of infants in the peripheral cannula arm having had a UAC (72.0% versus 50.0%) or UVC (48.0% versus 20.8%). No difference was seen in sepsis rates between infants in the longline or the peripheral cannula groups (45.8% versus 40.0%). The most common organism seen was coagulase negative Staphylococcus. However infants allocated to the peripheral cannula group received up to 11% less fluid (p=0.0014) than was prescribed through lack of venous access.

Conclusions: Percutaneously-inserted longlines do not significantly affect sepsis rate in babies receiving TPN. Use of peripheral cannulae may be associated with under-administration of TPN unless fluids are re-calculated each time a new cannula is inserted. We consider percutaneous longlines to be the preferred method of continuing TPN administration in ill infants.

G108 DO 'VANISHING TWIN' SINGLETON INFANTS DIFFER FROM OTHER SINGLETON PREGNANCY INFANTS?

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Aims: To identify if infants from a 'vanishing twin' (VT) pregnancy differ by sex, birthweight, or gestational age when compared with infants from singleton pregnancies.

Method: A 27 month retrospective cohort study. Data on birthweight, gestational age, sex and other variables were abstracted from the records of women who at first ultrasound examination had evidence of multiple pregnancy, but subsequently delivered only a single infant and a random sample of women in whom a single fetus was reported at first ultrasound.

Results: Data was collected on 64 VT pregnancies and compared with a random sample of 266 singleton pregnancies. There were a further 155 multiple pregnancies during the period. Compared with singleton pregnancies, survivors of VT pregnancies were significantly more likely to be girls (68.8% vs. 48.7%). The VT survivors were also more likely to be born earlier, (38.7 vs. 39.4 weeks). Mothers of VT infants had more pregnancies prior to the index pregnancy (25.4% vs 40.4% were gravida 1), although a similar number of previous births. Distribution of birthweight, apgar at 5 minutes and cord pH were similar in the two groups.

Conclusions: Survivors of a vanishing twin pregnancy are more likely to be female, and to be born earlier other singleton infants. Their mothers may have a poorer obstetric history when compared with their peers. Although the increases risks are small, this study provides further evidence that a 'vanishing twin' pregnancy does carry higher risks than other singleton pregnancies.

G109 RISK FACTORS FOR SEVERE IVH IN VERY PRETERM INFANTS IN THE AUSTRALIAN AND NEW ZEALAND NEONATAL NETWORK (ANZNN) 1995-1997

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Aims: The ANZNN consists of all level III neonatal intensive care units in Australia and New Zealand. The aims of this study were to identify trends in the rates of intraventricular/periventricular haemorrhage (IVH), to identify major risk factors and to develop a predictive model for grade 3-4 IVH.

Methods: The rates of IVH were analysed retrospectively in a cohort of 5712 infants of gestational age 24-30 weeks born in 1995-1997. Perinatal variables up to the 1 minute Apgar, which were significant on univariate analysis of 1995 and 1996 data, were entered into a multivariate logistic regression model and the model was validated on the 1997 data.

Results: The incidence of IVH decreased from 30.4 to 24.3% from 1995-1997. The median incidence of grade 3-4 IVH fell from 9.0 to 5.8%, but there was wide inter-unit variation (1.7-19.0% in 1997). Significant risk factors for grade 3-4 IVH after multivariate regression analysis (odds ratio, 95% confidence interval) were antenatal corticosteroids (decreased risk with greatest effect if given >24 hours prior to delivery, 0.5, 0.4-0.7 but also effective if given <24 hours 0.7, 0.5-1.0), gestational age (increased risk with decrease in gestational age from 30-24 weeks 11.1, 6.7-17.9), ex-utero transfer (increased risk 1.6, 1.2-3.2), 1 minute Apgar score <4 (2.4, 1.9-3.0) and male gender (increased risk 1.2, 1.0-1.5). Factors which were not significant included mode of delivery, pregnancy induced hypertension, birth weight percentile and congenital malformations.

Conclusions: This model may allow risk adjustment and meaningful inter-unit comparisons of rates of grade 3-4 IVH.

G110 SAFE REDUCTION IN ADMINISTRATION OF NALOXONE TO NEWBORN INFANTS

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Introduction: Guidelines for the use of naloxone during resuscitation of the newborn have been provided in the report "Resuscitation of Babies at Birth"(1). Our experience in a number of UK maternity units indicated excessive administration of naloxone to infants whose mothers had received opiates in labour and who had transient apnoea or cyanosis in the first 1-2 minutes after birth. This practice may have undesirable effects including the potential to induce a severe withdrawal reaction if the mother has been abusing opiates and the tendency for early administration of naloxone to distract from the priorities of airway management and adequate oxygenation.

Methods: A protocol for use of naloxone reflecting RCPCH guidelines was designed and implemented. Data was collected retrospectively on naloxone administration and on episodes of apnoea and cyanosis occurring before discharge in 1000 consecutive deliveries prior to protocol implementation and prospectively on 1000 deliveries following implementation.

Results: 44.3% of mothers received opiates during labour. Before implementation of the protocol, 7.3% of infants who had been exposed to opiates received naloxone at birth compared to 0.23% following protocol implementation (p<0.0001). There was no increase in morbidity; respiratory events were documented in 7.2% and 5.2% of infants respectively (p=0.48)

Conclusion: This study indicates a high incidence of naloxone administration to newborn infants which can be considerably reduced without ill effect and should prompt examination of current practice within maternity units.

