51ST SEMDSA Congress - Abstracts

Abstract Number: 1

The Mediating Effects Of Low-grade Systemic Inflammation And Neuropeptide Dysfunction In The Relationship Between Obesity And Cognition

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Background: Obesity, considered as a low-grade pro-inflammatory state, is associated with a reduction in the expression of genes coding for body fat-suppressing neuropeptides and with marked declines in cognitive performance. The purpose of this paper is to systematically review and summarise the extant literature (both human and animal studies) on the mediating effects of neuropeptide dysfunction and low-grade systemic inflammation in the relationship between weight excess and cognition.

Methods: PubMed, Web of Science and Scopus were searched for terms such as 'chronic inflammation', 'systemic inflammation', 'inflammatory responses', 'overweight', 'obesity', 'adiposity', 'body mass index', paired with 'cognition', 'cognitive function' or 'cognitive performance' and with 'neuropeptides', 'neuropeptide dysfunction' or 'neuronal signalling'. Articles were scanned to ensure that the associations between systemic inflammation, neuropeptide function and cognition were examined. Here we selected only articles that measured body composition, neuropeptide signalling and cognitive performance, with the primary aim of identifying the relationship between these three constructs.

Results: A prominent theme in the literature is that derangements in glucagon-like peptide-1 (GLP-1) precursor proglucagon (Gcg) and brain-derived neurotrophic factor (BDNF) have been linked with the formation of β-amyloid plaques within the brain, with neuronal tissue inflammation, and with increases in whole-body adiposity. Moreover, researchers demonstrate that weight gain is accompanied by insulin resistance and proliferations in localised brainstem and systemic inflammatory markers which have been shown to act negatively on cerebral metabolism. Cognitive deficits (especially in executive function) are therefore speculated to be corollaries of chronic inflammatory cascades as empirical reports consistently show us that weight excess coincides with reductions in (a) neurobehavioural governance over appetitive drive and (b) prepotent feeding responses.

Conclusion: Emerging data reveal that low-grade systemic inflammation coincides with decreases in anti-obesity peptides and with marked declines in cognitive performance. This review underscores the need for prospective and/or intervention studies to better understand the associations between systemic inflammation, neuronal signalling and executive brain function. Finally, the relationship between cognition and inflammation specific to dorsolateral prefrontal cortices respectively - must be examined.

Abstract Number: 2

The Analysis of Acute Precipitating Factors in the Patients with Diabetic Ketoacidosis

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Objective: The aim of the study was to demonstrate the acute predisposing factors in hospitalized patients in the intensive care unit with a diagnosis of diabetic ketoacidosis.

Material and Method: A total of 25 cases with diabetic ketoacidosis were admitted emergency department firstly (12-%48 type 1 Diabetes Mellitus, age 48.2 ± 26.4 years, male/woman: 12/13 (0.92)), who were hospitalized in intensive care unit of the internal medicine department were included in the study. Urgent medical treatments, intensive care and diagnostic protocols were also performed to all patients.

Results: The average diabetes duration of patients was 7.04 ± 8.8 years, average HbA1c level was 12.1 ± 2.6, the average fasting blood sugar level was 488± 146.9 mg/dL, in arterial blood gas analysis the average Ph was 7.20± 0.15, and the average HC03 was 10.9 ± 6,6 mEg/L. Acute precipitating factors were found in 52% of cases, when it was analyzed in terms of acute precipitating factors. Of all the factors, 46% caused by infection, 38% irregular drug use and the rest of 26% caused by other reasons (nutrition disorder, insulin pump corruption, operation, etc.)

Conclusion: Diabetic ketoacidosis is first of the immediate complications which is threatening life. The presence of acute precipitating factors is mentioned in a significant proportion of all the cases. In our study, we found that infections are the most common reason of acute precipitating factors. We consider that preventing of the precipitating factors is significant in terms of preventing of the emergence of this serious complication.

Abstract Number: 3

Anorexia Nervosa with Fatal Hypoglycemic Coma

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Introduction: Anorexia nervosa (AN) is a difficult to treat psychosomatic disease that may present with a variety of serious complications but hypoglycemic coma is an unusual complication of AN.

Case report: A 32-year-old woman with a 4-year history of AN was admitted because of unconsciousness. She was in a deep coma with a Glasgow Coma Score of 4. The electrocardiogram showed sinus rhythm and her pulse rate was 112/minutes and her blood pressure was 70/34 mmHg. Laboratory data revealed marked hypoglycemia (10 mg/dL) and hyponatremia (117 mmol/L), moderate elevation of transaminase (AST 160 u/L, ALT 137 u/L) levels. Prothrombin time was prolonged with 20 second and serum international normalized ratio (INR) was 1.69. Her full blood count showed leukopenia

(2890/mm3) and moderate thrombocytopenia (88.300/mm3). Insulin, C peptide, FSH, LH, prolactin and free T3 levels were suppressed that the hypoglycemia was related to severe malnutrition. Diffusion-weighted magnetic resonance imaging of the brain didn't show any abnormality except mild brain atrophy. Total parenteral nutrition, enteral tube feeding and electrolyte replacement therapy was started properly in the intensive care unit but no neurological response was observed and she died on the fifth day

Discussion: AN is associated with many medical complications such as cardiovascular problems, endocrine disorders, electrolyte and hematopoietic abnormalities, amenorrhea and osteoporosis. Although hypoglycemic coma is uncommon in AN, we should be careful of severe hypoglycemia especially when signs of liver damage are detected. The pathogenesis of hypoglycemia may be related to the depletion of liver glycogen, defective gluconeogenesis, failure of glucagon secretion and finally starvation-induced autophagy of the liver cells. Hypokalemia can be explained by the abuse of laxatives and diuretics. Hyponatremia is often due to excessive water intake but may also occur in chronic energy deprivation or diuretic misuse. Anemia, leukopenia and thrombocytopenia are all seen in severe AN. The (INR) level may be mildly elevated, due to liver damage and impaired synthesis of coagulation factors. Although hypoglycaemic coma frequently results in death, prompt treatment may result in full recovery. To prevent patients with AN from these mortal complications, they must be followed closely with multi-disciplinary approach.

Abstract Number: 4

Fasting Plasma Glucose with Waist Circumference In Middle Aged Women

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Objectives: The association between type 2 Diabetes Mellitus and Obesity is very close. Impaired Fasting Glucose (IFG) reflects an intermediate condition between normality and diabetes. Obesity is more common in middle aged women. Waist Circumference (WC) indicates both general as well as central obesity & both are prone for development of type 2 D.M. Early detection of obesity may delay or prevent the onset of type 2 D.M. The aim of this is to study the correlation of Fasting plasma Glucose (FPG) levels with WC in middle aged women that includes pre and post-menopausal women.

Method: FPG levels and WC were estimated in 100 asymptomatic middle aged women with no family history of type 2 Diabetes Mellitus.(D.M.) in pre and postmenopausal women. The results were analyzed statistically using ANOVA test.

Result: In the entire subject population (n=100) difference in mean age and FPG levels are found statistically significant in postmenopausal groups but no statistically significant difference for WC was noted in pre and post-menopausal women Mean values or age, FPG levels & WC were found higher in postmenopausal women

Conclusion: Obesity is present in both postmenopausal and premenopausal group and all value are higher in postmenopausal women so preventive measure should start at early to prevent the diabetes in both groups. WC should use as an important parameter for obesity which is simple, self-monitored & easy to interpret for early diagnosis of obesity and prevention of obesity & diabetes.

Abstract Number: 5

Islet Cell Antibodies among Children and Adolescents with Type 1 Diabetes Mellitus In South Africa

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Background: Type 1 diabetes mellitus is associated with specific pancreatic autoantibodies that are used to characterize and classify diabetes. There is a paucity of information on the prevalence of these antibodies in children of African descent. Published information suggests that these children have a lower prevalence of antibodies. This study was undertaken to determine the prevalence of GAD and IA2 antibodies in a group of South African children with T1DM and to determine whether there are differences in prevalence between ethnic groups

Methods: A review of patients presenting to a single practice was undertaken. The study population was limited to subjects that were less than 18 years at diagnosis, had onset if diabetes on/after 1 January 2002 and not later than 31 December 2014 and had a clinical diagnosis of type 1 diabetes. GAD and IA2 antibodies were performed by commercial laboratories. Ethnicity was determined by the families and the investigator.

Results: Of 392 subjects seen with a diagnosis of diabetes mellitus, 634 fulfilled entry criteria. The age at diagnosis ranged from 0.6 to 17 years (median=8.2 years). Of these, 91 (25%) were considered to be black Africa, 100 (27.5%) Asian, 162 (44.5%) white and 11 (3.0%) of mixed ethnicity (coloured). There was no data of Ab status in 68 of these subjects. Of the remainder, 33 (11.1%) were negative for 1 or both antibodies, 134 were positive for 1 Ab and 129 (43.6%) were positive for both antibodies. Thus, 263/296 (88.9%) had antibodies to 1 or both antibodies. There was no significant differences in prevalence of 1 or both antibodies among the different ethnic groups; 68/98 (87.2%) among black African children, 69/77 (89.6%) among Asian children, 118/132 (89.4%) among white children and 8/9 (88.9%) among coloured children. There was no difference when the study population was stratified by age at diagnosis or year of diagnosis.

Conclusion: The prevalence of Antibodies in children and adolescents with type 1 diabetes is similar to that described from developed countries. There was no difference in prevalence between difference ethnic groups, age at diagnosis or year of diagnosis.

Abstract Number : 6

Association Between Vitamin D Deficiency & Glycemic Control In Central Region - Saudi Arabia

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Background: Vitamin D is an essential micronutrient and have important role to human health.

Low level of vitamin D is one of the major problem around the world as well as diabetes mellitus.

Aim: Our main aim in this study to assess the association between low level of vitamin D and glycemic control .

Methods: This cross-sectional study revewing files of patients who have either vitamine D defeciency or suffeciency who performed hemoglobin A_{1C} fasting blood sugar, lipid profile, Ca, liver and renal functions and hemoglobin that done in Prince Sattam Bin Abdulaziz University Hospital at Al-Kharj city between Jan-1- 2015 & December-1- 2015.

Results: We identified 1200 patients with vitamin D deficiency insuffeciency, of those 200 patients (16.7%) were diabetic. More women had vitamin D deficiency and DM compared to males. HbA_{1C} ranged between (5.02 - 15.71) with mean of HbA1C for males was 7.16± 1.8 and for female was 6.98 ± 2.07 (P=0.54). Vitamin D levels ranged between (3.91 - 47.92) the mean of vitamin D for males was 20.54 ± 7.88 and for females was 20.08 ± 9.19 (P=0.7).

Conclusion: Vitamin D deficiency is frequent among diabetic patients. A significant inverse correlation was detected between vitamin D and HbA_{1C} . poor glycemic control leads to reduction in vitamine D level

Abstract Number: 7

Cardiac Tamponade due to Hypothyroidism: a Cluster of Cases.

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We report on three patients who were seen at our institution within a short period of 6 months, with a new diagnosis of severe primary hypothyroidism. Pericardial effusion was suspected on clinical and x-ray findings and confirmed with cardiac echocardiography in all cases. All patients had evidence of cardiac tamponade on echocardiographic criteria. Pericardiocentesis was performed in all cases and other causes for pericardial effusions were excluded. Although infrequently described in very large pericardial effusions and tamponade, hypothyroidism need to be considered in patients presenting as such.

Abstract Number: 8

Communication in Diabetes Management in South Africa: more than words

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Introduction: Communication between doctor and patient has always been regarded as an important aspect of the consultation and plays a particularly significant role especially in negotiating the complexity of diabetes. Medical education internationally and locally is embracing a competency-based framework which includes the role of communicator along with others such as a medical expert. Models of communication tend to be developed outside that of the local context and recent publications have begun to highlight the need for locally-adapted, culturally-relevant models.

Methodology: The aim of this study was to explore the relationships between doctors and patients in the context of diabetes in the multicultural context of KwaZulu-Natal with specific emphasis on the communication techniques and role of socio-cultural factors in communication. Two district hospitals were included (one urban, one rural) with a total of 24 routine doctor-patient consultations that were audio- and video-recorded. Ethnographic data as well as interviews with patients and doctors were undertaken to substantiate observed phenomena. A thematic analysis augmented by additional elements of conversational analysis techniques were used to substantiate meaning from the data.

Results: Both the structure and process of the consultation were seen to contribute to how the consultation was interpreted by doctors and patients. Initial opening and closing segments were key areas where the relationship was established and culturally appropriate communication, both verbally and non-verbally, could occur. The body of the consultation tended to deviate from traditional models in medical education but was expected as experienced clinicians developed their own styles. Most significantly, various process skills occurring during the consultation were seen to have been adapted from traditional communication models for use in the local socio-cultural context. The positive impact on interpersonal relationship in these instances was remarkable.

Conclusion: This research offers a theoretically sound and relatively unfamiliar methodology in clinical medicine which can enhance our understanding of the important role played by communication in the management of diabetes in South Africa. As medical education shifts towards a competency-based model and the role of communicator becomes more significant, imported communication models will certainly need to be adapted and scrutinised for local use.

Abstract Number: 9

Haplotypes Analysis of Adipoq Snps Among Saudi Arabian Women

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[1]University of Tabuk

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder in females and is associated with altered metabolic processes, in particular insulin resistance. Several studies have shown that polymorphisms in the adiponectin gene might be associated with the risk of PCOS.

In the present study, we assessed the relationship of haplotypes tagging nine common single nucleotide polymorphisms (SNPs) in the adiponectin gene(- 11391 G/A, - 11377 C/G, - 4041 A/C, - 3964 A/G, 45 T/G, 276 G/T, 349 A/G, 712 A/G, 1233 T/C) with the risk of PCOS. A case control study was conducted in total of 162 PCOS cases and 162 control subjects of Saudi Arabian women (Tabuk region) using high throughput genotyping methods.

Results: Overall, we didn't observe significant differences in genotype or allele frequencies for the nine SNPs. The analysis of different blocks haplotype based on the Linkage Disequilibrium (LD) given by haploview software coded major alleles as "1", while minor alleles were coded as "2". This analysis demonstrated that the frequency of the haplotype 21211 (rs2241766/ rs1501299/rs2241767/rs3774261/ rs17366743) is significantly high (P corrected= 0.009). This haplotype of susceptibility had been shown to increase the risk of PCOS (OR (IC 95%)=2.16 (1.22 - 3.82))

Moreover, our results reveal significant differences between the controls and cases on the frequency of (11211) haplotype (P corrected= 0.001) as protective haplotype against PCOS risk (OR (IC 95%)=0.24 (0.09 - 0.59)).

Conclusion: We can conclude that PCOS patients with the haplotype 21211 of adiponectin gene have higher susceptibility to the disease and those with haplotype 11211 have higher protection against the disease. However, there are not significant differences in the distribution of genotypes and alleles among PCOS patients and controls in Saudi Arabian women.

Abstract Number: 10

Prevalence of Chronic Kidney Disease and Associated Factors using Three Glomerular Filtration Rate Equations among patients with Type 2 Diabetes Mellitus at Muhimbili National Hospital, Tanzania.

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Background: Chronic kidney disease (CKD) classification is one of the most important statistical tools and clinical significance when evaluating the performance of an equation on an individual level. It is related to the percentage of patients correctly classified by eGFR into the different CKD stages in comparison with the confirmatory test of mGFR. An equation with high correct CKD classification would decrease the need for determining the mGFR and provide great confidence to the clinicians to implement an appropriate plan of action according to the individual's eGFR result.

The study was conducted to determine the prevalence of chronic kidney disease (CKD) defined as GFR less than 60 for each of the three equations (Cockcroft-Gault, MDRD and CKD-EPI); also determine factors associated with CKD for each equation.

