of T1D were examined over time, between areas of differing socioeconomic status, and in urban and rural Canterbury. Second, cluster analysis using the spatial scan statistic was employed to test for spatial-temporal clustering of T1D within the Canterbury region. Finally, Poisson and zero-inflated Poisson regression analyses were utilised to investigate the association between T1D and various measures of population mixing at the area level.

Standardised incidence ratios revealed that childhood T1D was higher in the more affluent CAUs in Canterbury, and in areas classed as satellite urban communities. Geographical patterns in incidence were evident and a number of significant spatial-temporal clusters of the disease were noted. Regression analyses revealed significantly higher T1D incidence rate ratios in CAUs which had increased the most in population mixing for three out of four of the analysis periods (1987-1992, 1993-1998 and 1999-2004). Supporting evidence for this relationship was especially strong in the most recent period (1999-2004) where T1D incidence was positively associated with three different population mixing measures: change in the percentage of total migrants, change in the percentage of child migrants and change in the one year mobility percentage. It is postulated that where population mixing is low in early life, children miss out on important immune system stimulation from common infectious exposure. Subsequent increases in population mixing which introduce new infections to the area could trigger the onset of T1D in genetically susceptible individuals.

This study is the first to consider the role of population mixing in the aetiology of type 1 diabetes in New Zealand. Study limitations mean that no causal relationships can be proved, but the associations found highlight the need to investigate the role of population mixing and infections in the pathogenesis of T1D further.

CD4-3

Vitamin D deficiency in the young population with Type 1 diabetes: a case-control study

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Background: To the best of our knowledge, there are no population-based studies that have examined the association between Vitamin D and Type 1 diabetes and the associated environmental risk factors in young children in Qatar.

Aim: The aim of this study was to examine the association between vitamin D and Type 1 diabetes mellitus, and then to study the difference in level of vitamin D in Type 1 diabetes and control subjects, and determine the associated environmental risk factors in the young Qatari population.

Design: Matched case-control study.

Subjects: Qatari nationals male and female aged below 16 years. The study subjects including 150 cases and 150 controls were matched by age and sex. The survey was conducted over the period from August to November 2007.

Methods: Face-to-face interviews were based on a questionnaire that included variables such as socio-demographic information, assessment of non dietary covariates, assessment of dietary intake, vitamin D intake, type of feeding, clinical manifestations and laboratory investigations. The participant's health status was assessed by medical conditions, family history, body mass index, past or present clinical manifestations, vitamin D level, calcium, alkaline phosphatase, phosphorus, HbA1c, parathyroid hormone, magnesium and creatinine analyses.

Statistical analysis: Student-t test and the nonparametric Mann-Whitney test were used to ascertain the significance of differences between mean values of two continuous variables. Chi-square analysis was performed to test for differences in proportions of categorical variables between two or more groups. In 2x2 tables, the Fisher's exact test (two-tailed) replaced the chi-square test if the assumptions underlying chi-square violated, namely in case of small sample size and where the expected frequency was <5 in any of the cells. A P value <0.05 was considered as the cut-off value for significance.

Results: The study revealed that vitamin D deficiency was considerably higher in children with Type 1 diabetes (66.0%) compared to controls (58.7%). There was a significant difference found in the mean value of vitamin D between children with Type 1 diabetes and children without Type 1 diabetes (p=0.027). There were statistically significant differences between children with Type 1 diabetes and control subjects with respect to mean age and occupation of the parents ($p<0.01$). Family history of vitamin D deficiency was considerably higher among children with Type 1 diabetes (59.3%) with a significant difference compared to controls (p=0.001). Vitamin D supplementation with breast milk was very poor in children with Type 1 diabetes (41.3%) compared to controls (43.2%). The majority of the studied subjects were breast fed children (96.0% of cases and 97.8% of controls).

Conclusion: The present study revealed that vitamin D deficiency was higher in children with Type 1 diabetes compared to controls. Moreover, vitamin D deficiency was common in the Qatari young population. Vitamin D intake was very poor in children and indicates that supplementing infants with vitamin D might be a safe and effective strategy for reducing the risk of Type 1 diabetes.

