subjects (neuromotor score, NMS ≥2, or Bayley Scales of Infant Development II or III MDI < 70 or cognitive score < 85).

Chorioamnionitis (42 subjects) was associated with a lower risk of moderate-severe brain injury (OR 0.3; 95%CI 0.1–0.7; p=0.003), and trended toward lower risk of adverse neurodevelopment. Infant infection (32 subjects) trended toward association with moderate-severe injury (OR 1.6; 95%CI 0.8–3.5; p=0.2), and was significantly associated with an abnormal NMS (OR 3.4; 95%CI 1.2–10.2; p=0.03) but not cognitive outcome. After adjusting for hypothermia and severity of encephalopathy, maternal infection remained associated with a lower risk of brain injury, whereas the association between infant infection and NMS was no longer significant.

These preliminary results are in keeping with animal studies that suggest that the timing of an inflammatory signal may determine whether infection is injurious or protective.

Acknowledgements NIH UL1 RR024131&P50NS035902.

290 GENES IMPORTANT IN INFLAMMATION, APOPTOSIS, TRANSCRIPTION REGULATION AND ANGIOGENESIS ARE INDUCED IN THE NEWBORN MOUSE BRAIN AFTER HYPOXIA-REOXYGENATION (HR)

doi:10.1136/archdischild-2012-302724.0290

[1,2]AGW Rognlien, [1,2]EJ Wollen, [2,3]M Atneosen-Åsegg, [4]M Bjørås, [1,2]OD Saugstad. *[1]Department of Pediatric Research, Oslo University Hospital HF; [2]Women and Children's Division, University of Oslo, Oslo; [3]Department of Clinical Molecular Biology and Laboratory Sciences, Akershus University Hospital, Lørenskog; [4]Department of Microbiology, Oslo University Hospital HF, Oslo, Norway*

Background and Aims Pathogenesis of birth asphyxia has yet to be fully elucidated. To explore the mechanism of HR injury we followed the temporal profile of *a priori* selected genes in the newborn mouse brain.

Methods 84 C57BL/6 mice (postnatal day 7) were randomized to 120 minutes of hypoxia (FiO_2 0.08, n=64) or 180 minutes in air (controls (C21), n=20). The hypoxia group was randomized to 30 min reoxygenation with FiO_2 0.60 (H60) or air ($H_2$1). After observation in air for 0, 150, 300 minutes or 3 days, organs were harvested. Homogenate of hippocampus and striatum was analyzed for mRNA expression of 44 genes by real-time PCR.

Results *Lcn2*, *Mt1, Hmox1 and Vegfa* were significantly up-regulated (p<0.05) after 0–300 min observation when comparing $H_2$1vsC21 and H60vsC21. *Ccl2*, *Ccl12* and *Tnf* were up-regulated from 0–150 min, *Stat3* from 150–300 min, while *Ccnd1* was down-regulated at 0 min in both comparisons. In the $H_2$1vsC21 comparison at 0 min, *Neil3* and *Apaf1* were down-regulated. When comparing H60vsH21, *Cxcl10* (0 min) and *Hmox1* (300 min) were up-regulated while *Neil3* (0 min) was down-regulated. There were no significant gene expression changes after 3 days.

Conclusions Genes important in inflammation (*Lcn2, Mt1, Ccl2*, *Ccl12*, *Cxcl10*, *Tnf*, *Hmox1*), apoptosis (*Lcn2*, *Mt1*, *Tnf*, *Hmox1*, *Vegfa*), angiogenesis (*Vegfa*), and transcription regulation (*Stat3*) were induced up to 300 minutes after hypoxia-reoxygenation while the DNA-glycosylase *Neil3* was suppressed. The up-regulation of the pro-inflammatory cytokine *Cxcl10* after hyperoxic compared to normoxic reoxygenation, confirms that hyperoxia induces additional inflammation.

