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Royal Victoria Hospital, Belfast

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	Novo Lecture	Nordisk Lecture
1976	D.K. O'Donovan	
1977	S. Bloom	
1978	J.H.S. Robertson	
1979	A.G. Cudworth	
1980	D.A.D. Montgomery	
1981	Peter Watkins	
1982	G. Joplin	
1983	D.R. London	
1984	A.X. Bertagna	
1985	Malcolm Nattrass	Laurence Kennedy
1986	Brian Frier	JB Ferriss
1987	Maurice Scanlon	TJ McKenna
1988	D.A. Heath	AB Atkinson
1989	J. Ward	GH Tomkin
1990	R. Volpe	KD Buchanan
1991	Michael Besser	PPA Smyth
1992	R.V. Ragontte	DH Hadden
1993	Bruce Weintraub	David Powell
1994	Oscar Croffard	Patrick Bell
1995	Robert Lindsay	Brian Sheridan
1996	C.R.W. Edwards	Rosemary Freaney
1997	Stephanie Amiel	David McCance
1998	Robert Turner	Randle Hayes
1999	Ian Hay Sean	K Cunningham
2000	Stephen O'Rahilly	Michael Cullen
2001	Andre Lacroix	Daphne Owens
2002	J. Tuomilehto	Chris Thompson
2003	Tony Weetman	John Nolan
2004	R.V. Thakker	RGR Firth
2005	P.M. Stewart	FMP O'Harte
2006	Kevin Docherty	CH Walsh
2007	Lynnette Nieman	Timothy O'Brien
2008	Ken Ho	Donal O'Shea
2009	Daniel J. Drucker	Steven Hunter
2010	Joseph G. Verbalis	James Gibney
2011	Thomas A. Buchanan	Maria Byrne
2012	Beverly M.K. Biller	Fidelma Dunne
2013	Mark McCarthy	Diarmuid Smith
2014	Karel Pacak	Sean F Dinneen
2015	European Society of Endocrinology meeting, Dublin	

Lifetime Achievement Award

2012 David Hadden
2013 T Joseph McKenna
2014 Gerard Tomkin

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Friday 14th of October 2016

1 pm to 1.45 pm **Poster Viewing Session**

1.50 pm **Welcome and Introduction**
Professor FPM O'Harte
President, Irish Endocrine Society

Friday Oral Presentations

2.00 pm **OC1. Epidemiology of Gestational Diabetes Mellitus according to IADPSG/WHO 2013 criteria among Obese Pregnant Women in Europe**

Egan AM[1], Vellinga A[1], Desoye G[2], van Poppel MNM[3], Simmons D[4], Dunne FP[1] on behalf of the DALI Core Investigator Group.
[1]National University of Ireland, Galway, Ireland, [2]Department of Obstetrics and Gynecology, Medizinische Universitaet Graz, Graz, Austria, [3]Department of Public and Occupational Health, EMGO[+]-Institute for Health and Care Research, VU University Medical Centre, Amsterdam, The Netherlands and [4]Institute of Metabolic Science, Addenbrookes Hospital, Cambridge, England and Macarthur Clinical School, Western Sydney University, Sydney, Australia

2.15 pm **OC2. Tumour necrosis factor related apoptosis inducing ligand (TRAIL) reduces oxidative stress in human aortic endothelial cells exposed to inflammatory stimuli**

Forde H,[1,2] Harper E,[2] Davenport C,[1] Rochford KD,[2] Cummins PM,[2] Smith D[1]
[1]Department of Endocrinology, Beaumont Hospital, Beaumont, Dublin 9, [2]Department of Endothelial Cell Biology, Dublin City University, Glasnevin, Dublin 9

2.30 pm **OC3. Abnormal aldosterone/renin ratio is common in patients of African compared to European origin, is associated with hypokalaemia and left ventricular hypertrophy, but is rarely associated with abnormal adrenal imaging characteristics**

Ahmed KS[1], Bogdanet D[1], Heshe S[2], Boran G[3], Behan LA[1], Sherlock M[1], Gibney J[1]
[1]Departments of Endocrinology, Cardiology[2] and Chemical Pathology[3], The Adelaide and Meath Hospital, Incorporating the National Children's Hospital, Tallaght, Dublin 24

2.45 pm **OC4. What are the clinical consequences of changes induced in the hypothalamic-pituitary-thyroid axis following growth hormone replacement?**

Glynn N1, Kenny H[2], Salim T[3], Halsall DJ[4], Boran G[5], Cook P[6], Smith D[1], Tun T[7], McDermott JH[7], Tormey W[8], Thompson CJ[1], McAdam B[3], McKenna MJ[9], O' Gorman DJ[2], Agha A[1]
Departments of Endocrinology[1], Cardiology[3] and Chemical Pathology[8], Beaumont Hospital, Dublin, Ireland. School of Health and Human Performance[2], Dublin City University, Ireland. Department of Clinical Biochemistry[4], Addenbrooke's Hospital, Cambridge, UK. Department of Clinical Biochemistry[5], Adelaide and Meath Hospital, Dublin, Ireland. Department of Chemical Pathology[6], University Hospital Southampton, UK. Department of Endocrinology[7], Connolly Memorial Hospital, Dublin, Ireland. Department of Endocrinology[9], St Vincent's University Hospital, Dublin, Ireland

3.00 pm **OC5. Insight into the molecular mechanisms underlying enhanced gonadotropin hormone receptor activity in polycystic ovarian syndrome**

Owens L, Lerner A, Sposini S, Christopoulos G, Liyanage M, Islam R, Lavery S, Tsui V, Hardy K, Franks S, Hanyaloglu A
Institute of Reproductive and Developmental Biology, Imperial College London

3.15 pm **OC6. How frequently can we predict failure of fluid restriction in SIAD (syndrome of inappropriate antidiuresis)? Results of a prospective, multicenter audit**

Cuesta M, Garrahy A, Slattery D, Ortolá A[1], Tormey W[2], Calle-Pascual AL[1], Runkle I[1], Thompson CJ
Academic Department of Endocrinology, Beaumont Hospital/RCSI Medical School, Dublin, Ireland, [1]Servicio de Endocrinología y Nutrición, Hospital Clínico San Carlos/Universidad Complutense de Madrid, España, [2]Department of Chemical Pathology. Beaumont Hospital/RCSI Medical School, Dublin, Ireland

3.30–4.25 pm **Coffee and Poster Viewing Session**

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4.30 pm **OC7. Characterisation of the biological activity and therapeutic effectiveness of bone-targeting forms of glucose-dependent insulinotropic polypeptide (GIP)**
Vyavahare S, Barrie JW, Hasib A, Flatt PR, Irwin N
School of Biomedical Sciences, University of Ulster, Coleraine, United Kingdom

4.45 pm **OC8. A polymorphism in the KRAS 3′ UTR microRNA binding site: A case–control analysis assessing impact on differentiated thyroid cancer risk**
Owens PW[1,2], McVeigh TP[1,2,3], Miller N[1], Guerin C[4], Sebag F[4], Quill D[1,2], Bell M[5], Lowery AJ6**, Kerin MJ[1,2]**
[1]Discipline of Surgery, Lambe Institute for Translational Research, National University of Ireland, Galway. [2]Department of Surgery, Galway University Hospital, Galway. [3]Department of Clinical Genetics, Our Lady's Children's Hospital Crumlin, Dublin. [4]Department of Endocrine Surgery, Hôpital de la Timone, Marseilles, France, [5]Department of Endocrinology, Galway University Hospital, Galway. [6]University of Limerick, Graduate Entry Medical School, Limerick

5.00 pm **Inaugural IES Hadden Lecture**
Controversies in Diabetes 2016: Where do we go from here?
Professor David M Nathan MD
Director MGH Diabetes Centre and Clinical Research Centre
Professor of Medicine, Harvard Medical School

Saturday 15th of October 2016

8.00–9.00 am **IES Annual General Meeting**

Oral Presentations

9.15 am **OC9. The synthetic analogue apelin-13 amide, improves acute glucose tolerance via activation of the APJ receptor in diet induced obese diabetic mice**
Parthsarathy V, Hogg C, Flatt PR, O'Harte FPM
The Saad Centre for Pharmacy and Diabetes, School of Biomedical Sciences, Ulster University, Coleraine, N. Ireland

9.30 am **OC10. Investigation into the impact of Glucagon like peptide-1 therapy on IL-1 beta production in obesity**
Mat A[1], Tobin L[1], O'Brien[1] A, Hogan A[1], O'Shea D[2]
[1]Education and Research Centre, St Vincent's University Hospital, Dublin 4
[2]Dept of Endocrinology, St Vincent's University Hospital, Dublin 4

9.45 am **OC11. Changes in adipose tissue gene expression profile and fat mass are associated with deteriorating glucose tolerance**
Woods CP[1], Crowley RK[2], Gathercole LL[3], Hughes B[4], Gray J[4], McCarthy T[4], Crabtree N[4], Stewart pm:[5], Tomlinson JW[3]
Naas General Hospital, Co Kildare[1], St Vincent's University Hospital, Elm Park, Dublin 4[2], Oxford Centre for Diabetes Endocrinology and Metabolism (OCDEM), NIHR Biomedical Research Centre, University of Oxford, Churchill Hospital, Oxford, UK[3], School of Clinical and Experimental Medicine, Institute of Biomedical Research, Centre for Endocrinology, Diabetes and Metabolism (CEDAM), University of Birmingham, UK[4], Department of Endocrinology, University of Leeds, UK[5]

10.00 am **OC12. Vertical sleeve gastrectomy attenuates diabetic kidney disease in a rat model of obesity and type 2 diabetes**
Nair M[1], Elliott J[1,2], Jackson S[1], Corteville C[3,4], Abegg K[3,5], Boza C[6], Lutz T[3,5], le Roux CW[1,7], Docherty NG[1,7]
[1]Diabetes Complications Research Centre, Conway Institute, School of Medicine, University College Dublin, Ireland. [2]Department of Surgery, Trinity Centre for Health Sciences, St. James's Hospital, Dublin, Ireland. [3]Institute of Veterinary Physiology, Vetsuisse Faculty, University of Zurich, Switzerland [4]Department of Surgery, University of Wurzburg, Wurzburg, Germany. [5]Zurich Center for Integrative Human Physiology, University of Zurich, Switzerland [6]Bariatric Surgery, Clinica Las Condes, Santiago, Chile [7]Gastrosurgical Laboratory, Sahlgrenska Academy, University of Gothenburg, Sweden

10.15 am **OC13. Effects of dapagliflozin and liraglutide on metabolic control and cognition in high fat fed mice**
Millar PJB[1], Pathak NM[1], Pathak V[1], Bjourson AJ[2], O'Kane MJ[2], Flatt PR[1], Gault VA[1]
[1]School of Biomedical Sciences, Ulster University, Coleraine, UK
[2]Northern Ireland Centre for Stratified Medicine, C-TRIC Building, Londonderry, UK. [3]Clinical Chemistry Laboratory, Western Health and Social Care Trust, Altnagelvin Hospital, Londonderry, UK

10.30 am **Inaugural IES McKenna Lecture**
"Pituitary replacement therapy: refinement, interactions and unanswered questions"
Professor Amar Agha MD FRCPI
Consultant Endocrinologist, Beaumont Hospital and Lecturer in the RCSI

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11.00–11.30 am Coffee and Poster Presentation session

11.30 am OC14. Evaluation of beta to alpha cell transformation in the INS-1 cell line
Tanday N, Moffett RC, McClean S, Flatt PR
School of Biomedical Sciences, Ulster University, Coleraine, United Kingdom

11.45 am OC15. Investigation of the regulatory role of GPR120 receptor on islet function and glucose homeostasis
McCloskey AG, Gormley NM, Flatt PR, McKillop AM
Biomedical Sciences Research Institute, Ulster University, Coleraine, Northern Ireland

12.00 pm OC16. Is it time for Renin Measurement to be part of the Diabetologist's Armamentarium?
Griffin TP[1], Wall D[2], Browne GA[3], Dennedy MC[1,3], O'Shea PM[4]
[1]Centre for Endocrinology, Diabetes and Metabolism, Galway University Hospitals, Galway, [2]School of Mathematics, Statistics and Applied Mathematics, National University of Ireland, Galway, [3]Discipline of Pharmacology and Therapeutics, Lambe Institute/Translational Research Facility, School of Medicine, National University of Ireland, Galway. [4]Department of Clinical Biochemistry, Galway University Hospitals, Galway

12.15 pm OC17. The elevated expression of the ER-stress induced miR-29a in individuals with type 1 diabetes Mellitus
Bacon S[1], Engelbrecht B[2], Schmid J[2,3], Pfeiffer S[2], Concannon CG[2], Mc Carthy A[1], Burke M[1], Prehn JHM[2,3], Byrne MM[1]
[1]Department of Endocrinology, Mater Misericordiae University Hospital, Eccles Street, Dublin 7, Ireland; [2]Department of Physiology and Medical Physics, [3]Centre for Systems Medicine, Royal College of Surgeons in Ireland, 123 St Stephen's Green, Dublin 2, Ireland

12.30 pm OC18. The effect of Vitamin D supplementation on insulin resistance in a pre-diabetic population: a double-blind randomised placebo controlled trial
Wallace HJ[1,2], Holmes L[2], Ennis CN[1,2], Cardwell C[2], Woodside JV[2], Young IS[2], Bell PM[1], McKinley MC[2], Hunter SJ[1]
[1]Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast, [2]Nutrition and Metabolism Group, Centre for Public Health, Queen's University Belfast

12.45 pm OC19. Postprandial studies unmask endothelial dysfunction in subjects with type 1 diabetes
McGowan A[1], Widdowson WM[1], Boran G[2], Moore K[1], Gibney J[1]
Departments of Endocrinology[1], and Chemical Pathology[2], The Adelaide and Meath Hospital, Incorporating the National Children's Hospital, Tallaght, Dublin 24

1.00 pm IES Summer Student Award Presentations

1.15 pm Presentation of Irish Endocrine Society O'Donovan Medal (best oral presentation) and Montgomery medal (best poster presentation)

Close of meeting

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Oral Presentations

OC1 Epidemiology of gestational diabetes mellitus according to IADPSG/WHO 2013 criteria among obese pregnant women in Europe

Egan AM[1], Vellinga A[1], Desoye G[2], van Poppel MNM[3], Simmons D[4], Dunne[1] FP on behalf of the DALI Core Investigator Group

[1]National University of Ireland, Galway, Ireland; [2]Department of Obstetrics and Gynecology, Medizinische Universitaet Graz, Graz, Austria; [3]Department of Public and Occupational Health, EMGO+-Institute for Health and Care Research, VU University Medical Centre, Amsterdam, The Netherlands; [4]Institute of Metabolic Science, Addenbrookes Hospital, Cambridge, England and Macarthur Clinical School, Western Sydney University, Sydney, Australia

Accurate prevalence estimates for gestational diabetes mellitus (GDM) in Europe are lacking. We aimed to calculate the prevalence of GDM in early, mid and late gestation in a cohort of women with body mass index (BMI) $\geq$ 29 kg/m^2 across 11 European centers using IADPSG/WHO 2013 diagnostic criteria and report pregnancy outcomes and important risk factors.

Pregnant women (n = 1023) with a BMI $\geq$ 29.0 kg/m^2 enrolled into the DALI (Vitamin D And Lifestyle Intervention for GDM prevention) pilot, lifestyle and Vitamin D studies of this trial, attended for oral glucose tolerance testing during pregnancy. Demographic, anthropometric and metabolic information were collected. Statistical analysis was performed using SPSS 21.0 (Chicago, USA).

Numbers recruited per country ranged from 80 to 217. Dropout rate (7.1 %) was low and 39 % developed GDM. Prevalence of GDM was 24 % (242/1023) in early pregnancy; 14 % (94/672) of the remaining cohort developed GDM in mid gestation (24–28 weeks); and 13 % (60/476) in late gestation (36 weeks). Demographics and lifestyle factors were similar between women with GDM and those who maintained normal glucose tolerance. Previous GDM (16.5 % vs 7.9 %, p = 0.002), congenital malformations (6.4 % vs 3.3 %, p = 0.045) and macrosomia (31.4 % vs 17.9 %, p = 0.001) were more frequent in women with GDM. Significant anthropometric and metabolic differences were present in early pregnancy between women developing GDM or not.

The prevalence of GDM in this cohort is substantial, posing a significant health burden to these pregnancies and the future well-being of the mother-offspring pair. Criteria for GDM in early pregnancy are needed to guide modern GDM screening and treatment strategies.

OC2 Tumour necrosis factor related apoptosis inducing ligand (TRAIL) reduces oxidative stress in human aortic endothelial cells exposed to inflammatory stimuli

Forde H,[1,2] Harper E,[2] Davenport C,[1] Rochford KD,[2] Cummins PM,[2] Smith D[1]

[1]Department of Endocrinology, Beaumont Hospital, Beaumont, Dublin 9; [2]Department of Endothelial Cell Biology, Dublin City University, Glasnevin, Dublin 9

Accumulating evidence suggests that increased oxidative stress has injurious effects within the vasculature. Excess reactive oxygen species (ROS) production leads to elevated expression of adhesion molecules, stimulation of vascular smooth muscle cell proliferation, and promotion of endothelial cell apoptosis; events which culminate in the formation and progression of atherosclerotic plaque. Tumour necrosis factor-related apoptosis-inducing ligand (TRAIL), a member of the tumour necrosis factor (TNF) superfamily, has been shown to exhibit anti-atherosclerotic properties in animal studies. Preliminary studies from our own group, indicate that under pro-atherogenic oscillatory flow, TRAIL treatment of human aortic endothelial cells (HAECs) can shift net gene expression toward an "atheroprotected" phenotype by up-regulating anti-oxidant genes e.g. superoxide dismutase 1, endothelial nitric oxide synthase. The aim of this study therefore was to confirm the anti-oxidant potential of TRAIL at a functional level. Primary-derived HAECs were cultured in 6-well plates and exposed to pro-oxidant conditions for 24 h (TNF-α 100 ng/ml or Glucose 30 mmol), in the presence and absence of TRAIL (100 ng/ml). Flow cytometry using dihydroethidium staining was utilised to measure ROS generation. TNF-α and hyperglycaemia both significantly increased ROS production within HAECs, whilst TRAIL alone had no effect on ROS production. TRAIL significantly attenuated ROS generation induced by either TNF-α or hyperglycaemia (n = 3, $p < 0.05$). In conclusion, TRAIL may impart protective pleiotropic effects on the vascular endothelium, in-part through reduction of oxidative stress. Though the anti-oxidant mechanism is unclear, this effect does not seem to be mediated by TNF-α antagonism.

OC3 Abnormal aldosterone/renin ratio is common in patients of African compared to European origin, is associated with hypokalaemia and left ventricular hypertrophy, but is rarely associated with abnormal adrenal imaging characteristics

Ahmed KS[1], Bogdanet D[1], Heshe S[2], Boran G[3], Behan LA[1], Sherlock M[1], Gibney J[1]

Departments of Endocrinology[1]; Cardiology[2] and Chemical Pathology[3]; The Adelaide and Meath Hospital, Incorporating the National Children's Hospital, Tallaght, Dublin 24

Adrenal mineralocorticoid biochemistry is known to differ between people of African and European ancestry. The aldosterone/renin ratio (ARR) is the initial screening test for primary hyperaldosteronism (PHA), but little data exists regarding ethnic variations in this.