References: (1). Joint Working Party of the RCPCH and the RCOG. *Resuscitation of Babies at Birth.* London: BMJ Publishing Group, 1997.

G111 NEURODEVELOPMENTAL OUTCOME IN PRETERM INFANTS TREATED WITH INHALED NITRIC OXIDE

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Background/Aims: Inhaled nitric oxide (iNO) is being used increasingly to treat preterm infants with hypoxaemic respiratory failure despite a lack of evidence of long term efficacy or safety. Uncontrolled studies have suggested that iNO therapy may be associated with adverse neurodevelopmental outcomes. The aim of this study was to investigate long term outcome in a group of high-risk preterm infants enrolled into a randomised controlled trial of iNO therapy.

Methods: 42 infants (20 iNO, 22 controls) were recruited into the original study; 25 infants survived to discharge from hospital and 22 infants were still alive at 2 years 6 months of age (corrected for prematurity). These infants were assessed in a blinded manner using the Bayley II Scales of Infant Development to obtain a Mental Developmental Index (MDI) and a Psychomotor Development Index (PDI) for each child. A standardised neurological examination was also performed.

Results: Formal assessment was carried out in 21 out of 22 survivors; one iNO-treated infant was lost to follow up. There were no statistically significant differences in long term survival or neurodevelopmental outcomes between iNO-treated infants and controls (table).

	iNO (n = 20)	Controls (n = 22)	RR (95% CI)
Death	12 (60%)	8 (36%)	1.65 (0.87-3.3)
MDI or PDI < 85	4/7 (57%)	9/14 (64%)	0.89 (0.37-1.75)
Cerebral Palsy	0/7	2/14 (14%)	*p = 0.53*

Conclusions: In this relatively small study, there was no evidence of a significant effect on either survival or long term neurodevelopmental outcome in survivors following inhaled nitric oxide therapy.

G112 QUANTITATIVE ASSESSMENT OF BRAIN DEVELOPMENT IN THE PREMATURE INFANT FOLLOWING POST-HEMORRHAGIC HYDROCEPHALUS

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Introduction: Injury to the cerebral white matter is the dominant form of injury in post-hemorrhagic hydrocephalus (PHH). Using an advanced 3-D volumetric MRI technique (1), we studied the impact of PHH on myelination of vulnerable white matter (WM) in the developing brain.

Patients and Methods: Sixteen preterm (gestational age 24 to 31 weeks) VLBW infants were studied, at post menstrual ages (PMA = Gestational age + Postnatal Age) 38 to 44 weeks using a 3D MRI technique to quantify cerebral tissue volumes and assess the effects of posthemorrhagic hydrocephalus on brain development. The Institutional Review Board of the hospital approved this study.

Results	Normals (n=11)	PHH (n=5)	p
Cortical GM(%)	41.51 ± 9.36	38.26 ± 8.27	0.52
Basal Ganglia (%)	5.90 ± 3.03	5.08 ± 1.19	0.57
MWM (%)	3.37 ± 1.47	1.76 ± 0.41	0.03
UMWM (%)	37.74 ± 6.63	33.97 ± 9.48	0.37
CSF (%)	11.48 ± 5.46	20.94 ± 9.38	0.02

Relative volumes of the different tissues are reported as percentage of total intracranial volume. Comparison of relative volumes in the two groups was made using two-tailed *t*- test.

Conclusion: This reduction in myelinated WM volume in the PHH group, with no significant changes seen in cortical GM, basal ganglia or unmyelinated WM volumes, demonstrated *in vivo* supports animal and human autopsy studies of PHH which demonstrate hypomyelination as a consequence of PHH.

References: (1) Huppi PS *et al.* 3D-Visualization and Quantitation of the Developing Human Brain in Vivo. *Annals of Neurology* 1998;**43**(2):224-35.

G113 DOES TOPICAL AMETHOCAINE GEL PREVENT OR REDUCE THE PAIN OF VENEPUNCTURE IN THE NEWBORN INFANT?

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Topical amethocaine provides effective pain relief during venepuncture in children. We have previously shown that it has a local anaesthetic action in the newborn.

Aim: To investigate the effect of topical amethocaine on the pain of venepuncture in the newborn.

Design: Randomised double blind, placebo controlled trial.

Subjects: 40 newborn infants, gestation 27 to 41 weeks (median 33), age 2 to 17 days (median 7), undergoing routine venepuncture.

Method: 1.5g of amethocaine gel, 4% w/w (Ametop) was applied to the skin under occlusion for one hour, then wiped away. Venepuncture was performed five minutes later. Facial reaction and cry were recorded on videotape. Pain was assessed using a validated adaptation of the neonatal facial coding score (NFCS). Five features were scored at one second intervals for five seconds before and after venepuncture. No or minimal pain was defined as a cumulative score of below 10 (out of 25) after venepuncture. Each author scored the tapes independently.

Results: There was close agreement on scoring of the tapes. One infant was excluded because of prevenepuncture restlessness. 16 of 19 (84%) amethocaine treated infants showed little or no pain compared with 6 of 20 (30%) in the placebo group (p=0.001, Fisher's exact test). The median cumulative NFCS over five seconds after venepuncture was 3 compared with 16 in the placebo group (p=0.001, Mann Whitney U test). Amethocaine treated infants were less likely to cry in the first ten seconds and if they did, their cry was shorter. No local reaction to amethocaine was seen.

Conclusion: Topical amethocaine provides excellent pain relief during venepuncture in the newborn.