Method: A cross-sectional study that consecutively enrolled 216 diabetic patients with type 2 diabetes mellitus was conducted between May 2009 and February 2010. Data were entered using STATA package with computed variables including mean and standard deviation. Differences between and within groups was assessed by test of ANOVA and post-hoc tests whenever necessary. A confidence interval of 95% was used to determine factors associated with CKD for each of three equations; with p-value of 0.05 or less was considered statistically significant.

Results: The prevalence of CKD (e GFR<60) was 53/216(24.5%) for Cockcroft-Gault (CG) formula, 22/216(10.2%) for MDRD equation and 30/216 (13.9%) for CKDEPI equation. Age, gender, body mass index, duration of diabetes mellitus and glycemic control were not associated with CKD in any of the three estimation equations. Proteinuria was significantly associated with e GFR of less than 60 for both MDRD and CKDEPI equation with p-values of 0.00 and 0.00 respectively.

Conclusion: Cockcroft Gault formula is widely used for estimation of GFR in settings where measured GFR is not possible. Results of this study suggest that; - CG equation has to be used with caution in diabetic patients as it may overestimate CKD prevalence. There is a need to conduct local studies to help clinicians determine the most precise equation in local setting.

Abstract Number: 11

Association of Tcf7l2 Gene Haplotypes with an Elevated Risk of PCOS in Saudi Arabian Women

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Background: Polycystic ovary syndrome (PCOS) is a common and heterogeneous endocrine disorder in females at reproductive age with well-established metabolic and hormonal abnormalities such as glucose homoeostasis and insulin resistance. Several reports have presented TCF7L2 (Transcription factor 7-like 2)as plausible gene associated with the risk of PCOS.

In the present study, we assessed the relationship of haplotypes tagging nine common single nucleotide polymorphisms (SNPs) in the TCF7L2 gene(rs7901695, rs4506565, rs7903146, rs12243326, rs7895340, rs11196205, rs12255372, rs11196229, rs11196236) with the risk of PCOS. A case control study was conducted in total of 162 PCOS cases and 162 control subjects of Saudi Arabian women (Tabuk region)

Results: Overall, although the minor allele frequency of the rs11196229 was in borderline of significance (P=0.06) we didn't observe significant differences in genotype or allele frequencies for the nine SNPs.

A statistically correlation clearly revealed that the homozygous genotype TT of rs4506565 was higher in PCOS case when analyzed under recessive genetic model compared to control subjects (P=0.022) with an increased risk to the disease which remain high even after adjustment for age and BMI (aOR= 2.28 (1.10-4.72)).

The analysis of different haplotype blocks based on the Linkage Disequilibrium (LD) given by haploview software demonstrated respectively that the frequency of the haplotypes T- *G*- *C*-G-G-T and T-A-G-G- *A*-T (rs12243326/ rs7895340/rs11196205/rs12255372/ rs11196229/rs11196236) were significantly high in PCOS women compared to control subjects (P corrected= 0.009 and 0.045). These haplotypes of susceptibility have been shown to increase the risk of PCOS as follow (OR=2.16 (1.22 - 3.82 (and OR=4.68 (1.04-21.06).

Conclusion: We can conclude that genetic polymorphisms of TCF7L2 are associated with increased risk of PCOS in Saudi Arabian women. PCOS patients with the haplotype T- *G*- *C*-G-G-T and T-A-G-G- *A*-T of TCF7L2 gene have higher susceptibility to the disease.

Abstract Number: 12

Obesity-associated Type 2 Diabetes Can Have Detrimental Effects On The Ability Of Mesenchymal Stem Cells (MSCS) To Aid Tissue Regeneration

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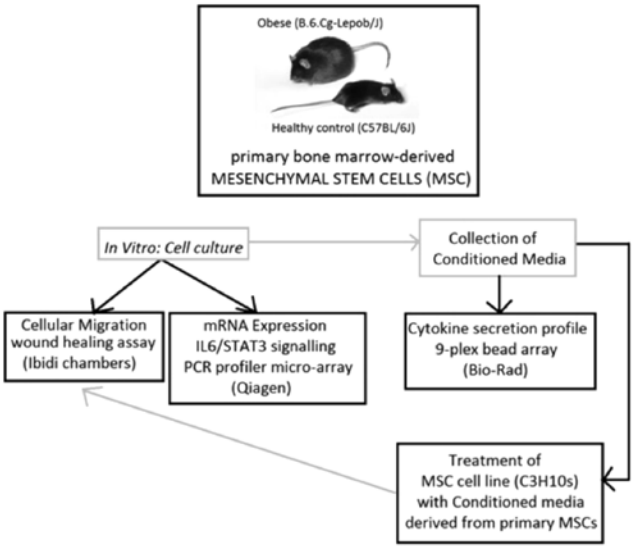
Background: The multi-functional properties of mesenchymal stem cells (MSCs) play a key role in wound healing and tissue regeneration. However, the implications of obesity-associated type 2 diabetes on MSC functionality is less well defined.

This study therefore aimed to investigate the a) in vitro migratory capacity b) cytokine secretion profile and c) mRNA expression profile



of MSCs derived from either healthy control (C57BL/6J) (control MSCs) or pre-diabetic obese (B.6.Cg-Lepob/J) mice (ob/ob MSCs). It furthermore aimed to elucidate the effects of conditioned media collected from the control MSCs or ob/ob MSCs on the migratory capacity of an immortalized MSC cell line (C3H10s).

Methods:

Results: Our results show that ob/ob MSCs had reduced viability and an impaired migration rate in vitro compared to control MSCs. The conditioned media collected from these impaired ob/ob MSCs did however promote the migration of immortalized MSCs (C3H10s), suggesting that ob/ob MSCs release specific chemo attractants. Analysis of the cytokine secretion and mRNA expression profile furthermore demonstrated that interleukin-6 (IL-6) deficiency was linked to the dysregulation of STAT3 signalling in ob/ob MSCs.

Conclusion: Long term exposure to a chronic inflammatory and hyperglycaemic micro-environment in vivo can affect MSC functionality through dysregulation of the IL-6/STAT3 signalling pathway.

Abstract Number: 13

Pseudohypoparathyroidism with Presumed Epileptic Seizures.

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Objective: Demonstration of misdiagnosis in a patient with Pseudohypoparathyroidism

Background: Pseudohypoparathyroidism (PHP) is a rare condition characterised by hypocalcaemia, hyperphosphataemia and elevated parathyroid hormone levels. It exists in several subtypes based on the presence or absence of PTH resistance and features of Albright Hereditary Osteodystrophy (AHO), which include short stature, rounded face, central obesity, subcutaneous ossification and mild mental retardation.

The patient is a 33 yr. female who first presented at age 11 with recurrent seizures and was treated for epilepsy for two years. Apart from short stature and overweight, the patient had no obvious AHO features of AHO. There was no cognitive impairment.

Results: and Discussion: Biochemical pattern revealed decreased calcium and elevation of both phosphate and PTH. Vitamin D levels and renal function were normal. The coexistence of hypocalcaemia, elevated PTH associated with hyperphosphataemia made the diagnosis of PHP a possibility. No other endocrine abnormalities such as thyroid or gonadotropin resistance were reported. The pattern is in keeping with Pseudohypoparathyroidism subtype 1b. As there was no evidence of previous genetic workup, a DNA sample was subsequently drawn for genetic analysis, and is currently being processed.

The patient was followed up at the endocrine clinic and managed on calcium supplements and active vitamin D, which led to the improvement of PTH levels although these levels remained persistently high. At the age of 29 years the patient complained of infertility associated with an abnormal menstrual cycle. Biochemical workup indicated unremarkable FSH, LH and Prolactin levels. An MRI scan was booked for the patient, however patient tested positive for pregnancy prior to the scan. She was then managed as a high risk pregnancy and had uneventful delivery.

Conclusion: Pseudohypoparathyroidism is a rare condition, the presentation of which can be confused with a neurological disorder particularly in the absence of typical features of AHO.

Abstract Number: 14

State Of The Art Work Up Of Pituitary Cushing's Disease In SA.

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A 50 year old obese woman was referred for evaluation of possible Cushing's syndrome. She had been diagnosed with diabetes mellitus and hypertension in the preceding year and had noted recent unexplained weight gain of 12kg in the preceding 3 months. She had no history of alcohol abuse or depression and took no medication apart from anti-hypertensives and oral diabetic drugs. On examination she had a BMI of 43kg/m ^{2}, thin skin, violaceous striae and facial plethora.

She failed to suppress on an overnight 1mg betamethasone suppression test (444 nmol/L). Twenty-four hour urine cortisol was elevated (1356 nmol/24hrs) and she also failed to suppress on prolonged low dose betamethasone testing. Adrenocorticotrophic hormone (ACTH) was 9.3 pmol/L (normal 1.1-10.2 pmol/L).

An overnight high dose betamethasone suppression test was performed, which demonstrated 89% suppression of serum cortisol, virtually diagnostic of pituitary Cushing's disease. Magnetic resonance imaging (MRI) showed 2 vaguely defined pituitary hypodensities (right and left). Dynamic contrast MRI of the pituitary revealed a 5mm hypodensity on the right, suggesting microadenoma .

Inferior petrosal sinus (IPS) sampling was performed, to confirm pituitary origin of ACTH. Desmopressin stimulation of ACTH during

the procedure has recently been shown to enhance diagnostic accuracy and was performed in this case. We also did simultaneous sampling of prolactin, which has been shown to enhance diagnostic accuracy of the test by identifying technical factors that may suggest false negative results.

Our patient had a high baseline central to peripheral (C:P) ACTH ratio of 12:1 on the right, which doubled with desmopressin stimulation. The prolactin C:P ratio of 5:1 confirmed accurate sampling from the right IPS. The ACTH level sampled from the left IPS catheter was not different to peripheral blood level, but neither was the prolactin C:P ratio on the left, confirming that sampling from the left catheter was not representative of pituitary values.

At pituitary surgery, a lesion was identified on the right and removed. Histology & immunohistochemistry confirmed the specimen to be a corticotroph microadenoma.

This case illustrates latest developments in the diagnosis & localisation of ACTH-dependent Cushing's, which is available in certain specialised centres in RSA

Abstract Number: 15

Coffee Or Tea: Could Your Daily "cuppa" Be Beneficial For Weight-loss?

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Background: Currently available weight-loss therapies are plagued by low efficacy and unacceptable side-effects. Aspalathin, a flavonoid uniquely found in caffeine-free Rooibos tea, has been found to be anti-hyperglycaemic in diabetic animal models, but its role in modulating adiposity in normoglycaemic individuals has not been investigated. Caffeine is a constituent of black and green teas and coffee, and is also commonly used at high doses in purported weight-loss supplements, but with a risk of adverse cardiac side-effects. However, caffeine is structurally and functionally similar to isobutyl-methylxanthine (IBMX), the non-selective phosphodiesterase inhibitor and adenosine receptor antagonist commonly used in the cocktail to stimulate adipogenesis in cultured pre-adipocytes. This study aimed to investigate the modulation of *in vitro* adipogenesis in cultured subcutaneous and visceral adipose-derived stromal cells (ADSCs) by aspalathin and caffeine, in order to determine whether these compounds may be able to regulate body weight through direct effects on adipocytes, possibly in an adipose depot-specific fashion.

Methods: Cultured naïve ADSCs, isolated from subcutaneous and visceral adipose tissue samples from adult male Wistar rats, were differentiated into mature adipocytes using adipogenic induction media, consisting of standard growth media supplemented with IBMX, insulin, indomethacin and dexamethasone (AM-IIDX). In parallel, cells were treated with AM supplemented with 50µM aspalathin (AM-IIDX-Asp) or AM with 0.3 mM caffeine (AM-IIDX-Caf), or with AM without IBMX (AM-IID) in the absence or presence of 0.3 mM caffeine (AM-IID-Caf). After 12 days, intracellular lipid accumulation was quantified using Oil Red O staining and image analysis.

Results: Omission of IBMX from AM strongly inhibited lipid accumulation. Caffeine, despite being structurally similar to IBMX, could not replace the adipogenic properties of IBMX, and also reduced AM-induced lipid accumulation in the presence of IBMX by 50-70%. Aspalathin resulted in approximately 30% reduction in lipid accumulation against the background of AM. Neither compounds appeared to have overt depot-specific effects.

Discussion: Both aspalathin and caffeine inhibited *in vitro* adipogenesis, although the concentration of aspalathin required was far higher than that found in a standard Rooibos tea extract. However, aspalathin mastill be considered for further development as a synthetic caffeine-free supplement supporting weight-loss therapy.

Abstract Number: 16

Glucocorticoids Reduce The Cell Viability Of Mscs Derived From The Proximal Femur But Not From Bone Marrow Of Rats

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Glucocorticoid induced osteoporosis (GIO) is associated with reduced numbers of osteoblast progenitor cells, namely mesenchymal stem cells (MSC) which results in lower bone formation and bone mineral density. We have previously found that vanadate, a non-specific protein tyrosine phosphatase inhibitor, prevents GIO in rats, but it is unclear whether vanadate directly prevented the glucocorticoid-induced reduction in osteoblast progenitor cells. It has been observed that the pathology of GIO does not manifest uniformly throughout the femur, but predominantly affects the proximal region of the femur. We therefore considered that glucocorticoids may negatively affect MSC populations in the proximal femur more rapidly than those in bone marrow, which has traditionally been assumed to be the source of osteoblastic progenitors. Consequently, we investigated the effects of glucocorticoids and vanadate on the viability of cultured MSCs from bone marrow (bmMSCs) and proximal femur (pfMSCs).

MSCs were isolated from the marrow cavity of the diaphysis and the hard tissue of the proximal region of femora excised from adult male Wistar rats. The cell surface marker profile of the cultured MSCs was characterized by flow cytometry, and multi-potentiality was assessed by osteoblastic and adipocytic differentiation. Cell density, cell viability and apoptosis were quantified by crystal violet staining, the MTT mitochondrial activity assay and the Annexin V-PE Apoptosis Detection Kit respectively.

pfMSCs exhibited a similar mesenchymal cell surface marker (CD90, CD106) profile to that of bmMSCs, with low expression of the hemopoietic marker CD45. However, the bmMSCs rapidly differentiated within 7 days to osteoblasts but required 21 days for adipocytic differentiation, while pfMSCs rapidly differentiated into adipocytes by day 7 but required 21 days for osteoblastogenesis. Dexamethasone treatment for 7 days did not affect the viability of bmMSCs, while in pfMSCs, dexamethasone caused a reduction in cell viability ($p = 0.021$) and an increase in early apoptosis ($p = 0.027$). However, these negative effects of glucocorticoids on pfMSCs could not be prevented by co-treatment with vanadate.

During GIO, glucocorticoids may directly cause apoptosis of osteoblastic precursors at the proximal region of the femur but it is unlikely that vanadate prevents GIO through restoring of pfMSC numbers.

Abstract Number: 17

An Extremely Rare Cause Of Cushing Syndrome In Childhood

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Cushing Syndrome is rare in childhood. Between 2-5 new cases per million people are diagnosed each year, of which only 10% are reported to occur within the paediatric population. There is a female predominance but a male predominance has been reported in infants. Classical clinical indicators of Cushing syndrome in childhood include central weight gain and growth failure. Other clinical manifestations include facial flushing, hypertension, hirsutism, pubertal delay, acne, striae and bruising. Compulsive overachieving behaviour is seen in about 40% of children and adolescents.

