Method STAK is a 12 week, activity programme including activity diary, street dance DVD, circuit training and, for children at or above the 91st centile weight for height, motivational interviewing and goal setting. STAK was evaluated in a cluster-randomised trial in 24 schools. Children aged 9 to 11 were screened for overweight, low exercise self-efficacy or asthma. Twelve schools were randomised to receive the STAK intervention and 12 to control. BMI, waist circumference and exercise self-efficacy were assessed at baseline and post intervention (4 months).
Results Of the 2479 children screened, 1065 children (43%) met the study inclusion criteria. Parents of 424 (40%) children consented to their child's participation with 4 months follow-up data available for 392 (92%). The groups were well matched at baseline. After controlling for baseline values and time between testing, children in the intervention group had higher total self-efficacy at 4 month follow-up. In the group of children who were overweight at baseline (=>91st centile), those in the STAK intervention group had smaller waist circumference and lower BMI at 4 month follow-up.
Conclusion Preliminary analysis suggests that a targeted activity intervention has benefits for children at risk of obesity. Future analyses will explore if benefits are sustained at 12 months follow-up.

49 GETTING UNDER THE SKIN: *STREPTOCCOCUS PYOGENES* IN TOXIC SHOCK

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Streptococcus pyogenes can cause a variety of diseases in immunocompetent individuals, from pharyngotonsillitis to life-threatening invasive diseases like streptococcal toxic shock syndrome and rapidly progressing deep tissue infections, such as necrotizing fasciitis. Necrotizing fasciitis is often seen in combination with toxic shock, which further increases morbidity and mortality.

To gain insight into the pathogenesis of severe deep tissue infections, we have utilized a snap-frozen tissue biopsy material collected from patients with various soft tissue infections, including necrotizing fascitiis, myositis, and cellulitis caused by *S. pyogenes*. All patients had received intravenous clindamycin in combination with a β-lactam antibiotic at admission.

The studies revealed that severe soft tissue infections are characterized by massive bacterial load, presence of important streptococcal virulence factors including soluble M1-protein, the cysteine protease SpeB and superantigens, DNAses, and heavy infiltration of inflammatory cells and inflammatory mediators. Analyses of host-microbe interactions at the tissue site of infection have furthermore provided *in vivo* evidence for many of the immune evasion strategies previously described *in vitro*. Important bacterial resistance mechanisms at the tissue site include exploitation of human phagocytic cells as host cells thereby allowing persistence intracellularly, as well as protection against antimicrobial peptides by SpeB retained at the bacterial surface through GRAB-a2-macroglobulin complexes. It is clear that the pathogenesis of severe streptococcal tissue infections is multifactorial in nature. This complexity is important to consider in the design of novel therapeutic strategies, where IVIG represent one immunomodulatory therapy that should be evaluated further.

50 LATE ONSET NEONATAL SEPSIS (LOS) IN VERY LOW BIRTH WEIGHT INFANTS: A MULTICENTRIC STUDY IN THE NEOCOSUR SOUTH AMERICAN NETWORK

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Background LOS is an important cause of mortality and morbidity among very low birth weight (VLBW) infants.
Aim To determine the incidence, bacteriology and associated morbidity to LOS over a 10 year period in a South American Network.
Methods Data were prospectively collected with predefined diagnostic criteria on all VLBW infants born in 18 centers from this Network, from 2001 through 2010. For numerical variables, mean and standard deviations were calculated. Students-t test or Chi Square tests were used for comparisons as appropriate. Logistic regression was used to assess association between sepsis and morbidity conditions.
Results 11651 VLBW were included, with a mean BW 1086±279 g and GA of 29.9±3 weeks. A 19% acquired LOS, with a slight decrease in incidence from 19.5% in the 2001–2005 period to 17.5% in 2010. There was a wide intercenter variability from 5.9% to 29.6 %. The most common pathogens were CONS (53%) and *Staphylococcus aureus* (11%). Infants who developed LOS were significantly smaller by weight and gestational age. Multivariate logistic regression analysis showed a positive association between LOS and an increased risk for patent ductus arteriosus (OR: 1.510 [95% CI: 1.113–2.049]), NEC (OR: 0.427 [95% CI: 0.373–0.488]) and mechanical ventilation (OR: 0.383 [95% CI: 0.327–0.449]).
Conclusions LOS remains an important cause of morbidity among VLBW infants with a wide intercenter variability. Decreasing LOS is a present important challenge for neonatal centers and networks may contribute in this purpose.

51 RESISTIN - A NOVEL FEATURE IN THE DIAGNOSIS OF SEPSIS IN PREMATURE NEONATES

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Objective To evaluate the efficacy of resistin in the diagnosis of sepsis and to compare with C-reactive protein (CRP) in preterm infants.
Study Design Totally 80 preterm infants were prospectively included in the study. Blood samples were collected within the first hour of life, on first and third days of sepsis for basal resistin, basal CRP, CRP-1, CRP-3, resistin-1 and resistin-3 levels. Septic patients were divided into two groups as Gr-negative and Gr-positive sepsis group.
Results Basal resistin and CRP levels were 14.0 (4.7–31.1) ng/ml and 0.5 (0–23) mg/dL. Culture-proven sepsis was diagnosed in 20 infants. Resistin-1 and resistin-3 were significantly higher than basal resistin levels ($p<0.01$) and positively correlated with CRP. The area under curve values for CRP and resistin were 0.714 and 0.984, respectively ($p=0.039$). Resistin-1 and resistin-3 levels were significantly higher in Gr-negative sepsis group than Gr-positive ($p<0.001$).
Conclusion We showed that resistin had an efficacy superior to that of CRP in the diagnosis of sepsis in preterm infants. Resistin can be used as an early marker for sepsis in premature infants. Further studies are needed in larger groups to better understand the role of resistin to determine cut-off values for Gram-negative and positive sepsis.

52 PAEDIATRIC NEUROLOGICAL DISEASES: WHAT DOES ACTIVE CANADIAN SURVEILLANCE TELL US?

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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 remarkedly. 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 TRANS-EPITHELIAL 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

a. 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.
b. 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 DEXMEDETOMIDINE WITH THERAPEUTIC HYPOTHERMIA IN A PIGLET ASPHYXIA MODEL

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Background Dexmedetomidine (DXM) is a potent, selective a2 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.