CD4-4

Exendin-4 treatment expands graft β-cell mass in diabetic recipients with a marginal number of fresh islets

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Background: It has shown that transplantation of islets precultured with exendin-4 increases the reversal rate of hyperglycaemia in rodents. However, post-transplant exendin-4 treatment did not improve glucose homeostasis in diabetic mice syngeneically transplanted with a large number of freshly isolated islets. The aim of this study was to test if exendin-4 is beneficial for hyperglycemic transplant recipients with a marginal number of fresh islets.

Methods: We syngeneically transplanted 150 C57BL/6 mouse islets under the kidney capsule of inbred streptozotocin-diabetic mice, and then treated the recipients with and without exendin-4 for 6 weeks. After transplantation, blood glucose, body weight and intraperitoneal glucose tolerance test were measured. At 6 weeks, the grafts were removed to determine β-cell mass.

Results: Blood glucose levels in both groups decreased progressively after transplantation, with the exendin-4-treated group having lower blood glucose than controls. By 6 weeks, euglycemia was achieved in 16/16 (100%) of mice treated with exendin-4 vs. 6/13 (46%) of controls (p=0.001). Normoglycemia was observed at 12±8 days in the exendin-4-treated group and at >30±14 days in controls (p=0.001) Blood glucose at 6 weeks was 122±5 and 186±19 mg/dl in the exendin-4-treated group and con-

trols, respectively (p=0.008). Additionally, the exendin-4 treated group had better glucose tolerance than controls at 2, 4 and 6 weeks ($p<0.01$). However, both groups exhibited increased body weight over time, and weight changes did not significantly differ between the two groups throughout the study period. At 6 weeks, body weight was 24.9±1.0 and 25.1±1.6 g (p=0.621), and weight gain was 3.5±1.7 and 3.2±1.7 g (p=0.673) in the exendin-4-treated group and controls, respectively. At 6 weeks after transplantation, grafts in the exendin-4-treated group were more prominent than those of controls. Graft immunohistochemistry revealed a larger number of insulin-stained cells in the exendin-4-treated group than in controls. The exendin-4-treated group had twice the β-cell mass of the graft than controls (0.8±0.05 vs. 0.13±0.01 mg, p=0.034).

Conclusions: Our results indicate post-transplant exendin-4 treatment expands transplanted β-cell mass and improves transplantation outcome in diabetic recipients with a marginal number of fresh islets.

CD5-1

Serum extra domain B containing fibronectin (EDB FN) – a biomarker for proliferative diabetic retinopathy

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Introduction: Diabetic eye diseases are one of the leading causes of blindness in both developed and developing countries. Diabetic microangiopathy, one of the common causes for visual impairment, is characterized by increased extra cellular matrix protein production. Fibronectin, a predominant extra cellular matrix protein, plays an important role in angiogenesis and cell proliferation. We have demonstrated previously increased production of a splice variant of fibronectin, i.e., extra domain B containing fibronectin (EDB FN), in diabetic retinopathy and that this variant may provide outside in-signaling and VEGF up regulation leading to angiogenesis and cell proliferation.

Aim: The aim of this study was to investigate whether EDB FN can be used as a biomarker for proliferative diabetic retinopathy.

Methods: We collected serum and vitreous samples from 16 patients with proliferative diabetic retinopathy (age range 30-70 yrs). We also collected serum and vitreous samples from 6 non-diabetic patients undergoing vitrectomy for other indications (age range 62-87 years). Serums from 8 healthy controls were also collected to compare the serum EDB FN levels. EDB FN protein levels were analyzed using an ELISA developed in our laboratory. mRNA analysis of vitreous samples was carried out using real time RT-PCR analysis.