Causes of Cushing syndrome include the exogenous administration of glucocorticoids and ACTH, pituitary adenomas (Cushing disease), adrenal tumours and very rarely ectopic ACTH production. It has been reported that ectopic ACTH production accounts for less than 1% of causes of Cushing Syndrome in adolescents. Tumours that secrete ACTH include small cell carcinoma of the lung, carcinoid tumours of the bronchus, thymus or pancreas, pheochromocytomas and neuroendocrine tumours, particularly that of the pancreas and gut.

We report a rare case of a 3 year old child who presented with Cushings Syndrome secondary to ectopic ACTH production from a pancreatoblastoma.

Pancreatoblastoma, a pancreatic neuroendocrine tumour known to produce ACTH is a very rare malignant tumour. It arises from multipotential stem cells and may bear resemblance to other embryonic neoplasms such as nephroblastoma and hepatoblastoma. . These tumours usually occur in the first decade of life and there is a slight male predominance. An incidental mass is the most common form of presentation. The head and tail of the pancreas is the most common site of tumour occurrence while the liver is the most frequent site of metastatic disease. Complete surgical resection of the tumour is the treatment of choice. Chemotherapy maybe beneficial prior to surgery to reduce tumour size. Even though these tumours are curable, long-term surveillance for recurrence is mandatory.

The clinical presentation, management and outcome of this rare tumour in a 3 year old child will be presented in this paper.

Abstract Number: 18

Prevalence And Determinants Of Metabolic Syndrome Among Adults Attending General Medical Outpatient Clinics In Botswana.

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Background: Developing countries including Botswana are facing rising prevalence of obesity and related cardio-metabolic complications. We aimed to assess the prevalence and identify determinants of metabolic syndrome among the general outpatients' attendances in Botswana.

Methods: A cross -sectional study was conducted from August to October 2014 involving outpatients aged 20 years without diagnosis of diabetes mellitus. A pre-coded questionnaire was used to collect data on participants' socio-demographics, risk factors, and anthropometric indices. Fasting blood samples were drawn and analyzed for glucose and lipid profile. Metabolic syndrome was assessed using National Cholesterols Education Program _ Adult treatment panel III criteria.

Results: In total, 291 participants were analyzed, 215(74.2%) were females. The mean age of the total population was 50.1(±11) years. The overall prevalence of metabolic syndrome was 79 (27.1 %), with no significant difference between the gender (female = 29.6 %, Men= 20% P-Value =0.11). A triad of central obesity, Low HDL-Cholesterols and elevated blood pressures constituted the largest proportions cases of metabolic syndrome, 38(13.1%), followed by a combination of low HDL, elevated Triglycerides, central obesity and elevated blood pressure, 17(5.8%). Independent determinants of Metabolic syndrome were antihypertensive use and increased waist circumference.

Conclusion: Metabolic syndrome is highly prevalent in the general medical outpatients' clinics. Proactive approaches to screen and manage cases targeting its most important predictors are needed.

Abstract Number: 19

The Durban Diabetes Study: Prevalence Of Diabetes And The Utility Of Hba1c For Detection Of Diabetes In Urban South Africans.

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Introduction: Glycated haemoglobin (HbA_{1c}) is recommended as an additional tool to glucose-based measures (fasting plasma glucose [FPG], 2-hr plasma glucose [2PG] during OGTT) for the diagnosis of diabetes; however, its use in sub-Saharan African populations is

not established. We assessed the prevalence of diabetes and the detection of diabetes based on OGTT and HbA_{1c} in an urban black South African population.

Methods: We conducted a population-based cross-sectional survey using multistage cluster sampling of adults aged 18 years in the eThekwini municipality (Durban) in KwaZulu-Natal. All participants had a 75-g OGTT and HbA_{1c} measurements. The 1999 World Health Organization (WHO) diagnostic criteria for disorders of glycaemia were used for the PG results and the 2011 WHO criteria for diabetes for the HbA_{1c}. Receiver operating characteristic (ROC) analysis was undertaken in participants without known diabetes, to assess the overall diagnostic accuracy of HbA_{1c}, using OGTT as the reference, and to determine optimal HbA_{1c} cut-offs.

Results: Of 1300 individuals invited to join the study, 1204 participated (response rate 92.6%); this analysis includes 1190 subjects (851 women) on whom complete data was available. The age-standardised prevalence of diabetes was 12.9% based on OGTT, with a higher prevalence in women (14.0%) than in men (8.5%). Peak prevalence was in the oldest age-group (≥65 years) in women (39.3%) and in the 55-64-year age-group in men (29.0%). Among the 150 participants with diabetes, 24.7% were previously undiagnosed. The age-standardised prevalence of diabetes based on HbA_{1c} ≥6.5% was 13.1%. Using OGTT as the reference, an HbA_{1c} ≥6.5% detected diabetes with 70.3% sensitivity (95%CI: 52.7 - 87.8) and 98% specificity (95%CI: 97.9-99.4) (AUC 0.94 [95%CI 0.89-1.00]). The optimal HbA_{1c} cut-off for detection of diabetes was 6.0% (sensitivity 89.2%, [95% CI 78.6-99.8]; specificity 92.0%, [95% CI 90.3-93.7]).

Conclusion: We find that the prevalence of diabetes is high in urban black South Africans, particularly in women, and provide evidence for the utility of HbA_{1c} for detecting DM in this population. However, prospective studies are needed to establish optimal cutoffs for the use of HbA_{1c} as a diagnostic and screening tool in this and other SSA populations.

Abstract Number: 20

Intestinal Absorption And Metabolism Of Bush Tea Major Phenolic Compounds Exhibiting Anti-diabetic Activity

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Background: *Athrixia phylicoides*, popularly known as `bush tea`, is an indigenous aromatic shrub found in mountainous and grassland areas of eastern parts of Southern Africa. The plant is traditionally used for the treatment of several ailments, including hypertension and coughing. *A. phylicoides,* has been shown to contain abundant levels of phenolic acids and to display antidiabetic properties by improving glucose uptake when tested in muscle, liver and fat cells. There is limited knowledge available about the absorption and metabolism of the bioactive phenolic compounds of *A. phylicoides*, and thus, we aim to study the bioavailability and metabolism of these active compounds using Caco-2 monolayers.

Methods: HPLC-DAD analysis was used for phenolic profile characterization of the bioactive components of an aqueous *A. phylicoides* extract. Cell viability was determined at the highest soluble extract concentration. HPLC and LC MS was used to identify the constituents transported across the Caco-2 monolayer.

Results: *A. phylicoides* was not found to be toxic at the highest soluble concentration (5 mg/mL). HPLC-DAD and LC MS analysis identified protocatechuic acid, caffeic acid and p-coumaric acid as major phenolic acids that were transported across the Caco-2 cell monolayer, with Papp values of 5.93, 2.15 and 3.27 ($x10^{-7}$), respectively.

Conclusion: To our knowledge, this is the first report of bioavailability and absorptive potential of the three major phenolic acids present in *A. phylicoides* namely, protocatechuic acid, caffeic acid and p-coumaric acid with a relatively slow absorption rates and low bioavailability. These findings will be presented, together with mechanism(s) of transport of *A. phylicoides* phenolic compounds still under investigation and remains the subject of subsequent studies.

Abstract Number: 21

Flying Under The Radar- Adrenal Steroids In Androgen Excess

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Background: The biosynthesis of adrenal hormones in the androgen, mineralo-, and glucocorticoid pathways is well established. Recent advances in analytical technologies have, however, placed adrenal steroids under the spotlight. We reported that 11β-hydroxyandrostenedione (11OHA4) is a major adrenal androgen- one not previously included in the adrenal androgen pathway. We characterized its biosynthesis by cytochrome P450 11β-hydroxylase (CYP11B1) in androstenedione's (A4) conversion, and its downstream metabolism to steroids capable of activating the androgen receptor (Fig. 1).

Here 11β-hydroxysteroid dehydrogenase type 2 (11βHSD2) plays a pivotal role in activating 11OHA4 as well as 11β-hydroxytestosterone (11OHT). We hypothesized that other adrenal steroids would contribute to the steroid pool in hyperandrogenism and adrenal disorders, by metabolic pathways similar to that of 11OHA4.

Methods: We investigated the catalytic activity of CYP11B1 towards the C21 adrenal steroids and the downstream conversions catalyzed by 11βHSD2 and 5α-reductase (SRD5A). Circulating levels of adrenal steroids and their metabolites were confirmed by UPC ^{2}-MS/MS.

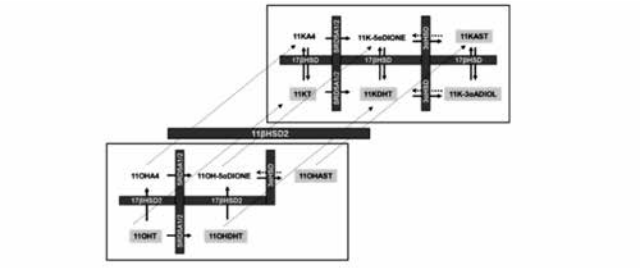

Figure 1: C11 hydroxy- and keto- C19 steroids metabolism in the 11OHA4-derived pathway. 11OHA4, 11β-hydroxyandrostenedione; 11OHT, 11β-hydroxytestosterone; 11KA4, 11-ketoandrostenedione; 11KT, 11-ketotestosterone; 11OH-5aDIONE, 11β-hydroxy-5α-androstenedione; 11K-5aDIONE, 11-keto-5α-androstenedione; 11KDHT, 11-ketodihydrotestosterone; 11OHDHT, 11β-hydroxy-dihydrotestosterone; 11OHAST, 11β-hydroxyandrosterone; 11KAST, 11-ketoandrosterone; 11K-3aADIOL, 11-keto-5α-androstane-3α, 17β-diol. Reactions are catalysed by 17β-hydroxysteroid dehydrogenase (17βHSD) type 3, 5 and 2; 5α-reductase (SRD5A) type 1 and 2; 3α-hydroxysteroid dehydrogenase (3αHSD) (AKR1C1 and AKR1C2) and 11β-hydroxysteroid dehydrogenase type 2 (11βHSD2). Boxed steroids are potential uridine diphosphate glucuronosytransferases (UGT2B15, UGT2B17) substrates.

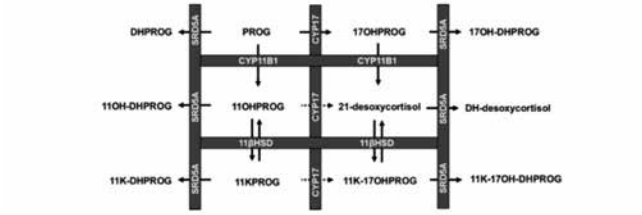

Figure 2: Biosynthesis and metabolism of C11-oxy C21 adrenal steroids. PROG, progesterone; 17OHPROG, 17α-hydroxyprogesterone; 11OHPROG, 11β-hydroxyprogesterone; 11KPROG, 11-ketoprogesterone; 11K-17OHPROG, 11-keto-17α-hydroxyprogesterone; DHPROG, dihydroprogesterone; 11OH-DHPROG, 11β-hydroxy-dihydroprogesterone; 11KDHPROG, 11-ketodihydroprogesterone; 17OH-DHPROG, 17α-hydroxy-dihydroprogesterone; DH21-desoxycortisol, dihydro-21-desoxycortisol; 11K-17OH-DHPROG, 11-keto-17α-hydroxy-dihydroprogesterone. Reactions are catalysed by cytochrome P45011β-hydroxylase (CYP11B1); cytochrome P45017α-hydroxylase (CYP17A1); 5α-reductase (SRD5A) type 1 and 2; 11β-hydroxysteroid dehydrogenase (11βHSD) type 1 and 2.

Results: CYP11B1 catalyzes the hydroxylation of progesterone (PROG), 80% after 12h, and 17α-hydroxyprogesterone (17OHPROG), 60% after 24h, yielding 11β-hydroxyprogesterone (11OHPROG), and 21-desoxycortisol, respectively. The subsequent conversion of 11OHPROG and 21-desoxycortisol to 11keto-progesterone (11KPROG) and 11keto-17OHPROG (11K-17OHPROG) was catalyzed by 11βHSD2 (75 -80% conversion after 12h), with the reverse reactions catalyzed by 11βHSD1, comparable to cortisone's conversion to cortisol (50-60% after 12 h). These steroids, in turn, served as novel substrates for SRD5A yielding dihydro steroid metabolites (Fig. 2).

Circulating levels of A4, testosterone (T) and their metabolites were 22-57nmol/L while 11OHA4, 11OHT and their metabolites were 50-140nmol/L. PROG metabolite profiles showed that dihydroprogesterone (DHPROG) and 11keto-dihydroprogesterone (11K-DHPROG) were the most abundant C21 steroids, 10-40nmol/L. Pregnanetriol, ±10nmol/L, and 21-desoxycortisol, <2nmol/L, are routinely measured in CAH.

Summary: 11OHA4 is not considered in the diagnoses of hyperandrogenism. While T and A4 are measured routinely in PCOS patients, reports have suggested that A4 can be ignored. However, 11OHA4 and its metabolites are significantly higher than A4 and its metabolites while C21 steroids, DHPROG, 11OHPROG and 11K-DHPROG were far higher than 21-desoxycortisol. It is apparent that these C19 and C21 adrenal steroids warrant consideration as they may impact on disease states.

Abstract Number: 22

Efficacy and Safety of Liraglutide versus Sulfonylurea both in combination with Metformin during Ramadan in Subjects with Type 2 Diabetes (LIRA-Ramadan): A Randomized Trial

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Background: Subjects with type 2 diabetes (T2D) who fast during Ramadan have a 5- and 7.5-fold increased risk of severe hyper- and hypoglycemia, respectively. The effect of liraglutide (lira) vs sulfonylurea (SU), both + metformin (Met), on glycaemic control in subjects with T2D who fasted during Ramadan was evaluated.

Methods: In this up to 33-week, open-label trial, adults (HbA_{1c} 7-10%; BMI ≥20 kg/m ^{2}; stable SU + Met; intent to fast during Ramadan) were randomized to either switch to once daily lira 1.8 mg (N=172) or continue pretrial SU (N=171), both + Met. After 3-week dose escalation, a 6-19-week maintenance period preceded Ramadan. Primary endpoint was change in fructosamine (FA) from start to end of Ramadan (lira N=151; SU N=165).

Results: During Ramadan, despite lower mean FA & HbA_{1c} at start of Ramadan in the lira arm, a similar reduction in FA with lira and SU was seen. (Mean reduction 12.8 umol/L and 16.4 umol/L respectively). Confirmed hypoglycemic episodes appeared to be lower with lira & fewer subjects withdrew during Ramadan (lira 3, SU 11). During Ramadan Lira was associated with greater wt. loss (1.4 kg compared to SU (0.89kg). AE frequencies appeared similar: lira 23.7%; SU 20.9%. GI AEs were more common for lira (10.5%; SU 3.7%). A low incidence of SAEs was observed (lira 1.3%; SU 0%).

Conclusion: During Ramadan, lira showed similar improvements in glycaemic control based on FA & HbA_{1c} levels compared to SU with a similar number of AEs, apparently fewer confirmed hypoglycemic episodes and better weight control.

Abstract Number: 23

Evaluation Of Excipients For Enhanced Intestinal Absorption Of Rooibos Flavonoids

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Background: Rooibos flavonoids, such as the *C*-glucosyl dihydrochalcone aspalathin, have been shown to ameliorate insulin resistance, improve glycaemia and have a cardioprotective effect in cell and animal models. However, the poor bioavailability of aspalathin limits its potential as a nutraceutical. This study investigated the use of excipients to improve aspalathin bioavailability in Caco-2 monolayers.