Following clinical observation of a high prevalence of abnormal (increased) ARR in patients of African origin, we retrospectively reviewed all ARR measurements in a single centre over 10 years. Rates of hypokalaemia and intraventricular septal thickness (IVS, by echocardiography) were studied as end-points of PHA, and adrenal imaging was reviewed. Data are expressed as median (range) and analysed using Student's *t* test and Chi square test as appropriate. ARR was available in 1947 patients, and abnormal in 315 (16.2 %). Abnormal ARR occurred in 267/1823 (14.6 %) of European-origin and 48/124 (38.7 %) of African-origin patients ($p < 0.05$). Among those with abnormal ARR, hypokalaemia (< 3.5 mmol/l) was documented on at least one occasion in 153/267 (57.3 %) European-origin and 33/48 (68.8 %) African-origin patients (p = ns). Median (range) IVS was 1.57 (0.78 to 2.80) cm in African-origin and 1.2 (0.69 to 2.18) cm in European-origin patients ($P < 0.005$). Adrenal adenoma was identified in 2/48 (4.3 %) African-origin and 41/267 (15.4 %) of European-origin patients ($P < 0.05$). In summary, ARR was abnormal in 39 % of African-origin patients screened at an Irish hospital, but only 4.3 % had demonstrable adrenal pathology. Rates of hypokalaemia were similar between European-origin and African-origin patients, while cardiac hypertrophy was more marked in African-origin patients. These findings have implications for the use of current screening guidelines for ARR in African-origin patients and also for

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the mechanistic role of aldosterone in hypertensive complications in African-origin patients.

OC4 What are the clinical consequences of changes induced in the hypothalamic-pituitary-thyroid axis following growth hormone replacement?

Glynn N[1], Kenny H[2], Salim T[3], Halsall DJ[4], Boran G[5], Cook P[6], Smith D[1], Tun T[7], McDermott JH[7], Tormey W[8], Thompson CJ[1], McAdam B[3], McKenna MJ[9], O' Gorman DJ[2], Agha A[1]

Departments of Endocrinology[1]; Cardiology[3] and Chemical Pathology[8]; Beaumont Hospital, Dublin, Ireland. School of Health and Human Performance[2]; Dublin City University, Ireland. Department of Clinical Biochemistry[4]; Addenbrooke's Hospital, Cambridge, UK. Department of Clinical Biochemistry[5]; Adelaide and Meath Hospital, Dublin, Ireland. Department of Chemical Pathology[6]; University Hospital Southampton, UK. Department of Endocrinology[7]; Connolly Memorial Hospital, Dublin, Ireland. Department of Endocrinology[9]; St Vincent's University Hospital, Dublin, Ireland

Alterations in hypothalamic-pituitary-thyroid (HPT) axis have been reported following growth hormone (GH) replacement. However, the clinical significance of GH-induced alterations is unclear. We aimed to examine the relationship between changes in serum concentration of thyroid hormones and known biological markers of thyroid hormone action.

Twenty hypopituitary men were prospectively studied before and after routine GH replacement. Serum TSH and thyroid hormone (free and total T4, free and total T3, reverse T3) were measured. Changes in thyroid hormone concentrations were compared to alterations in serum biomarkers of thyroid hormone action. Resting energy expenditure (REE) and cardiac time intervals were also evaluated as sensitive markers of peripheral thyroid hormone exposure.

GH replacement provoked a decline in freeT4 concentration (-1.09 ± 1.99 pmol/L, $p = 0.02$); freeT3 level increased (+0.34 ± 0.15; $p = 0.03$). REE did not rise, as expected, with GH substitution. Sex hormone binding globulin level was unchanged. However, decline in serum ferritin (-26.6 ± 8.5 ng/ml; $p = 0.005$) correlated with fall in freeT4. Significant increases were recorded in serum bone turnover markers—procollagen type 1 amino-terminal propeptide +57.4 %; $p = 0.0009$, osteocalcin +48.6 %; $p = 0.0007$; c-terminal telopeptides of type I collagen +73.7 %; $p = 0.002$. Changes in bone formation markers occurred in parallel with fluctuations in thyroid hormone. Alterations in lipid profile, including a rise in large high density lipoprotein subfractions and Lp (a) (+2.1 ± 21.1 nmol/L; $p = 0.002$) did not correlate with thyroid hormone levels. Cardiac time intervals were not significantly altered. In conclusion, changes in the HPT axis, following GH replacement, are reflected in hepatic and bone markers of thyroid hormone action.

OC5 Insight into the molecular mechanisms underlying enhanced gonadotropin hormone receptor activity in polycystic ovarian syndrome

Owens L, Lerner A, Sposini S, Christopoulos G, Liyanage M, Islam R, Lavery S, Tsui V, Hardy K, Franks S, Hanyaloglu A

Institute of Reproductive and Developmental Biology, Imperial College London

Polycystic ovary syndrome (PCOS) is a common endocrine disorder, affecting 5–10 % of women of reproductive age, and is the major cause of anovulatory infertility. Aberrant secretion and/or action of gonadotropins are implicated but, to date, we have only limited knowledge about the precise mechanisms involved. Recent genome wide association studies have discovered signals at loci close to the genes coding for gonadotropin receptors. The functional significance of these polymorphisms is, as yet, unclear and represents a key area for research. In this study granulosa-lutein cells were obtained from women with and without PCOS undergoing IVF. RNA was extracted and qPCR performed to analyse differential gene expression. Cyclic AMP production was measured after administration of luteinising hormone (LH) and follicle stimulating hormone (FSH) to cultured cells using a second messenger accumulation assay. Intracellular calcium signalling was measured after administering LH using calcium fluorescent indicators. Increased expression of full-length FSH ($p = 0.02$) and LH ($p = 0.05$) receptor RNA was seen in PCOS, along with increased expression of signaling/trafficking molecules β arrestin-2 ($p = 0.03$), PDZ-protein GIPC ($p = 0.07$) and APPL1 ($p = 0.005$). No significant differences were seen in expression of LH receptor splice variants. cAMP level measured after administration of LH for 5 min was higher in cells from women with PCOS than from controls (× 4 fold). Cyclic AMP measured after administration of FSH for 5 min however was negligible in both groups, suggesting involvement of an alternative to the traditional Gs pathway. Administration of LH activated a calcium signaling response in granulosa cells. These provisional results reveal multiple molecular alterations of LH receptor action and downstream signaling in PCOS.

OC6 How frequently can we predict failure of fluid restriction in SIAD (syndrome of inappropriate antidiuresis)? Results of a prospective, multicenter audit

Cuesta M, Garrahy A, Slattery D, Ortolá A[1], Tormey W[2], Calle-Pascual AL[1], Runkle I[1], Thompson CJ

Academic Department of Endocrinology, Beaumont Hospital/RCSI Medical School, Dublin, Ireland; [1]Servicio de Endocrinología y Nutrición, Hospital Clínico San Carlos/Universidad Complutense de Madrid, España; [2]Department of Chemical Pathology. Beaumont Hospital/RCSI Medical School, Dublin, Ireland

Context: Fluid restriction (FR) is recommended as first line therapy for SIAD by both the European and the American guidelines. The American guidelines have identified clinical predictors of failure to respond to FR. These include 1. Urine osmolality (UOsm) > 500 - mOsm/Kg 2. Furst formula (ratio UNa + UK/pNa) > 1, and 3. 24 h-urine volume <1500 ml.
Objective: To ascertain the frequency with which patients with SIAD display at least one criterion for prediction of no response to FR.
Design: Prospective, non-interventional, multicenter study in Hospital Clínico San Carlos (Madrid) and Beaumont Hospital (Dublin)0.183 patients with SIAD were prospectively and consecutively recruited, 51 from Madrid and 132 from Dublin. The investigators did not interfere in the management of hyponatraemia unless specifically requested. Results are expressed as the absolute number or percentage for categorical variables and median with interquartile range (IQR) for quantitative as appropriate.
Results: There was 100 % ascertainment of the full diagnostic criteria for diagnosis of SIAD.75/183 (41 %) patients had UOsm > 500 mOsm/kg, 48/183 (26 %) a Furst formula > 1, 49/103 (47 %) urinary volume <1500 ml/24 h. 109/183 (59 %) had at least one criterion predicting no response to FR.

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Conclusion: More than half of SIAD patients had at least one criterion which have been recommended to predict failure to respond to FR, the first line therapy for SIAD. If the predictors of non-response to FR are correct, our data challenges the conventional wisdom that FR is first line treatment for SIAD. Further studies are needed to test the validity of the predictors of non-response in the US guidelines.

OC7 Characterisation of the biological activity and therapeutic effectiveness of bone-targeting forms of glucose-dependent insulinotropic polypeptide (GIP)

Vyavahare S, Barrie JW, Hasib A, Flatt PR, Irwin N

School of Biomedical Sciences, University of Ulster, Coleraine, United Kingdom.

The incretin hormone glucose-dependent insulinotropic polypeptide (GIP) possesses a well-characterised insulin secretory function following feeding, but has also been shown to have direct positive effects on bone strength and quality. This bone-specific action could be further harnessed by generation of bone-targeting GIP forms, through addition of six C-terminal acidic L-Asp amino acid residues that encourage binding to hydroxyapatite. The present study has investigated the effects of an enzymatically stable GIP analogue, [D-Ala^2]GIP, and an L-Asp C-terminally extended form, [D-Ala^2]GIP-Asp, on alkaline phosphatase (AlkP) activity in osteoblastic SaOS-2 cells and insulin secretion form BRIN BD11 beta-cells. We also examined effects of once-daily administration of both peptides (25 nmol/kg) for 42 days on bone mineral density (BMD) and content (BMC), and metabolic control in high-fat fed mice. AlkP activity in SaOS-2 cells was enhanced (10^{-9} to 10^{-6} M, $P < 0.01$) after 24, 48 and 72 h incubations with [D-Ala^2]GIP and [D-Ala^2]GIP-Asp. Both peptides significantly ($P < 0.001$) augmented insulin secretion from BRIN BD11 cells. Once daily injection of the peptides had no effect on body weight or food intake in high-fat mice, but circulating glucose was significantly ($P < 0.001$) reduced by day 42. Interestingly, glucose tolerance was enhanced by [D-Ala^2]GIP, but not [D-Ala^2]GIP-Asp. DEXA analysis revealed no difference in overall, femoral and lumbar BMD and BMC between groups of mice. However, assessment of tibia BMC uncovered marked ($P < 0.01$) benefits of [D-Ala^2]GIP-Asp. In conclusion, we show that biologically active, bone-targeting, forms of stable GIP analogues can be produced, and merit further investigation for the treatment of bone-related diseases.

OC8 A polymorphism in the KRAS 3′ UTR microRNA binding site: a case–control analysis assessing impact on differentiated thyroid cancer risk

Owens PW[1,2], McVeigh TP[1,2,3], Miller N[1], Guerin C[4], Sebag F[4], Quill D[1,2], Bell M[5], Lowery AJ[6], Kerin MJ[1,2]

[1]Discipline of Surgery, Lambe Institute for Translational Research, National University of Ireland, Galway; [2]Department of Surgery, Galway University Hospital, Galway; [3]Department of Clinical Genetics, Our Lady's Children's Hospital Crumlin, Dublin; [4]Department of Endocrine Surgery, Hôpital de la Timone, Marseilles, France; [5]Department of Endocrinology, Galway University Hospital, Galway; [6]University of Limerick, Graduate Entry Medical School, Limerick

Multiple low risk germline mutations may exert a polygenic influence on differentiated thyroid cancer (DTC) risk. One such variant in the KRAS 3′-untranslated region (UTR) of a miRNA binding site (rs61764370, T→G) has been implicated in susceptibility to subsets of breast, ovarian and head and neck cancers, although controversy exists as to its specificity as a biomarker. While other mutations at this 3′UTR are associated with DTC, little is known about rs61764370 and thyroid cancer risk. Tissue samples were obtained from patients with DTC attending tertiary referral centres in Ireland and France. Controls comprised cancer-free individuals over the age of 60. Germline DNA was isolated from whole blood and buccal swabs by *ethanol precipitation*. Genotyping was performed using Taqman-based PCR. The variant frequency was assessed in 948 samples (279 DTC cases, 669 controls). 210 (75 %) of cases were female. 85 % (219/258) with available histology were papillary subtype; the remaining were follicular. Distribution of the rs61764370 mutation did not vary significantly between groups, with both having minor allele frequencies (MAF) of 0.08. Genotypic odds ratios confirmed a lack of association with DTC; OR = 1.2 (95 % CI 0.68–1.49, p = 0.888) for heterozygous carriers vs wild type homozygotes; and OR = 1.0 (95 % CI 0.68–1.49, p = 0.997) for rare homozygotes vs wild type homozygotes. Presence of this 3′UTR polymorphism does not increase DTC susceptibility. While conflicting evidence exists as to the clinical utility of this polymorphism as a biomarker for other cancers, we can conclude that there is strong evidence against an association between rs61764370 and DTC susceptibility.

OC9 The synthetic analogue apelin-13 amide, improves acute glucose tolerance via activation of the APJ receptor in diet induced obese diabetic mice

Parthsarathy V, Hogg C, Flatt PR, O'Harte FPM

The Saad Centre for Pharmacy and Diabetes, School of Biomedical Sciences, Ulster University, Coleraine, N. Ireland

Apelin is an adipokine peptide secreted by adipocytes and has been identified as an endogenous ligand of the APJ receptor. Here we examined the ability of the novel stable apelin-13 amide analogue to combat acute glucose intolerance in a high-fat fed diet induced obese (DIO) insulin resistant mouse model. Male NIH Swiss mice were maintained on a high fat diet (45 % fat, 20 % protein, 25 % carbohydrate) from 8 weeks of age for 20 weeks to induce obesity and glucose intolerance. Fasted mice (18 h) were given an ipGTT (18 mmol/kg bw) glucose alone or in combination with apelin-13, apelin-13 amide or (Ala^{13})apelin-13 a known APJ receptor antagonist (all at 25 nmol/kg bw). Blood glucose and plasma insulin analysis was performed on tail blood samples at regular intervals up to 105 min. Apelin-13 amide significantly reduced (49 %) the glucose $AUC_{(0-105\ min)}$ ($P < 0.01$) compared to i.p. glucose alone, whereas apelin-13 had no effect and the antagonist (Ala^{13})apelin-13 caused an 18 % rise in blood glucose (Students t-test, $P < 0.05$). Effects of these peptides on insulin secretion demonstrated a 55 % increase ($P < 0.001$), no change and a 20 % reduction ($P < 0.05$), respectively. Furthermore, in a separate ipGTT co-administration of (Ala^{13})apelin-13 specifically antagonised the antihyperglycaemic ($P < 0.01$; AUC 22 % rise) and insulinotropic ($P < 0.01$; AUC 45 % decrease) actions of apelin-13 amide. These data show that apelin-13 amide markedly improves glycaemic control in DIO mice and is significantly more potent than native apelin-13. These actions can be attenuated in the presence of a specific APJ receptor antagonist.

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OC10 Investigation into the impact of glucagon like peptide-1 therapy on IL-1 beta production in obesity

Mat A[1], Tobin L[1], O'Brien A[1], Hogan A[1], O'Shea D[2]

[1]Education and Research Centre, St Vincent's University Hospital, Dublin 4; [2]Dept of Endocrinology, St Vincent's University Hospital, Dublin 4

Glucagon-like peptide-1 (GLP-1) receptor agonists are currently licensed for use in T2DM and Obesity. Previous reports showed that GLP-1 therapy reduces IL-1β levels in T2DM patients. IL-1β is a pro-inflammatory cytokine that has been implicated in the pathogenesis of T2DM and Obesity. The aim of the current study is to elucidate the mechanisms through which GLP-1 reduces the production of IL-1β. We recruited 47 patients who started GLP-1 therapy (liraglutide) for management of their T2DM or Obesity. Research samples were taken before commencement of therapy and after 12 weeks. Peripheral blood mononuclear cells (PBMC) were isolated and stimulated ex vivo with LPS for 24 h and the level of IL-1β was measured in the cell culture supernatants by ELISA. To investigate the impact of GLP-1 on IL-1β production in vitro, THP-1-derived macrophages were activated in the presence LPS and treated with varying concentrations of GLP-1. The levels of pro-IL-1β were analysed by real-time quantitative PCR, and active IL-1β was measured by ELISA. To date, 12 participants (58 % male; mean age 51.6 year) completed the study. GLP-1 therapy was associated with a reduction in mean BMI from 44.6 to 42.8 kg/m^2 ($p = 0.002$) and mean HbA1c from 52.5 to 47.8 mmol/mol ($p = 0.01$). FBG also decreased from 7.8 to 7.3 mmol/L ($p = 0.04$). Cholesterol profiles were not significantly affected. IL-1β production was reduced from mean of 3065.6 pg/ml pre-treatment to 392.6 pg/mL ($p = 0.02$). Our preliminary results show that IL-1β is reduced in T2DM patients 12 weeks post GLP-1 and this may be a direct cellular effect.

OC11 Changes in adipose tissue gene expression profile and fat mass are associated with deteriorating glucose tolerance

Woods CP[1], Crowley RK[2], Gathercole LL[3], Hughes B[4], Gray J[4], McCarthy T[4], Crabtree N[4], Stewart PM[5], Tomlinson JW[3]

[1]Naas General Hospital, Co Kildare; [2]St Vincent's University Hospital, Elm Park, Dublin 4; [3]Oxford Centre for Diabetes Endocrinology and Metabolism (OCDEM), NIHR Biomedical Research Centre, University of Oxford, Churchill Hospital, Oxford, UK; [4]School of Clinical and Experimental Medicine, Institute of Biomedical Research, Centre for Endocrinology, Diabetes and Metabolism (CEDAM), University of Birmingham, UK; [5]Department of Endocrinology, University of Leeds, UK

Increasing adiposity is associated with worsening glucose tolerance and insulin resistance. Not all obese individuals share the same risk of metabolic deterioration. We studied obese individuals to identify factors; including subcutaneous adipose tissue (SAT) gene expression profiles, that may predict, or track with worsening metabolic phenotype. 65 overweight/obese persons (women = 40, BMI = 33 ± 4.4kgs/m^2, age = 50.3 ± 7.3 years) were recruited into a prospective cohort study. Metabolic phenotype, including oral glucose tolerance testing (OGTT), body composition analysis using DXA and SAT biopsy were performed with a mean length of time to follow-up of 3.9 ± 1.5 years. Analysis was performed, using last observation carried forward and categorising patients into those whose glucose tolerance (as measured by AUC glucose across the OGTT) deteriorated ('*deteriorators*') or improved ('*improvers*') over the duration of the study. Baseline BMI and fat mass (total and regional) were not different between *deteriorators* or *improvers*. However, lean mass was significantly higher at baseline in those that glucose tolerance improved (59,038 ± 11,000 vs 50,727 ± 14058 g, $p < 0.05$). Increasing fat mass was associated with worsening glucose tolerance (36,325 ± 8134 to 39,588 ± 10190 g, $p < 0.005$). SAT gene expression profiles in the *deteriorators* demonstrated significant increased expression of genes involved in lipid metabolism (CD36, LPL, PNPLA2 and, DGAT) adipocytokines (LEP and ADIPO1), adipocyte differentiation (PPARG, GPD and CEBPA/B) and ER stress and Inflammation (HSPA5 and TNF). We have demonstrated that lower lean mass, increasing fat mass and altered SAT gene expression profiles are associated with worsening glucose tolerance. These factors may identify individuals at risk of developing metabolic disease and in whom interventions should be prioritised.

