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## DOES PHENOBARBITAL IMPROVE THE EFFECTIVENESS OF THERAPEUTIC HYPOTHERMIA IN INFANTS WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY?

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**Objective:** To determine whether Phenobarbital (PB) given before therapeutic hypothermia to infants with hypoxic-ischemic encephalopathy (HIE) augments the neuroprotective efficacy of hypothermia.

**Methods:** Records of 68 asphyxiated infants of ≥ 36 weeks' gestation, who received hypothermia for moderate or severe HIE were reviewed. Some of these infants received PB prophylactically or for clinical seizures. All surviving infants had later brain MRI. The composite primary outcome of HIE-related neonatal death, and MRI abnormalities consistent with hypoxic-ischemic brain injury, were compared between the infants who received PB before initiation of hypothermia (PB group, n= 36) and the infants who did not receive PB before or during hypothermia (no PB group, n= 32). Logistic regression analysis determined which of the pre-hypothermia clinical and laboratory variables predict the primary outcome.

**Results:** The two groups were similar for severity of asphyxia as assessed by Apgar scores, initial blood pH and base deficit, early neurologic examination, and presence of an intrapartum sentinel event. The composite primary outcome was more frequent in infants from the PB group (PB 78% versus No PB 44%, p=0.006, OR 4.5, 95% CI 1.6 12.8). Multivariate analysis identified only the PB receipt before initiation of hypothermia (p=0.002, OR 9.5, 95% CI 2.3 39.5), and placental abruption to be independently associated with a worse primary outcome.

**Conclusions:** The combination of therapeutic hypothermia and PB may be associated with an increase in the composite outcome of HIE-related neonatal death and the brain MRI abnormalities, but the long term outcomes have not yet been evaluated.

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## FETAL ALCOHOL SYNDROME (FAS); ARE WE GETTING THE MESSAGE ACROSS? AUSTRALIAN, DANISH AND BRITISH DATA ANALYSED AND COMPARED

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**Background and aims:** To report on surveys of health professionals: 1443 in Western Australia, 165 in Denmark & 40 in the UK who were asked about their knowledge & practice regarding FAS & alcohol use during pregnancy.

**Methods:** In Australia & in the UK an anonymous postal questionnaire consisting of 44 multiple choice, Likert scale & open-questions was used. The Danish study used face-to-face interviews (open-ended questions). Analysis: descriptive statistics & the Statistical Package for the Social Sciences (SPSS).

**Results:** Study response rates; Australia 79%, Denmark 77.5% & UK 72.5%.

12% of Australian participants could identify the 4 FAS diagnostic features compared with 10% in the UK (no DK data).

In Australia (A) 45% routinely asked pregnant women about alcohol intake compared with 85% in Denmark (DK) & 100% in the UK, but only 25% (A), 64% (DK) & 55% (UK) routinely gave advice. Abstaining from binge-drinking (n=≥5 drinks) was advised by 29% (A), 28% (DK) & by none in the UK. Total alcohol abstention was recommended by 87% in Australia, 28% in Denmark & 100% in the UK.

Only 13% of Australian & none of the Danish or UK participants provided information in accordance with their countries' national guidelines.

**Conclusions:** These international data suggest that knowledge about FAS is limited, that consistent, evidence-based alcohol advice is not provided & that

further education of health professionals and their clients is essential if we are to improve knowledge, practice & prevention of FAS worldwide.

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## THE RNA-BINDING PROTEIN RBM3 IS INVOLVED IN HYPOTHERMIA INDUCED NEUROPROTECTION

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**Background:** Induced hypothermia is the only therapy with proven efficacy to reduce brain damage after perinatal asphyxia. While hypothermia downregulates global protein synthesis and cell metabolism, low temperature induces a small subset of proteins that includes the RNA-binding protein RBM3, which is transcriptionally induced also in response to hypoxia and has recently been implicated in cell survival.

**Methods/results:** We studied RBM3 expression in the developing murine brain by immunohistochemistry and found RBM3 widely expressed in neurons of the hippocampus, the subventricular zone, and the cerebellum during the first postnatal days. In adult brains, RBM3 was present only in neuronal precursor and stem cells, characterized by the presence of doublecortin. Hypothermia profoundly promoted RBM3 expression in juvenile as well as in mature neurons, and hypothermia-induced RBM3 expression was associated with protection of primary neurons and neuronal cell lines from forced apoptosis. Blocking RBM3 expression by siRNAs in neuronal cells significantly diminished the neuroprotective effect of hypothermia while vector-driven RBM3 overexpression prevented activation of caspase-3.

**Conclusion:** Together, the RNA-binding protein RBM3 protects neuronal cells from apoptosis. RBM3 upregulation apparently accounts for a substantial proportion of hypothermia-induced neuroprotection.

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## HYDROCORTISONE VERSUS DEXAMETHASONE TREATMENT FOR BRONCHOPULMONARY DYSPLASIA AND NEUROLOGICAL OUTCOME IN PRETERM INFANTS

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**Background and aims:** At present, hydrocortisone (HC) as well as dexamethasone (DXM) are used to treat preterm infants at risk for bronchopulmonary dysplasia. Our aim was to determine the influence of HC- and DXM-therapy in preterm infants on neurodevelopmental outcome assessed by the quality of general movements (GMs) until three months after term.

**Methods:** Thirty-six preterm infants were included, 18 infants received HC (BW range 630−1700 grams, GA range 24.9−31.0 weeks), 18 infants received DXM (BW range 700−1800 grams, GA range 26.0−30.3 weeks) in a mean cumulative equivalent cortisol dose of 113.3 mg/kg resp. 166.3 mg/kg. After videotape recording, we analyzed each recording on the quality of GMs as normal or abnormal. Additionally, we performed a Motor Optimality Score (MOS) on details of the GMs (range 5−28).

**Results:** No difference in GM quality was found between HC- and DXM infants, neither before treatment, nor in the first week after treatment or at term. At 3 months, HC infants had a higher median MOS than DXM infants (24 vs. 21, $p$ =0.025). This effect became stronger after correction for equivalent dose of cortisol, BW and GA ($p$ =0.005). In the DXM group, but not in the HC group, MOS on day 1 of treatment was lower than before treatment (10 vs. 11, $p$ =0.030).

**Conclusions:** Our study indicates that the quality of GMs is impaired in DXM treated infants, in particular on the first day following treatment. HC treatment is associated with a better quality of GMs 3 months after term.