Methods: Three different types of green rooibos extracts (60% ethanol, 80% ethanol and aqueous extracts), as well as commercialized green rooibos extract (GRT, Afriplex), were assessed for cytotoxicity and their bioavailability in terms of aspalathin. Two batches were selected from each extract type based on (i) activity and (ii) chemical dissimilarity in polyphenol content. Caco-2 cells were used as a model to assess bioavailability. The passage of aspalathin in the extracts was monitored by HPLC-DAD in the presence and absence of excipients (β-cyclodextrin and inulin). Relative bioavailability is expressed as Papp values representative of the rate of transport across the monolayer.

Results: Each extract (standardized to 150 µM aspalathin content) was deemed not cytotoxic (80% cell viability). The rate of transport of aspalathin (1.59 x 10 $^{-6}$ cm/s ^{2}) and its flavone derivatives, was not markedly altered by extraction method and thus extract composition. Furthermore, absorption of aspalathin was not increased by the addition of β-cyclodextrin (6.99 x 10 $^{-7}$ cm/s ^{2}) or inulin (1.21977 x 10 $^{-6}$ cm/s ^{2}), implying that these excipients did not enhance intestinal absorption of aspalathin (similar results were observed for its flavones).

Conclusion: This study has provided novel information about the bioavailability of aspalathin and its flavones which was not altered by the use of excipients, extraction method and chemical composition of the extracts.

Abstract Number: 24

11-ketotestosterone And 11-keto-5α-dihydrotestosterone Are Potent Androgens Comparable To Testosterone And 5α-dihydrotestosterone

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Background: Castration resistant prostate cancer (CRPC) is dependent on adrenal androgen precursors which are converted to active androgens. DHEA and androstenedione (A4) serve as precursors to the potent androgen 5α-dihydrotestosterone (DHT), while the abundant adrenal steroid 11β-hydroxyandrostenedione (11OHA4) is the precursor to the novel androgens, 11-ketotestosterone (11KT) and 11-keto-5α-dihydrotestosterone (11KDHT). The objective of this study was to characterise the androgenic activity of 11KT and 11KDHT and assess their potential contribution to the development of CRPC.

Methods: Competitive whole cell binding assays and transactivation assays were used to determine the binding affinities, potencies and efficacies of 11KT and 11KDHT. The androgenic activity of 11KT and 11KDHT were subsequently assessed in two androgen dependent cell prostate cancer cell lines (LNCaP and VCaP) using qPCR, mass spectrometry based proteomics and cell growth assays. The metabolism of 11KT and 11KDHT were measured using ultra-performance convergence chromatography tandem mass spectrometry (UPC ^{2}-MS/MS).

Results: 11KT and 11KDHT bind to the human androgen receptor (AR) with affinities similar to that of testosterone (T) and DHT. The potencies and efficacies of 11KT and 11KDHT are comparable to that of T and DHT, respectively. In most cases, 11KT and 11KDHT upregulated AR-regulated gene expression (KLK3, TMPRSS2 and FKBP5) and increased LNCaP cell growth to a significantly higher extent than T and DHT. In addition, 11KT and 11KDHT, like T and DHT, resulted in the upregulation of multiple AR-regulated proteins in VCaP cells, with 11KDHT regulating more AR-regulated proteins than DHT. 11KT and 11KDHT were metabolised at a significantly lower rate than T and DHT, respectively, in both cell lines.

Conclusions: 11KT and 11KDHT are potent and efficacious androgens. The reduced rate of metabolism observed for these steroids suggest that they have the potential to remain active longer than T and DHT, and in so doing drive the expression of AR-regulated genes and cell growth to a greater degree than equal concentrations of T or DHT. The role of 11OHA4 as an androgen precursor should therefore no longer be overlooked when considering androgen dependent diseases such as CRPC.

Abstract Number: 25

Glucose Tolerance and Insulin Resistance in Trained Cyclists Eating a Low-Carbohydrate High-Fat Diet Over the Long Term

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Background: A low-carbohydrate high-fat (LCHF) diet has been implicated in the development of insulin resistance and post-prandial hyperglycemia. Short term exposure (3 - 15 days) to a LCHF diet reduces insulin sensitivity during a hyperinsulinemic-clamp and reduces glucose tolerance during an oral glucose tolerance test (OGTT). This has been observed even in healthy, aerobically trained participants. However, it is not clear whether reduced insulin action and glucose tolerance would persist, progress or reverse with long-term exposure to a LCHF diet. Therefore, as part of a larger study, we investigated glucose tolerance in trained athletes that had been eating a LCHF or a mixed diet (Mix) for longer than eight months.

Methods: Fourteen male endurance-trained cyclists (7 LCHF; 7 Mix) matched for age, body composition and cycling ability were recruited. On the morning after an overnight fast, they ingested a 75 g glucose drink. Samples for the determination of serum insulin and plasma glucose were collected prior to and 30, 60, 90 and 120 min after the ingestion of glucose. Participants were required not to exercise for two days prior to the OGTT. Insulin-sensitivity was assessed by the Homeostatic Model Assessment (HOMA-IR) and the Matsuda Index.

Results: The HOMA-IR scores were not significantly different between groups (1.04 ± 0.52 LCHF; 0.89 ± 0.40 Mix, p=0.80). The LCHF group tended to have a lower Matsuda Index compared to the mixed diet group (1.53 ± 0.64 LCHF; 2.29 ± 0.85 Mix, p = 0.07). At all OGTT time points after baseline, plasma glucose was significantly higher in the LCHF group (p<0.01). The insulin profile was significantly different between groups. Serum insulin in the mixed group peaked at 30 min and returned to baseline by 60 min whereas serum insulin peaked at 60 min and returned to baseline after 120 min in the LCHF group (p=0.03).

Discussion:. The elevated plasma glucose and delayed insulin peak suggests a reduced capacity for the LCHF adapted cyclists to metabolise ingested glucose. This is likely due to their reliance on fat as their primary fuel source and a concomitant down-regulation of carbohydrate oxidation enzymes.

Abstract Number:26

The Prevalence of the Metabolic Syndrome and its Components in South Africans with Psoriasis

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Background :Psoriasis (PsO) is an immune-mediated inflammatory disorder in which cardiometabolic comorbidities are being increasingly recognised. There are no data from sub-Saharan Africa on the relationship between PsO and cardiometabolic disease risk factors. The objective of this study was to determine the prevalence

of the metabolic syndrome (MS) and related disorders in PsO patients.

Methods: Adult PsO patients, excluding HIV-associated PsO, were recruited from the Dermatology and Rheumatology clinics at hospitals of the Wits Academic Complex. Demographic, anthropometric and cardiometabolic data were recorded. Disease severity of PsO was assessed using the psoriasis area and severity index (PASI) scoring method. Hypertension and MS were defined according to the harmonized guidelines, type 2 diabetes (T2D) was diagnosed using ADA criteria and hypercholesterolaemia was diagnosed using the ATPIII criteria.

Results: A total of 95 patients (44 male, 51 female; 41 Indian, 28 coloured, 15 black, 11 white) were recruited. The mean (±SD) age and PsO disease duration were 52.6±14.6 and 17.6±13.3 years, respectively. The mean BMI and waist circumference were 31.9±8.64 kg/m ^{2} and 101.4±16.9 cm, respectively. The prevalence (% [95% CIs]) of obesity was 51.6 [41.3, 61.8], of T2D was 31.2 [20.6, 41.7], of hypertension was 76.8 [68.2, 85.5], of hypercholesterolaemia was 54.2 [42.4, 65.9] and of psoriatic arthritis (PsA) was 27.4 [18.2, 36.5]. The prevalence of MS was 58.1 [46.6, 69.6] % . Multivariate logistic regression analysis showed that Indian ethnicity was associated with a higher risk of MS (odds ratio [95 % CIs]: 6.64 [1.28, 34.4]; p=0.02), as was a higher PASI score (4.34 [1.00, 18.9]; p=0.05) whilst a higher socio-economic status (SES) was associated with a lower risk of MS (0.14 [0.02, 0.84]; p=0.03).

Conclusions: The prevalence of obesity and its associated complications is high in this population suggesting that screening for cardiometabolic diseases should form part of routine care in patients with psoriasis. Furthermore, the risk of MS increases with increasing severity of psoriasis.

Abstract Number: 27

Obesity Phenotypes In African People Living With Hiv Infection: Overall Prevalence And Effects Of Antiretroviral Therapy On The Distribution

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[3]Cape Peninsula University of Technology
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[5]Global Evaluation Science

Objectives: The distribution of body size phenotypes in people with human immunodeficiency virus (HIV) infection has yet to be characterised. We assessed the distribution of body size phenotypes overall, and according to antiretroviral therapy (ART), diagnosed duration of the infection and CD4 count in a sample of HIV infected people recruited across primary care facilities in the Western Cape Province, South Africa.

Methods: Adults aged ≥18 years were consecutively recruited using random sampling procedures, and their cardio-metabolic profile assessed during March 2014 and February 2015. They were classified across body mass index (BMI) categories as normal-weight (BMI<25 kg/m ^{2}), overweight (25 /uBMI30 kg/m^2), and obese (BMI 30 kg/m^2), and further classified according to their metabolic status as "metabolically healthy" vs. "metabolically abnormal" if they had less than two vs. two or more of the following abnormalities: high blood glucose, raised blood pressure, raised triglycerides and low HDL-cholesterol. Their cross-classification gave the following six phenotypes: normal-weight metabolically healthy (NWMH), normal-weight metabolically abnormal (NWMA), overweight metabolically healthy (OvMH), overweight metabolically abnormal (OvMA), obese metabolically healthy (OMH), and obese metabolically abnormal (OMA).

Results: Among the 748 participants included [median age 38 years (25 th-75 th percentiles: 32-44)], 79% were women. The median diagnosed duration of HIV was 5 years; the median CD4 count was 392 cells/mm ^{3} and most participants were on ART. The overall distribution of body size phenotypes was the following: 31.7% (NWMH), 11.7% (NWMA), 13.4% (OvMH), 9.5% (OvMA), 18.6% (OMH), and 15.1% (OMA). The distribution of metabolic phenotypes across BMI levels did not differ significantly in men vs. women (p=0.062), in participants below vs. those at or above median diagnosed duration of HIV infection (p=0.897), in participants below vs. those at or above median CD4 count (p=0.447), and by ART regimens (p=0.205).

Conclusions: In this relatively young sample of HIV-infected individuals, metabolically abnormal phenotypes are frequent across BMI categories. This highlights the importance of general measures targeting an overall improvement in cardiovascular health across the spectrum of BMI distribution in all adults with HIV. This should be coupled with targeted screening to identify those more likely to benefit from aggressive metabolic risk factor control interventions.

Abstract Number: 28

Primary Hypophysitis: A Case Series

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Primary hypophysitis, previously regarded as a rare inflammatory condition of the pituitary gland, is becoming an increasingly recognized diagnosis. The radiographic and clinical presentation of primary hypophysitis is extremely varied. There are three histopathological variants of primary hypophysitis namely: lymphocytic hypophysitis (the most common variant), granulomatous hypophysitis and xanthomatous hypophysitis (very rare). Clinical presentation can be limited to either anterior or posterior pituitary dysfunction, or may involve both anterior and posterior components of the gland. In addition, lymphocytic hypophysitis which has a predilection in women, often presents in the postpartum period or third trimester of pregnancy.

We describe three cases of primary hypophysitis. The first two cases are both 24 year old women presenting in the postpartum period with anterior hypopituitarism. Magnetic resonance imaging varied considerably, with the first case demonstrating a mass lesion with optic chiasm compression, and the second an empty sella. Surgery was performed in the case with the mass lesion and histology revealed the diagnosis of lymphocytic hypophysitis. The third case is a 50 year old woman who presented with diabetes insipidus and subsequently developed panhypopituitarism. Imaging in this case revealed stalk thickening and an anterior pituitary mass.

These three clinical cases demonstrate the varied presentation of primary hypohysitis and how it can mimic other more common forms of pituitary disease. As such, knowledge of this disease entity is important when considering pituitary lesions.

Abstract Number: 29

Perceptions Of Body Size, Obesity Threat And The Willingness To Lose Weight Among Black South African Adults: A Qualitative Study

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Background: The obesity epidemic is associated with rising rates of cardiovascular disease (CVD) among adults, particularly in countries undergoing rapid urbanisation and nutrition transition. This study explored perceptions of body size, obesity risk awareness, and the willingness to lose weight among adults in a resource-limited urban community to inform appropriate community-based intervention for the prevention of obesity.

Method: This is a descriptive qualitative study. Semi-structured focus group discussions were conducted with purposively selected black men and women aged 35-70 years living in an urban South African township. Weight and height measurements were taken, and the participants were classified into optimal weight, overweight and obese groups based on their body mass index. Participants were asked to discuss perceived obesity threat and risk of CV, body image perceptions and the willingness to lose excess body weight. Discussions were conducted in the local language (isiXhosa), transcribed and translated into English. Data was analysed using the thematic analysis approach.

Findings: Participants generally believed that obesity could lead to health conditions such as heart attack, stroke, diabetes, and hypertension. However, the severity of obesity was perceived differently in the groups. Men in all groups and women in the obese and optimal weight groups recognized obesity to be a serious threat to their health, whereas the overweight women did not. Obese participants who had experienced chronic disease conditions indicated strong perceptions of risk of obesity and CVD. Obese participants, particularly men, expressed willingness to lose weight, compared to the overweight ones. The belief that overweight is 'normal' and not a disease, subjective norms, and inaccessibility to physical activity facilities, negatively influenced participants' readiness to lose weight.

Conclusion: Low perception of the threat of obesity to health, particularly among overweight women in this community indicates a considerable challenge to obesity control. Community health education and promotion programmes that increase awareness about the risk associated with overweight, and improve motivation for physical activity and maintenance of optimal body weight are needed.

Abstract Number: 30

Development Of An Alternative Non-obese Non-genetic Rat Model Of Type 2 Diabetes Using Caffeine And Streptozotocin

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The present study was to develop an alternative non-obese non-genetic rat model for type 2 diabetes (T2D). Six-week-old male SD rats were randomly divided into six groups, namely: Normal Control (NC), Diabetic Control (DBC), STZ+Caffeine 5 mg/kg BW (CAF5), STZ+Caffeine 10 mg/kg BW (CAF10), STZ+Caffeine 20 mg/kg BW (CAF20) and STZ+ Caffeine 40 mg/kg BW (CAF40) and were fed a normal rat pellet diet and drinking water *ad libitum* throughout the experimental period. After a one week acclimatization period, diabetes was induced in the animals in DBC and all CAF groups with an injection (i.p.) of the respective dosages of caffeine 15 min before the injection of STZ (65 mg/kg BW) when normal saline was injected to the DBC group instead of caffeine. The NC group was received normal saline and buffer instead of caffeine and STZ, respectively. One week after the STZ injection, animals with non-fasting blood glucose > 300 mg/dl were considered as diabetic. Three weeks after the STZ injection, the animals in the CAF5 and CAF10 groups were eliminated from the study due to the severity of diabetes the experiment was continued with remainder groups for a 13 weeks period. The data of food and fluid intake, body weight, blood glucose, glucose tolerance test, serum insulin, fructosamine, lipid profile and organ specific enzymes, anti-diabetic drug response tests, HOMA-IR, HOMA-beta and pancreatic histopathology suggest that CAF20 group can be an excellent alternative model of non-obese non-genetic model of type 2 diabetes.

Abstract Number: 31

Assessment of chemical markers as surrogates for safety and efficacy of rooibos

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Background: Research interest in the bioactive polyphenols of rooibos to which health-promoting properties are attributed has escalated. These phytochemicals could serve as critical quality attributes for assessing the efficacy of rooibos health products and must be defined and quantified as part of a quality control system. For this study particular focus will be drawn to the *C*-glucosyl dihydrochalcone, aspalathin, demonstrated to have antidiabetic properties in various in vitro and in vivo models.

