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Background Paediatric neurological diseases individually are rare; however, collectively affect thousands of children and have life-long impacts. The incidence of many of these is not readily available, and yet essential for improving clinical care, advocacy and health service planning.

Aims To obtain/examine national population-based data, in a timely manner, on acute flaccid paralysis (AFP), progressive intellectual and neurological deterioration (PIND), acquired demyelinating syndromes of the central nervous system (ADS), congenital myotonic dystrophy (CMD) and paediatric myasthenia (PM).

Methods Studies were conducted through the Canadian Paediatric Surveillance Program, a network of >2,500 paediatricians, reporting cases monthly according to preset protocols. Confidentiality is mandatory; studies receive ethical approval.

Results The AFP study, with 657 cases in 15 years, affirms that Canada is free of wild-type poliovirus. The PIND study demonstrated several genetically defined neurodegenerative disorders, and only one case of iatrogenic Creutzfeldt-Jakob disease. A yearly incidence of 0.9 per 100,000 was estimated to affect Canadian children during the ADS study, with optic neuritis being the most common presentation. Awareness of multiple sclerosis as a possible outcome of ADS increased remarkably. Of 38 confirmed CMD cases in six years, 61% were index cases for families. In year one of surveillance, 33 cases of PM were confirmed; almost half not having elevated titers of acetylcholine receptor antibodies, and 21% having other co-existing or familial immune disorders.

Conclusion Active national surveillance has more reliably characterized several rare neurological disorders and their associated burdens, supporting and informing the development of medical and public health interventions.

53 THE IMPORTANCE OF SECRETORY IGA ON TRANSEPI- THELIAL TRANSPORT OF COMMENSAL BACTERIA AND ITS CONSEQUENCES ON NEONATAL IMMUNE DEVELOPMENT: PRECLINICAL ASSESSMENT

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Background and aims Secretory IgA (SIgA) naturally binds to commensal bacteria and is able to cross back through the intestinal epithelium to promote immune responses. The aim of the present work was to investigate the contribution of SIgA on the trans-epithelial transport of commensal bacteria, such as probiotics, and its consequences on neonatal immune development as such process may also occur with SIgA originating from breast milk.

Methods A) Fluorescent bacteria alone or associated with SIgA as immune complexes (IC) were administered into intestinal loops containing one Peyer's patch (PP) in SPF or germ-free mice. Fate of bacteria within PP over time was analyzed by confocal microscopy.

B) After day 7 of life, germ-free mouse neonates were conventionalized to induce natural neonatal gut colonization and supplemented up to weaning with either placebo, probiotics or IC. Immune maturation was then assessed by measuring mucosal IgA production (ELISPOTs) in PPs.

Results

- Natural entry of commensal bacteria into PP was speeded up when administered in the form of IC. In germ-free mice, lacking endogenous SIgA, a very low level of trans-epithelial transport of commensal bacteria was observed, which was restored with IC.

- While early-life supplementation with probiotics alone significantly enhanced occurrence of IgA producing cells in PPs of pups as compared to controls, IC feeding significantly further increased it.

Conclusions SIgA-mediated entry of commensal bacteria in PPs represents a mechanism ensuring the continuous dialogue between the host and its microbiota, particularly relevant for neonatal immune development.

54 CEACAM1 IN BRAIN DEVELOPMENT AND PRETERM BRAIN INJURY

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Background and aims About 10% of all neonates are born preterm before 37 weeks of gestation. These babies are at high risk to develop morbidities such as neurocognitive disorders (encephalopathy of prematurity) which are a huge burden on the children and their families. Multiple factors are causal, e.g. hyperoxia and maternal/neonatal inflammation. We demonstrated that CEACAM1, a member of the carcinoembryonic antigen-related cell adhesion molecule (CEACAM) family, is expressed ontogenetically in oligodendrocytes of the developing brain. Since CEACAM1 is involved in inflammation-associated signaling we hypothesize that CEACAM1 might contribute to inflammation-induced preterm brain injury.