OC12 Vertical sleeve gastrectomy attenuates diabetic kidney disease in a rat model of obesity and type 2 diabetes

Nair M[1], Elliott J[1,2], Jackson S[1], Corteville C[3,4], Abegg K[3,5], Boza C[6], Lutz T[3,5], le Roux CW[1,7], Docherty NG[1,7]

[1]Diabetes Complications Research Centre, Conway Institute, School of Medicine, University College Dublin, Ireland; [2]Department of Surgery, Trinity Centre for Health Sciences, St. James's Hospital, Dublin, Ireland; [3]Institute of Veterinary Physiology, Vetsuisse Faculty, University of Zurich, Switzerland; [4]Department of Surgery, University of Wurzburg, Wurzburg, Germany; [5]Zurich Center for Integrative Human Physiology, University of Zurich, Switzerland; [6]Bariatric Surgery, Clinica Las Condes, Santiago, Chile; [7]Gastrosurgical Laboratory, Sahlgrenska Academy, University of Gothenburg, Sweden

Glomerulomegaly, progressive increases in urinary protein excretion and accelerated decline of glomerular filtration rate (GFR) are typical features of diabetic kidney disease (DKD). Vertical sleeve gastrectomy (VSG) involves resection of > 80 % of the stomach and results in 40 % of patients achieving diabetes remission at 1 year. The aim of the present study was to investigate the impact of VSG on proteinuria and glomerulomegaly in the Zucker Diabetic Fatty (ZDF) rat model of DKD.

Eighteen week old ZDF fa/fa rats underwent VSG (n = 5) or sham surgery (n = 5). Zucker fa/+ rats (n = 5) acted as healthy, lean controls. Glycaemic control was monitored over the subsequent 12 week period. Glomerular volume and urinary protein-creatinine ratio were assessed following harvest at post-operative week 12.

Sham operated ZDF rats developed overt hyperglycemia associated with proteinuria and glomerulomegaly. VSG significantly improved glycaemic control versus sham operated rats ($p < 0.01$). This was associated with significant attenuation of proteinuria (A) and paralleled at the histopathological level by significant reductions in glomerular volume (B) ($p < 0.05$).

Biochemical and histopathological indices of DKD in the ZDF rat are reduced following VSG surgery in tandem with improved glycaemic control. VSG may be of value as an intensive intervention in patients with poorly controlled diabetes and DKD.

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OC13 Effects of dapagliflozin and liraglutide on metabolic control and cognition in high fat fed mice

Millar PJB[1], Pathak NM[1], Pathak V[1], Bjourson AJ[2], O'Kane MJ[2], Flatt PR[1], Gault VA[1]

[1]School of Biomedical Sciences, Ulster University, Coleraine, UK; [2]Northern Ireland Centre for Stratified Medicine, C-TRIC Building, Londonderry, UK; [3]Clinical Chemistry Laboratory, Western Health and Social Care Trust, Altnagelvin Hospital, Londonderry, UK

The pathophysiology of type 2 diabetes is complex and no single therapy can adequately manage the disorder and related comorbidities. It is therefore necessary to develop safe combination therapies with distinct and complementary mechanisms of action. In the present study, metabolic and neuroprotective actions of SGLT2 inhibitor dapagliflozin was examined in combination with GLP-1 receptor agonist liraglutide using obese diabetic high fat fed mice. Mice received dapagliflozin-plus-liraglutide (1 mg/kg *po* and 200 μg/kg *ip*, respectively), dapagliflozin alone, liraglutide alone, or vehicle once-daily over 28 days. Energy intake, body weight, glucose and insulin concentrations, glucose tolerance, insulin sensitivity, hormone and biochemical analysis, DEXA scanning, object recognition, and islet histology were assessed. Once-daily administration of dapagliflozin-plus-liraglutide was generally superior to either treatment alone. Dual therapy resulted in significant decrease ($p < 0.05$–$p < 0.001$) in body weight, percentage body fat loss, circulating glucose and insulin concentrations, which were independent of changes in energy intake. Similar beneficial metabolic improvements ($p < 0.05$–$p < 0.001$) were observed following oral glucose tolerance, insulin sensitivity, HOMA-IR, HOMA-β, HbA1c and lipid profile. Recognition memory was significantly ($p < 0.01$–$p < 0.001$) improved without affecting motor activity or anxiety levels. Circulating plasma glucagon, GLP-1 and IL-6 levels were significantly increased ($p < 0.05$–$p < 0.001$) and corticosterone concentrations decreased ($p < 0.05$) in dapagliflozin-plus-liraglutide treated mice. Furthermore, alpha cell area, pancreatic glucagon and insulin content were increased ($p < 0.01$–$p < 0.001$). These data demonstrate that combination therapy with dapagliflozin and liraglutide exerts beneficial metabolic and neuroprotective effects in diabetic mice, highlighting an important personalized approach which requires further clinical evaluation in the treatment of diabetes and associated neurodegenerative disorders.

OC14 Evaluation of beta to alpha cell transformation in the INS-1 cell line

Tanday N, Moffett RC, McClean S, Flatt PR

School of Biomedical Sciences, Ulster University, Coleraine, United Kingdom

The role of insulin secreting beta cells transdifferentiating into alpha cells has yet to be determined in the pathogenesis of diabetes. This cellular plasticity could account for declining beta cell function and increasing alpha cell mass observed in type-2 diabetes. We look to see whether this transformation process occurs in the rat derived INS-1 beta cell line in order to generate an in vitro model of beta cell transdifferentiation. Cells were exposed to high glucose [25 mM], lipotoxic [0.25 mM palmitate], glucolipotoxic [25 mM glucose + 0.25 mM palmitate], low and high cytokine [100/300U/ml IL1β/IFNγ + 20/40U/ml TNFα] conditions for 24/48 h to examine whether this transformation occurs. Cell viability, insulin content/secretion and expression of insulin, glucagon and various beta and alpha markers were examined both at protein and gene expression levels by immunocytochemistry and qPCR, respectively. As expected viability was reduced when cells were exposed to cytokines ($p < 0.05$), lipotoxic ($p < 0.001$) and glucolipotoxic ($p < 0.05$) conditions. After 48 h of lipotoxicity, immunocytochemical expression of insulin was reduced ($p < 0.05$) whilst expression of glucagon positive cells were increased ($p < 0.01$) with the appearance of cells expressing both hormones ($p < 0.01$). Gene expression of alpha cell markers (glucagon, Arx) and progenitor marker neurogenin-3 were increased ($p < 0.01$) whilst beta cell markers (Glut2, Foxo1) appeared reduced in cytokine groups. These results suggest that INS-1 cells are capable of beta to alpha cell transformation and that this process occurs through downregulation of mature beta cell markers, reactivation of progenitor markers ultimately leading to upregulation of alpha cell markers and production of glucagon.

OC15 Investigation of the regulatory role of GPR120 receptor on islet function and glucose homeostasis

McCloskey AG, Gormley NM, Flatt PR, McKillop AM

Biomedical Sciences Research Institute, Ulster University, Coleraine, Northern Ireland

Type-2-diabetic therapies which enhance beta cell regeneration and function are needed and interest has focused on G-protein coupled receptors (GPCRs). The biological activation of GPR120 as a new therapeutic target was studied by investigating the functional role of the receptor and downstream signalling events activated by GPR120 agonists. Insulinotropic activity of agonists was examined in rodent (BRIN-BD11) and human (1.1B4) pancreatic cell lines; and glucagon secretion in α-TC1.9 cells. Expression of GPR120 was determined by RT-PCR and western blotting in BRIN-BD11 cells and lean and high fat fed (HFF) NIH-Swiss mice.

Endogenous ALA (10^{-9} to 10^{-4}M) and synthetic GW-9508 (10^{-8} to 10^{-4}M) agonists increased insulin secretion at 5.6 mM ($p < 0.01$–$p < 0.001$) and 16.7 mM ($p < 0.01$–$p < 0.001$) glucose in BRIN-BD11 and 1.1B4 cells. No cytotoxicity was observed as assessed by MTT. GPR120 ($p < 0.05$) and insulin ($p < 0.01$) mRNA expression was upregulated in HFF pancreas, compared to lean control. Incubation of BRIN-BD11 cells with ALA and GW-9508 increased GPR120 ($p < 0.05$) and insulin ($p < 0.01$) mRNA expression at 16.7 mM glucose, and the increase in GPR120 ($p < 0.01$) protein expression was confirmed by western blotting. Glucagon secretion was decreased with ALA (10^{-6} to 10^{-4}M) in αTC1.9 cells ($p < 0.05$–$p < 0.01$) and isolated islets ($p < 0.01$). GW-9508 (10^{-8} to 10^{-4}M) augmented glucagon secretion at 5.6 mM ($p < 0.05$–$p < 0.001$) and 16.7 mM ($p < 0.01$–$p < 0.001$) glucose in α-TC1.9 cells and isolated islets ($p < 0.05$–$p < 0.01$). Specificity of agonist activation was confirmed using the GPR120 antagonist AH7614 (10^{-4} M), resulting in no inhibition of glucagon secretion by ALA in α-TC1.9 cells. These studies suggest that the regulatory role of GPR120 in islet cell function and glucose homeostasis may have potential in the development of a novel therapy for type-2-diabetes.

OC16 Is it time for Renin Measurement to be part of the Diabetologist's Armamentarium?

Griffin TP[1], Wall D[2], Browne GA[3], Dennedy MC[1,3], O'Shea PM[4]

[1]Centre for Endocrinology, Diabetes and Metabolism, Galway University Hospitals, Galway; [2]School of Mathematics, Statistics and Applied Mathematics, National University of Ireland, Galway;

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[3]Discipline of Pharmacology and Therapeutics, Lambe Institute/ Translational Research Facility, School of Medicine, National University of Ireland, Galway; [4]Department of Clinical Biochemistry, Galway University Hospitals, Galway

Introduction: Hyperglycaemia increases succinate levels and succinate receptor (GPR91) activation in the kidney resulting in renin release. The aim of our study was to determine if there was an association between glycaemic control and markers of the Renin-Angiotensin-Aldosterone-System (RAAS).
Methods: A prospective cross-sectional study was conducted at Galway University Hospitals (GUH) between December 2014 and March 2015. Patients with diabetes were identified through interrogation of the electronic patient database, DIAMOND®, using non-probability consecutive sampling. Baseline clinical demographics, aldosterone, plasma renin activity (PRA), direct renin concentration (DRC) and aldosterone-to-renin ratio (ARR) measured using PRA and DRC, urea and electrolytes, glycated haemoglobin (HbA_{1c}), cholesterol, urine sodium and albumin:creatinine ratio were recorded.
Results: There was a significant positive linear correlation between HbA_{1c} and renin [both PRA ($p = 0.002$) and DRC ($p = 0.008$)] and between serum creatinine and aldosterone measured using radioimmunoassay (RIA) ($p = 0.008$) and immunochemiluminometric assay (ICMA) ($p = 0.008$). There was a significant negative linear correlation between serum sodium ($p = 0.005$) and DRC ($p = 0.015$) and between estimated glomerular filtration rate (eGFR) and aldosterone measured using RIA ($p = 0.020$) and ICMA ($p = 0.016$). A significant negative linear correlation also exists between urine sodium and PRA ($p = 0.040$) and aldosterone measured using RIA ($p = 0.045$).
Conclusions: There is a direct positive association between glycaemic control and renin. We advocate for renin measurement to be part of the diabetologist's armamentarium to assess, guide and optimise antihypertensive therapeutic strategies in patients with diabetes.

OC17 The elevated expression of the ER-stress induced miR-29a in individuals with type 1 diabetes mellitus

Bacon S[1], Engelbrecht B[2], Schmid J[2,3], Pfeiffer S[2], Concannon CG[2], Mc Carthy A[1], Burke M[1], Prehn JHM[2,3], Byrne MM[1]

[1]Department of Endocrinology, Mater Misericordiae University Hospital, Eccles Street, Dublin 7, Ireland; [2]Department of Physiology and Medical Physics; [3]Centre for Systems Medicine, Royal College of Surgeons in Ireland, 123 St Stephen's Green, Dublin 2, Ireland

Background and aims: MicroRNAs are 19–25 noncoding RNA molecules functioning as post-transcriptional regulators and play a crucial role in insulin secretion and action. Metabolically-stressed β-cells display markers of endoplasmic reticulum (ER)-stress and apoptosis. The expression of two specific microRNAs; miR-29a and miR-376a have been identified by our group as being induced during ER-stress. We aimed to determine the expression of the ER-stress induced miR-29a and miR-376a in human participants with T1DM and T2DM.
Materials and methods: 65 individuals participated with a mean duration of diabetes of 13 years. Participants were phenotyped and levels of serum miR-29a and 376a determined using RT PCR. We correlated expression levels with clinically relevant indices.
Results: Expression of miR-29a was higher in T1DM than in the T2DM cohort (448,000 [9,183,000–2×10^6] vs 240,500 [58,425–485,750], $p = 0.01$). miR-376a expression levels were not significantly different between the groups. No significant correlation was observed between miR-29a/miR-376a and markers of insulin resistance including BMI, OGIS, AUC insulin, HDL, triglyceride level or CRP. There was a significant correlation between miR-29a and diastolic blood pressure in the T2DM cohort ($rho = -0.4$, $p = 0.01$).
Conclusion: We demonstrate the higher expression of the ER-stress induced miR-29a in T1DM when compared to T2DM. ER-stress is implicated in the β-cell failure associated with T2DM. However, the role of ER-stress in the propagation of T1DM remains undefined. In the β-cells of a NOD mouse model, the over expression of miR-29a promotes apoptosis by decreasing levels of the anti-apoptotic protein Mcl-1. Our findings suggest that there is ongoing ER-stress in T1DM despite a long duration of diabetes.

OC18 The effect of vitamin D supplementation on insulin resistance in a pre-diabetic population: a double-blind randomised placebo controlled trial

Wallace HJ[1,2], Holmes L[2], Ennis CN[1,2], Cardwell C[2], Woodside JV[2], Young IS[2], Bell PM[1], McKinley MC[2], Hunter SJ[1]

[1]Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast; [2]Nutrition and Metabolism Group, Centre for Public Health, Queen's University Belfast

Observational studies have suggested an inverse association between low serum 25-hydroxyvitamin D (25(OH)D) concentrations and insulin resistance. High-quality trials are required to test the hypothesis that vitamin D is a direct contributor to type 2 diabetes pathogenesis. This study investigated the effect of vitamin D supplementation on insulin resistance in sixty-six individuals with pre-diabetes (impaired fasting glucose or impaired glucose tolerance) and low serum 25(OH)D concentrations (< 50 nmol/l). Subjects were randomised to receive 3000 IU (75 μg) cholecalciferol or placebo daily for 26 weeks. Compliance was monitored by pill count and change in serum 25(OH)D concentration using ultra performance liquid chromatography (UPLC). Insulin resistance was assessed pre and post intervention using a two-step euglycaemic-hyperinsulinaemic clamp technique. Between group comparisons of change were made using ANCOVA. Sixty-four subjects (placebo n = 30, vitamin D n = 34) completed the study. No hypercalcaemia or adverse effects were recorded. Mean change in serum 25(OH)D concentration was higher within the vitamin D compared to placebo group (70.5 nmol/l ± 31.4 versus 5.3 nmol/l ± 18.6, respectively; $p < 0.001$). Weight was unchanged throughout the study. Mean change in glucose infusion rate was −0.4 and 0.9 μmol/kg/min during step 1 and 0.6μol/kg/min and 0.3μol/kg/min during step 2, respectively ($p = 0.16$ Step 1, $p = 0.94$ Step 2). There was no significant difference in between group change in fasting plasma glucose, serum insulin or HbA1c ($p = 0.22$, 0.33 and 0.67, respectively). This study employed a robust assessment of insulin resistance and targeted a high-risk population with low 25(OH)D status at baseline and found that Vitamin D supplementation had no effect on insulin resistance in people with pre-diabetes.

OC19 Postprandial studies unmask endothelial dysfunction in subjects with type 1 diabetes

McGowan A[1], Widdowson WM[1], Boran G[2], Moore K[1], Gibney J[1]

Departments of Endocrinology[1]; and Chemical Pathology[2], The Adelaide and Meath Hospital, Incorporating the National Children's Hospital, Tallaght, Dublin 24

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Postprandial metabolic changes impair endothelial function, which is associated with development of cardiovascular disease in type 2 diabetes (T2DM) and non-diabetic subjects. Little data exists in type 1 diabetes (T1DM).

Subjects with T1DM (n = 20) and controls (n = 24) were studied fasting and 8 h following 2 mixed meals. Measurements taken included Apolipoprotein-B48(ApoB48) a marker of intestinally-derived lipoproteins, and flow-mediated-dilatation (FMD) of the brachial artery; a non-invasive measure of endothelial function. Additional control subjects (n = 98) were studied to further explore variables associated with endothelial function.

Fasting and postprandially, glucose and ApoB48 but not triglyceride concentrations were greater in T1DM subjects. Fasting FMD did not differ between groups but decreased significantly postprandially in T1DM subjects only. Pooled data (n = 142) revealed negative correlation (R = 0.27, P < 0.005) between peak-glucose concentration and postprandial FMD measurements.

	Mean Plasma Glucose (mmol/L)	Mean Triglyceride (mmol/L)	Mean ApoB48 (mcg/ml)	Flow Mediated Dilatation of brachial artery (Mean % change)
Controls Fasting	5.00 ± 0.44	1.25 ± 0.83	7.60 ± 5.01	6.90 ± 2.73
Controls Postprandial	4.93 ± 0.37	2.27 ± 1.67	14.10 ± 7.93	6.02 ± 2.07
T1D Fasting	9.89 ± 4.22**	1.02 ± 0.47	12.09 ± 3.94**	6.32 ± 3.34
T1D Postprandial	10.32 ± 4.49**	1.59 ± 0.88	22.1 ± 13.81*	3.17 ± 2.66**$^{\#}$

Mean ± S.D. Independent T-Tests

*p < 0.05 vs controls; **p < 0.001 vs controls; $^{\#}$p < 0.001 vs fasting

T1DM is associated with glucometabolic changes resulting in endothelial dysfunction, possibly mediated through postprandial glucose excursions

Poster Presentations

P1 Influence of chronic kidney disease aetiology on outcomes of multi-disciplinary diabetic renal clinic attendance

Martin WP[1], Griffin TP[1], Lappin D[2], Griffin D[2], O' Brien T[1,2], Griffin MD[1,2]

[1]Regenerative Medicine Institute (REMEDI), National University of Ireland, Galway, Ireland; [2]Endocrinology and Nephrology Services, Galway University Hospitals, Saolta University Health Care Group, Galway, Ireland

Background: Combined Diabetology and Nephrology care may benefit patients with type 1 (T1D) or type 2 (T2D) diabetes and chronic kidney disease (CKD). We aimed to assess the impact of CKD aetiology on outcomes of Diabetic Renal Clinic (DRC) attendance.

Methods: Patients attending a DRC at a tertiary referral centre during 2008–2012 were identified. Serial renal and metabolic indices were recorded from 2004 to 2014, and compared pre- and post-first DRC attendance using paired t-tests conducted through SPSS v22.