Methods: One water-based and two solvent-based (60% and 80% ethanol) extracts were prepared from the same batches of unfermented rooibos. HPLC-DAD analysis was performed to quantify aspalathin and other major flavonoids present in the extracts. Glucose uptake was assessed using C2C12 murine skeletal muscle cells exposed to 1 and 10 µg/mL of the extracts.

Results: HPLC-DAD analysis of the different extracts demonstrated that the 80% ethanol extract yielded the highest level of enrichment

of the final extract (18.5% aspalathin), compared to 60% ethanol and water extracts (13.5% and 9.6% aspalathin, respectively). Preliminary bioactivity data demonstrated that glucose uptake was dependent on the aspalathin content, as the 80% and 60% ethanol extracts performed better than the aqueous green rooibos extract.

Conclusion: The efficacy of glucose uptake increased in proportion to the concentration of the major flavonoid, aspalathin, however, the presence of other phenolic and non-phenolic compounds in the extract may also have contributed to the observed effect.

Abstract Number: 32

Prevalence And Determinants Of Vitamin D Deficiency In Human Immune Deficiency Virus Positive Patients At Tshwane District Hospital

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Introduction: Vitamin D deficiency has been found to be prevalent in most populations around the world. Various studies of patients with Human Immune deficiency Virus (HIV) infection have shown an even higher prevalence of vitamin D deficiency than the population at large. South Africa has an HIV prevalence of around 10 percent but there is little data regarding vitamin D status in this population group.

Objective: To investigate the prevalence of vitamin D deficiency and insufficiency and its determinants in an HIV positive population.

Subjects and methods: We conducted a cross-sectional descriptive study of 295 patients at Tshwane District Hospital's Retroviral Disease clinic, in Pretoria, South Africa. Vitamin D sufficiency, insufficiency, and deficiency were respectively defined as levels above 30ng/ml (75nmol/L), between 20 and 30ng/ml (50-75nmol/L), and below 20ng/ml (50nmol/L) For analytical purposes the vitamin D deficient and insufficient patients were grouped together and compared to patients with normal vitamin D levels. Numerous patient variables were assessed for statistically significant associations.

Results: Almost 98% of the patients were black, and 77.3% were female. Forty five patients (15%) were found to be vitamin D deficient, 121 (41%) were found to be insufficient with 129 (44%), falling in the sufficient range. In the univariate analysis female gender ($p = 0.009$) as well as weight ($p = <0.001$) was statistically significant for low vitamin D levels. In the multivariate analysis after adjustment for weight and gender, only the use of Efavirenz, Zidovudine (AZT) or Bactrim remained statistically significant, with odds ratios for a low vitamin D level ranging between 1.97 and 3.20.

Conclusion: The prevalence of vitamin D deficiency and insufficiency was high in our population at 56%, which is much higher than in the general South African population, but lower than the reported prevalence in Europe and North America. Predictors of low vitamin D levels in this population were gender, weight, and the use of Efavirenz, AZT or Bactrim.

Abstract Number: 33

Effect Of Clinically Relevant Weight Loss On Heart Rate Variability And Preconscious Brain Processing During Laboratory Induced Stress.

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Background: While clinically relevant weight loss (CWL; ≥ 5% reduction in body weight) is sufficient to enhance physical health; its effect on autonomic nervous system (ANS) regulation is unclear. Our aim was to determine if CWL was associated with alterations in heart rate variability (HRV; marker of cardiac ANS regulation) during a Stroop Task interspersed with 20 picture prompts of high calorie food items. A further aim was to correlates HRV with preconscious brain processing during the Stroop Tasks to determine whether this correlation is different in CWL vs. control (CTL) participants.

Methods: 45 women were recruited into 2 groups; successful dieters (CWL: $n = 20$) and age and BMI-matched controls with no history of weight loss (CTL: $n = 25$). Participants first completed a familiarization Stroop Task interspersed with 20 white squares, followed by the completion of 2 independent Stroop Tasks (one with 20 food-related image inserts, another with 20 neutral, office-related image inserts.

Results & Discussion: We found a significant correlation between the mean heart rate and % body fat across all subjects both at rest ($R = 0.44$, $P < 0.005$) and during the Stroop Tasks ($R = 0.35$, $p < 0.05$). The SD of heart rate (SDHR: a marker of vagal activation) *decreased* from the Food to Office Stroop Tasks in CTL, but *increased* in CWL participants ($p < 0.05$). Furthermore, there was a significant correlation between the high frequency power (HFP) in the cardiac spectrogram of CWL subjects and the latency of their P200 component (associated with preconscious emotional processing) of the event related potentials (ERP) measured during the Food Stroop Task ($R = 0.66$, $p < 0.01$); there was no such correlation in CTL.

The inverse SDHR changes form Food to Office Stroop Tasks in CWL vs. CTL suggests altered ANS reactivity to food picture prompts; further confirmed by the significant correlation between the HFP in their cardiac spectrogram and the latency of their P200 waveform generated by food picture prompts.

Conclusion: Good evidence of strong attentional processing of environmental food prompts in both the heart and brain of CWL participants.

Abstract Number: 34

Bioavailability And Transport Characteristics Of The Rooibos C-glucosyl Dihydrochalchone Aspalathin

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Background: The health benefits of plant-derived polyphenols have been well documented for flavonoids, including aspalathin, a

C-glucosyl dihydrochalcone, novel to rooibos (*Aspalathus linearis*). The mechanism of aspalathin intestinal transport, bioavailability and metabolism will provide important information for dose optimisation as a nutraceutical. We aim to showcase the metabolite formation of pure synthetic aspalathin both *in vitro* and *in vivo.*

Methods: *In vivo* metabolism was determined, by analysing whole blood and urine samples, collected from mice dosed orally with aspalathin. Samples were extracted following protein precipitation and analysed by LC-MS. The passage of aspalathin was monitored across CaCo2 cell monolayers in the presence and absence of inhibitors to help elucidate mechanisms of transport across the monolayer. Collected samples were analysed by HPLC-DAD and LC-MS.

Results: Metabolites of aspalathin, mainly sulphated, glucuronidated and methylated derivatives, were found in the mouse urine samples. No metabolites were detected in the *in vivo* blood samples. In Caco2 monolayers aspalathin was transported across the intestinal barrier at a rate typical of moderately absorbed compounds (1.59×10^{-6} cm/s [2]). Major glucose transporters, SGLT-1 and GLUT-2, were shown not to be primary transporters, nor was aspalathin significantly effluxed back into the gut lumen (1.9×10^{-6} efflux ratio: 1.2). The rate of absorption was not affected by the presence of other polyphenols present in aspalathin-enriched extracts, but was affected by glucose concentration (2.9×10^{-7} cm/s [2] at 20.5 mM glucose).

Conclusion: Aspalathin is poorly absorbed *in vivo* from the small intestine and its metabolites are detectable in the urine, but not the blood. Mechanistically we showed that aspalathin is not actively transported by the glucose transporters across Caco2 monolayers, but presumably passes across the monolayer paracellularly.

Abstract Number: 35

Audit Of Standard Of Care Measures And Complications In A Tertiary Type I Diabetic (dm1) Clinic: A Different Perspective.

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Background: Guidelines for the care of diabetics allow clinicians to deliver appropriate standards of care. The uptake rate of recommended preventive measures offered at an adult DM1 clinic (tertiary level), was assessed in a 2014 audit, together with a review of disease severity and complications in these patients. The results of this audit were presented at SEMDSA 2015, where the data was analyzed solely at a per visit level. Because of concern expressed about potential under- or over-representation of uptake rate in some screening areas, or in the prevalence of complications, the data has now been re-analysed at a per patient level.

Aims: (1) Conduct an audit of the quality of care delivered to adult diabetics who attend our DM1 clinic. (2) Characterize their burden of illness. (3) Compare results of the 2 analyses.

Methods: A retrospective chart review of all patients attending the DM1 clinic in 2014 was performed and re-analysed at a patient-level. If a patient had more than one visit, results were averaged for all visits and the mean was used.

Results: 174 patients who attended the clinic during a 12-month period (totaling 455 patient visits), were analysed. When compared to the visit-level analysis, the only notable differences detected were in both the uptake rates of screening for peripheral neuropathy and vascular disease, as well as in the prevalence of these specific complications. The differences were statistically significant ($p<0.05$) with confidence intervals that did not overlap. Results were as follows: screening for neuropathy was 80.5% (vs. 58.0%) and 54.5% for vascular disease (vs. 34.0%). Neuropathy was present in 32.1% (vs. 28.0%) of patients, while vascular disease was present in 6.4% (vs. 3.0%).

Conclusion: Analysing data per patient, rather than per visit, revealed significantly improved screening of and increased prevalence of neuropathy and vascular disease.

Abstract Number: 36

High Fat Programming Impairs Hepatic And Skeletal Muscle Insulin Receptor Immunoreactivity In Neonatal Rats

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Background: Impaired insulin signaling contributes to insulin resistance systemically and in metabolic organs. Programming by exposure to either a stimulus or insult during fetal life alters progeny physiology and metabolism with immediate, transient and durable effects. The liver and skeletal muscle are glucose recipients and maintenance on a fetal diet high in fat content may programme insulin resistance in both organs. This study investigated the effects of maternal diets, varying in fat content (10-40% fat as energy), on hepatic and skeletal muscle expression of the proximal insulin signalling cascade.

Methods: Pregnant rats were randomised into groups and maintained on diets with varying fat proportions: 10% (control), 20% (20F), 30% (30F) and 40% (40F) fat as energy throughout gestation. Neonatal liver and skeletal muscle were collected to determine the proximal insulin signalling expression profiles of the target factors: insulin receptor (IR), insulin receptor substrate 2 (IRS2) and phosphoinositide 3-kinase (PI3K). Quantitative polymerase chain reaction (qPCR) was applied to determine mRNA expression of these target insulin signalling factors. Immunostaining of the target proteins in the liver and skeletal muscle was performed followed by relative quantification with image analysis.

Results: Hepatic PI3K mRNA expression was elevated in 30F neonates compared to 20F neonates with no changes in hepatic IR or IRS2 mRNA expression. In skeletal muscle, IR and PI3K mRNA expression were reduced in the 30F and 40F neonates compared to 20F neonates. Hepatic IRα immunoreactivity was reduced in 40F neonates compared to control and 20F neonates. Further, skeletal muscle IRα immunoreactivity was reduced in 30F and 40F neonates compared to control neonates.

Conclusion: Fetal high fat programming reduced both hepatic and skeletal muscle IRα immunoreactivity which reflects impaired insulin signalling at the receptor level. Proper maternal nutrition during gestation is critical to avoid the programming of disrupted insulin signalling in their neonatal progeny.

Abstract Number: 37

High Fat Programming Of Beta And Alpha Cell Trajectories In Neonate, Weanling And Adolescent Rats

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Background: Islets are dynamic throughout life and influenced by metabolic states. Altered metabolic states such as hyperglycemia and insulin resistance contribute to islet cell compensatory responses. Nutritional programming, such as maintenance on a high fat diet during critical developmental life stages, shapes islet cell structure and function. We assessed beta and alpha cell trajectories in neonate, weanling and adolescent rats during development and after maintenance on a high fat diet.

Methods: Pancreata from neonatal (one-day-old), weanling (three-week-old) and adolescent (three-month-old) rats were double immunolabeled with insulin and glucagon in control progeny (10% fat diet) and progeny maintained on a high fat diet (40% of mainly saturated fat as energy) during fetal, lactational and/or postnatal life (high fat programming). Beta and alpha cell number, size and volume were assessed.

Results: Postnatal high fat maintenance induced beta cell hyperplasia at weaning which persisted into adolescence concomitant with beta cell hypertrophy at adolescence. Physiologically and more markedly after postnatal high fat maintenance, alpha cell numbers increased with age, emerging at weaning and prevailing into adolescence. Alpha cell hyperplasia was maintained after fetal and postnatal high fat maintenance at weaning and adolescence. After postnatal high fat maintenance, alpha cell hypertrophy emerged earlier at weaning and persisted into adolescence. Alpha cell volume was consistently enhanced at weaning.

Conclusion: :Beta and alpha cell populations vary in number, size and volume throughout development and are altered in response to high fat programming. Postnatal high fat maintenance appears to trigger a beta cell compensatory response. Proper and balanced nutrition during critical life stages is required for normal islet cell development.

Abstract Number: 38

High Prevalence Of The Metabolic Syndrome In Urban-dwelling South Africans With Hypertension

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Background: In light of the clustering of cardio-metabolic abnormalities, the aim of this study was to determine the prevalence and associations of the metabolic syndrome, identified by the 2009 Joint Interim Statement criteria, in 25-74-year-old urban Africans with hypertension in Cape Town.

Methods: In 2008/09, a representative cross-sectional sample, stratified for age and gender, was randomly selected. Cardio-metabolic abnormalities were determined by administered questionnaires, clinical measurements and biochemical analyses, including fasting and 120 minute blood samples. Logistic regression analysis assessed the independent effects of socio-demographic variables on the metabolic syndrome in hypertensive participants.

Results: Of the 1099 study participants, 461 (162 men and 299 women) were identified with hypertension. The metabolic syndrome was present in 30.5% (95% confidence interval (CI) 23.0-39.4) and 80.1% (95%CI: 73.3-85.6) of hypertensive men and women, respectively. The most prevalent metabolic syndrome components accompanying hypertension were central obesity (men: 27.5%, women: 93.3%) and low high-density lipoprotein cholesterol (men: 28.0%, women: 71.8%). Dysglycaemia and raised triglycerides were equally high in hypertensive men (26.6%) while in hypertensive women these were 38.4% and 17.8%, respectively. In the multiple logistic model, participants with hypertension who were older (odds ratio (OR): 1.03, 95%CI: 1.01-1.06, p=0.028), women compared to men (OR: 9.93, 95%CI: 5.63-17.52, p<0.001), employed (OR: 3.04, 95%CI: 1.49-6.20, p=0.002) or receiving a pension (OR: 2.45, 95%CI: 1.07-5.60, p=0.034) compared to their unemployed counterparts, and wealthier compared to being the poorest (middle tertile: OR: 2.31, 95%CI: 1.16-4.57, p=0.017) were more likely to have the metabolic syndrome.

Conclusions: The high prevalence of the metabolic syndrome in hypertensive urban Africans reinforces that hypertension rarely occurs in isolation. This highlights the importance of examining for other cardio-metabolic abnormalities in the presence of hypertension in this population because of the overall higher cardiovascular risk associated with having multiple abnormalities.

Abstract Number: 39

Sweet Talk: Communication Practices And Perceptions At An Urban Clinic For Gestational Diabetes Mellitus

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Background: South Africa provides a unique context for the examination of the influence of linguistic and cultural diversity on diabetes management. Previous research has identified links between communication practices and health outcomes and attitudes towards conditions and treatment. However, these links have not been explored in the field of GDM in South Africa. Furthermore, little attention has been given to issues related to patients' lifeworlds, empowerment, nursing, stigma and information-giving in the context of GDM in South Africa. This study explores the communication practices and perceptions of nurses and patients at an urban GDM clinic in South Africa.

Methods: A qualitative study was conducted at an urban clinic involving, including ethnographic observations, focus groups (4 groups with a total of 19 patients), semi-structured interviews (12 interviews) and video recordings of nurse-patient interactions (6 recorded interactions). Purposive sampling was adopted. Data analysis included thematic analysis and an interactional analysis of the nurse-patient interactions at the clinic.

