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TYPE 1 DIABETES IN NEW ZEALAND CHILDREN AND ADOLESCENTS: INCIDENCE, PREVALENCE AND MORTALITY

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Background: Type 1 diabetes results from the autoimmune destruction of pancreatic beta cells. Epidemiological studies from many populations and geographical contexts reveal increases in the incidence of type 1 diabetes with time. This study in Canterbury (New Zealand) determined the incidence of type 1 diabetes from 1970 to the present, the prevalence mid-way through the study period and mortality rates at 9 and 15 years follow-up.

Methods: Prospective ascertainment of incident cases aged 0–19 years commenced in 1982. Cases presenting 1970–82 were ascertained from hospital records. The prevalence of type 1 diabetes in the population was determined in January 1994 via a community survey based in retail pharmacies. The prevalence cohort was followed up at 9 and 15 years to establish vital status.

Results: Incidence rates ranged from 2.40 to 26.59 cases/100 000 person years over the three decades, increasing by 0.59 cases/100 000 per year or 5% annually. The prevalence of type 1 diabetes mid-way through the observation period was 0.3 and 1.8 per 1000 for the 0–9 and 10–19 year age groups respectively. At follow-up after 15 years, the standardised mortality ratio for individuals diagnosed with diabetes before age 30 was 2.7 for females and 3.0 for males. That is, a diagnosis of diabetes prior to 30 years of age is associated with a three-fold increase in mortality compared with non-diabetic children in the background population. While cardiovascular disease accounted for the highest absolute mortality rate, the standardised mortality rates for hypoglycaemia, and for renal failure were 7.52 and 35.74 respectively.

Conclusion: The incidence rate of type 1 diabetes is increasing significantly over time. A diagnosis of diabetes is associated with considerable excess mortality.

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NF-KAPPA B ACTIVATION AND APOPTOSIS IN LUNG NEUTROPHILS FROM INFANTS WITH HYALINE MEMBRANE DISEASE

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Background: Sequestration and the persistence of neutrophils in the lungs of infants with hyaline membrane disease (HMD) have been associated with pulmonary injury and the subsequent development of chronic lung disease (CLD). While activation of the transcription factor, NF-kappa B, in these cells could upregulate the expression of various mediators that enhance the pulmonary inflammatory process, apoptosis of neutrophils may promote the resolution of lung inflammation. We aimed to determine the proportion of tracheal aspirate samples from infants with HMD that had neutrophils showing evidence of NF-kappa B activation and/or apoptosis.

Methods: Tracheal aspirates were collected from mechanically ventilated infants who were diagnosed to have HMD. The cells in the samples were pelleted after centrifugation, fixed and stained for immunofluorescence microscopy. The neutrophils from each sample were stained using anti-p65 antibody to assess for NF-kappa B activation and cleaved caspase-3 antibody for the detection of apoptosis.

Results: A total of 172 tracheal aspirates from 59 premature infants were studied. The median gestational age and birthweight were 27 weeks (range, 23 to 36 weeks) and 855 g (range, 500 to 3200 g) respectively. The median age when aspirates were obtained was day four of life and the median number of samples per infant was two. Fifty-four (31%) samples from 33 (56%) infants had neutrophils with evidence of NF-kappa B activation. A total of 68 tracheal aspirates from 27 infants were available for concomitant assessment for neutrophil apoptosis. Eleven (16%) samples from seven (26%) infants showed evidence of neutrophil apoptosis. With the exception of one sample, tracheal aspirates with neutrophils showing NF-kappa B activation or apoptosis were mutually exclusive events.

Conclusion: A majority of infants with HMD had indication of a pro-inflammatory milieu in their lungs with tracheal aspirate neutrophils showing activated NF-kappa B. We speculate that NF-kappa B activation in neutrophils may reflect conditions that are anti-apoptotic, and thus be associated with persistent neutrophilic inflammation implicated in the process of lung injury and the development of CLD.

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VITAMIN K DEFICIENCY BLEEDING (VKDB) IN NEW ZEALAND INFANTS: RESULTS OF SURVEILLANCE OVER FIVE YEARS (1998 TO 2002)

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Background: There have been several changes in the recommended prophylaxis of VKDB in New Zealand over the past decade. Preceeding the introduction of a new preparation, Konakion MM, in 2001, a consensus statement from professional organisations representing paediatricians, midwives, nurses, GPs and obstetricians was published. This recommended that all babies should receive vitamin K prophylaxis and that the preferred route is intramuscular (i.m.). Where parents did not agree to i.m. vitamin K, a regime of three repeat oral doses was recommended. We aimed to determine the annual incidence of, morbidity from and circumstances surrounding, cases of VKDB, defined as "spontaneous bruising or bleeding associated with prolonged clotting time, but not due to an inherited coagulopathy or disseminated intravascular coagulation, in an infant <6 mths old".