Results: 200 subjects were identified (44 (22.0 %) T1Ds and 156 (78.0 %) T2Ds). An alternative aetiology for CKD was found in 2 (4.5 %) T1Ds (both interstitial renal disease) and 34 (21.8 %) T2Ds: 22 (14.1 %) hypertensive renal disease, 12 (7.7 %) other.

Table 1 Laboratory indices pre- and post-first attendance

	Type 1 diabetic nephropathy (n = 42)				Type 2 diabetic nephropathy (n = 122)				Other CKD aetiology (n = 36)			
	Pre-first clinic	Post-first clinic	n (%)	p	Pre-first clinic	Post-first clinic	n (%)	p	Pre-first clinic	Post-first clinic	n (%)	p
Rate of eGFR decline (mean ± SD; mL/min/SA/year)	−1.97 ± 4.36	−2.88 ± 3.43	26 (61.9 %)	0.379	−3.09 ± 4.61	−2.38 ± 3.18	81 (66.4 %)	0.233	−3.65 ± 4.27	−1.60 ± 2.86	26 (72.2 %)	0.038
Mean $HbA1_c$ (mean ± SD; mmol/mol)	80.47 ± 19.42	72.58 ± 17.80	40 (95.2 %)	0.001	63.03 ± 15.19	61.51 ± 13.80	110 (90.2 %)	0.241	59.25 ± 10.85	58.02 ± 10.08	35 (97.2 %)	0.523
Mean LDL cholesterol (mean ± SD; mmol/L)	2.75 ± 0.88	2.49 ± 0.89	38 (90.5 %)	0.030	1.91 ± 0.73	1.83 ± 0.69	96 (78.7 %)	0.218	2.03 ± 0.96	1.92 ± 0.81	29 (80.6 %)	0.331

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Conclusions: Attendance at a multi-disciplinary DRC improved renal functional course for patients with diabetes and an alternative CKD aetiology, and metabolic indices in subjects with T1D.

P2 Association of vitamin D receptor TaqI gene variant in Exon 9 and ApaI in intron 8 with uncontrolled paediatric asthma in Ireland

Hutchinson K[1,4], Kerley CP[3], Cormican L[2], Faul J[2], Greally P[3], Coghlan D[3], Louw M[1], Elnazir B[3], Rochev Y[4]

[1]Biomnis Ireland, Sandyford, Dublin 18, Ireland; [2]Asthma Research Centre, Connolly Hospital, Dublin 15, Ireland; [3]Adelaide and Meath Hospital, Tallaht, Dublin 24, Ireland; [4]NCBES, National University of Ireland, Galway, Ireland

Asthma is a chronic heterogeneous respiratory disease and affects around one out of every five children in Ireland. Vitamin D receptor (VDR) polymorphisms have been associated with asthma risk. We aimed a) to determine the VDR TaqI gene variant in exon 9 (T/C) (rs731236) and ApaI (rs7975232) in intron 8 (C/T) in 45 paediatric patients with uncontrolled asthma and in 29 healthy volunteers and b) to investigate the impact of this polymorphism in asthma susceptibility in relation to 25-hydroxyvitamin D (25OHD) status and other biochemical and immunological indices. Genotypes were performed using TaqMan® Assay. We found that the distribution of T and C alleles and genotype frequencies differed significantly between asthmatics and controls for both polymorphisms (p value <0.05). No association was observed between genotypes and 25OHD levels, lung function and other biomarkers including IgE, Eosinophil Cationic Protein, Cathelicidin antimicrobial peptide and CRP, with the exception of IL-10. IL-10 levels were significantly low in asthmatics with TC genotype for TaqI polymorphism (p value <0.003) and were significantly high in patients with TT genotype for ApaI gene variant (p value <0.005). Our report suggests that TaqI and ApaI polymorphisms are associated with uncontrolled asthma in Irish children. Further studies are warranted to investigate the importance of decreased IL-10 levels in uncontrolled paediatric asthmatics with specific genotypes that could help us to understand the mechanism involved in the development of paediatric asthma.

P3 Audit of re-attendance of patients defaulting from the Endocrine clinics at Connolly Hospital

Plaisir C, Cheah SK, Kyaw Tun T, McDermott J, Sreenan S

Department of Endocrinology, Royal College of Surgeons in Ireland, Connolly Hospital Blanchardstown, Dublin 15, Ireland

Current HSE and hospital policy recommends discharge of patients following one missed outpatient appointment, a policy which is difficult to enforce on patients living with diabetes for which expertise in the primary care setting is limited or complex endocrine conditions that are beyond the scope of management in the community.

We reviewed electronic records of missed endocrinology and diabetes clinics from December 2011 to December 2014. Approximately 52 % of the records were available. There were 723 defaulting endocrinology and 1202 diabetes patients. Of these, 62 % (endocrinology) and 73 % (diabetes) received clinic recalls and 92 % had had no previous default, 71 % had 1, 59 % had 2 and 42 % had more than 2 previous defaults ($p < 0.01$). Of those offered further appointments, 31 % of patients defaulted again from Endocrinology, while 49 % defaulted from the diabetes clinic ($p < 0.01$). Overall, for those with no prior history of failed attendance, 38 % defaulted compared to 41 % if 1 previous default, 63 % if 2 previous defaults, and 56 % if > 2 defaults ($p < 0.01$). The time lapse to the next offered appointment did not impact on compliance.

We conclude that significant numbers of patients who miss appointments will present if offered further visits and those with fewer previous defaults are more likely to comply. Given the many possible reasons for failure to attend at clinic we feel that flexibility should be permitted in the offering of further appointments to the Endocrine Service.

P4 Tighter glycemic control in elderly type 2 diabetes patients attending a hospital diabetes clinic

Duane C, Cheah SK, Durak A, Kyaw Tun T McDermott J, Sreenan S

3U Diabetes, Department of Endocrinology, Royal College of Surgeons in Ireland, Connolly Hospital Blanchardstown, Dublin 15, Ireland

To compare glycemic control in elderly patients to younger age groups, we retrospectively reviewed HbA1c (A1c) measured in 1078 type 2 Diabetes (T2DM) patients consecutively attending for annual diabetes review. The overall mean ± SD A1c was 55.1 ± 16 mmol/mol. Patients >65 year (N = 462, mean ± SD age 73.3 ± 6 year, mean BMI 31.4 ± 5.5 kg/m^2) had a lower mean A1c of 52.7 ± 14.1 mmol/mol when compared with their counterparts aged <65 (N = 616, mean ± SD age = 53.5 ± 8 year, mean BMI 32.4 ± 6.8 kg/m^2) who had a mean HbA1c of 56.9 ± 17.0 mmol/mol, $p < 0.05$ for comparison of A1c. Insulin use and number of oral hypoglycemic medications were similar in those < and >65 year. Mean A1c in patients >40 year declined when compared in 10-year age brackets ($p < 0.05$, Table 1) and was 9.4 and 7.1 mmol/mol lower in patients aged 81–90 and 71–80 years, respectively compared to those aged 41–50 ($p < 0.05$). We conclude that these data may reflect overtreatment of T2DM and importance of individualised treatment in elderly.

Table 1 Mean HbA1c ± SD (mmol/mol) by 10-year age bracket

41–50	59.1 ± 19.5 (N = 147)
51–60	57.0 ± 16.3 (N = 289)
61–70	54.6 ± 15.6 (N = 315)
71–80	52.0 ± 11.9 (N = 209)
81–90	49.7 ± 11.8 (N = 67)

P5 Impact of obesity on management of type 2 diabetes

Cheah SK, Duane C, Durak A, Kyaw Tun T, McDermott J, Sreenan S

3U Diabetes, Department of Endocrinology, Royal College of Surgeons in Ireland, Connolly Hospital Blanchardstown, Dublin 15, Ireland

Type 2 diabetes (T2D) comprises a spectrum from thinner patients who may be more insulin deficient to those who are overweight/obese and insulin resistant. To compare management between these phenotypes, we reviewed 1007 T2D patients attending annual review. Patients were divided into quartiles by body mass index and those in

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the lowest (n = 252, age 63 ± 13 years) and highest (n = 252, age 60 ± 12) quartiles were compared (data are mean ± standard deviation. p = 0.001 for comparison of age). Phenotypic and biochemical data were compared using t tests while Chi square-test was used to compare proportions on different treatments. Systolic blood pressure, total and LDL cholesterol and eGFR, were not different between the groups. Mean BMI (kg/m^2) in the lowest quartile was 25.1 ± 2 compared to 40.2 ± 5 in the highest quartile, p < 0.001). Mean HbA1c (mmol/mol) was 54 ± 15 in the lowest quartile compared to 59 ± 19 in the highest, p = 0.001. In the lowest quartile, 14 % of patients were on insulin, 28 % on sulfonylureas and 71 % on metformin, compared to 25, 37 and 81 % in the highest quartile, respectively, p < 0.05 in each case. More patients in the highest quartile were on GLP-1 agonists (13 vs 2 % in the lowest quartile) but DPP4 inhibitors use was similar. In summary, thinner patients were slightly older and had slightly better glycemic control, despite less aggressive glycemia management. We believe that this reflects a different underlying pathophysiology of diabetes between these phenotypes and highlights the need for a personalised management approach.

P6 A study on age and nodule size in affecting decision for repeat thyroid FNAC after one benign cytology

Pierce B[1], Cheah SK[1], Premkumar A[1], Hickey N[2], Walsh T[3], Leen E[4], Sabah M[4], McDermott J[1], Sreenan S[1], Kyaw Tun T[1]

[1]Department of Endocrinology; [2]Radiology; [3]Surgery and [4]Histopathology, Connolly Hospital Blanchardstown, Dublin 15, Ireland

The British Thyroid Association (BTA) recently updated guidelines recommending that an FNAC that initially yields benign cytology (Thy2) should be repeated if there is any clinical or ultrasound (US) suspicion. We postulate that there is a tendency for a more conservative approach in older age groups with smaller thyroid nodules.

From our multidisciplinary meeting database for thyroid nodules under investigation from 2012 to 2015, we identified 126 cases with a single Thy2 cytology. Cases were recommended for conservative approaches (US and clinical surveillance) or more invasive approaches (repeat FNAC or surgery). Mean age and nodule size were compared between these groups, with independent t-test applied for the mean difference.

Patients recommended for US (36 cases, 29 %) or clinical surveillance (28 cases, 22 %) had a mean age of 56.7 ± 16.7 years with a mean nodule size of 25.1 ± 15.2 mm (mean ± standard deviation). Patients recommended for surgery (9 cases, 7 %) or repeat FNAC (53 cases, 42 %) were younger with a mean age of 47 ± 15.2 years and a larger mean nodule size at 33.7 ± 15.2 mm. 9 patients recommended for surgery included 5 cases with tracheal compression, 2 cases for concomitant hyperthyroidism, 1 case for cosmetic reason and 1 case unspecified.

Between these groups, there is a mean difference of 9.7 years (p = 0.001) for age and 8.5 mm for nodule size (p = 0.002).

After one benign cytology, there is a tendency for a more conservative approach in older patients with smaller nodule. The thresholds directing such decisions lie at approximately 50 years of age and a nodule size of 30 mm.

P7 Atlantic DIP: pregnancy and beyond: an evaluation of women with diabetes 1 year post delivery

Egan AM, Carmody L, Kirwan B, Dunne FP

Galway Diabetes Research Centre, National University of Ireland Galway, Galway, Ireland

During pregnancy women are motivated to achieve treatment goals and typically receive intensive support from a specialist service. This study sought to examine if positive changes observed during pregnancy were sustained at 12 months postpartum.

We included women with type 1 and 2 diabetes attending three centres along the Irish Atlantic Seaboard for antenatal care from January 2006 to December 2014. Women were evaluated at 6 months prepregnancy, during pregnancy and at 12 months postpartum. Statistical analysis was performed using SPSS 21.0 (SPSS Inc, Chicago, USA).

269 women were included, 177 (66 %) with type 1 and 92 (34 %) with type 2 diabetes. 117 (44 %) attended prepregnancy care. At 12 months postpartum, 70 (26 %) were attending prepregnancy care, 26 (9.7 %) were pregnant, 40 (14.9 %) were lost to follow up and133 (49.5 %) were attending routine diabetes clinics.

Despite achieving tight glycaemic control by the first trimester of pregnancy (mean HbA1c 7.2 ± 1.6 %), there was no significant difference in HbA1c before and 12 months after pregnancy (before: 7.8 ± 1.9 %, after: 7.6 ± 1.7 %, p = 0.26). There was no difference in blood pressure, lipid profile, albumin-creatinine ratio or weight in women before and after pregnancy. The subgroup of women who achieved a first trimester HbA1c of <7.0 % continued to demonstrate superior glycaemic control at 12 months postpartum (6.8 ± 1.3 vs 8.4 ± 1.8 %, p < 0.001).

By 12 months postpartum, glycaemic control has deteriorated in women with diabetes. These findings highlight the postpartum period as a crucial time to engage women to maintain the positive changes observed during pregnancy and impact on long-term outcomes.

P8 EMERGE: a randomized placebo controlled trial of early metformin in addition to usual care in the reduction of gestational diabetes mellitus effects

Dunne F[1], Devane D[1], Newell J[1], Gillespie P[2], Tuthill A[3], Donnell MO[1]

[1]College of Medicine Nursing and Health Sciences; [2]Health Economics, National University of Ireland, Galway and [3]Department of Medicine, Cork University Hospital, Cork

Gestational diabetes is common. Despite current management with diet exercise and insulin adverse outcomes of macrosomia and excessive maternal gestational weight gain (GWG) continue to be problematic. We will evaluate whether the initiation of early metformin (at GDM diagnosis) in women of all BMI categories undergoing universal screening with IADPSG criteria, improves glycaemic control, reduces excessive GWG, improves perinatal outcome and postpartum maternal glucose status compared to placebo. Detailed cost benefit and cost utility analyses will be conducted.

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A parallel double blind placebo controlled trial of metformin in addition to usual care will be conducted in the routine clinical environment. The primary outcome is the proportion of women requiring insulin initiation, or have hyperglycaemia at weeks 32 and 38. The secondary outcome is the proportion of women displaying excessive GWG. A total sample of 552 participants (significance level of 0.05, 80 % power) is required and takes account of a dropout rate of 5 % and non-adherence of 8 % in metformin group.

EMERGE is in progress and will inform clinical practice by providing evidence of the effectiveness of early active management with metformin at the time of diagnosis in a broader GDM population.

P9 A case of high bone mineral density presenting with 'rugger jersey spine'

Loughrey PB[1], Hunter SJ[2], Lindsay JR[1]

[1]Osteoporosis and Bone Metabolism Service, Musgrave Park Hospital, Belfast, Northern Ireland; [2]Regional Centre for Diabetes and Endocrinology, Royal Victoria Hospital, Belfast, Northern Ireland

Raised bone mineral density is a common finding on dual X-ray absorptiometry (DXA) scanning, primarily arising from degenerative disease, vertebral fracture or more rarely a range of skeletal dysplasias.

We report a case of 25 year old man with a 7 year history of low back pain referred for a metabolic bone opinion. Past medical history included a fracture of the left scaphoid bone at the age of 18. Pertinent family history includes an uncle with severe back pain from his early teenage years.

At presentation X-ray of the whole spine revealed prominent dense sub-endplates throughout the thoracic and lumbar vertebrae in keeping with "rugger jersey spine". DXA demonstrated a Z score of +5.8 (lumbar spine) and +2.8 (left hip). The main differential diagnoses of "rugger jersey spine" include hyperparathyroidism and renal osteodystrophy, which were excluded. Initial investigations confirmed normal renal function (eGFR $>$ 60 mls/min), alkaline phosphatase (72 U/L), adjusted calcium of 2.37 mmol/L. There were features of mild vitamin D insufficiency at 47 nmol/L, and normal parathyroid hormone levels at 31 pg/mL. The clinical presentation is in keeping with a mild phenotype of autosomal dominant osteopetrosis type II, which presents with generalised increased bone density. The genetic defect is likely to be on the CLCN7 gene. This case illustrates the challenges of interpretation and investigation of increased bone mineral density discovered on DXA scanning. Further characterisation through family screening and genetic screening may inform future management decisions. Risk of future fractures, delayed healing and osteomyelitis remain high despite increased bone mineral density.

P10 Investigating the protective effect of TRAIL on RANKL-induced calcification using a vascular cell co-culture model

Harper E[1], Forde H[1,2], Davenport C[2], Rochfort KD[1], Smith D[2], Cummins PM[1]

[1]School of Biotechnology, Dublin City University, Glasnevin, Dublin 9; [2]Department of Academic Endocrinology, Beaumont Hospital, Dublin 9

Cardiovascular death remains the leading cause of mortality in type-2 diabetes mellitus (T2DM), in which a high prevalence of vascular calcification (VC) is a significant risk factor. Both receptor-activator of NF-κB ligand (RANKL) and tumour necrosis factor-related apoptosis-inducing ligand (TRAIL) are believed to co-interact to regulate the VC process. RANKL promotes calcification and, whilst TRAIL is believed to be anti-calcific, its vascular function is less clear. We propose that TRAIL can exert protective effects on the vasculature via attenuation of RANKL-induced calcification. To investigate this hypothesis, cultured human aortic endothelial cells (HAECs) and human aortic smooth muscle cells (HASMCs) were individually treated for 72 h with either RANKL (25 ng/ml) or TRAIL (5 ng/ml), or were co-treated with both. In HAECs, RANKL induced bone morphogenetic protein-2 (BMP-2) release and NF-κB/p52 activation in a dose-dependent manner, pro-calcification effects that were subsequently blocked with TRAIL co-treatment. In HASMCs, TRAIL could attenuate RANKL-induced Runx2 expression, a pro-calcification transcription factor. Finally, a HAEC:HASMC co-culture model was employed to approximate the structure of the vasculature. In this model, HAEC treatment with RANKL caused elevated calcification in neighbouring HASMCs, the primary location of vascular mineralisation in vivo, via paracrine signalling. Furthermore, co-treatment of HAECs with TRAIL attenuated RANKL-induced BMP-2 release, pro-calcific alkaline phosphatase activity/expression, and anti-calcific osteoprotegerin down-regulation in HASMCs. Thus, in both mono- and co-culture models, TRAIL has the ability to block the pro-calcifying actions of RANKL on vascular cells, yielding valuable information on VC pathogenesis and on the potential therapeutic value of TRAIL in this context.

P11 A novel hybrid peptide of glucose-dependent insulinotropic polypeptide (GIP) and xenin exhibits enhanced metabolic actions in a diet-induced mouse model of diabetes

Ng MT, Hasib A, Parthsarathy V, Flatt PR, Irwin N, Gault VA

School of Biomedical Sciences, Ulster University, Coleraine, UK

GIP and xenin are hormones secreted from intestinal enteroendocrine K-cells that exert important metabolic effects on glucose homeostasis and insulin secretion. In this study, we evaluated metabolic properties of a novel GIP-xenin hybrid peptide (GIP-XEN). GIP-XEN was incubated with DPP4 (5 mU) to confirm enzyme stability and clonal BRIN-BD11 beta cells to evaluate insulin secretion. Acute and persistent effects of GIP-XEN on food intake, glucose and insulin concentrations were examined in Swiss mice. For long-term studies, high fat fed mice with established obesity-diabetes received twice-daily injections of vehicle or test peptides (25 nmol/kg) for 21 days. Energy intake, body weight, circulating glucose and insulin concentrations, glucose tolerance (18 mmol/kg), biological response to GIP, insulin sensitivity (25 U/kg) and islet histology were examined. GIP-XEN was resistant to DPP4 degradation ($>$ 12 h) and concentration-dependently ($p < 0.001$) enhanced insulin secretion. Acute injection of GIP-XEN together with glucose significantly ($p < 0.05$) lowered glucose and increased insulin concentrations and reduced food intake ($p < 0.01$). Twice-daily administration of GIP-XEN for 21 days to high fat fed mice returned circulating glucose concentrations to levels similar to normal controls ($p < 0.01$). There was no effect on body weight, energy intake or circulating insulin at the dose administered. However, glucose tolerance ($p < 0.05$), insulin sensitivity ($p < 0.001$) and GIP-mediated glucose insulinotropic effects were markedly ($p < 0.001$) improved. Islet and beta-cell ($p < 0.001$) area together with insulin content ($p < 0.01$) were augmented. In

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conclusion, GIP-XEN exhibits beneficial metabolic effects in high fat fed mice highlighting clear potential of GIP-xenin hybrid based approach to treatment of type 2 diabetes.