291 PROGNOSTIC TESTS IN TERM NEONATES WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY: A SYSTEMATIC REVIEW

doi:10.1136/archdischild-2012-302724.0291

[1]H van Laerhoven, [2]TR de Haan, [3]M Offringa, [4]B Post, [5]JH van der Lee. *[1]Academic Medical Center - Emma Children's Hospital; [2]Neonatology, Academic Medical Center - Emma Children's Hospital, Amsterdam, Netherlands Antilles; [3]Hospital for Sick Children Research Institute, Toronto, ON, Canada; [4]UMCN St Radboud, Nijmegen; [5]Woman and Child Centre, Academic Medical Centre, Amsterdam, Netherlands Antilles*

Background and Aims Hypoxic Ischemic Encephalopathy (HIE) following perinatal asphyxia in term neonates is associated with long term neurological sequelae or demise. The aim of this systematic review was to investigate the prognostic value of currently used clinical tests in neonatal patients with HIE.

Methods MEDLINE, EMBASE, Central and CINAHL were searched until November 2011. Studies were included if they: (1) concerned infants with a gestational age ≥ 36 weeks suffering perinatal asphyxia and HIE; (2) evaluated prognostic tests in either cooled or non-cooled patients; (3) reported on neurodevelopmental outcome results at a follow up age ≥ 18 months. Study selection, assessment of methodological quality, and data extraction was performed by three independent reviewers. Pooled sensitivities and specificities of investigated tests were calculated when possible.

Results Included in the analysis were 29 studies describing 13 different prognostic tests conducted 1631 times in 1306 term neonates. Investigated tests comprised a range of imaging modalities, neurophysiological tests and clinical neurological exams. Most promising neurophysiology tests (first week of life) were: aEEG (sens. 0.93, [95%CI 0.78–0.98]; spec. 0.90 [0.60–0.98]); EEG (sens. 0.92 [0.66–0.99]; spec. 0.83 [0.64–0.93]) and VEP (sens. 0.90 [0.74–0.97]; spec. 0.92 [0.68–0.98]).

Conclusions The available evidence suggests an important role for aEEG, EEG, and VEP. Given the heterogeneity of the tests' performance and outcomes studied, accurate predictions of long term outcomes in these critically ill neonates await the results of well designed large prospective studies that evaluate the best possible combination and timing of diagnostic tests.

292 THE IMPACT OF HYPOTHERMIA ON POST-NATAL BLOOD BIOMARKERS OF NEONATAL HYPOXIC ISCHAEMIC ENCEPHALOPATHY

doi:10.1136/archdischild-2012-302724.0292

BH Walsh, GB Boylan, EM Dempsey, DM Murray. *Neonatal Brain Research Group, Department of Paediatrics and Child Health, University College Cork, Cork, Ireland*

Numerous post-natal biomarkers of hypoxic ischaemic encephalopathy (HIE) severity have been proposed before the era of hypothermia. It is unclear if hypothermia impacts upon these potential biomarkers, and therefore whether previous findings are now valid. The aim of this study was to determine if hypothermia alters the discriminative ability of post-natal nucleated red blood cells (NRBCs) to distinguish between mild and moderate/severely encephalopathic infants.

Methods A prospective cohort study recruited term infants with HIE. The grade of HIE was categorised using Sarnat score, and multi-channel EEG. The recruitment period (2003–2012), spanned the introduction of hypothermia. Therefore the discriminative ability of the NRBC count for grade of encephalopathy could be compared in moderate/severely encephalopathic infants who did and did not receive hypothermia.

Results 86 infants with HIE were included in the study, 40 were mild, 26 moderate (14 normothermic, 12 hypothermic), and 18 severe (10 normothermic, 8 hypothermic). In the normothermic group, the NRBC count discriminated between mild and moderate/severe Sarnat scores (p=0.016), but not in the hypothermic group (p=0.297). This change was due to a decrease in NRBCs among infants with a moderate Sarnat score receiving hypothermia, This occurred despite these infants having a significantly worse 5 minute Apgar score (p<0.001) and background EEG at 6 hours (p=0.032) than their normothermic counterparts.

Conclusion This study has demonstrated that hypothermia can impact upon early post-natal blood biomarkers of HIE. We therefore advise caution in the use of these samples when studying novel diagnostic biomarkers for HIE in the hypothermic era.