Methods: The standard methods of the NZPSU were used. Each month all paediatricians were sent either a reply-paid card or email to indicate if they had seen a child with VKDB in the previous month. Following a "yes" response, a two page questionnaire was sent to ascertain details of the case. VKDB was included on the NZPSU card from its inception in January 1998 and has remained under surveillance subsequently.

Results: 19 cases were reported in the five years 1998 to 2002; 1 report was not valid, 3 were double reports. Of the 15 remaining cases, 6 were in the first week of life ("Early") and 9 were from day 8 to 6 months ("Late-onset"). Amongst early, 4 were confirmed of Classical type (day 2 to 7), all were breast fed and none received vitamin K; 2 cases were in the first day of life and unusual (pulmonary haemorrhage, sub-dural haemorrhage) and were only possible cases. Amongst late-onset, 1 had i.m. vitamin K at birth, had severe liver disease of unknown cause and required repeat doses of vitamin K; 8 were fully breast fed and had not received vitamin K , 4 had liver disease, 3 had intracerebral haemorrhage (all surviving, 2 with hydrocephalus), and 1 died. One case is only probable because no coagulation studies were performed before vitamin K was given. The annual incidence of confirmed early VKDB (4 cases) was 1.4 per 100, 000 births, and of confirmed late-onset VKDB (8 cases) was 2.9 per 100,000.

Conclusion: Cases of VKDB in New Zealand are virtually confined to breast fed infants who have not received prophylactic vitamin K at birth either i.m. or orally.

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SIZE MATTERS: THE RISK OF CHRONIC LUNG DISEASE AND SIGNIFICANT RETINOPATHY OF PREMATURITY

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Aims: To identify prenatal risk factors for hospital–based outcomes in very preterm infants.

Methods: ANZNN prospectively audits all high-risk infants (gestation <32 completed wks or birthweight (BW) <1500g) admitted to each level III newborn intensive care unit in Australia and New Zealand. Two outcomes were selected for individual analysis; chronic lung disease (CLD-any respiratory support at 36wks post-menstrual age-PMA); significant retinopathy of prematurity (ROP-stage III or greater). As local criteria for ROP screening is most often <31wks gestation or <1250g BW, a subset of babies born at <29wks was used to prevent bias towards small for gestational age infants. Data were excluded if no eye examination was recorded (n=176, 7.7%). Univariate analysis of 23 variables was undertaken and variables not significant at P <0.05 eliminated; the remainder being entered stepwise into a multivariate logistic model and rejected when they lost significance at P <0.01.

Results: The study group consisted of 5599 babies born during 1998–99 who survived to 36wks PMA. Of these, 1235 (22%) had CLD. On univariate analysis having a mother who had a previous perinatal death, antepartum haemorrhage, male sex, 1 min Apgar <4, lower gestational age, lower BW for gestation, ethnicity, pregnancy induced hypertension, and both the method and presentation of birth were associated with CLD. Pre-term pre-labour rupture of the membranes was protective. ROP exams were recorded for 2111 babies born at 22 to 28 weeks gestation; stage III or more being detected in 203 (9.6%). Significantly associated with ROP on univariate analysis were gestation, BW for gestation, 1 min Apgar <4, sex and prolonged rupture of membrane. For both models, after simultaneous adjustment, factors that remained in the multivariate model were gestation, sex and BW for gestation. A dose response was demonstrated for gestation (trend P <0.0001) and BW for gestation (trend P <0.0001), with the risk of poor outcome increasing with decreasing gestation and increasing growth restriction. Being female was protective. The models were validated on comparable groups born in 2000–2001 with all Receiver Operating Characteristic curve statistics >0.80.

Conclusion: The association of CLD with reduced fetal growth is biologically plausible and may be causal, as it has been demonstrated in other populations. The relationship is less clear for ROP, where historically populations have been based on BW.