Material and Methods In a rat model of inflammation-induced encephalopathy of prematurity (LPS at p3), changes in CEACAM1 expression were quantified on RNA level at p6 and p11. Animals were anesthetized, transcardially perfused, and forebrains were immediately removed and snap-frozen. RNA from forebrains was isolated according to standard protocols. CEACAM1 isoform expression was quantified by qRT-PCR.

Results LPS exposure at p3 induces significant changes in CEACAM1 expression in the developing brain. We report a significant increase of the soluble isoform CEACAM1-4C2 at p6, and a subsequent increase of the CEACAM1-4L isoform and an isoform shift from CEACAM1-4S towards CEACAM1-4L at p11.

Conclusions Although underlying mechanisms are still elusive we demonstrate that CEACAM1 expression in oligodendrocytes is significantly altered in a model of inflammation-induced encephalopathy of prematurity. This finding emphasizes our hypothesis that CEACAM1 is involved in detrimental processes in the immature brain.

55 ADVERSE EVENTS FOLLOWING THE COMBINATION OF DEXMETOMIDINE WITH THERAPEUTIC HYPOTHERMIA IN A PIGLET ASPHYXIA MODEL

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Background Dexmedetomidine (DXM) is a potent, selective α_2 adrenoceptor agonist which exerts sedative, neuroprotective, analgesic and anti-inflammatory properties that may be beneficial for neonatal asphyxia. The safety of DXM combined with therapeutic hypothermia is unknown.

Aim To assess safety of low (0.6–1.5mcg/kg/h) and high dose (10mcg/kg/h) DXM with hypothermia as part of a larger study investigating neuroprotection with DXM-augmented cooling.

Methods Following a quantified hypoxic-ischaemic insult, 16 male piglets were randomized to either hypothermia alone (33.5°C from 4–22h, n=7) or DXM plus hypothermia (n=9). Mean arterial blood pressure (MABP) was measured continuously; when MABP was < 40mmHg, a saline bolus was given followed by inotropes. At 48 h the experiment was terminated.

Results There was no difference in baseline variables. Compared to hypothermia only, the DXM hypothermia group required more saline, adrenaline and cardiac arrests (all $p<0.05$). These adverse events occurred at both high and low dose DXM.

Abstract 55 Table 1 Volume replacement, adrenaline and cardiac arrests

	Hypothermia alone (n=7)	Hypothermia plus DXM (n=9)
Saline replacement (ml/kg)	0.45±0.18	0.88±0.29*
Adrenaline for resuscitation (μ)	28.57±23.82	211.11±69.29*
Cardiac arrest	2 out of 7	7 out of 9 ^
Fatal cardiac arrest	1 out of 7	4 out of 9

* $p<0.05$ unpaired t test ^ $p<0.05$, Chi squared test

Conclusion Adverse cardiovascular events with low and high dose DXM combined with cooling occurred mainly after 16 h and could be due to perturbed central autonomic function, vasoconstriction via peripheral alpha adrenoceptor stimulation or effects on the imidazoline receptor.

56 SAFETY OF HIGH-DOSE ERYTHROPOIETIN FOR NEUROPROTECTION IN PRETERM INFANTS

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Background Erythropoietin has been shown to be protective against hypoxic-ischaemic and inflammatory injuries in cell culture, animal models of brain injury, and in clinical trials in human adults. A multicentre randomized placebo-controlled trial was started to investigate whether early administration of high dose recombinant human erythropoietin (rhEpo) in very preterm infants improves neuro-developmental outcome at 24 months.

Aim Interim analysis of neonatal complications until discharge from hospital.

Results 395 preterm infants were recruited in 5 centres. 206 infants had received (n) 3,000 U/kg body weight rhEpo, and 189 infants NaCl 0.9% intravenously at 3, 12–18 and 36–42 hours after birth.