P12 Development of novel antagonists of the incretin hormone gastric inhibitory polypeptide (GIP)

Perry RA, Flatt PR, Gault VA

School of Biomedical Sciences, Ulster University, Coleraine, UK

Recent studies suggest that GIP plays a key role in lipid metabolism, brain function and bone turnover but lack of specific and potent GIP antagonist has hampered progress in exploiting its full extra-pancreatic actions. In this study, N- and C-terminally truncated human GIP peptides (GIP 1–42; 1–30; 3–30; 5–30; and Glu → Pro substitution at position 3 in GIP (3–30) were synthesised and preliminary biological actions evaluated. Insulin-releasing actions of GIP peptides were tested in BRIN-BD11 beta cells at 5.6 and 16.7 mM glucose in absence and presence of native GIP. Glucose concentrations were measured in Swiss mice (n = 6) prior to and after intra-peritoneal administration of glucose (18 mmol/kg) together with GIP peptides (25 nmol/kg), and in presence of native GIP (25 nmol/kg). All peptides purified to homogeneity by HPLC displayed retention times ranging from 19.8 to 20.9 min. Experimental masses confirmed by MALDI-ToF MS: GIP 1–42 (4982.8 Da); GIP 1–30 (3530.6 Da); GIP 3–30 (3296.3 Da); GIP 5–30 (3110.2 Da); and GIP Pro3–30 (3263.4 Da) correlated with theoretical masses. In BRIN-BD11 cells, GIP 1–42 and GIP 1–30 equi-potently stimulated insulin secretion (1.3-fold; $p < 0.01$–$p < 0.001$) compared to glucose. At higher concentrations, GIP 3–30, GIP 5–30, and GIP Pro3–30 weakly stimulated insulin secretion and significantly ($p < 0.01$) inhibited GIP-stimulated insulin secretion. Furthermore, GIP Pro3–30 significantly increased glucose concentrations (131 %; $p < 0.05$) and countered ($p < 0.05$) glucose-lowering action of GIP in vivo. These data demonstrate that N- and C-terminally truncated GIP peptides, especially Glu to Pro substitution at position 3, may provide a functional GIP antagonist for further evaluation.

P13 Novel mutations Of POLD1 and WRN genes in a case of adipose redistribution syndrome associated with hypothyroidism

Mat A[1], McIntyre A[2], McKenna M[1], Hegele RA[2], O'Shea D[1]

[1]Dept of Endocrinology, St Vincent's University Hospital, Dublin 4; [2]Robarts Research Institute, Western University, Ontario, Canada

Adipose Redistribution Syndrome (ARS) is a rare condition associated with lipoatrophy, lipohypertrophy and significant metabolic derangement. Here we report a case of florid ARS in a hypothyroid patient with rare genetic mutations. A 52-year-old woman complained of gradual facial and body habitus change over 3 years. There was significant lipoatrophy of Bichat facial fat pads, upper arms, breasts, abdomen, buttocks and upper thighs and lipohypertrophy of dorsocervical fat pad with symmetrical fat deposits over her scapulae extending over the shoulder girdles, supraclavicular, infraclavicular and axillary regions. There was severe hypothyroidism (TSH 120.4 mIU/L, T4 < 5.15 pmol/L and T3 of 1.03 nmol/L; anti-TPO antibody 355 kIU/L [n: 0–5.61 kIU/L]). BMI was 33 kg/m2. Fasting glucose and Insulin were 6.2 mmol/L and 57.5 mU/L (n: 3–25 mU/L), respectively. OGTT and HbA1c were normal. Total cholesterol was 11.2 mmol/L, LDL was 7.53 mmol/L and triglyceride was 2.33 mmol/L. 8 AM cortisol was 503.8 nmol/L (n: 171–536 nmol/L); Dexamethasone Suppression Test showed appropriate response (cortisol 15.5 nmol/L). Leptin was 46.6 ug/L (n: 12.2–67.5 ug/L), complement C3 was 1.86 g/L (n: 0.9–1.8 g/L) and C3 nephritic factor was negative. Other blood tests were normal including PRL and IGF1. Serology for hepatitis B, C and HIV viruses were negative. Genetic analysis revealed heterozygous mutations in POLD1 (p.V70F) and WRN (p.V114F) genes which is the first time demonstrated in ARS. We are uncertain if these mutations interact (oligogenic interaction) and caused the phenotypic and metabolic pathologies observed.

P14 Oxytocin: improves glucose homeostasis, beta cell proliferation and survival

Mohan S, Khan D, Moffett RC, McKillop AM, Flatt PR

School of Biomedical Sciences, Ulster University, Coleraine, United Kingdom

Oxytocin, a nine amino acid peptide is mainly associated with child birth and lactation. However, recent studies have shown the expression of oxytocin receptors in the pancreatic islets and its possible involvement in beta cell regulation. In the present study we examined the expression of oxytocin and its receptor in rodent and human insulin secreting cell lines and assessed its role in regulation of beta cell function, proliferation and protection against streptozotocin induced DNA damage. In both rodent BRIN BD11 cells and human 1.1B4 cells oxytocin significantly ($p < 0.001$) stimulated insulin secretion in a concentration dependent manner at basal and elevated glucose (5.6 mM and 16.7 mM) (10^{-6} M to 10^{-9} M). Similar insulinotropic activity of oxytocin was observed with isolated mouse islets. To assess the mechanism of action, membrane potential and $[Ca^{2+}]_i$ were examined in BRIN BD11 cells. Oxytocin increased intracellular calcium with no apparent change of membrane potential. *In vivo* administration of oxytocin (25 nmol/kg body weight) to overnight fasted mice significantly ($p < 0.05$) reduced blood glucose and increased plasma insulin in response to glucose (18 mmol/kg). Oxytocin receptor mRNA was significantly ($p < 0.001$) expressed in mouse islets, BRIN BD11 cells and 1.1 B4 cells when compared to *Gipr*, a well-known beta cell GPCR. Interestingly, Ki67 staining showed direct stimulating effect of oxytocin in beta cell proliferation ($p < 0.01$) when 1.1B4 cells were cultured with oxytocin. Additionally, oxytocin countered beta cell DNA damage by streptozotocin in BRIN BD11 cells. In conclusion, the results indicate a role of oxytocin and its receptor in beta cell function.

P15 In vitro insulinotropic activities of frenatin peptides in rat clonal pancreatic beta cell line

Musale V, Owolabi BO, Conlon JM, Flatt PR, Abdel-Wahab YHA

SAAD Centre for Diabetes and Pharmacy, School of Biomedical Sciences, University of Ulster, Coleraine, Northern Ireland, BT52 1SA, UK

Frenatin peptides have been previously reported to exhibit antimicrobial and immunomodulatory activities. The present study investigated the insulinotropic effects of frenatin-2D from *Discoglossus sardus,* and frenatin-2.1S, 2.2S and 2.3S from *Sphaenorhynchus lacteus* using the clonal pancreatic beta cell, BRIN-BD11. Acute insulin-release studies were carried out in Krebs–Ringer

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bicarbonate buffer supplemented with 5.6 mM glucose in the presence of peptides (0–3μM). Insulin-release was measured by radioimmunoassay while membrane potential and intracellular calcium were evaluated by a fluorometric assay using FLEXstation™. Cytotoxicity was assessed by measuring cellular lactate dehydrogenase (LDH) release using a commercially available kit (Promega). Metabolic stability was determined in the presence of mouse plasma. At 5.6 mM glucose, all the four peptides significantly stimulated ($P < 0.001$) insulin-release without beta cell cytotoxicity. The stimulatory response of frenatin-2.2S persisted to as low as 30 pM ($P < 0.05$) while the threshold concentration (lowest stimulatory concentration) for frenatin-2.1S and 2.3S was 0.1 nM ($P < 0.05$). Frenatin-2D was found to be the most potent of the four peptides exhibiting an EC50 of 0.1 nM compared to frenatin-2.1S (1 nM), 2.2S (10 nM), 2.3S (1 nM) and a threshold concentration of 30 pM ($P < 0.01$). Frenatin-2D did not induce membrane depolarization or increase intracellular Ca^{2+} suggesting that alternative pathways are involved. Frenatin-2D was resistant to plasma degradation up to 4 h. In conclusion, frenatin-2D represents to be a promising compound for the development of new treatment for type 2 diabetes. Further studies are needed to investigate possible pathways by which it exhibits its insulinotropic activities.

P16 Acute airway compromise due to haemorrhage into a parathyroid tumour

Garrahy A[1], Hogan D[2], O'Neill J[2], Agha A[1]

[1]Department of Endocrinology, Beaumont Hospital, Dublin; [2]Department of Otolaryngology, Head and Neck Surgery, Beaumont Hospital, Dublin

A 45 year old female presented to the emergency department (ED) with a 3 day history of shortness of breath and chest discomfort. She had been recently diagnosed with primary hyperparathyroidism (baseline aCa^{2+} 3.33 mmol/L, PTH 367 pg/ml) with mild symptoms only.

One day prior to presentation Sestamibi/SPECT CT revealed a 3.7 cm mass in the right tracheoesophageal groove extending to the upper mediastinum. Ultrasound neck 6 weeks prior reported to show a 6 mm probable right inferior parathyroid lesion. On arrival to ED, she was tachycardic and a biphasic stridor was noted. Emergency CT neck revealed significant increase in size of the mass since the scan 2 days prior, measuring 5.2 × 4.2 × 10.7 cm, with a fluid level. The trachea was narrowed measuring 0.4 cm at the level of the sternoclavicular joints. She was admitted to ICU, electively intubated and brought to theatre the following morning. Pre-op, calcium levels normalised and PTH had fallen to 77 pg/ml suggesting infarction of the gland. There was no tracheal invasion on bronchoscopy. The cystic mass was identified posterior and inferior to the right hemithyroid with surrounding haemorrhage. Decompression of the cyst allowed complete dissection and removal en-bloc. She was extubated without complication on the first post-operative day. Histopathology confirmed a parathyroid neoplasm with extensive haemorrhage and necrosis; MIB-1 index <5 %. Post-operative calcium remained normal. Functional parathyroid cysts are rare and may be differentiated from thyroid cysts by demonstration of high levels of PTH in aspirate. Haemorrhage into a parathyroid cyst is an exceptionally rare entity and can present with acute airway compromise.

P17 Paediatric cushing's syndrome: a case series

Garrahy A[1], Noctor E[1], Dineen R[1], McGurren K[1], Byrne M[2], O'Grady M[3], Costigan C[4], Javadpour M[2], Agha A[1]

[1]Dept of Endocrinology and 2. Dept of Neurosurgery, Beaumont Hospital; [2]Dept of Endocrinology, Mater Misericordiae University Hospital; [3]Depts of Paediatric Endocrinology Midland Regional Hospital, Mullingar and [4]Our Lady's Hospital for Sick Children, Crumlin, Dublin

Cushing's Syndrome is very rare in the paediatric population. We present a series of 4 such patients (2 males) treated in our institutions. 3 patients had Cushing's disease and one had an adrenal adenoma. All had weight gain, two had stunted growth, one primary and one secondary amenorrhoea. Two had cyclical Cushing's disease. All patients were in remission following surgery (3 had endoscopic trans-sphenoidal surgery (TSS), one laparoscopic adrenalectomy). 3 patients had evidence of growth hormone (GH) deficiency post-op and were treated with GH. Cushing's syndrome in children is associated with significant morbidity and requires prompt diagnosis and treatment. Trans-sphenoidal surgery by an experienced surgeon is successful in inducing remission in Cushing's disease.

Clinical features	Dynamic testing and imaging	Outcome
7 year male, height 2nd–9th centile, weight >91st centile Weight gain, early adenarche, growth retardation	Cyclical cortisol hypersecretion High ACTH IPSS: central/gradient confirmed MRI pituitary unremarkable	Remission after TSS. Histology: corticotroph hyperplasia ACTH + GH deficient
13 year male, height 2nd–9th centile, weight > 99.6th centile Weight gain, proximal myopathy. Fatty liver. Day-to-day variability in symptoms	Cyclical cortisol hypersecretion High ACTH CRH test: ↑ ACTH × 1.7 fold IPSS: central/gradient confirmed MRI pituitary unremarkable	Remission after TSS. Histology: corticotroph hyperplasia ACTH + GH deficient; hypothyroidism
14 year female, height 50th–75th centile, weight >99.6th centile Primary amenorrhoea, IGT, Fatty liver	Cyclical cortisol hypersecretion High ACTH CRH test: ↑ ACTH × 5 fold MRI pituitary: Microadenoma	Remission after TSS Histology: corticotroph adenoma ACTH + GH deficient
16 year female, Height 25–50th centile, weight 75–91st centile Weight gain, Hirsutism, secondary amenorrhoea	Cortisol hypersecretion Suppressed ACTH CT adrenals: 3.7 cm adrenal mass	Remission after adrenalectomy Histology: benign tumour

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P18 Myxoedema masquerading as severe dementia, cardiomyopathy and bowel obstruction

Ayoub J, Goulden E, Garrahy A, Agha A

Department of Endocrinology, Beaumont Hospital, Dublin

Myxodema is a severe form of hypothyroidism that is characterised by cognitive impairment and multisystem dysfunction which is rarely seen now in developed countries.

A 63 year old woman presented with cognitive decline, anorexia, abdominal discomfort and low mood including suicidal ideations. She was hypothermic, had abdominal distention with absent bowel sounds, dry skin, frontal balding, periorbital, sacral and pretibial oedema with erythema ab-igne on both lower limbs. She had a marked flat affect. Abdominal radiograph showed large bowel dilatation consistent with pseudo-obstruction. Laboratory tests revealed hypokalaemia, hypomagnesaemia and hypoalbuminaemia. Echocardiogram showed reduced ejection fraction at 35 % and findings consistent with restrictive cardiomyopathy

Thyroid function tests showed an undetectable Free T4 and T3 levels with a TSH $>$ 100 mu/l. TPO antibodies were positive. Initially she was commenced on oral thyroxine but absorption studies showed poor blood T4 response so this was changed to I.V T3. Glucocorticoid cover was added but later the short synacthen test showed a normal response. Her condition gradually improved and she was later converted to PO L-thyroxine and underwent intensive rehabilitation. She was discharged well after 33 days and when seen in the clinic 12 weeks later she was markedly better, asymptomatic and independent with a normal TSH.

Although rare, physicians need to be aware of the possibility of myxoedema in the differential diagnosis of patients presenting with similar features. Prompt treatment initially with IV T3 or T4 due to absorption uncertainty followed by oral replacement results in reversal of clinical features.

P19 Genetic diagnosis of hepatic nuclear factor 4-alpha maturity onset diabetes of the young (HNF4A-MODY) alters clinical management

Ioana IA[1], Bacon S[1], Byrne MM[1]

[1]Department of Diabetes, Mater Misericordiae University Hospital, Dublin, Ireland

HNF4A-MODY accounts for 6–10 % of all MODY. It is an autosomal dominant form of diabetes (DM), characterized by an increased incidence of neonatal hypoglyaemia and sensitivity to sulphonylurea (SU). The aim was to phenotype individuals with HNF4A-MODY (from the Mater MODY-cohort) and establish optimal diabetic therapy. We studied 22 HNF4A subjects from 8 pedigrees (17DM, 5 IGT), average age 39.5 years, known diabetic for 12.45 $\pm$ 13.13 years. The average age of MODY diagnosis was 35.0 $\pm$ 15.8 years with 8.2 year interval between diabetes and genetic testing. 5 of 17 diabetic subjects, were on insulin. Three, including 1 on continuous subcutaneous insulin infusion (CSII), were switched to SU after 24 $\pm$ 14.7 years of insulin therapy (mean 23.3 $\pm$ 15.7units/day) with an improvement in HbA1c from 72.3 $\pm$ 8.6 to 53 $\pm$ 16 mmol/mol. The mean dose of SU (diabrezide) was 226.6 $\pm$ 83.2 mg. 2 remained on insulin, one planning pregnancy (12units/day), and 1 discontinued CSII with significantly lower insulin requirement on SU (56–20 units/day). 8 patients on SU for 5.2 $\pm$ 4.7 years had their doses optimized, HbA1c improved from 55.42 $\pm$ 16.43 to 48.13 $\pm$ 11.16 Units, 1 patient had recurrent hypoglycaemia on SU and is on metformin. 3 patients remained diet controlled. The IGT group remained on diet with HbA1c minimally changed from 33.2 to 34 mmol/mol after 5.5 $\pm$ 3.8 years. Overall, 36 % had background retinopathy, 1 individual had proliferative retinopathy, none had neuropathy. 14 had microalbuminuria, only one had MACR $>$ 2.5 mg/mmol. One smoker had PVD. The incidence of hypertension was 22.7 %. An accurate diagnosis of HNF4A-MODY allows discontinuation of insulin therapy and good control on SU. Relatively few diabetic complications were noted.

P20 In-hospital mortality rates is lower in SIAD (syndrome of inappropriate antidiuresis) than in hypervolaemic or hypovolaemic hyponatraemia; results of a prospective, single-center study

Cuesta M, Garrahy A, Slattery D, Gupta S, Hannon AM, Forde H, McGurren K, Tormey W[1], Sherlock M[2], Thompson CJ

[1]Academic Department of Endocrinology and [1]Department of Chemical Pathology. Beaumont Hospital/RCSI Medical School, Dublin, Ireland; [2]Department of Endocrinology, The Adelaide and Meath Hospital, Dublin/Trinity College, Dublin, Ireland

Background: Hyponatraemia is associated with increased mortality, but the mortality associated with SIAD is unknown. The hypothesis of this study was to that mortality was lower in SIAD than in hypervolaemic (HEN) or hypovolaemic (HON) hyponatraemia.
Design: Prospective, single center, non-interventional study of all patients with hyponatraemia ($\leq$ 130 mmol/l) between January and October 2015. Patients were identified from computerised laboratory records and were assessed by a single experienced investigator (MC), who ensured full data collection, but otherwise did not intervene in therapy. Patients were allocated to SIAD, HEN or HON groups by international guidelines. Mortality rates are presented as risk ratios with the 95 % confidence interval (CI) compared to a normonatraemic control group (NN).
Results:1323 admissions with hyponatraemia were prospectively evaluated and 1136 NN patients. 431 (32.6 %) had HON, 573 (43.3 %) SIAD, 275 (20.8 %) HEN, 3 (0.002 %) patients primary polydipsia; 41 (3.1 %) had insufficient data for accurate classification. 121 (9.1 %) patients died during 1323 admissions with hyponatraemia compared to 38/1136 (3.3 %) NN patients ($p < 0.0001$). The risk ratios for in-hospital mortality were 1.76 (95 % CI 1.08–2.8) for SIAD, 2.77 (1.8–4.3) for HON and 4.9 for HEN (3.2–7.4). 9/121 (7.4 %) patients died with plasma sodium $\leq$ 125 mmol/l, 4 with plasma sodium <120 mmol/l
Conclusion: We confirmed that hyponatraemia is associated with higher all-cause mortality than NN, with the novel demonstration that mortality is higher in HON and HEN than in SIAD. Mortality rates reported for hyponatraemia are not applicable to SIAD.