Results: Diabetic patients with proliferative retinopathy showed a 2-fold increase in serum EDB FN levels compared to non-diabetic retinopathy subjects. Both diabetic and non-diabetic retinopathy patients have significantly higher EDB FN in the serum compared to normal subjects (mean ± std error in proliferative diabetic retinopathy - 8.48±1.6μg/ml, in non-diabetic proliferative retinopathy - 3.82±0.85μg/ml, normal subjects - 0.077±0.033μg/ml. In the vitreous, EDB FN mRNA levels showed a 33% increase in patients with diabetic retinopathy. We further showed a 42% increase in vitreal ET-1 mRNA expression and a 140% increase in TGF-β transcript. EDB FN levels in the vitreous correlated with EDB mRNA and TGF-β mRNA in the vitreous.

Conclusion: Data from this study indicates that diabetic microangiopathy may result in increased EDB FN, possibly via TGFβ1 and ET-1. EDB FN may be potentially useful as a screening tool for diabetic microangiopathy.

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CD5-2

Autonomic neuropathy and hypertension in Type 1 and Type 2 diabetes mellitus: is there a relationship?

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Background and aims: Cardiovascular autonomic neuropathy carries a five-fold risk for mortality in diabetic patients, but the factors leading to increased mortality have not been clarified entirely up to now. The aim of our study was to evaluate a possible connection between autonomic neuropathy (AN) and 24-hour blood pressure profile in patients with Type 1 and Type 2 diabetes mellitus.

Materials and methods: The five standard cardiovascular reflex tests were used to assess autonomic function in 102 patients with diabetes who had no history of hypertension. We examined 32 patients with Type 1 diabetes (mean age: 37.8±12.7 years), 70 normoalbuminuric patients with Type-2 diabetes (mean age: 52.3±7.6 years) and 29 healthy control subjects (mean age: 51.8±9.5 years). The severity of autonomic neuropathy was characterized by an autonomic score. Ambulatory 24-hour blood pressure monitoring (ABPM) was performed by a MEDITECH ABPM 04 device. Among the ABPM parameters we evaluated the blood pressure load (%-time when day-time blood pressure was above 140/90 mmHg and night-time blood pressure was above 120/80 mmHg) and the hyperbaric impact values (the area under the blood pressure curve exceeding 140/90 mmHg during day-time and 120/80 mmHg during night-time).

Results: There was a significant correlation between the severity of autonomic neuropathy and the blood pressure load (systolic: $p<0.001$; diastolic: $p<0.01$), the hyperbaric impact values (systolic: $p<0.01$; diastolic: $p<0.05$) and microalbuminuria ($p<0.001$) in patients with Type 1 diabetes. Autonomic neuropathy as well as microalbuminuria were independently associated with hypertension among patients with Type 1 diabetes. Among patients with Type 2 diabetes, the severity of AN correlated positively with 24-hour mean blood pressure, the blood pressure load (systolic: both $p<0.0001$; diastolic: both $p<0.01$), and also with systolic ($p<0.001$) and diastolic ($p<0.05$) hyperbaric impact values. Analyzing the relationship between ABPM parameters and the five cardiovascular reflex tests separately, in patients with Type 1 diabetes, a significant negative correlation was found with two tests only, the 30/15 ratio and Valsalva ratio, both tests reflecting mainly parasympathetic function. Among patients with Type 2 diabetes, also two predominantly parasympathetic tests, the heart rate variation during deep breathing and the Valsalva ratio, were inversely related to the ABPM parameters. The Valsalva ratio correlated negatively with the 24-hour systolic blood pressure standard deviation ($p<0.01$). These relationships remained significant after adjustment for age, sex, body mass index and smoking.

Conclusion: Autonomic neuropathy is independently associated with elevated 24-hour ABPM parameters in patients with both Type 1 and Type-2 diabetes. Our data suggest that a relative sympathetic overactivity due to predominantly parasympathetic neuropathy might be responsible for the higher ABPM indices and also increased blood pressure variability in patients with Type 1 or Type 2 diabetes. ABPM is suggested to be performed for the early assessment of hypertension in diabetic patients with autonomic neuropathy and vice versa: autonomic function should be screened as part of the cardiovascular risk assessment in diabetic patients with hypertension. Higher 24-hour-long blood pressure values and increased blood pressure variability may both contribute to the poor prognosis associated with cardiovascular autonomic neuropathy in diabetic patients.