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Collaborative placebo-controlled trial of dexamethasone for neonatal chronic lung disease: a 3 year follow-up

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287 preterm babies from 31 European and North American centres who were oxygen-dependent aged 3 weeks or more were randomized to dexamethasone or placebo. Active treatment was associated with reduced time on assisted ventilation and no observed increase in serious immediate side-effects. 62 infants died. Survivors were followed up at 3 years of age, using questionnaires to GPs, health visitors and parents. Data are available for 209 infants (93% of survivors and 100% of UK residents).

Random allocation to:	Dex (n=100)	Placebo (n=109)
Home on suppl O_2 (%)	18	22
Median times GP gave antibiotics	7	5
Children re-admitted to hospital (%)	65	61
Frequent cough or wheeze (%)	39	38
Weight below 3rd centile (%)	41	27
Height below 3rd centile (%)	26	20
Head circ. below 3rd centile (%)	22	19
Cerebral palsy (%)	20	17
Poor vision or blind (%)	8	7
Moderate or severe deafness (%)	11	20
DQ below 50 on Minnesota scale (%)	9	9
Overall disability - severe (%)	18	20

Despite early benefits, there were no clear effects on respiratory morbidity, rates of infection, or overall disability. An 39% of the placebo group later received open steroids, even a trial of this size would have limited statistical power to detect a moderate effect on these adverse outcomes. Irrespective of random allocation, overall morbidity was high. A trial of prophylactic dexamethasone is planned.

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NEONATAL VISUAL RESPONSES AND NEURODEVELOPMENTAL OUTCOME AT 8 YEARS IN VERY PRETERM INFANTS. Vincent Kirkbride, Jenny Baudin, Jan Townsend, Simon Roth, David McCormick, Osmund Reynolds, Ann Stewart. Dept of Paediatrics, University College London Medical School, London, UK.

The purpose of this study was to investigate the longterm significance of abnormal visual responses in the neonatal period in very preterm (<33w) infants. All infants had ultrasound brain scans (US), and visual responses to an Albert Einstein Bullseye were elicited in the course of neurological examination. 111 infants born in 1983 were examined at a gestational equivalent age of 38-48 weeks without knowledge of the US findings. Nystagmoid movements (NM) and absent or limited (tracking in one plane only) responses were considered abnormal. 105 infants were re-examined at 99 ± 4.7 months with clinical and neurological examinations, tests of vision, hearing, visual-motor integration (VMI), cognition (WISC-R) and school performance. The main results were:

Neonatal					Eight years		
Visual responses.	n	US Abn*	Impairment Major	Minor	Help/special schooling	WISC IQ±sd	VMI centile±sd
present	83	43	10	26	16	101±19	38±29
limited	13	10	1	5	3	96±18	40±31
absent/NM	9	9	3	3	3	95±34	48±31

Visual impairment (amblyopia) at 8 years was noted in only 1 of the 22 infants with abnormal responses. We conclude that the abnormal neonatal visual responses were central in origin and indicated brain damage likely to cause adverse neurological and cognitive outcomes at 8 years.
* $p<0.005$, df 2

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EFFECT OF HIGH FREQUENCY OSCILLATORY VENTILATION (HFOV) ON ARTERIAL AND VENOUS CEREBRAL BLOOD FLOW VELOCITIES IN NEONATES. Lindner W., Saritas S., Münch G., Sökefeld C, Nicolai T
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The different ventilatory pattern of HFOV and conventional ventilation (IPPV) may differently affect cerebral hemodynamics in neonates. Using color Doppler sonography we measured left ventricular output (LVO), the mean blood flow velocity (BFV,cm/s) in the median cerebral artery (MCA) and in the great cerebral vein (GCV) in 10 critically ill neonates [GA 27 (25-37) wks, weight 980 (530-2500) g, age 8 (1-36) d] during IPPV and 3 (2-18) h after initiating HFOV (Infant Star). Indication for HFOV: Air leak (n=8), failure of IPPV (n=2).
RESULTS: Data are medain and range. MAP = mean airway pressure (mmHg) OI = oxygenation index (OI = FiO2 x MAP x 100 / paO2). * = $p < 0.05$.

	MCA*	GCV*	LVO	pCO2*	PEEP*	MAP	OI*
IPPV	14 (7-41)	5 (3-7)	200 (130-255)	44 (27-103)	4 (2-6)	12 (6-27)	12 (4-18)
HFOV	21 (9-42)	3 (2-6)	201 (144-289)	51 (35-107)	8 (3-24)	12 (4-31)	9 (3-16)

During IPPV, LVO was low and MCA-BFV normal compared to data of 54 stable ventilated (IPPV) preterm neonates [GA 28(23-35)wks; LVO: 248(212-316), mean MCA-BFV: 10(5-28)]. During HFOV the blood flow in the MCA was oscillating synchroneously with the oscillations of the ventilator and arterial cerebral BFV was increased in all infants (increased pCO2) compared to IPPV. Venous cerebral BFV however was decreased (up to 45%), possibly due to the increased PEEP during HFOV. CONCLUSION: HFOV affects cerebral hemodynamics and may cause cerebral congestion in neonates at risk of intracranial hemorrhage.