P21 The contribution of undiagnosed adrenal insufficiency to euvolaemic hyponatraemia: results of a large prospective single-center study

Cuesta M, Garrahy A, Slattery D, Gupta S, Hannon AM, Forde H, McGurren K, Sherlock M[1], Tormey W[2], Thompson CJ

Academic Department of Endocrinology, Beaumont Hospital/RCSI Medical School, Dublin, Ireland; [1]Department of Endocrinology, The

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Adelaide and Meath Hospital, Dublin/Trinity College, Dublin, Ireland; [2]Department of Chemical Pathology, Beaumont Hospital/ RCSI Medical School, Dublin, Ireland

Objective: The syndrome of inappropriate antidiuresis (SIAD) is the commonest cause of hyponatraemia. Data on SIAD is mainly derived from retrospective studies, often with poor ascertainment of the minimum criteria for the correct diagnosis. Reliable data on the incidence of adrenal failure in SIAD is therefore unavailable. The aim of the study was to describe the aetiology of SIAD, and in particular to define the prevalence of undiagnosed adrenal insufficiency.
Design: Prospective, single centre, non-interventional, observational study of patients admitted to Beaumont Hospital with euvolaemic hyponatraemia (plasma sodium ≤ 130 mmol/l) between January 1st and October 1st 2015.
Patients: 1323 admissions with hyponatraemia were prospectively evaluated; 573 (43.4 %) initially classified as SIAD.
Main Outcome Measures: 1. Aetiology of SIAD, defined by diagnostic criteria. 2. Incidence of adrenal insufficiency.
Results: CNS diseases were the commonest cause of SIAD (n = 148, 26 %) followed by pulmonary diseases (n = 111, 19 %), malignancy (n = 105, 18 %) and drugs (n = 47, 8 %). 22 patients (3.8 %), initially diagnosed as SIAD, were reclassified as secondary adrenal insufficiency on the basis of cortisol measurements and clinical presentation. 9/22 cases had undiagnosed hypopituitarism. 13/22 patients had secondary adrenal insufficiency due to exogenous glucocorticoid administration.
Conclusions: In a large, prospective and well-defined cohort of euvolaemic hyponatraemia, undiagnosed secondary adrenal insufficiency co-occurred in 3.8 % of cases initially diagnosed as SIAD. Undiagnosed pituitary disease was responsible for 1.5 % of cases presenting as euvolaemic hyponatraemia.

P22 Novel fatty acid modified apelin-13 analogues show efficacy in alleviating chronic diet induced obesity diabetes in mice

O'Harte FPM, Hogg C, Parthsarathy V, Flatt PR

The Saad Centre for Pharmacy and Diabetes, School of Biomedical Sciences, Ulster University, Coleraine, BT52 1SA, N. Ireland

Apelin is an adipokine that activates the APJ receptor which is found in many tissues including the β-cells of the pancreatic islets. Here we compared the therapeutic potential of two fatty acid modified (acylated) analogues of apelin-13 with liraglutide for their antidiabetic actions in diet induced obese (DIO) diabetic mice. Male Swiss TO mice were pre-conditioned to develop insulin resistance and hyperglycaemia by feeding a high fat diet (HFD, 45 % fat) for 4 months. Once daily intraperitoneal (i.p.) injections of saline control, (Lys^8-GluPAL)apelin-13-amide, pGlu (Lys^{8}GluPAL)apelin-13-amide, or liraglutide, were given to DIO mice in a 28 day intervention study. After 28 days, pGlu (Lys^{8}GluPAL)apelin-13-amide, (Lys^{8}GluPAL)apelin-13-amide and liraglutide treatment reduced bodyweight by 6.4, 4.4 and 3.1 %, respectively. Furthermore, pGlu (Lys^{8}GluPAL)apelin-13-amide; (Lys^{8}GluPAL)apelin-13-amide and liraglutide treatment significantly decreased non-fasted blood glucose (ANOVA, $P < 0.05$ to $P < 0.001$) and increased non-fasted plasma insulin ($P < 0.05$ to $P < 0.01$) versus saline-treated controls. Furthermore, (Lys^{8}GluPAL)apelin-13-amide, pGlu (Lys^{8}GluPAL) apelin-13-amide and liraglutide significantly improved both i.p. and oral glucose tolerance after chronic treatment ($P < 0.05$ to $P < 0.001$). Insulin sensitivity was improved by both apelin analogues ($P < 0.01$) and liraglutide ($P < 0.05$) and all three peptides produced a significant reduction in HbA_{1c} concentration ($P < 0.05$ to $P < 0.01$). The acylated analogue pGlu (Lys^{8}GluPAL)apelin-13-amide also reduced plasma cholesterol concentrations ($P < 0.01$), triglycerides ($P < 0.001$), increased HDL-C ($P < 0.01$) and decreased LDL-C ($P < 0.01$) compared to high-fat fed saline-treated control mice. Overall these results indicate that chronic treatment with acylated apelin-13 analogues showed similar or enhanced therapeutic responses compared to the GLP-1 receptor mimetic liraglutide. Thus, acylated apelin-13 analogues possess promising anti-obesity and anti-diabetic therapeutic potential for these metabolic disorders.

P23 Inadequate transition services for young adults with type 1 diabetes

Davenport C[1], O'Riordan SMP[2], Moore KB[1]

[1]Department of Endocrinology and Diabetes, Adelaide and Meath Hospital, Tallaght, Dublin, Ireland; [2]Department of Paediatrics, Cork University Hospital, Cork, Ireland

Young adults with type 1 diabetes mellitus (T1DM) have poor glycaemic control, high diabetic ketoacidosis rates and increased mortality relative to their older and younger counterparts. It has been suggested that transition clinics may improve some of these outcomes. The present study examined current transition and young adult care practices in the Republic of Ireland.

An online structured questionnaire was distributed to paediatric and adult diabetes centres between June and October of 2015. The survey was completed by one senior member (doctor or nurse) per centre.

Eleven paediatric and 15 adult centres completed the survey. 3/11 (27 %) of paediatric and 6/15 (40 %) of adult centres have a specific policy for transitioning patients. A specific transition clinic is provided in 2/11 (18 %) of paediatric and 5/15 (33 %) of adult centres. In the absence of a transition clinic, 7/9 (77 %) of paediatric centres refer patients to a young adult clinic and 2/9 (23 %) refer to adult clinics. 8/11 (72 %) of paediatric and 11/15 (73 %) of adult centres do not have access to clinical psychology support or mental health services in any form. However, 7/11 (64 %) of paediatric and 15/15 (100 %) of adult clinics have dietitians in attendance at their clinics.

These data indicate poor access to key services for young adults with T1DM in Ireland during transitional care. The lack of key members of staff may contribute to poor outcomes in this vulnerable population. Dedicated transition clinics and access to mental health services including clinical psychological support must be addressed nationally as a matter of urgency.

P24 The successful use of online learning to improve insulin prescribing practice in foundation year zero doctors

D'Arcy R[1], O'Kane A[2], Graham UM[1,2]

[1]Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast; [2]Centre for Medical Education, Queen's University Belfast

National Inpatient Diabetes Audits consistently demonstrate a high prevalence of insulin prescription errors in hospital inpatients. Variable access to inpatient diabetes teams often leaves insulin prescribing to junior medical staff making training in insulin prescribing essential in this group. To address this we designed and delivered an online, interactive, insulin prescribing module to foundation year zero (FY0)

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doctors. In a pilot group of FY0 doctors we aimed to: 1. Determine the "readiness" of FY0 doctors for insulin prescribing; 2. Evaluate the impact of our novel insulin prescribing module on prescribing accuracy; 3. Assess the students' responses and attitudes to the module.

200 FY0 doctors undertook the structured e-learning programme. Before and after the module, they completed an assessment involving ten insulin prescribing scenarios which were marked by a blinded examiner awarding scores for correct prescription of insulin type and dose. Students also completed a questionnaire on their attitudes to insulin prescribing before the module, and to evaluate the module afterwards.

The majority of students felt apprehensive about insulin prescribing before the module citing insulin to be a "dangerous drug". Prescribing accuracy improved following module participation (75.5 % to 84.2 % $p = < 0.0001$). Students felt the module to be useful and interactive, helping to prepare them for practice.

This structured case-based e-learning module demonstrates a significant improvement in insulin prescribing accuracy among FY0 doctors. It is hoped that this will translate to improved inpatient insulin prescribing and glucose management as they enter clinical practice.

P25 Should we measure Parathyroid Hormone-Related Peptide (PTHrP)?

Bogusz P[1], Abid N[2], Spence K[3], Mullan K[1]

[1]Regional Centre for Endocrinology Royal Victoria Hospital BHSCT; [2]Royal Belfast Hospital for Sick Children BHSCT; [3]Regional Endocrine Laboratory Royal Victoria Hospital Belfast

Case 1: A 70 year old woman was admitted with a 3 weeks history of night sweats, weight loss and lethargy. Calcium corrected (Ca(c)) was 3.14 mmol/L (2.2–2.6) and phosphate (PO4) was 1.04 mmol/L (0.8–1.5). Abdominal imaging was in keeping with gallbladder carcinoma and liver metastases. A bone scan did not show metastases and intact PTH was low at 8 pg/ml (15–65). PTHrP was available posthumously 3 weeks after admission and was elevated at 20.6 pmol/l ($n < 1.8$).

Case 2: A baby girl was delivered at 36 weeks due to foetal distress. She required intubation and ventilation and was noted to have an abdominal mass and hypertension with blood pressure of 107/75 ($n < 64/40$). Renal profile was normal. Ca(c) was 3.24 mmol/L, PO4 1.76 mmol/L, PTH <5 pg/ml, PTHrP 5.5 pmol/L. Imaging revealed a renal mass and a mesoblastic nephroma was confirmed at surgery. Post-operative PTHrP <1.0 pmol/l and he remains well.

High levels of PTHrP have been associated with more severe weight loss, attenuated responses to bisphosphonates and lower median survival rates. Therefore PTHrP may be of benefit in helping to counsel patients and their carers about these parameters as well as offering a tumour maker in rare cases such as Case 2. Although the assay cost is modest (~£50 to 60) its value is attenuated by the long laboratory turn-around time of any send away assay. Anti-PTHrP antibody therapy is currently showing promise in animal models and therefore in the future we require a more accessible assay.

P26 Expression of gastrin family peptides in pancreatic islets and their role in beta cell function and survival

Khan, Vasu S, Moffett RC, Flatt PR

School of Biomedical Sciences, Ulster University, Coleraine, United Kingdom

In addition to insulin, glucagon, somatostatin and PP, pancreatic islets express several other regulatory peptides. Cholecystokinin and gastrin, ligands for CCKA and CCKB type G-protein coupled receptors have been reported to be expressed in pancreatic islets. In the present study, we demonstrated the cellular co-localization of classical gut hormone CCK-8 with insulin/glucagon and gastrin immunoreactivity with glucagon in mouse pancreatic islets. The presence of CCK receptors on rodent and human islet cells and the effects of CCK-8 and gastrin on beta-cell function, cell proliferation and apoptosis were examined. Immunohistochemistry revealed no co-localization of CCK and gastrin with nerve ending marker tyrosine hydroxylase or vesicular acetylcholine transporter. CCK A and B receptors mRNA were differentially expressed in mouse islets, BRIN BD11 cells and 1.1 B4 cells compared to Gipr, a well-known beta cell GPCR. *In vitro*, CCK-8 and gastrin (10^{-6} to 10^{-8}M) stimulated ($p < 0.05$ to $p < 0.001$) insulin secretion at both 5.6 mM and 16.7 mM glucose from cultured rodent and human beta-cells. However, CCK-8 stimulated ($p < 0.05$) insulin secretion from isolated mouse islets and improved glucose disposal in vivo following an i.p. 18 mmol/kg glucose challenge in NIH-Swiss mice. Administration of CCK-8 markedly reduced ($p < 0.05$) food intake in overnight fasted mice. Both peptides significantly ($p < 0.05$ to $p < 0.01$) increased human and rodent beta-cell proliferation as demonstrated by Ki67 staining. CCK-8 and gastrin protected human 1.1B4 cells from streptozotocin induced DNA damage. These data highlight that intra-islet expression of these peptides and activation of CCK receptors could play an important role in beta cell function.

P27 Loss of NK cell effector function in childhood obesity is associated with dysregulated cell metabolism

Tobin L[1], Mavinkurve M[1,2], Donnelly R[3], Mat A[1], Carolan E[1,2], Gardiner C, Finlay D[3], Cody D[2,4], Hogan A[1,2], O'Shea D[1,5]

[1]Obesity Immunology Group, Education and Research Centre, St Vincent's University Hospital, University College Dublin 4, Ireland; [2]National Children's Research Centre, Dublin 12, Ireland; [3]Trinity Biomedical Sciences Institute, School of Biochemistry and Immunology, Trinity College Dublin, Dublin, Ireland; [4]Department of Diabetes and Endocrinology, Our Lady's Children's Hospital Crumlin, Dublin, Ireland; [5]Department of Endocrinology, St Vincent's University Hospital, University College Dublin 4, Ireland.

Childhood obesity is increasing in both prevalence and severity. It is well established that childhood obesity tracks strongly into adulthood. Natural Killer (NK) cells are innate effector cells that are capable of carrying out potent cytotoxic actions against tumour cells without previous immunization. They are potent producers of a key cytokine, interferon gamma (IFNγ), which is capable of activating inflammatory responses essential for anti-tumour and anti-viral immunity. Loss of NK cell frequencies and effector functions have previously been described in obese adults. However, it has not yet been established if NK cells are affected in childhood obesity prior to the onset of metabolic complications such as type 2 diabetes mellitus (T2DM). The aim of this study was to determine the impact of childhood obesity on NK cell effector functions and elucidate the impact of obesity on cellular metabolism. We found that NK cell frequencies were reduced in obese children in a BMI dependent manner. In our cohort of obese children, NK cells had reduced ability to lyse tumour cells and secrete IFNγ when compared to lean counterparts. Cell intrinsic metabolic pathways control the effector function of NK cells. NK cell require glucose and the activation of the nutrient sensor mTOR to generate effector molecules such as IFNγ. Obese children displayed reduced glucose uptake and phosphorylation of mTOR.

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This failure in metabolic reprogramming may explain why NK cells from obese children show defective functions. Overall our data shows that obesity dysregulates NK cell function, which may lead to increased susceptibility to malignancies and infections.

P28 A review of clinical and molecular features of non-syndromic phaeocromocytoma/paraganglioma and renal tumour association (PARTA)

Casey R[1], Warren A[2], Maher ER[1]

Department of Medical Genetics[1]/Pathology[2], Cambridge University Hospital

Sixty years ago, the co-occurrence of phaeochromocytoma and renal tumours was linked to VHL disease. Subsequently, other genetic causes of renal tumours in combination with phaeochromocytoma/paraganglioma have been described. Our aim was to better define the clinical and molecular features of PARTA (defined as the co-occurrence of tumours from both classes in the same individual or in first degree relatives after exclusion of VHL disease) by literature review and characterisation of a large case series of patients. A literature review revealed evidence of an association, between germline mutations in *SDHA, SDHB, SDHC, SDHD, FH, TMEM127* genes. In the literature review and our case series of 20 probands with non-VHL PARTA, *SDHB* mutations were the most frequent cause. A genetic cause was identified in a minority of the probands (25 %). In addition to SDHB mutations we identified the first known case of MAX-associated malignant renal tumour. In our case series, the presence of a detectable germline mutation was not associated with the age at onset, renal tumour type or malignant PGL ($p > 0.05$). Renal tumours and PC/PGL tumours share common molecular and clinical features and may cluster within families because of mutations in a variety of genes. We propose an algorithm for genetic testing and recommend that the diagnostic criteria for PARTA should cover both sympathetic and parasympathetic paragangliomas and both renal cell carcinoma and oncocytomas.

P29 Metabolomic profiling of phaeochromocytomas: a journey from diagnostic application to identification of metabolic therapeutic targets

Casey R[1], Bassetti M[2], McLean M[3], Gallagher F[3], Maher ER[1]

Department of Medical Genetics[1]/Radiology[3]; CRUK[2], Cambridge University Hospital

Phaeochromocytomas are recognised to be the most heritable tumour, with 40 % having a genetic defect. Mutations in the succinate dehydrogenase complex of genes (SDH) are the most frequently implicated. SDH is a citric acid cycle enzyme thus defects in the encoding gene has significant consequences on tumour cell metabolism. The aim was to investigate the role of metabolomics to identify patterns of metabolite dysregulation in SDH tumours. An ex vivo technique called high resolution magic angle spinning (HRMAS) was applied to fresh frozen tumour samples. 7 tumour samples were included in an initial pilot study (2 SDH tumours, 5 sporadic tumours.) The mean succinate level in the SDH tumours (22.3 mM) was ten fold higher than the non-SDH tumours (2.3 mM). Other significant differences included asparatate, which was undetectable in the SDH tumours verses a mean of 18.8 mM in the non SDH tumours. The mean glutamine level was lower in the SDH group but not statistically significant (p-value 0.25). This study highlights succinate as a metabolic biomarker in SDH tumours. Applications include, verification of variant pathogenicity and identification of somatic mutations. The low aspartate and glutamine levels in SDH tumours suggest an alternative metabolic shunt to achieve anabolism and further studies using in vivo MRI spectroscopy and a larger HRMAS study are underway to further investigate this potential metabolic vulnerability.

P30 Radiological surveillance in multiple endocrine neoplasia type 1: a double edged sword?

Casey R[1], Saunders D[2], Challis B[1], Cheow H[2], Shaw A[2], Simpson H[1]

Department of Endocrinology[1]/Radiology[2], Cambridge University Hospital, Cambridge, UK

MEN1 is a hereditary condition characterised by hyperplasia or solitary adenomas of multiple endocrine glands. The associated mortality necessitates a vigorous surveillance protocol, however the clinical practice guideline recommendations report a lack of consensus on the optimum radiological surveillance. We sought to determine if cumulative radiation exposure as part of the recommended radiological surveillance programme posed a distinct and independent risk in this cohort of patients with hereditary endocrine neoplasia. A retrospective review of patients with MEN1 attending our institution was carried out, including all radiological procedures performed as part of MEN1 surveillance between 2007 and 2015. An estimated radiation effective dose (ED) for each individual patient was calculated. Epidemiological data has suggested an ED of 50 mSv as the minimum threshold for the development of solid tumours A total of 43 patients were included. The mean ED was 121 mSv and the estimated mean lifetime risk of cancer secondary to radiation exposure was calculated as 0.49 %. Patients with malignant neuroendocrine tumours (NETS) had significantly higher ED levels compared to patients without metastatic disease (p-value <0.00002) and functional pancreatic neuroendocrine tumours (PNETS) were also associated with a higher ED (p-value 0.002). This study highlights the effects of long term radiological surveillance and the need for a multimodality imaging approach in patients with hereditary cancer syndromes requiring life-long follow up.