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GENDER-RELATED DIFFERENCES IN PLASMA LEPTIN LEVELS AMONG OBESE CHILDREN WITH IMPAIRED GLUCOSE TOLERANCE OR TYPE 2 DIABETES

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Plasma leptin has been shown to correlate positively with many indices of obesity, as well as insulin resistance. Previous studies have reported that leptin levels are similar in diabetic and nondiabetic individuals. However, these studies were not performed in newly diagnosed diabetics, and other variables (such as gender) could have confounded the results.

Aim: The aim of the study was to explore the influence of the glucose tolerance status on plasma leptin in obese children, separately girls and boys. **Material and methods:** The study group consisted of 67 obese subjects (28 boys and 39 girls), aged 7–17 years. Among them 61 were glucose intolerant (IGT) and 6 had diabetes mellitus type 2, according to ADA criteria. The control group comprised 64 obese children (30 boys and 34 girls). Both groups were well matched for age, % overweight, and body mass index (BMI). Measurements of weight, height, waist and hip circumferences were performed with the using of standardized techniques. Fat mass was measured by bioimpedance method. Plasma insulin was measured using a commercialised enzyme immunoassay kit. Fasting plasma leptin was determined by RIA (Linco Research).

Results: Mean plasma leptin level was significantly lower in entire study group than in control group (17.0±7.5 ig/L vs. 21.0±7.4 ig/L; p<0.05). Leptin levels were, on average, 36% lower in girls with diabetes or IGT versus control girl (17.7±6.5 ig/L vs. 23.1±7.7 ig/L; p<0.001). No such between-group difference was observed in boys. In a multiple regression model adjusting for age and BMI in the female subgroup, plasma insulin and glucose concentrations 2-h after glucose load were the best predictors of fasting plasma leptin (r=0.38; p<0.05 and r=0.60; p<0.001, respectively).

Conclusion: Leptin synthesis by adipose tissue is more susceptible to regulation by insulin and glucose in girls than in boys. Lower plasma leptin levels in obese girls with IGT or type 2 diabetes than in control girls suggest that hyperglycemia may interfere with the stimulatory effect of insulin on leptin synthesis.

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ABNORMAL ORAL MUCOSAL LIGHT REFLECTANCE IN BRONCHOPULMONARY DYSPLASIA

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Background: Bronchopulmonary dysplasia(BPD)remains an important cause of mortality and morbidity in preterm infants. A disordered vascular development and a decreased production of angiogenic factors in BPD have been recently reported. Extracellular matrix (ECM) is known to play an important role on angiogenesis and blood vessel geometry and changes in ECM components have been previously reported in experimental models and patients with BPD. In the present study, we tested the hypothesis of abnormal reflectance of the oral mucosa in BPD.

Methods: Fifteen preterm infants with BPD(M:9,F:6; gestational age:27.5±2.0 wk, birth weight:850±125 gr) and 15 gender and gestational age-matched control infants without BPD (M:9, F:6; gestational age: 27.6±2.6 wk, birth weight: 865±135 gr) were examined. Mean blood concentrations of major chromophores, including hemoglobin and bilirubin (P= 0.95) and total bilirubin (P= 0.88) were comparable between the groups. Reflectance was measured on high-resolution photographs of the lower lower gingival and vestibular oral mucosa, using an imaging spectrophotometer. Spatially averaged spectra were used in order to estimate the oral mucosal color in the 400–700 nm wavelength electromagnetic spectral range. Derived spectral data were reproducible [intra- and inter-observer coefficients of variation (mean±SD),1.46±0.89% and 3.72±1.75%, respectively], and qualitatively comparable (±2%shift) to those obtained by direct measurements (absolute spectral error~0.4). Reflectance values from 50–100 different artifact-free and vessel-free areas were measured, and mean values were used for data analysis. The predictive accuracy of oral spectrophotometry was calculated using receiver operating characteristic curve analysis.

Results:BPD patients showed significantly lower light reflectance values in the red (610–700 nm; t values range:4.552–6.775, df=28,P<0.0001), with higher values in the violet (400nm, P=.0056;430nm, P=.014), and blue-green (480–500 nm, P≤.024) sections of the spectrum. A low reflectance value in the 640–700 nm wavelengths interval was found to identify BPD patients with 100% sensitivity and 100% specificity (640nm: cutoff≤44.91%;650nm:≤ 45.64%;660nm:≤46.56%; 670nm:≤47.14%;680nm:≤47.56%;690nm:≤ 48.95%;700nm:≤50.81%).

Conclusion: These findings indicate the presence of previously unrecognised, early abnormalities of the average optical properties of the oral mucosa in BPD infants.