Results: Multiple themes, facilitators and barriers to communication emerged from the study, including communication difficulties between nurses and patients, patient dissatisfaction with communication at the clinic, uncertainty about GDM and living with the condition, negative attitudes and preconceptions among

nurses, intra-professional conflict and environmental barriers. Findings highlighted the barriers to information giving which included cultural and linguistic mismatch, a lack of skills and knowledge amongst nurses, resource shortages, differing nurse-patient agendas and negative attitudes of nurses and patients. A paradox between patient reports and observations at the clinic also emerged. All of these factors appeared to affect the satisfaction, lifeworld, empowerment and attitudes of the patients attending the clinic, as well as nurses' job satisfaction.

Conclusions: GDM is a complex condition and communication appears to play an important role in facilitating positive health outcomes, attitudes, satisfaction and treatment adherence, especially in a diverse population. The findings inform important implications related to communication training and policy related to GDM care in South Africa.

Abstract Number: 40

Prevalence Of Low Serum Testosterone Levels In South African Men With Type 2 Diabetes Attending An Outpatient Diabetes Clinic

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Background: To determine the prevalence of a low serum testosterone level and its association with metabolic parameters among men with type 2 diabetes mellitus (T2DM) attending the outpatient tertiary diabetes clinic at Inkosi Albert Luthuli hospital (IALCH) in Durban, Kwa-Zulu Natal

Methods: This was a cross-sectional observational study among men with T2DM attending the adult diabetes clinic at IALCH. Information collected from patients included smoking and medication history, clinical examination and laboratory tests. Blood tests included serum total testosterone (TT), sex-hormone binding globulin (SHBG), calculated free-testosterone (fT) and free-androgen index, leutinising hormone (LH), HbA1c, fructosamine, lipid profile, full blood count, urea and electrolytes and liver function tests. Symptoms were assessed using the Ageing Male's Symptom Scale (AMS) questionnaire. TT, SHBG and fT levels were also measured in male control subjects with no history of diabetes. Low testosterone level was defined as a free testosterone <180 pmol/l.

Results: A total of 197 men were recruited: African n:87, Indian n:58, White n:3. The mean age, mean duration of diabetes and mean BMI was 57.5±11.2 years, 11.4±9.0 years and 29.8±6.0 kg/m^2 respectively. Prevalence of metabolic syndrome was 86.4% (n:127). Low serum free testosterone (LST) was found in 15.6% of men (n:23). A high AMS score of $\geq$27 was noted in 75.5% of all subjects (n:111). When compared with men with normal serum testosterone levels (NST), men with LST had had higher waist circumference (108.3 vs 102.3 cm, p=0.04) but no differences were found with respect to BMI, WHR, HbA1c and serum lipids; all subjects with LST had normal or low LH levels. Non-diabetic control subjects had significantly higher levels of TT and fT compared to the diabetic study population (18.8 vs 14.5 nmol/l, p <0.001 and 351.7 vs 265.9 pmol/l, p<0.001 respectively) and significantly lower BMI (27,1 vs 29.8 kg/m^2, p=0.01).

Conclusion: Low serum free-testosterone (LST) levels and symptoms of androgen deficiency occur often among South African men with T2DM. The significance of these findings need further evaluation.

Abstract Number: 41

Gluconeogenesis During Endurance Exercise In Cyclists Habituated To A Long-term Low Carbohydrate High Fat Diet

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Endogenous glucose production (EGP) occurs via hepatic glycogenolysis (GLY) and gluconeogenesis (GNG) and plays an important role in maintaining euglycemia. Rates of GLY and GNG increase during exercise in athletes following a mixed macronutrient diet; however these processes have not been investigated in athletes following a low carbohydrate high fat (LCHF) diet. Therefore, we studied 7 well-trained male cyclists that were habituated to either a LCHF (7% carbohydrate, 72% fat, 21% protein) or mixed diet (51% carbohydrate, 33% fat, 16% protein) for longer than 8 months. After an overnight fast, participants performed a 2-hour laboratory ride at 72% of maximal oxygen consumption. Glucose kinetics were measured at rest and during the final 30 minutes of exercise by infusion of [6,6- $^2H_2$]-glucose and the ingestion of ^2H_2O tracers. Rates of EGP and GLY both at rest and during exercise were significantly lower in the LCHF group than the mixed diet group (Exercise EGP: LCHF, 6.0 ± 0.9; Mixed, 7.8 ± 1.1 mg/kg/min, $p < 0.01$. Exercise GLY: LCHF, 3.2 ± 0.7; Mixed, 5.3 ± 0.9 mg/kg/min, $p < 0.01$). Conversely, no difference was detected in rates of GNG between groups at rest or during exercise (Exercise: LCHF, 2.8 ± 0.4; Mixed, 2.5 ± 0.3 mg/kg/min, $p = 0.15$). We conclude that athletes on a LCHF diet do not compensate for reduced glucose availability via higher rates of glucose synthesis compared to athletes on a mixed diet. Instead, GNG remains relatively stable while glucose oxidation and GLY are influenced by dietary factors.

Abstract Number: 42

Athrixia Phylicoides (bush Tea) Extract Protects Pancreatic Beta Cells Against Oxidative Stress And Lipotoxicity

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Background: Currently, drugs used to treat type 2 diabetes (T2D) help to manage hypoglycaemia in the short term but fail to protect the β-cells and prevent the pathophysiological deterioration of the disease. Sourcing therapeutic agents from natural sources, which protections β-cells from diabetic stressors provides a unique opportunity for the development T2D adjuvant therapeutics. The phenolic constituents of *Athrixia phylicoides*, a shrub indigenous to South Africa, make it a promising candidate to reduce inflammation and oxidative stress, and thus protect β-cells.

Methods: Rat (RIN-5F) beta cells, were exposed to a range of concentrations of an aqueous extract of *A. phylicoides* (0.00001 - 1000 µg/mL) for 1, 3 and 24 hours, respectively to determine if the extract was toxic to the cells. The cells were then exposed to oxidative stress and lipotoxic conditions using 10 mM streptozotocin (STZ) and 1 mM palmitate (PA), respectively. The ability of *A. phylicoides*

to protect the RIN-5F cells against oxidative stress was assessed by measuring cellular ATP, apoptosis and while glucose stimulated insulin secretion was assessed under lipotoxic conditions.

Results: *A.phylicoides* showed to be toxic only at the highest concentration tested (1000 µg/mL). Optimal extract concentrations (0.001, 0.1 and 10 µg/mL) were selected from the toxicity study. RIN-5F cells exposed to STZ and treated with the extract showed increased cellular ATP, decreased caspase 3/7 activation by ca. 29% and increased PA reduced glucose stimulated insulin secretion by ca. 243%.

Conclusion: This study indicates that an aqueous extract of *A. phylicoides* has some ability to protect RIN-5F pancreatic beta cells against oxidative stress induced apoptosis and restore cellular function under lipotoxic conditions.

Abstract Number: 43

Overweight Female Runners More Fat But Just As Healthy As Lean Counterparts

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Background: There is a growing prevalence of recreational endurance athletes who are overweight despite regular exercise. We investigated whether they are metabolically ill and the potential contributory lifestyle factors.

Methods: Twenty female runners [10 'Overweight (OW)', BMI ≥ 25kg/m ^{2} and 10 'Lean (L)', BMI <23kg/m ^{2}], aged 30-45 years and who had been running half-marathon distances for the previous 5 years, were recruited for the study. Body fat percentage (BF%) was determined by DXA. After an overnight fast, participants had their blood pressure taken and blood drawn for cardio-metabolic parameters and hepatic insulin-sensitivity (HOMA-IR). Peripheral insulin-sensitivity was assessed by an Oral Glucose Tolerance Test (Matsuda).

Results: OW and L were well-matched for age (OW, 38.7 ± 4.6; L, 37.7 ± 4.3), years of running experience (OW, 7.1 ± 4.4; L, 8.0 ± 3.7), current mileage in km/week (OW, 42.0 ± 10.9; L, 44.5 ± 12.1) and running calibre taken as energy expenditure (kcal/min) in their most recent half-marathon. OW exhibited higher adiposity including BF% (32.1 ± 3.9 vs. L, 21.8 ± 3.9, p < 0.0001), and had higher systolic (118 ± 10 vs. L, 107 ± 5, p 0.05), but not diastolic blood pressure. There were no differences in blood parameters except OW had higher (p 0.05) C-reactive-protein (1.30 ± 0.97 vs. L, 0.59 ± 0.35), cholesterol/HDL-C (2.70 ± 0.40 vs. L, 2.30 ± 0.42) and LDL-C (2.99 ± 0.65 vs. L, 2.43 ± 0.72). Insulin-sensitivity was similar between groups owing to considerable intra-group variation in HOMA-IR (OW, 0.62 - 2.25 vs. L, 0.53 - 1.23) and Matsuda (3.26 - 10.63 vs. L, 6.95 - 15.10). Three OW and two L runners had impaired fasting glucose (≥ 5.56 mM) and two OW runners exhibited insulin-resistance (Matsuda < 5); but no participants had metabolic syndrome. There were no significant differences in lifestyle factors including habitual diet, sleep and physical activity.

Conclusions: Despite elevated adiposity, OW female runners were not metabolically ill compared to matched L runners. Large inter-individual variation in metabolic parameters, however, suggests some OW runners may be at risk and motivates further exploration of the OW athlete phenotype.

Abstract Number: 44

Metabolic And Anti-diabetic Effects Of Athrixia Phylicoides

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Background: Insulin resistance is the major risk factor for type 2 diabetes (T2D) and cardiovascular disease. There is a need to find alternative and/or supplementary treatments that can improve insulin sensitivity to prevent or delay the onset of this serious metabolic disease. An aqueous extract of *A. phylicoides* has previously displayed anti-oxidant and anti-diabetic properties *in vitro* and is therefore likely that *A. phylicoides* can also modulate glucose metabolism *in vivo*. This study investigated the effect of an aqueous extract on glucose metabolism in differentiated, insulin resistant C2C12 myocytes and in diabetic db/db mice .

Methods: Insulin resistance was induced in C2C12 myocytes using palmitic acid (500 µM) for 16 hours, followed by treatment with two concentrations (10 and 100 µg/ml) of an aqueous *A. phylicoides* extract in the presence and absence of insulin. Cellular ATP content was served as a measure of cell viability and glucose uptake was measured using a glucometer. Six-week old obese C57BLKS db/db mice were treated with *A. phylicoides* extract (20 and 200 mg/kg body weight) for 28 days. Body weights, fasting blood glucose levels, food and water intake were monitored weekly followed by an oral glucose tolerance test. Serum lipids were also assessed.

Results: Preliminary results suggested that *A. phylicoides* increased basal glucose uptake, but not in insulin resistant C2C12 myocytes. *A. phylicoides* had no effect on body weight, fasting blood glucose or plasma lipids in diabetic db/db mice.

Conclusion: Current results suggest that *A. phylicoides* is unable to alleviate insulin resistance *in vitro* and hyperglycemia in a spontaneous diabetic db/db mouse model. However, the preventive potential on insulin resistance before the onset of T2D has not been assessed. Further investigation into underlying mechanisms will be discussed.

Abstract Number: 45

The Differential Effects of Insulin Treatment on Hypoxia and Extracellular Matrix Expression In mature 3T3-L1 Adipocytes

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Objective: Compared to white South African (SA) women, black SA women have less abdominal and greater gluteal-femoral fat, but

paradoxically are more insulin resistant and hyper-secrete insulin to maintain normoglycaemia. Insulin resistance in black women was associated with their greater gluteal subcutaneous adipose tissue (SAT) cell size, and higher hypoxia inducible factor 1 (*HIF-1α*), and extracellular matrix (ECM) component (collagen V α1 (*Col5a1*) and collagen VI α1 (*Col6a1*)) gene expression. Using a cell culture approach we tested the effects of chronic high insulin treatment on ECM and gene expression under hypoxic vs. normoxic conditions

Methods: Differentiated *3T3*-L1 adipocytes were cultured in increasing concentrations of insulin (baseline (0.02nM), medium (2.5 μM) and high (12.5 μM)) for 8 hours under hypoxic (5%O_2) vs. normoxic (21%O_2) conditions. Oil-red-O staining, quantitative real time PCR (qRT-PCR) and Western blotting was used to determine the effects of increasing insulin concentrations on triglyceride content and *HIF 1α*, *Col5a1*- and *Col6a1* expression.

Results: Insulin treatment significantly reduced triglyceride content in adipocytes, and the effect was exacerbated in the hypoxic vs. normoxic condition (interaction effect, p<0.001). Compared to the normoxia condition, *HIF-1α* mRNA and protein expression was significantly higher in the hypoxia treated cells (oxygen effect, p<0.001). Also, insulin treatment resulted in higher *HIF-1α* mRNA levels compared to the baseline insulin controls in both the normoxic and hypoxic conditions (insulin effect, P<0.001) but *HIF-1α* protein was only increased in the highest insulin concentration compared to the baseline insulin control in the normoxia condition, with no significant effect seen in the hypoxia condition. Conversely, Hypoxia but not insulin resulted in an increased COL5a1 and COL6a1 protein expression (oxygen effect, p<0.001) when compared to the normal control, whereas no effect was observed on mRNA level.

Conclusion: Hypoxia and high insulin treatment during normoxia increased *HIF-1α* protein and mRNA expression and reduced cellular triglyceride content. Hyper-insulinemia and the *in-vivo* hypoxia signal may share a common aim to reduce excess fat accumulation through increased triglyceride oxidation. However, hypoxia but not insulin resulted in increased *COL5a1*- and *COL6a1* protein expression and indicates that the effect of hypoxia on *Col5a1* and *Col6a1* is independent of insulin.

Abstract Number: 46

Epidemiology Of Hyperglycemia In Tuberculosis Patients In An Urban Cape Town Township

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Background: Diabetes (DM) is a significant risk factor for developing tuberculosis (TB). We describe the patterns of hyperglycemia and DM in TB patients from Khayelitsha, South Africa.

Methods: TB cases were identified at Ubuntu clinic Khayelitsha. Participants were screened at baseline for DM with fasting glucose (FG), HbA_{1c}, and oral glucose tolerance test (OGTT). Hyperglycemia definition was:FG>5.6 or OGTT>7.8 or HbA_{1c}>5.7%. DM definition was:FG>7 or OGTT>11.1 or HbA_{1c}>6.5. Demographic information, risk factors for non-communicable diseases (NCDs), and body mass index (BMI) were also recorded. HIV status was obtained.

Results: TB cases were mostly male (58%, 95%CI 53.2-62.6) with a median age of 35.4 (IQR 29.6-42.6) and a median BMI of 21.4 (IQR 19.1-24.9). HIV co-infection was 64.1% (95%CI 59.3-68.79). The overall prevalence of hyperglycemia amongst TB cases was 74.2% (95%CI 69.7-79.5) whereas the overall DM prevalence was 13.6% (95%CI: 10.4-17.3). Table 1 shows hyperglycemia and DM prevalence stratified by blood test.

Table one: Hyperglycemia and DM prevalence by blood test

	Hyperglycemia (95% CI)	**Diabetes** (95% CI)
FG	10.65% (8.8-12.7)	4% (2.3-6.1)
OGTT	21.3% (18.8-24)	3% (1.2-4.4)
HbA1c	40% (36.9-43.1)	10% (7-12.7)

Table two shows hyperglycemia and DM by HIV status.