P31 Prolonged episodes of hypoglycaemia in HNF4A-MODY mutation carriers with IGT. Evidence of persistent hyperinsulinism into early adulthood

Bacon S[1], Kyithar MP[1], Condron EM[1], Vizzard N[1], Burke M[1], Byrne MM[1]

Department of Diabetes and Endocrinology, Mater Misericordiae University Hospital, Dublin 7, Ireland

HNF4A is an established cause of Maturity Onset Diabetes of the Young (MODY). Congenital hyperinsulinism can also be associated with mutations in the *HNF4A* gene. A dual phenotype is observed in HNF4A-MODY with hyperinsulinaemic hypoglycaemia in the neonatal period progressing to diabetes in adulthood. The nature and timing of the transition remains poorly defined. We performed an

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observational study to establish changes in glycaemia and insulin secretion over a 6 year period. We investigated glycaemic variability and hypoglycaemia in HNF4A-MODY using a continuous glucose monitoring system (CGMS). An OGTT with measurement of glucose, insulin and C-peptide was performed in *HNF4A* participants with diabetes mellitus (DM) (n = 14), *HNF4A*-IGT (n = 7) and age-and BMI-matched MODY negative family members (n = 10). Serial assessment was performed in the *HNF4A*-IGT cohort. In a subset of HNF4A-MODY mutation carriers (n = 10), CGMS was applied over a 72 h period. There was no deterioration in glycaemic control in the *HNF4A*-IGT cohort (initial AUC glucose:29.5 mmol/L/120 min vs AUC glucose @ 6 yr. follow-up: 34.8 mmol/L/120 min, p = 0.9). Likewise, there was no change in AUC insulin over the study period (888 pmol/L/120 min vs 932 pmol/L/120 min, p = 0.7). CGMS profiling demonstrated prolonged periods of hypoglycaemia in the *HNF4A*-IGT group when compared to the *HNF4A*-DM group (432 min. vs 138 min. p = 0.04). In a young adult *HNF4A*-IGT cohort, we demonstrate preserved glucose, insulin and C-peptide secretory responses to oral glucose. Utilising CGMS, prolonged periods of hypoglycaemia are evident despite a median age of 21 years. We propose a prolonged hyperinsulinaemic phase into adulthood is responsible for the notable hypoglycaemic episodes.

P32 Does implementation of fracture risk thresholds for access to dual energy densitometry (DXA), using FRAX, impact management outcomes?

Wilson C, Loughrey PB, Cummings B, McNally C, Lindsay JR

Osteoporosis and Bone Metabolism Service, Musgrave Park Hospital, Belfast, Northern Ireland

Fracture risk assessment using FRAX, uses clinical risk factors (CRFs) to estimate 10-year fracture probability. The SIGN guideline group recently suggested a fracture risk threshold of 10 % as an indication for DXA[1]. In order to determine the impact of this recommendation on management, we undertook a prospective audit of our direct access DXA and health promotion service. FRAX scores and treatment recommendations were obtained.

Charts from 61 consecutive patients were reviewed (54F/7 M, Mean age 60.4 years). 18 patients had sustained a fragility fracture at time of referral. A range of clinical risk factors (CRFs: 0, n = 4; 1, n = 28; 2 = 15; 3 = 8; > 3 = 6) were observed. Treatment at referral included calcium/vitamin D (n = 17), bisphosphonate (n = 1), or combination of both (n = 2).

No referrals included a prospective FRAX score. Retrospective FRAX assessment showed 27/61 patients had a <10 % probability of 10 year major fracture risk and would not have met SIGN criteria for DXA. Direct access DXA identified 25 patients with osteopenia and 18 with osteoporosis. 16/61 patients with low bone mineral density (BMD) might have been excluded from accessing the DXA/health promotion service using SIGN thresholds. Based on National Osteoporosis Guideline Group algorithms management recommendations included DXA (30/61), lifestyle advice (18/61) or pharmacological therapy (10/61).

This audit reveals a low adherence to NICE guidelines for assessment of fracture risk in those referred for direct access DXA. Our data highlights that some patients with modifiable low BMD would have been excluded from scanning using proposed fracture risk thresholds for access to DXA.

[1]Scottish Intercollegiate Guidelines Network (SIGN) 142. Management of osteoporosis and the prevention of fragility fractures (March 2015).

P33 Effects of glucagon from the paddlefish *Polyodon spathula* on insulin secretion from BRIN-BD11 beta-cells

Graham G, Flatt PR, Conlon JM, Abdel-Wahab YHA

SAAD Centre for Diabetes and Pharmacy, School of Biomedical Sciences, University of Ulster, Coleraine, Northern Ireland, BT52 1SA, UK

The paddlefish is a phylogenetically ancient species related to the sturgeons. The insulinotropic properties of paddlefish glucagon were assessed in vitro using the BRIN-BD11clonal pancreatic beta cell line. Prior to the acute insulin-release studies, the cells were incubated in Krebs–Ringer bicarbonate buffer supplemented with 1.1 mM glucose. The test incubations were performed for 20 min at 37^0 C using the same buffer supplemented with 5.6 mM glucose in the presence of peptides at concentrations from 0 to 3 μM. The receptor antagonist studies was performed by incubating 0.1 μM of peptide in the presence and absence of 1 μM of Glucagon-like peptide-1 (GLP-1), glucagon and glucose-dependent insulinotropic peptide (GIP) receptor antagonists. The release of insulin was measured by radioimmunoassay. Paddlefish glucagon significantly ($p < 0.05$) enhanced secretion of insulin from BRIN-BD11 beta cells compared to 5.6 mM glucose control at a concentration of 30 pM with $EC_{50} = 1.6$ μM. The in vitro insulinotropic activity of paddlefish glucagon was decreased after incubating BRIN-BD11 cells with the GLP-1 receptor antagonist, exendin-4 (9–39) ($p \leq 0.001$). The glucagon receptor antagonist (desHis1Pro4Glu9) glucagon amide also partially blocked the activity of paddlefish glucagon ($p \leq 0.01$). The action of the peptide was not antagonized by the selective GIP receptor antagonist, GIP (6–30) Cex-K40 [Pal] suggesting that GIP receptors are not a target for the peptide. The study suggests that a piscine proglucagon-derived molecule of ancient origin activates both GLP-1 and glucagon receptors. The peptide has the potential for development into an agent for the treatment of type 2 diabetes.

P34 Getting to the heart of hypopituitarism

Martin-Grace J[1], Feeney ER[2,3], Crowley RK[1,3]

[1]Department of Endocrinology and Diabetes Mellitus, St Vincent's University Hospital; [2]Department of Infectious Disease, St Vincent's University Hospital; [3]University College Dublin

A 53 year old woman presented with dyspnoea, chest pain and hyponatraemia. A large pericardial effusion was seen on a CT pulmonary angiogram. Echocardiogram showed features of tamponade despite no clinical signs, and the effusion was drained. She was investigated for the cause of the effusion. Microbiological and autoimmune investigations were negative, but she was diagnosed with secondary hypothyroidism, with TSH 0.73 IU/l, free T4 6.3 nmol/l (12–22), T3 0.44 pmol/l (1.3–3.1). Further investigations showed FSH/LH <0.5 IU/l, cortisol of 48 nmol/l, ACTH 13.4 ng/l, total prolactin 184 mU/L, and an empty sella on MRI pituitary. The diagnosis of hypopituitarism was made. The pericardial drain was successfully removed without re-accumulation following commencement of hydrocortisone and levothyroxine replacement.

Cardiac tamponade in hypopituitarism is rare. There are features common to both cardiac tamponade due to primary hypothyroidism and to hypopituitarism, including the absence of classical signs such as tachycardia, raised JVP and pulsus paradoxus. This is not true of tamponade associated with primary adrenal insufficiency, however the relatively volume deplete state of secondary hypoadrenalism in

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hypopituitarism may mask the clinical signs of an evolving tamponade, as the rise in right atrial pressure is less marked even in the presence of large effusion[1]. Our case demonstrates the importance of a high index of suspicion of cardiac tamponade in this subset of patients with large pericardial effusions even in the absence of clinical signs.

P35 Screening for cystic fibrosis related diabetes using oral glucose tolerance test

Hatton S[1], Martin-Grace J[1], Suzanne Kearns[2], Yassir Elamin[1], Crowley RK[1,3]

[1]Department of Endocrinology and Diabetes Mellitus, St Vincent's University Hospital; [2]National Adult Cystic Fibrosis Referral Centre, St. Vincent's University Hospital; [3]University College Dublin

Cystic fibrosis-related diabetes (CFRD) has a reported prevalence of up to 20–40 %, and a negative impact on pulmonary function[1]. Annual screening for all CF patients who have not been previously diagnosed with diabetes is recommended from 10 years to identify those likely to benefit from insulin therapy and referral to diabetes services[1]. The oral glucose tolerance test (OGTT)is the gold standard screening tool in this population to identify patients likely to benefit from insulin therapy.

Annual screening for CFRD using OGTT in 362 patients attending the CF service was audited. 62 patients with a known diagnosis of CFRD were excluded. 64 % of eligible patients were screened within the last 2 years. 13.7 % had a positive OGTT result. 12 % of eligible patients not screened using OGTT had HbA1c measured within the last 4 years, however HbA1c has been shown to correlate poorly with glucose tolerance status in this cohort. In total, 23 % of patients attending CF services have a diagnosis of CFRD, or a positive OGTT result. However, only 30.6 % are currently attending the diabetes service, and only 28.6 % have had urinary albumin:creatinine ratio measured within the last 4 years.

This audit emphasises the need for both regular screening for CFRD, and the continued involvement of the diabetes multidisciplinary team in CF services, in both in-patient and out-patient setting. A CFRD nurse specialist was appointed in 2015, and we plan to reaudit in autumn 2016 to measure progress in screening rates, referral to diabetes services and monitoring for development of complications such as microalbuminuria.

P36 Audit of diabetes retinal screening service on Connolly Hospital Blanchardstown patients

Kgosidialwa O, Gajewska K, Malik R, Comerford C, Kyaw Tun T, Mcdermott JH, Sreenan S

Department of Endocrinology and Diabetes, Connolly Hospital Blanchardstown, Dublin, Ireland

The prevalence of diabetic retinopathy (DR) is estimated at 34.6 % globally. The national diabetes retinal screening (NDRS) programme was introduced in Ireland in February 2013. We aimed to assess uptake of screening and patients' experiences with the programme as outlined in the NDRS standards for quality assurance. This was a cross sectional study using structured interviews to collect data at patients' routine diabetes clinic visits. Data were analysed using stata software. Of the sixty patients interviewed, the majority had type 2 diabetes (90.0 %). The mean age and duration of diabetes was 58.5 (95 % CI 55.1, 62.2) years and 9.5 (95 % CI 7.7, 11.4) years respectively. Most, 90.0 %, of the patients were aware of the NDRS programme and 86.7 % were enrolled. Of those enrolled, 63.3 % were registered by a healthcare professional. Of the 6 patients who were not enrolled, 4 did not have fundoscopy within the last year. Of the total, 21.6 % had a prior history of DR with 15.4 % receiving active ophthalmology treatment. The first appointment for 68.3 % of the patients was received within 6 months of registering but only 10.1 % within 4 weeks. 72 % of the patients received their results, 60.0 % within 1 month of screening and 25.0 % had received notice of their next appointment. In summary, within our cohort of diabetes patients in CHB retinal screening uptake within NDRS program is near the recommended goal of 95 %; however some deficiencies have been noted. Reasons for these targets not being met need to be explored further and addressed.

P37 A case of autoimmune pancreatitis presenting as a deterioration in glycaemic control in a patient with pre-existing type 2 diabetes

Forde H, Slattery D, Smith D

Department of Endocrinology, Beaumont Hospital, Beaumont, Dublin 9

We report a case of type 1 autoimmune pancreatitis (AIP) presenting as a rare cause of worsening hyperglycaemia in a patient with type 2 diabetes. A 69 year old man was referred to the diabetes clinic with poor glycaemic control despite escalation of oral hypoglycaemic therapy. At presentation to the diabetes clinic, his BMI was 24 kg/m^2 with a HbA1c of 8.1 % on Gliclazide 120 mg daily and Pioglitazone 15 mg daily. A previous trial of Metformin and Saxagliptin had been ineffective at lowering blood glucose levels and so he was commenced on Insulin Detemir once daily to optimise diabetes control. In view of significant weight loss and hyperglycaemia despite multiple agents, computerised tomography (CT) of the pancreas was arranged. This revealed pancreatic duct dilatation within an atrophic pancreatic tail. Magnetic Resonance Cholangiopancreatography (MRCP) demonstrated a prominence in the pancreatic head and neck region which appeared malignant when further imaged with endoscopic ultrasound (EUS). Though biopsy of the pancreatic head yielded insufficient material for diagnosis, the patient proceeded to Whipples procedure due to the high index of suspicion for malignancy arising from the clinical and radiological findings. Histopathology revealed an area of chronic pancreatitis with features of IgG4 related autoimmune pancreatitis. Currently he has excellent glycaemic control on a low dose of basal insulin, Metformin 1 g daily and Gliclazide 30 mg daily. This case highlights the importance of investigating atypical presentations of type 2 diabetes and the need to consider AIP in the differential diagnosis of pancreatic cancer.

P38 Descriptive analysis of patients with type 1 diabetes mellitus, categorised by age decile, attending a tertiary referral centre

Forde H, Wrigley S, Siddique N, Agha A, Thompson CJ, Smith D

Department of Endocrinology, Beaumont Hospital, Beaumont, Dublin 9

It is well established that young adults with type 1 diabetes mellitus (T1DM) often fail to meet the recommended standards for glycaemic

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control. Thus, long term clinical outcomes for this cohort are poor. There is however little data on glucose control in older patients with T1DM. The aim of this study was to determine whether treatment regimes, metabolic control, and presence of co-morbidities differ amongst patients with T1DM according to their age. A retrospective review of patients with T1DM attending Beaumont hospital (n = 771) was carried out. Patients were stratified according to age decile, with the first decile defined as those between 10 to 20 years of age. The majority of patients were in the 3rd decile (n = 200). Patients in the 1st decile had the poorest glycaemic control with only 10.1 % achieving a HbA1c <7 % and 47.8 % had a HbA1c >9 %. The proportion of patients with optimum glycaemic control (HbA1c <7 %) increased with each progressive decile and all patients in the 7th decile (n = 14) had a HbA1c <8 %. There were similar proportions of patients on insulin pumps in the 1st, 3rd and 4th decile (24.6, 21 and 21.38 %, respectively). The use of mixed insulins was most common in the 8th decile (50 %). The prevalence of nephropathy, neuropathy and cardiovascular disease all increased with age. The findings in this study are consistent with the literature and further highlight the need to improve service delivery to young adults with T1DM.

P39 Five year outcomes of patients attending the diabetic foot clinic in a tertiary referral centre

Wrigley S, Forde H, Agha A, Thompson CJ, Smith D

Department of Endocrinology, Beaumont Hospital, Beaumont, Dublin 9

Diabetic foot ulcers (DFU) are associated with an increased risk of lower limb amputation and death. Reported mortality rates for patients with DFU are as high as 55 % after 5 years[1]. The aim of this study was to examine the 5 year clinical outcomes of patients with high risk diabetic foot disease attending Beaumont Hospital. A retrospective review of patients attending a specialist foot clinic in Beaumont Hospital between 2007 and 2010 was conducted. Clinical information was obtained from the Cellma database and laboratory results were extracted from the Beaumont Hospital information system. In total, 140 patients with high risk feet attended the foot clinic over the 4 year period. Outcome data was missing in 11 patients. The mean HbA1c, (first reading recorded during the study period) was 7.56 ± 1.88 %. The 5 year mortality rate was 19.3 % with an amputation rate of 26.4 %. The presence of coexistent nephropathy and chronic renal failure was significantly associated with mortality (p = 0.009 and p = 0.001, respectively). 32.1 % of patients had recurrent/new DFU after 5 years of follow up. Poor glycaemic control was not associated with mortality or amputation. Diabetic foot disease is an important cause of morbidity and mortality in clinical practice. It remains to be seen whether implementation of the national model of foot care in 2011 will improve outcomes for patients with high risk diabetic foot disease.

P40 Comparison of glycaemic control in patients with type-1 diabetes mellitus (DM) on continuous subcutaneous insulin infusion (CSII) therapy with different basal rates

Yunus S, Forde H, Moore A, Fanning E, Smith D

Department of Endocrinology and Diabetes Mellitus, Beaumont Hospital, Dublin, Ireland

Background: There are very few studies comparing glycaemic control in patients with different basal rates on CSII, so the ideal number of basal rates for a patient is unclear.
Objective: To compare glycaemic control between patients with different basal rates (BRs).
Methods: Data was collected from hospital's database and by contacting patients via phone.
Results: 75 patients were evaluated. 46 (61.3 %) were female. All had type-1 DM except two (one with type-2 DM and the other had DM after pancreatic disease). Patients were divided in two groups based on using <5 BRs and ≥5 BRs over 24 h. Out of 33 patients in the group on <5 BRs, 63 % were female. Mean age was 42.7 ± 10.3 (mean ± SD) years with BMI of 25.9 ± 3.4 kg/m^2. Duration of DM was 19.3 ± 11.0 years and on CSII for 5.5 ± 3.4 years. Out of 42 patients in the group on ≥ 5 BRs, 54.5 % were female. Mean age was 38.7 ± 9.3 years with BMI of 25.9 ± 4.6 kg/m^2. Duration of DM was 19.3 ± 9.5 years and on CSII for 4.9 ± 2.9 years. In both groups, similar number of patients (69.6 %) experienced at least one episode of hypoglycaemia per week. Mean HbA1c in those on <5 BRs was 7.8 ± 0.8 % (61.7 ± 9 mmol/mol) versus 8.08 ± 0.7 % (64.8 ± 7.7 mmol/mol) in those on ≥ 5 BRs *(p-value = 0.16).*
Conclusion: In our study there was no difference in glycaemic control between the patients on fewer (< 5) or more (≥ 5) basal rates. The characteristics of both groups were similar so advice on the optimal number of basal rates for a patient appears to vary from individual to individual.

P41 Impact of DAFNE and subsequent continuous insulin infusion (CSII) therapy on glycaemic control in type-1 diabetes mellitus

Yunus S, Forde H, Browne S, Twamley H, Fanning E, Smith D

Department of Endocrinology and Diabetes Mellitus, Beaumont Hospital, Dublin, Ireland

Background: Dose Adjustment for Normal Eating (DAFNE) structured education programme is an effective tool in improving glycaemic control in patients with type-1 diabetes while reducing the frequency of hypoglycaemia. DAFNE however, does not solve all glucose problems and patients often proceed to continuous insulin infusion (CSII) therapy post DAFNE.
Objective: Out of our 370 DAFNE graduates, 46 have subsequently gone on to CSII. The aim of our audit was to examine glycaemic control of these 46 graduates before and after DAFNE, before and after starting CSII and the reasons for CSII.
Methods: Data was collected using hospital's database (cellma and pipe) and by contacting patients via phone.
Results: 56 % patients were female. Mean age was 40 ± 9.4 (mean ± SD) years with BMI of 26.6 + 4.5 kg/m^2. Mean duration of diabetes was 17.2 ± 8.5 years. Duration since completion of DAFNE was 5.8 ± 2.2 years. Duration of CSII therapy was 4.0 ± 2.2 years. HbA1c before DAFNE was 8.3 ± 1.2 % (67.2 ± 9.8 mmol/mol) compared to 8.05 ± 1.0 % (64.5 ± 11 mmol/mol) 12 months post DAFNE (*p-value* = 0.31). The indication of commencement of CSII was to improve overall glycaemic control in 45 % patients, impaired hypoglycaemic awareness in 26 % and patient preference in 23 %. HbA1c before commencement of CSII was 8.3 % ± 1.07 (67.2 ± 11.7 mmol/mol) compared to 7.9 % ± 0.9 (62.8 ± 9.9 mmol/mol) after 12 months of CSII therapy (*p-value = 0.04).*
Conclusion: DAFNE is an effective programme for patients with type-1 Diabetes but may not improve glycaemic control in all.