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AMINOPHYLLINE AND CAFFEINE HAS DIFFERENT EFFECTS ON CBF.

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Background Studies using Doppler ultrasonography have been unable to identify a direct effect of aminophylline and caffeine on Cerebral Blood Flow(CBF) of neonates. In one study using Xe-clearance, CBF decreased following intravenous administration of aminophylline.
Design As part of a double-blind, randomised, clinical study of preterm neonates recieving either caffeine or aminophylline, CBF and Left Ventricular Output(LVO) were measured in 35 spontaneously breathing infants (GA median 28 wks, BW mean 1129 gr). Measurements were done at a mean postnatal age of 137 min., two hours after an intravenous loading dose (aminophylline 5mg/kg., caffeine 10mg/kg).
Methods CBF was measured using the ^{133}Xe clearance method. LVO was estimated using M-mode echocardiography and Doppler ultrasound velocimetry.
Results Values are mean(SD).

	Caffeine(n=14)	Aminophylline(n=21)	p-value
CBF ml/100g/min	18.2(6.6)	13.0(2.9)	0.003
LVO ml/kg/min	217(43)	243(74)	0.26

No differences in GA, BW or MABP, HR, pCO_2, pO_2 and a/A-ratio at the time of measurements were found between the groups.
Conclusion These results apparently reflect differences in the ability of aminophylline and caffeine to block adenosine-induced vasodilation with the doses used. Aminophylline and caffeine may have different affinity for A_1- and A_2- adenosine receptors or subtypes of receptors.

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Title: EFFECT OF INCREASED INTRAABDOMINAL PRESSURE ON FENTANYL ELIMINATION IN NEONATAL LAMBS

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Increased intraabdominal pressure (IAP) might occur during closure of abdominal wall defects. IAP has been shown to reduce clearance of fentanyl. MAGEY et al. found acutely decreased portal flow with IAP. As it is important to also measure ductus venosus (DV) shunt and not hepatic blood flow to calculate clearance of fentanyl, we studied 6 neonatal lambs aged 4-46 hours. Fentanyl concentration was kept at 20 ng/ml. Organ blood flows were determined by a standard method, using radiolabelled microspheren. IAP was produced by a blood pressure cuff around the abdomen.

IAP(cm H_2O)	0	12	18
DV Shunt (% portal Blood flow)	23.5±6.4%	11.7±9.6%	7.0±6.7%
Hepatic artery flow (ml/min)	37.1±28.7	26.9±12.4	27 ±17.2
Spleenic flow (ml/min)	19.3±9.9	17.3±10.3	12.9±11.3
Mesenteric flow (ml/min)	355±126	293±104	244±91
Totalportal flow (ml/min)	370±131	341±140	326±123
Net hepatic flow (ml/min)	284±103	278±105	260±85.7
Hep. fentanyl clearance (ml/min)	53.9±25.5	21.1±16.2	20.1±17.8

Conclusion: Our study confirms that in neonatal lambs with IAP hepatic fentanyl clearance goes down. In addition we showed that DV shunt also decreases significantly, whereas no significant changes were found in portal or hepatic blood flow with IAP.

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SECONDARY ENERGY FAILURE AFTER ACUTE CEREBRAL HYPOXIA-ISCHAEMIA IN NEWBORN PIGS. Ann Lorek, Yukito Takei, Donald Peebles, David Edwards, Simon Roth, Ern Cady and John Wyatt for University College London Perinatal Brain Research Group. Departments of Paediatrics and Medical Physics, University College London Medical School, London, UK.

Phosphorus (^{31}P) magnetic resonance spectroscopy (MRS) of the brains of severely birth asphyxiated infants shows delayed "secondary" energy failure during the first 2 days of life (1). Our aim was to find out if this was i) reproducible in the newborn pig and ii) whether the severities of primary and secondary energy failure were related. 14 newborn pigs were anaesthetised and ventilated, and continuous ^{31}P MRS observations were made for 48 hours. An acute cerebral hypoxic-ischaemic insult causing severe intracellular acidosis and depletion of cerebral high-energy phosphorus compounds was made in 8 piglets and followed by resuscitation. The other 6 piglets were controls. During the insult, the phosphocreatine/inorganic orthophosphate ([PCr]/[Pi]) ratio fell from a mean of 1.59(SD 0.43) to 0.02(SD 0.02), but subsequently recovered. By 24 hours [PCr]/[Pi] was below both pre-insult and control values ($p<0.05$); it fell further to 0.46(SD 0.44) during the next 24 hours ($p<0.01$). Intracellular pH was no different from pre-insult values. Minimum [PCr]/[Pi] was related inversely to the acute depletion of nucleotide triphosphates. We conclude that secondary energy failure can be reproduced in the newborn pig and that its extent is related to the severity of the acute insult.

1. Azzopardi et al. Pediatric Research 1989;25:445-451