Abstract 56 Table 1

	EPO (n=206)	Placebo (n=189)	p
GA (wks); mean (SD)	29.3 (1.6)	29.3 (1.6)	0.99
BW (g); mean (SD)	1232 (373)	1231 (314)	0.99
Death n (%)	12 (5.9)	11 (5.9)	0.99
Severe adverse events SAEs n	46	45	0.82
Bronchopulmonary dysplasia n (%)	21 (10.8)	24 (13.5)	0.53
Retinopathy of prematurity n (%)	12 (6.4)	14 (8.3)	0.64
Intraventricular haemorrhage n (%)	38 (18.4)	28 (14.8)	0.41
Haemangioma n infants (%)	35 (17.0)	34 (18.0)	0.89
Haematocrit day 7–10, mean (SD)	47.3 (7.9)	44.8 (7.1)	0.002

Conclusions No significant adverse effects of early high-dose rhEpo treatment in very preterm infants were identified. The neuroprotective effect will be evaluated in 24 months.

57 ASSOCIATION BETWEEN SECRETORY PHOSPHOLIPASE A2 SUBTYPE V (PLA2G5) GENOTYPE AND ACUTE RESPIRATORY DISTRESS SYNDROME IN INFANTS

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Background Secretory Phospholipase A2 (PLA2) has been linked with acute respiratory distress syndrome (ARDS) and its clinical severity and mortality. The enzyme subtype -V (PLA2G5) is expressed in the lung tissue. We aimed at sequencing its gene (HGNC:9038) in infants with ARDS. This study is a part of a multicentre project whose protocol has been published elsewhere.[1]

Methods 24 ARDS and 24 age-matched babies with no lung disease were enrolled. 50 healthy adult volunteers, who never had neither ARDS nor chronic pulmonary diseases, served as another control group. Genomic DNA was extracted from leukocytes, amplified by PCR and sequenced, analyzing the coding regions by SeqScape. Basic clinical data were recorded.

Results A polymorphism (p.G3G=c.9C>T) was detected in the gene PLA2G5 (exon 1). This variation was present in heterozygosis in 42% of controls and in 17% of patients, while homozygosis was detected in 21% of patients and in no controls ($p=0.022$). Heterozygosis and homozygosis were present in 54% and 10% of adult controls, respectively. Homozygosis for such polymorphism led to an increased risk of ARDS (OR: 6.7; 95% C.I.: [1.3–34.2]). Patients carrying this polymorphism had lower PaO₂/FiO₂ ratio (104±29 vs 147±53; $p=0.039$) and higher lung injury score at the diagnosis (3.7±0.2 vs 3.2±0.4; $p=0.031$).

Discussion These are the first findings about genetic association between PLA2 and ARDS. Variation in the PLA2G5 gene might be associated to an increased risk for ARDS as it may represent a marker of variations in other genes nearby PLA2G5, that may be involved in inflammation pathway.

[1] De Luca D, Capoluongo E, Rigo V & Study group on Secretory Phospholipase in Paediatrics. BMC Pediatr 2011; 11:101.

58 EFFECT OF VARESPDLADIB-PROTECTED SURFACTANT IN CULTURED RAT ALVEOLAR MACROPHAGES STIMULATED WITH LPS

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Background Secretory phospholipase A2 (sPLA2) is a crucial enzyme for inflammatory response and surfactant catabolism. Acute lung injury (ALI) is a life-threatening syndrome characterized by surfactant dysfunction and raised levels of sPLA2. Varespladib is a potent selective sPLA2 inhibitor that is effective in animal models of ALI. Nothing is known about the joint administration surfactant+varespladib and we aimed at studying the effect on the sPLA2 pathway.

Methods 1x10⁶ normal alveolar macrophages (from *Rattus Norvegicus*) were cultured in Ham'sF12 medium + 2% fetal bovine serum. Cultures were incubated with 15 ng/mL LPS for 24h, then treated with 200 μg poractant-α, 90 μM varespladib, both or nothing. These concentrations were those achieving 50% sPLA2 activity reduction in previous experiments. After 24h, culture supernatants were assayed for sPLA2 activity, free fatty acids (FFA) and total proteins concentrations.

Results sPLA2 activity corrected for the protein level is 0.26±0.02, 0.24±0.02, 0.24±0.02 and 0.28±0.02 IU/μg in cultures treated with