Table two: Hyperglycemia and DM prevalence by HIV status

	HIV positive (95% CI)	**HIV negative** (95% CI)	
Hyperglycemia	72.62% (66.8-77.9)	62.7% (53.- 71.7)	p=0.047
Diabetes	11.11% (7.6 -15.6)	14.29% (8.7-21.6)	p=0.37

There was no difference in hyperglycemia prevalence between HIV infected and uninfected patients when each blood test was considered in turn (FG:12.65%vs12.82% p=0.963; OGTT:22.76%vs15.74% p=0.133; HbA1c:50%vs52.14% p=0.702). DM prevalence was only statistically significantly lower in HIV-infected versus uninfected persons when diagnosed by FG but not using the HbA1c or OGTT tests (FG:3.04%vs7.94% p=0.032; OGTT:3.04%vs3.17% p=0.943; HbA1c:8.75%vs.11.11% p=0.457).

Conclusions: TB cases had a high prevalence of hyperglycemia with HIV infected patients having a higher prevalence than HIV uninfected. Antiretrovirals may contribute to this finding, and this requires further investigation. Overall, DM prevalence was lower and with no difference between HIV infected and uninfected. Both hyperglycemia and DM were most prevalent when diagnosed by HbA_{1c}, which needs to be explored further by comparing HbA_{1c} concentration with haemoglobin levels and investigating if HbA_{1c} levels remain high post completion of TB therapy.

Abstract Number: 47

Development Of A Method For Studying The In Vitro Formation Of Foam Cells From Human Monocytes.

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Background: Atherosclerosis is a chronic inflammatory disease characterized by lipid and cholesterol accumulation within the walls of arteries. Atherosclerosis has a complex aetiology and there are a number of factors that contribute to the onset and progression of the disease. Formation of macrophage foam cells (FC) is a major hallmark of early stage atherosclerotic lesions. The formation of FCs is the rate-limiting step in the development of fatty streaks and, subsequently, of more advanced atherosclerotic lesions. Currently there is a lack of suitable cellular models to study FC formation *in vitro*. Therefore the aim of this study was to develop a method for converting peripheral blood mononuclear cells (PBMC) into FCs.

Methods: Healthy volunteers were recruited and 40ml of blood collected in EDTA tubes. Buffy coats were harvested by centrifugation, separated by a Ficoll-Hypaque gradient (density 1.07 g/ml) and the monocyte layer isolated. The monocytes were washed three times in sterile PBS and cultured overnight with RPMI medium supplemented with 10% human serum. After 24 hours of culture the monocytes adhered to the culture plate and non-adherent lymphocytes were removed through washing with RPMI. The monocytes were then differentiated into macrophages by incubation over 5 days in standard media supplemented with macrophage colony-stimulating factor (M-CSF (100 ng/ml)). FC formation was induced through exposure of macrophages to copper oxidized human low density lipoprotein (OxLDL) at a concentration of 3.0 µg/ml for 48 hours. FC formation was determined through the ability of macrophages to accumulate lipid in the presence of OxLDL and was confirmed by Oil red O staining of the intra-cellular lipid.

Results: The addition of OxLDL to macrophages resulted in enhanced intracellular lipid accumulation and under microscopic examination they were seen to exhibit classic foam cell morphology with pronounced staining of intra-cellular lipid droplets.

Conclusion: This work resulted in the development of a method allowing for the *in vitro* generation of FCs from human monocytes and represents a useful tool for studying the molecular mechanisms involved in the control of FC formation. Further work will be undertaken to confirm the presence of foam cell-specific proteins, in particular the scavenger receptor.

Abstract Number: 48

Relationship Between The Vitamin D System And Autoimmunity In African Type 1 Diabetic Patients

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Background: Recent studies have associated vitamin D deficiency with type 1 diabetes (T1D), a chronic autoimmune disease characterised by the destruction of insulin secreting β-cells in the pancreas. The vitamin D binding protein (VDBP) is essential for biological actions and transport of vitamin D. Polymorphisms in the VDBP gene alter the protein structure and may be responsible for a decreased affinity for vitamin D. Our aim was to determine if there are any associations between serum levels or genotypes of the VDBP with T1D and associated immunological markers in a South African black population.

Methods: Clinically diagnosed black South African T1D patients (n=103) were recruited from Chris Hani Baragwanath and Charlotte Maxeke Johannesburg Academic Hospitals. Healthy black non-diabetic controls (n=96) were recruited from blood drives. Participants were genotyped for the presence of two single nucleotide polymorphisms (SNPs; rs7041 and rs4588) in the VDBP gene by PCR-RFLP. VDBP levels, GAD65 and IA2 autoantibody positivity were measured by ELISA. Vitamin D concentrations were determined by HPLC. Data is expressed as mean ± SD or median [interquartile range] and analysed using ANCOVA.

Results: There was no significant difference in age (29.3 ± 9.64 vs. 28.7 ± 9.22 years; p=0.66), VDBP (303 ± 140 vs. 322 ± 88.7 ng/L; p=0.29) or vitamin D levels (64.8 [52.4, 79.6] vs. 61.3 [48.8, 76.9] nmol/L; p=0.20) between patients and controls, respectively. However, BMI was significantly lower in patients than controls (23.7 [21.0; 28.0] vs. 26.6 [23.5; 31.6]; p=0.0001). There were no differences in VDBP SNP allelic frequencies between the two groups and there were no genotype associations with vitamin D or VDBP levels. The VDBP levels were lower in GAD-positive than GAD-negative cases (222 ± 100 vs. 283 ± 122 ng/L; p=0.03), whilst vitamin D levels were significantly higher in IA2-positive than IA2-negative cases (86.9 [60.7, 98.6] vs. 61.5 [50.5, 77.0] nmol/L; p=0.01).

Conclusion: Autoantibody positivity in African T1D subjects is associated with higher systemic levels of vitamin D and lower systemic levels of VDBP. This data suggests that the vitamin D system is linked to the autoimmune process in diabetic subjects, and warrants further investigation.

Abstract Number: 49

Chronic Inflammation As A Target For Prevention and/or Alleviation Of Metabolic Diseases

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Background: Chronic inflammation is a common underlying and, potentially, causative feature in the development of non-communicable diseases, such as type 2 diabetes and cancer. It is often overlooked as a target to prevent and/or alleviate such diseases of lifestyle. Recent evidence suggests that systemic low-grade inflammation may be initiated in the gastrointestinal tract due to dietary factors including high fat diets, which can alter the composition of gastrointestinal microbiota and decrease the integrity of the intestinal epithelial lining. The interaction between intestinal microbiota and the immune system is thought to be mediated by increased systemic lipopolysaccharide (LPS) levels as a result of reduced intestinal barrier function and subsequent activation of epithelial cells.

Methods: To investigate potential anti-inflammatory effects of Z-2-(β-D glucopyranosyloxy)-3-phenylpropenoic acid (PPAG), its effect on TNF-α release in LPS-stimulated THP-1 cells was investigated. A co-culture cell model was established using differentiated Caco-2 cells represented intestinal lining and differentiated THP-1 cells as immune cells. The co-culture was stimulated with 10 ng/ml LPS for 24 hours. Transepithelial electrical resistance (TEER) of the Caco-2 monolayer was determined and cytokine release into the apical and basolateral compartments was screened using an MSD V-Plex pro-inflammatory cytokine panel.

Results: PPAG only minimally decreased TNF-α release in LPS-stimulated THP-1 cells. TEER values decreased significantly ($P < 0.05$) when the co-culture was exposed to LPS in the basolateral compartment, but it was high enough for an intact monolayer. No difference was observed when LPS was added to the apical compartment. Cytokines released in significant amounts into the basolateral compartment following LPS stimulation included TNF-α, interleukin-8 (IL-8), IL-1β and IL-6, while IL-12p70, interferon-γ and IL-10 were only detectable at the lower detection limit of the Mesoscale instrument.

Conclusion: While PPAG showed only small anti-inflammatory effects in LPS-stimulated THP-1 cells, future studies will further investigate other factors contributing to the loss of intestinal barrier function, such as the modulation of apoptosis and its effects using the newly established co-culture model.

Abstract Number: 50

Tissue Non-specific Alkaline Phosphatase Is A Positive Mediator Of Intracellular Cholesterol Accumulation In The Y1 Adrenocortico Murine Cell Line

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Introduction: Cholesterol esters (CE) accumulate in the cells of the adrenal cortex and are used for the synthesis of steroid hormones. The full molecular pathways involved in mediating the accumulation of CEs within the adrenal cortex are yet to be elucidated. Tissue non-specific alkaline phosphatase (TNAP) is needed for intracellular lipid accumulation of triglycerides in adipocytes and is also expressed in the cortical cells of the adrenal gland. Therefore we aimed to determine if TNAP is needed for the accumulation of CEs within the murine Y1 adrenal cortex cell line.

Methods: The Y1 cells were induced to accumulate CE's by incubating them in medium containing cholesterol-BSA-oleic acid. The effect of TNAP inhibition on intra-cellular CE accumulation was determined through measurement of Oil Red O-stained intracellular lipids in the presence and absence of the TNAP inhibitor levamisole. The activity of TNAP in cell extracts was measured using an automated chemistry analyzer. Immunohistochemistry was used to determine the intracellular localisation of TNAP within the adrenocortical cells.

Results: The activity of TNAP in Y1 cells increased significantly after the initiation of CE accumulation reaching 233 ± 11.9% of baseline levels ($p<0.5$) within the initial 24 hours. Maximal levels of TNAP activity were achieved by day 4 (445 ± 71.43%; $p<0.05$ vs. baseline levels). In cells incubated with levamisole TNAP activity was significantly lower at all time points ($p<0.05$) whilst CE accumulation was lower on day X and day Y ($p<0.05$) when compared to cells not incubated with levamisole. Immunocytochemical staining showed that TNAP activity was localised to the lipid droplets of the Y1 cells.

Abstract Number: 51

McCune Albright Syndrome: The Spectrum Of G Protein Disease

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McCune Albright Syndrome (MAS) consists of a triad of café au lait patches, polyostotic fibrous dysplasia and hyperfunctioning endocrinopathies (classically precocious puberty, although hyperthyroidism, gigantism, renal phosphate wasting and rarely Cushing syndrome have been described). It is caused by sporadic somatic mutations in the GNAS gene, most commonly an amino acid substitution of arginine at position 201. This mutation leads to constitutive activation of the stimulatory subunit alpha of the G protein, leading to high cyclic AMP levels and resultant autonomous endocrine hyperfunction. Clinical manifestations and severity vary due to the mosaic distribution of affected cells.

Precocious puberty and fibrous dysplasia are the most common initial findings. This case series describes 3 patients with different clinical presentations to highlight the variable spectrum of endocrinopathies in MAS.

Patient 1 presented at age 5 to orthopaedic services with a limp, X-rays revealed a pathological right femur fracture. She was subsequently referred to oncology services where she was noted to have café au lait patches and precocious puberty. She had a suppressed TSH, but normal T4 and was clinically euthyroid. Serum phosphate was normal and she displayed good bone healing. She was commenced on Tamoxifen.

Patient 2 was initially seen at age 2 with rapid weight gain; he was referred to tertiary services at the age of 8 with refractory hypertension and noted to have a Cushingoid appearance. He had no café au lait patches, but had an obvious bony deformity over the frontal aspect of the skull. Imaging revealed extensive fibrous dysplasia of the skull and a pituitary microadenoma. Cushing syndrome was confirmed on the basis of a suppressed ACTH and loss of diurnal variation. Bilateral adrenalectomy was performed and histology showed bilateral nodular hyperplasia.

Patient 3 presented at age 3 with a painful hip and X rays revealed fibrous dysplasia. He was clinically thyrotoxic with multiple café au lait patches. He was initiated on Neomercazole and bisphosphonate therapy.

These cases highlight the variable spectrum of endocrine involvement in MAS and the importance of screening for other endocrinopathies in all cases.

Abstract Number: 52

Is genotyping useful in neonatal diabetes mellitus?

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Background: Little is known about the genotype of neonatal diabetes mellitus (NDM) in South Africa. This case series describes the clinical presentation of 5 patients identified with NDM at Tygerberg Children's Hospital (TCH), the course of the disease, and how genotyping influenced management of the identified patients.

Methods: NDM patients ≤6 months were identified by searching the diabetes register and hospital records from August 2007 - January 2016.Clinical and laboratory information was extracted from clinical records of TCH and the National Health Laboratory system. Genotyping was performed at the Molecular Genetics Laboratory at the University of Exeter Medical School in the UK. Patients' treatment and progress was extracted from medical records at Tygerberg hospital.

Results: Four girls and 1 boy with NDM were identified. Three patients were from mixed race and 2 from black ethnic groups. Patient 1 presented with transient NDM with uniparental paternal disomy of chromosome 6 who re-developed diabetes mellitus at age 7 years and is currently treated with NPH and regular insulin. Patient 2 presented with permanent NDM (PNDM) with mutations in the

KCNJ11 and ABCC8 genes and is treated with glibenclamide. Patient 3 has PNDM, is heterozygous for a missense INS mutation, p.G47V and is treated with NPH insulin. Patient 4 presented with PNDM, is heterozygous for INS missense mutation,p.A24V and is treated with NPH and regular insulin. Patient 5 presented with PNDM, seizures and hypoparathyroidism (which resolved). The Kir6.2 mutation for DEND syndrome was negative. She is on insulin glargine and insulin aspart. These patients are progressing well, growing along their weight and height percentiles and have HbA1c values ranging from 6 to 8,6%.

Conclusion: Each patient with NDM had a different genotype. This identified the patient treatable with sulphonylureas and helped to predict the course of the disease. A nationwide study investigating the South African-specific genotype is recommended.

Abstract Number: 53

Health Related Quality Of Life And Functional Disability Among South African Older Adults With Diabetes: Results From Study On Global Ageing And Adult Health (sage).

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Introduction: A search of the literature on quality of life in older adults in South Africa has yielded little information and in particular none specifically related to older adults living with diabetes.Indeed diabetes overwhelms leads to reduced self-care, which in turn leads to deteriorated glycaemic control and increased risks for complications. Quality of life is a vital health outcome in its own right, representing the ultimate goal of all health interventions. This study examined the association between health-related quality of life and sociodemographics, health risk behaviours and coexisting chronic conditions among older people with diabetes in South Africa.

Methods: We studied nationally representative survey data from (3840) South Africans adults older than 50 years of age who participated in Wave 1 of the Study of Global Ageing and Adult Health (SAGE) over the period (2007-2008). Multivariable regressions describe the relationship between diabetes, sociodemographics, health risk behaviour and coexisting chronic conditions and multiple indicators of quality of life (WHOQoL) and functional ability (WHODASi).

Results: The prevalence of diabetes was 9.8%.fifty four percent of the study sample were black African 44% of them were diabetics. Approximately 60% were females in the study population.44% of the study respondents were aged between 50-59 years. 60% of the respondents were married or cohabiting at the time of the survey. Overall, there was wealth gradient among diabetics groups. In multivariable analysis, functional disability, lack of quality of life was associated with self-reported diabetes. Gender, currently married, ethnicity, work status, wealth, and chronic morbidities (such as arthritis, asthma, depression hypertension) and physical activity were significant in association with diabetes ($p<0.01$).

Conclusions: In the next decades the prevalence of older adults with diabetes is anticipated to rise significantly. Improving quality of life for older people in South Africa through access to appropriate health care is an absolute imperative. There is a need to develop sustainable policies for healthy ageing at the local and national levels through promoting healthy eating behaviours and increase physical activity. This requires, identifying research priorities, allocating resources, and setting effective health care strategies.

Abstract Number: 54

Hypoglycaemia In Patients With Type 1 Diabetes At Inkosi Albert Luthuli Central Hospital (IALCH), Kwazulu-Natal.

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Background: Hypoglycaemia is an important acute metabolic complication of type 1 diabetes. Fear of hypoglycaemia may influence self-management strategies. Limited data exists on the prevalence and risk factors for hypoglycaemia in subjects with type 1 diabetes in South Africa.

Aim: The study aimed to assess the prevalence of hypoglycaemia in subjects with type 1 diabetes attending the adult Diabetes Clinic at IALCH in Durban. In addition, the study aimed to determine patient's fear of hypoglycaemia and behaviour patterns in response to hypoglycaemia.

Methods: Patients with type 1 diabetes attending the Diabetes Clinic were enrolled at the time of clinic attendance. Demographic and clinical data were recorded from patient files. Data on frequency and severity of hypoglycaemia over the previous 12 weeks was obtained from glucose meter downloads as well as diary records. Each patient completed the Hypoglycaemia Fear Survey questionnaire as well as a clinic-devised questionnaire on hypoglycaemic episodes.

Results: The study enrolled 151 subjects (58% female). The (mean± SD) age was 29.9 ± 11.8 years, duration of diabetes 13.2 ± 9.4 years, BMI 26.5 ± 5.2 kg/m^2 and HbA1c 9.6 ± 2.2%. "Any" hypoglycaemia occurred in 148 (98%) subjects. Of 143 respondents, "severe" hypoglycaemia occurred in 107 (74.8%) subjects, 65 (45.5%) had more than 2 severe episodes per year and 27 (18.9%) required hospitalisation for hypoglycaemia in the last year. The most frequent behavioural change in response to hypoglycaemia was insulin dose self-adjustment and the commonest concern was the possibility of becoming emotionally upset and difficult to deal with during hypoglycaemia.

Conclusions: In a tertiary diabetes clinic in KwaZulu-Natal, patients with type 1 diabetes experienc ed a high prevalence of hypoglycaemia with the majority experiencing more than 2 severe episodes in the year prior to clinic attendance. The commonest behavioural response to hypoglycaemia was insulin dose adjustment with the commonest concern being the possibility of becoming emotionally upset and difficult to deal with during hypoglycaemia.

Abstract Number: 55

Anti- Nmda Encephalitis. A Rare Endocrine Emergency.

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A case report that shows the presentation of a rare disease -NMDA MENINGOENCEPHALITIS

Case report: A 19year old female presented with a few days history of headache and photophobia. Initial lumbar puncture showed an elevated protein and lymphocytosis and she was started empirically on treatment for a viral encephalitis. Approximately 48 hours later she deteriorated-developing mutism, confusion and ataxia. Clinical examination revealed frontal and cerebellar signs, meningism, hirsuitism and tachycardia of 140 beats/min. She remained apyrexial.

It was established that she had a 4 month history of progressive hirsutism and a family history of Autoimmune disease. Over the next few days she developed labile blood pressure and blood glucose levels, suggestive of Autonomic dysfunction. A repeat Lumbar puncture now showed lymphocytes, neutrophils and elevated protein. NMDA receptor antibodies in the CSF were positive. She was diagnosed with NMDA meningoencephalitis.

Cardiac autonomic dysfunction was managed with Beta Blockers and K channel inhibitors, mania and psychosis were managed with antipsychotics. She was treated with Aciclovir, high dose corticosteroids and immunoglobulins. A unilateral ovarian teratoma was identified. All medication was stopped 2 months after oophorectomy.

ANTI - NMDA RECEPTOR ENCEPHALITIS: The NMDA receptor (N-methyl-D-aspartate) is a glutamate receptor found in nerve cells. When activated, it allows for the influx of sodium and calcium and the efflux of potassium. Calcium influx is important for memory and learning -the so-called "plasticity" of the brain.

This rare disease was originally described in 2007. It is more common in females and typically presents around 20 years. It presents with an acute onset of psychosis, with prominent oro-facial movements and autonomic dysfunction. It is thought to be a paraneoplastic presentation of an ovarian teratoma, where the body produces antibodies against the teratoma which has cross-reactivity with the NMDA receptors in the brain. The body fails to recognize "self"- leading to an attack via anti-NMDA receptor antibodies. Not all cases are associated with ovarian teratomas, and in the absence of a teratoma, the exact pathophysiology is poorly understood and the recurrence risk is higher.

Surgical removal of the teratoma leads to reversal of the symptoms, and cure.

Abstract Number: 56

The phenotype and natural history of ketosis-onset diabetes in Cape Town, South Africa

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Background: Many adults presenting with diabetic ketoacidosis (DKA) in South Africa do not have the classical clinical features of type 1 diabetes (T1DM). Elsewhere, studies have shown that patients with the clinical phenotype of type 2 diabetes (T2DM), particularly if they have negative antibodies and preserved beta cell function, may not require long term insulin therapy. We set out to describe the phenotype of patients presenting with a first episode of DKA in Cape Town.

Methods: All patients 18 years old, presenting with a first episode of DKA to 4 hospitals in the UCT/Groote Schuur Academic Health complex were prospectively enrolled. Patients were reviewed 1-3 weeks post discharge for clinical, biochemical and immunological testing, and were then followed up closely for the next year. If possible, patients were weaned from insulin according to a standard protocol.

Results: Of the 116 patients enrolled: 52% are men, the mean age is 37years and the ethnic distribution is 54% black and 46% coloured. In 78% there was no prior diagnosis of diabetes ("Ketosis-onset diabetes"); the mean duration of diabetes in the 22% previously diagnosed was 7 years.

Based on clinical impression at first visit 65% were classified as T2DM. On preliminary analysis this group differed from those clinically classified as T1DM with respect to BMI (33.4 vs 21.6 kg/m^2), presence of acanthosis (65% vs 0%), family history of diabetes (65% vs 24%), proportion with low C-peptide secretion (< 0.9ng/ml) 27% vs 84% and positive antibodies (anti GAD and anti IA2) 23% vs 72%.

In 50% of patients (44/88) with 6 months follow-up, insulin has been stopped. Initial predictors for insulin withdrawal were: clinically classified as T2DM, negative antibodies and preserved beta cell function. Mean HbA_{1c} off insulin was 6.9% vs 8.4% for patients on insulin.

Conclusions: In Cape Town, South Africa, the most common phenotype of adults presenting with 1st onset DKA is that of T2DM. 80% of newly diagnosed patients clinically classified as T2DM could be completely weaned off insulin by 6 months with an HbA_{1c} at target.

Abstract Number: 57

A case of Idiopathic Granulomatous hypophysitis presenting with acute meningitis

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Introduction: Idiopathic Granulomatous Hypophysitis is a rare inflammatory disease of the pituitary gland. It usually presents like a nonfunctioning pituitary adenoma both clinically and radiologically

and uncommonly presents acutely with features of meningitis. Diagnosis is frequently made after surgery through histological examination which reveal granulomatous hypophysitis.

Case presentation: A 34 year old female who was previously well presented with 1 week history of deteriorating headache, vomiting, fever, photophobia and worsening vision. On examination, she was apyrexial, had a bi-temporal hemianopia and neck rigidity. Brain CT showed a sellar mass. Lumbar puncture revealed a cerebrospinal fluid lymphocytic pleocytosis and an elevated protein level. Endocrine studies demonstrated secondary hypothyroidism with hypogonadotropic hypogonadism: TSH 0.33 mIU/L(0.27-4.2) FT4 7 pmol/l (12-22) FT3 2 pmol/l (3.9-6.7) Prolactin 5.4 ug/l (4.8-23.3) FSH 2.2 iu/l (1.7-21.5) LH 0.1 iu/l (1.0-95.6)

A magnetic resonance imaging study showed a 18*18 mm pituitary mass for which she underwent endoscopic transhenoidal hypophysectomy. Histopathological examination revealed non caseating granulomatous inflammation with numerous multinucleated giant cells. Secondary causes were excluded and the diagnosis of idiopathic granulomatous hypophysitis was made.

Abstract Number: 58

Is low ATM protein responsible for myocardial insulin resistance associated with obesity?

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Ataxia-telangiectasia (A-T), an autosomal recessive disorder caused by mutations in the ataxia-telangtiectasia mutated gene, is coupled to low or no expression of ATM, a ser/thr protein kinase.

A-T patients suffer from insulin resistance/type 2 diabetes mellitus, atherosclerosis and ischaemic heart disease.

Aim: Since obesity may alter ATM expression, its myocardial levels and role in obesity-induced insulin resistance were studied.

Methods: Male Wistar rats were rendered obese and insulin resistant by diet (HFD) and compared to chow-fed controls (C). Measurements: IPGTTs, biometric and biochemical parameters, *ex vivo* perfused working hearts (functional performance), resistance to ischaemia/reperfusion and infarct development. Insulin sensitivity, measured by accumulation of [^{3}H]2DG in ventricular cardiomyocytes. Thoracic aortas tested in a PowerLab system and aortic endothelial cells (AEC's) used to determine NO production. A specific ATM inhibitor, KU60019, was used, protein expression determined by western blotting and NO measured by FACS analysis.

Results: (i) HFD cardiocytes were insulin resistant with reduced ATM and PKB/Akt expression: insulin-stimulated 2DG uptake 17.6±4.6 vs 27.5±3.2 pmol/mg prot/30min in C ($p<0.05$). (ii) KU inhibited insulin-stimulated 2DG uptake in C and HFD cells to 17±4.1 and 12.3 ±3.9 pmol/mg prot/30min respectively ($p<0.05$). (iii) HFD lowered expression of both ATM and PKB/Akt in myocytes by 60% (1±0.1 vs 0.4±0.1 ADU, $p=0.002$) and (1±0.05 vs 0.37±0.09, $p=0.0001$). (iv) KU significantly inhibited insulin-stimulated phosphorylation of both ATM ($p<0.001$) and PKB/Akt ($p=0.04$). (iii) KU increased coronary flow of both C and HFD hearts ($P<0.0001$), NO production by AEC's (23% increase in DAF fluorescence) and eNOS-mediated aortic relaxation. However. (iv) hearts from HFD but not C animals had significantly decreased coronary flow recovery on reperfusion following ATM inhibition. In contrast, KU in HFD animals was infarct sparing.

Conclusion: This is one of the first studies aimed to elucidate the importance of ATM in cardiac function. We showed downregulated expression of ATM in the heart in obesity coupled to insulin resistance in cardiomyocytes. Inhibition of ATM with KU mimicked this, also resulting in inhibition of insulin-stimulated PKB/Akt activation. ATM is therefore a prerequisite for insulin-mediated PKB/Akt activation and glucose uptake in cardiomyocytes and low ATM in HFD may be partly responsible for insulin resistance. In addition, we demonstrated an important role for ATM in vascular responsiveness.

Abstract Number: 59

A preclinical evaluation of the anti-hypertensive properties of an aqueous extract of *Agathosma* (Buchu)

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Hypertension, currently a pandemic, is one of the main risk factors for cardiovascular disease, hypertrophic heart disease, renal disease, stroke and blindness. Ischaemic heart disease and stroke are currently the top 2 causes of death worldwide. In view of the growing interest in the utilization of herbal remedies as treatment options, either alone or in conjunction with pharmaceuticals, this study investigated the anti-hypertensive properties of an aqueous extract of *Agathosma* (Buchu).

Methods: Male Wistar rats received normal rat chow (C) or a high-fat (40% fat) diet (HFD) for 16 weeks. A group of both C and HFD rats received: (i) Buchu extract as replacement for water from day 1 (prevention) or (ii) from week 12 (treatment) of the 16 weeks. Blood pressure (BP), food and water intake were monitored throughout and urinary production measured. At termination, body weight and visceral fat were determined. Blood was collected and serum insulin, c-peptide, leptin, aldosterone (ELISA) and ACE activity (FRET) determined.

Results: (i) The HFD elevated body weight and visceral fat gain while the Buchu extract significantly decreased both. (ii) BP rose steadily in HFD while this rise was completely prevented by the Buchu extract ingestion and normalised when used as treatment, having no effect on BP in C. (iii) Food and water intake were not affected and no diuretic effect was observed. (iv) Buchu ingestion decreased leptin levels and normalised the aldosterone levels that was increased by HFD. (v) No ACE inhibitor effect could be detected.

Conclusion: This aqueous extract of Buchu may serve as an alternative, cost effective natural therapy for the improvement of hypertension, also causing weight loss and an improved RAS.

Abstract Number: 60

Hypothalamic-Pituitary dysfunction in a patient with MELAS

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MELAS (Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like episodes), is a multisystem disorder, affecting predominantly the central nervous system. Endocrine dysfunction in mitochondrial disease is predominantly restricted to diabetes mellitus, due to the association with the heteroplasmic mitochondrial DNA (mtDNA) mutation, mA3243G. Other endocrinopathies are less frequently described.

We describe a 26 year old male presenting with lactic acidosis. Other common causes of lactic acidosis were excluded. He presented with a right hemiparesis, receptive aphasia and a reduced level of consciousness. CT and MRI were in keeping with ischaemia involving the left temporal and parieto-occipital regions. This did not conform to a specific vascular territory and was considered to be a stroke-like episode. Ancillary investigations exploring the involvement of other systems confirmed sensorineural deafness.

Notably he had proportionate short stature without dysmorphic features. Tanner staging was in keeping with a delay in secondary sexual characteristics. Bone age was 16 years of age, a delay of 10 years. Severe secondary hypogonadism was confirmed biochemically (testosterone <0.7nmol/l and 2.7nmol/l). Imaging showed a normal pituitary. There was no evidence of diabetes mellitus and thyroid disease. Further investigation of the hypothalamic-pituitary axis is being undertaken. The diagnosis of MELAS was supported by an elevated serum and CSF lactate to pyruvate ratio > 20. mtDNA sequencing confirmed MELAS.

Mitochondrial diseases are a heterogeneous group of disorders characterised by a respiratory chain deficiency, due to a mtDNA mutation of maternal inheritance. In MELAS there is dysfunction in oxidative phosphorylation which contributes to the pathogenesis of the stroke-like episodes. Hypothalamic-pituitary impairment typically occurs with severe mitochondrial phenotypes and thus presents in childhood but rarely in adults. We believe that this is the first report from South Africa describing hypogonadism in adults with MELAS.

Abstract Number: 61

Risk factors for incident diabetes in a cohort taking first line non-nucleoside reverse transcriptase inhibitor-based antiretroviral therapy

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Background: Efavirenz is the preferred non-nucleoside reverse transcriptase inhibitor (NNRTI) in first line antiretroviral therapy (ART) regimens in low and middle-income countries, where the prevalence of diabetes is increasing. Randomised control trials have shown mild increases in plasma glucose in participants in the efavirenz arms, but no association has been reported with overt diabetes. We explored the association between efavirenz exposure and incident diabetes in a large Southern African cohort commencing NNRTI-based first line ART.

Methods: Our cohort included HIV-infected adults starting NNRTI-based ART in a private sector HIV disease management programme from January 2002 to December 2011. Incident diabetes was identified by the initiation of diabetes treatment. Patients with prevalent diabetes were excluded.

Results: We included 56,298 patients with 113,297 patient-years of follow-up (PYFU) on first line ART. The crude incidence of diabetes was 13.24 per 1000 PYFU. Treatment with efavirenz rather than nevirapine was associated with increased risk of developing diabetes (Hazard ratio 1.27 (95% confidence interval 1.10 to 1.46) in a multivariate analysis adjusting for age, sex, body mass index, baseline CD4 count, viral load, NRTI backbone, and exposure to other diabetogenic medicines. Zidovudine and stavudine exposure were also associated with an increased risk of developing diabetes.

Conclusion: We found that treatment with efavirenz, as well as stavudine and zidovudine, increased the risk of incident diabetes. Interventions to detect and prevent diabetes should be implemented in ART programmes, and use of antiretrovirals with lower risk of metabolic complications should be encouraged.

Notes

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