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Selected patients may benefit from going on to CSII therapy post DAFNE and this can be associated with an improvement in HbA1c.

P42 To Determine the barriers to the uptake of the national diabetic retinal screening programme by patients over the age of 16, presenting to the outpatient diabetes clinic in CUH or to primary care

Bennett GH[1], Tuthill A[2]

[1]School of Medicine, University College Cork; [2]Department of Endocrinology, University College Hospital, Cork

Diabetic Retinopathy is a significant complication of diabetes, and the most common cause of blindness under 65 years. The National Diabetic Retinal Screening Programme (Diabetic RetinaScreen) aims to detect sight threatening retinopathies earlier leading to better outcomes. The purpose of this study is to determine the barriers to the uptake of Diabetic RetinaScreen, to investigate discrepancies between patients attending diabetes outpatients and attending general practice, and to evaluate general practitioner's satisfaction. This is a cross-sectional study. Two questionnaires were developed, one for general practitioners (n = 72). Another was developed for patients attending CUH diabetes outpatients (n = 102) and general practice (n = 45). 55.6 % of general practitioners surveyed were satisfied to refer to Diabetic RetinaScreen. Only 18 % considered a phone call to be the best referral method. Online referral, which has recently been introduced was most popular (53 %). 91.2 % of patients were familiar with, and 63.3 % had attended Diabetic RetinaScreen. There was no significant difference between patients attending outpatients or general practice as regards attendance (OR 0.793, 95 % CI 0.373 to 1.687). Older age (OR 1.023, 95 % CI 1.001 to 1.046) and complications of diabetes, excluding eye complications, (OR 2.741, 95 % CI 1.158 to 6.489) were associated with increased attendance. Factors which did not influence uptake include: gender, education, type of diabetes, length of disease, and ocular complications. Online referral is now available and the preferred method of referral. Efforts to encourage younger patients who do not yet have complications of diabetes may be beneficial. These changes could increase the uptake of Diabetic RetinaScreen.

P43 A rare case of infertility

Bogdanet D, Griffin T, Bell M

Department of Endocrinology, Galway University Hospital

The testicular disorder of sexual differentiation (DSD) is a rare clinical condition with an incidence of 1:20 000 newborn males. It is characterized by a male phenotype with 46XX karyotype. There are three clinical phenotypes: normal male phenotype, males with genital ambiguities true hermaphrodites. This condition results from the translocation of a Y chromosome segment containing the SRY gene during spermatogenesis.

A 33 years old male presented with his wife to the fertility clinic with a 3 years history of primary infertility. The patient's wife had no significant past medical history, her clinical examination was unremarkable and her biochemical and hormonal investigations were all normal. The patient had a past medical history of undescended testes in childhood. There was no significant family history. He had normal libido and sexual function. Clinical examination revealed a normal height and bilateral small testes. His total testosterone was 6.7 nmol/l, LH was 4.4 IU/l and FSH was 43.1 IU/l. A sample was sent for sperm analysis which revealed azoospermia. The patient was sent for chromosomal analysis and karyotyping. This revealed a 46XX SRY positive karyotype through translocation of the SRY gene between the × and the Y chromosome—46XX der(X)t(X;Y)(p22.3;p11.3)(SRY+).

Patients with azoospermia should be karyotyped. Sperm donation remains a fertility treatment option for these patients and had a successful outcome in this patient. Such patients require lifelong follow-up led by an endocrinologist with regular imaging of their gonads, bone density measurements, and testosterone supplementation.

P44 Thyroid function and glucose metabolism in adults after hematopoietic stem cell transplantation and total body irradiation

Bogdanet D[1], Stankard A[1], O'Kelly B[2], Hayden P[2], Healy ML[2]

[1]Galway University Hospital; [2]St. James's Hospital, Dublin

Endocrine and metabolic disorders are among the most common complications in survivors after hematopoietic stem cell transplant (HSCT). The aim of this study was to evaluate thyroid function and glucose abnormalities in patients treated with HSCT. This was a retrospective study which included 257 adult patients who underwent allogeneic HSCT between 2002 and 2014. Thyroid function was assessed early post HSCT (0–3 months), in the intermediate period (3–12 months) and late post HSCT (>12 months). The median age of the patients at diagnosis was 33 years (SD 10.45) with a median age at treatment of 35.3 years old (SD 10.27). 25 patients had thyroid function assessment in the early period out of which 32 % had thyroid dysfunction. In the intermediate period, 86 patients were assessed 19.76 % of which had thyroid abnormalities. In the late period, 172 patients had thyroid function assessment with an impressive 38.95 % having an abnormal test. The most frequent abnormalities were subclinical hypothyroidism and a low T4 with a low/normal TSH. 45 patients had HbA1c testing 48.88 % of which were diagnosed with diabetes (HbA1c >6.5 %) and 11.11 % with prediabetes. Our study provides evidence that the incidence of thyroid dysfunction and glucose metabolism abnormalities is higher than in the general population. This emphasizes the need for regular long term monitoring of thyroid function and risk of diabetes following HSCT.

P45 ATLANTIC DIP: insulin therapy for women with IADPSG-diagnosed gestational diabetes mellitus

Bogdanet D, Egan AM, Kirwan B, Carmody L, Dunne FP

Galway Diabetes Research Centre, NUIG

The objective of this study was to assess if women with gestational diabetes (GDM) diagnosed according to the IADPSG criteria treated with insulin have comparable pregnancy outcomes to women with normal glucose tolerance (NGT). This retrospective cohort study included 752 women diagnosed with GDM and treated with insulin and 2496 women with NGT during pregnancy. Multiple maternal and fetal outcomes were examined. Infants of women with GDM treated with insulin were more likely to be hypoglycemic at birth (adjusted odds ratio (aOR) 7.27, 95 % CI 2.49–21.22). They were more likely to be born prematurely (aOR 0.46 95 % CI 0.27–0.78) and require admission to NICU (aOR 13.90 95 % CI 10.23– 8.87). There was no difference in the rate of mortality, macrosomia, large and small for

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gestational age between the two groups. Women with GDM treated with insulin were at increased risk of polyhydramnios (aOR 8.52 95 % CI 4.40–16.47). Women with GDM had a significantly higher BMI (BMI >30 64.19 % GDM; 20.41 % NGT, $p < 0.01$) a higher rate of family history of diabetes (68.05 % GDM; 31.91 % NGT, $p < 0.01$) and history of smoking (11.79 % GDM; 6.89 % NGT, $P < 0.01$). Insulin treatment for women with IADPSG-diagnosed GDM may be successful in lowering rates of certain adverse outcomes. While offspring of women receiving insulin therapy during pregnancy have increased rates of prematurity and hypoglycemia, mortality rates are not elevated.

P46 Discordant thyroid function tests: case series from the Ulster Hospital

McNabb BM[1], Trinick T[2], Duly E[2], McHenry C[1]

[1]Department of Endocrinology, Ulster Hospital, Belfast; [2]Department of Biochemistry, Ulster Hospital, Belfast

Thyroid function tests (TFT) are among the most common biochemical investigations requested within our healthcare setting. Interpretation is usually straightforward, confirming the clinician's impression regarding thyroid status. However, results may be discordant; either not in keeping with the clinical picture or incongruent with each other. In this instance, once confounders are excluded, it is important to consider assay interference and genetic or acquired disorders of the hypothalamic–pituitary–thyroid axis.

We studied clinical records over an 18-month period of patients in whom TFT showed incongruent results (normal or elevated TSH with elevated Free T4 (FT4)) wherein samples were sent to Edinburgh Royal Infirmary (ERI) for analysis on a different immunoassay over 18 months. Sixteen patients' records were reviewed. The presenting incongruent TFT showed mean FT4 of 27.9 ± 7.3 pmol/L and TSH 2.7 ± 2.8 mU/L and were referred to ERI. Twelve of 16 (75 %) patients had normal TFT (FT4 16.8 ± 7.3 pmol/L; TSH 1.8 ± 1.9 mU/L) when checked on their assay. Eleven were asymptomatic, one had classical thyrotoxic symptoms. Incongruent TFT were confirmed in the remaining four (thyroid hormone resistance, renal impairment with normalisation of TFT post-transplant, variable compliance of thyroxine replacement, declined investigation). Where most TFT results fit with clinical assessment of thyroid status, a small subset of patients exhibit results that are discordant with the clinical picture or incongruent with each other. This study highlights when confounders are excluded, close liaison with clinical biochemists to exclude thyroid hormone and TSH assay interference is essential. Only then should further complex investigation be performed.

P47 A case of thyroid hormone resistance

McNabb B[1], Hunter SJ[2], McHenry CM[1]

[1]Department of Endocrinology, Ulster Hospital, Belfast; [2]Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast

A 45 year old female presented with anxiety and was noted to be tachycardic. Thyroid function tests (TFT) showed incongruent results (free T4 33.6 pmol/L; NR 10.6–23.2: TSH 4.39 mU/L; NR 0.3–4.2) prompting Endocrinology referral. There were no other symptoms of thyrotoxicosis. She was euthyroid with a small diffuse goitre. Visual acuity and fields were normal. TFT were repeated on a Roche assay and a further sample sent for testing on an alternative assay (Abbott). TFT remained incongruent. Further investigation included α-subunit, MRI pituitary, T3 suppression and TRH stimulation tests.

MRI pituitary and α-subunit were normal. TRH test showed basal TSH 4.72 mU/L, TSH at 20 and 60 min of 48.65 and 32.88 mU/L, respectively. T3 suppression test (T3 20mcg q.d.s for 8 days) showed baseline free T4 30.3 pmol/L, TSH 3.84 mU/L. Following T3 administration, free T4 17.2 pmol/L, TSH 0.16 mU/L. The exaggerated response to TRH and suppression of TSH with T3 suggested Thyroid Hormone Resistance (THR). Genetic testing demonstrated THRbeta mutation: c.1013G>T, p.(Arg338Leu) in T3 binding domain. The patient was counselled regarding 50 % chance her daughter is affected which could have future implications if she became pregnant. THR is an autosomal dominant inherited syndrome of reduced end-organ responsiveness to thyroid hormone. The paucity of symptoms includes goitre, tachycardia and hyperactivity, all of which our patient demonstrated. Tachycardia relates to predominant expression of THRalpha in the heart. Differentials include TSHoma and endogenous antibodies to T4 and T3. When assay interference is excluded, it is important to carefully evaluate discordant TFT.

P48 Optimal medical management of patients with maternally inherited diabetes and deafness (MIDD)

McCarrick CJ[1], Ioana J[1], Bacon S[1], Burke M[1], O'Sullivan E[2], Byrne MM[1]

[1]Diabetes Day Centre, Mater Misericordiae University Hospital, Dublin 7; [2]Bon Secours Hospital, Cork

An estimated 2.8 % of diabetic patients have MIDD. In clinical practice, MIDD presents similarly to T1DM or T2DM depending on the degree of insulinopenia. A suspicion for MIDD should be raised if there is matrilineal transmission of diabetes particularly in the presence of sensorineural deafness. MIDD can be associated with advanced microvascular complications for a given duration of diabetes and requires multidisciplinary input. This study aimed to review the optimal management and complication rate associated with the Mater MIDD cohort. A retrospective chart review of N = 29 patients with a mitochondrial mutation referred to the Mater MIDD clinic was performed. Data are presented as Mean and SEM. 66 % of the cohort had diabetes (N = 19), with a mean 10.4 year interval between diabetes diagnosis and confirmation of an MIDD mutation. The mean BMI was 22.8 kg/m^2 (N = 15). Sensorineural-deafness was present in 95 % (N = 18). 42 % had hypertension (N = 8), and on echocardiography 42 % had LVH (N = 8). The mean lactate level was 2.81 mmol/L (N = 14). Myopathy was described in 21 % (N = 4). Macular dystrophy was detected in 15.7 % (N = 3). The average urinary ACR (albumin creatinine ratio) was 14.03 mg/mmol (N = 18). Treatment: Metformin was discontinued in 42 % (N = 8). Insulin was required in 68 % of the diabetic cohort with an average of 43.7 units/day (N = 13). The mean HbA1c for those on insulin was 64 mmol/mol, an average of 11.9 mmol/mol higher than those not requiring insulin ($p = 0.027$). Mitochondrial based therapy in the form of co-enzyme-Q10 was prescribed in 68 % with the average dose being 236 mg/day (N = 11). Mitochondrial diabetes is increasingly being diagnosed on next generation sequencing. It is an important diagnosis to make as it requires genetic counselling and the anticipation of both iatrogenic and non-iatrogenic complications.

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P49 Identifying incomplete atypical femoral fractures with single-energy absorptiometry femur exam: declining prevalence

McKenna MJ[1,2], McKiernan FE[3], McGowan B[4], Silke C[4], Bennett K[5], van der Kamp S[1], Ward P[6], Hurson C[7], Heffernan E[6]

DXA Unit[1]; Department of Diagnostic Imaging[6], and Department of Orthopaedic Surgery[7]'; St. Vincent's University Hospital, Dublin; School of Medicine and Medical Sciences, University College Dublin[2]; Marshfield Clinic Research Foundation, Marshfield, Wisconsin, USA[3]; [4]The North Western Rheumatology Unit, Our Lady's Hospital, Manorhamilton[4]; Division of Population and Health Sciences, Royal College of Surgeons in Ireland, Dublin[5]

Atypical femur fractures (AFF) are associated with long-term bisphosphonate (BP) therapy. Single energy X-ray absorptiometry (SE) is an imaging method recently shown to detect incomplete AFF (iAFF) prior to fracture completion.

Patients (n = 173), who had been prescribed BP therapy for greater than 5 years, were assessed for iAFF using SE femur imaging at their presentation for routine bone mineral density testing between May 2013 and September 2014. National trends In Ireland for femur fracture incidence were calculated from 2005 to 2014 by extracting data from a national computer-based discharge abstracting system using the ICD 10 codes for the following specific hip fractures types: neck of femur (S720), pertrochanteric (S721), subtrochanteric (S722), and shaft of femur (S723). Trends in BP prescribing were calculated from 2009 to 2014 using a national primary care prescribing database.

No patients had iAFF using SE femur imaging compared to a prevalence of 2.7 % in the earlier study using dual-energy X-ray absorptiometry (DXA) imaging. Between 2005 and 2009, the yearly rates of hospitalisations in Ireland for all femur fractures increased by 7.2 % (p = 0.121) and for S722/S723 by 29.1 % (p = 0.030) with non-significant changes between 2010 and 2014 at -3.5 % (p = 0.672) and 6.7 % (p = 0.644), respectively. Between 2010 and 2104, BP prescribing declined by 14 % (p = 0.209) at a time when calcium prescription increased by 26 % (p = 0.023). Point of service SE imaging can identify iAFF prior to fracture completion that, in turn, might avert morbidity associated with fracture completion. The declining trend in AFF is coincident with declining national trends in BP prescribing in Ireland.

P50 Anorexia nervosa with severe hyperphosphataemia as a consequence of high bone turnover and functional FGF23 resistance

McKenna MJ[1], Kilbane M[2], Crowley R[1], O'Keane M[2], Maher C[3], Twomey P[2]

Departments of Endocrinology[1]; Clinical Chemistry[2]; and Psychiatry[3]; St. Vincent's University Hospital, University College Dublin, Ireland

We reported previously a case of X-linked hypophosphataemia with hypoparathyroidism post parathyroidectomy, in whom renal handling of phosphorus (as estimated by TmP/GFR) normalised despite > 10-fold elevation in fibroblast growth factor 23 (FGF23). Parathyroid hormone (PTH) concentration was undetectable suggesting the primacy of PTH over FGF23 in the renal handling of phosphorus. A 51 years old postmenopausal woman presented with an incomplete fragility fracture on the outer aspect of left femur neck. At presentation her weight was 27.1 kg; body mass index was 10.0 kg/m^2. She was monitored according to protocol for refeeding syndrome. After 6 weeks, adjusted serum total calcium was high-normal, 2.60 mmol/L (N: 2.20–2.60); serum phosphorus was high, 2.23 mmol/L (N: 0.84–1.48); TmP/GFR was high, 1.93 mmol/L (N: 0.84–1.48); 25OHD was sufficient, 57 nmol/L; PTH was low-normal, 15.7 ng/ml (N: 15–65); C-terminal FGF23 was high, 293HRU/ml (N: <100); eGFR was 90 ml/min. Bone turnover was markedly elevated: serum C-terminal telopeptide of type I collagen (CTX) 5.140 μg/L (N: 0.016–0.584); urinary N-terminal telopeptides of type I collagen (uNTX) 760nMBCE/mMCr (N: 25 –73); serum total procollagen type I amino-terminal propeptide (PINP) > 1200 μg/L (N: 17–-96); serum osteocalcin (OC [1–43]) 280 μg/L (N: 11–43). Denosumab 60 mg subcutaneous was administered. Two months later, resorption markers had normalized and formation markers were improved but still high: CTX, 0.366 μg/L; uNTX, 74nMBCE/mMCr; PINP, 489 μg/L; OC[1–43], 78.6 μg/L. PTH was mildly elevated, 95.1 ng/ml; TmP/GFR normalised, 1.23 mmol/L; and FGF23 was within the reference range, 60HRU/ml. This case report is further support for the primacy of PTH over FGF23 in renal handling of phosphorus.

P51 Cystic fibrosis related diabetes: a challenging cohort of patients that require multidisciplinary management

Ryan D[1], Burke H[1], Ryan O[2], O'Mahony M[2], Dineen S[1], O'Sullivan E[1], Bell M[1]

[1]Department of Diabetes and Endocrinology, University Hospital Galway; [2]Department of Respiratory Medicine, University Hospital Galway

50 % of cystic fibrosis (CF) sufferers over 30 have Diabetes Mellitus (DM)[1] Cystic fibrosis related Diabetes Mellitus (CFRD) is associated with increased mortality and worsening FEV1 %. Screening for DM has led to improvements in mortality. Decline in FEV1 % correlates with insulin insufficiency. BMI and nutrition improve with better glycaemic control. American Diabetes Association (ADA)/CF Foundation guidelines recommend CFRD patients should attend multidisciplinary clinics with expertise in DM and CF. CFRD patients attending UHG were identified (n = 13) through the Diamond database. Demographic and clinical data were obtained. Clinical outcomes were assessed and it was concluded that the management of this patient cohort is not optimal.

Table 1 CFRD patients in University Hospital Galway

Sex (male/female)	Male 8	Female 5
Age (years)	Mean 29.4	Range 19–47
Age at diagnosis (years)	Mean 25.46	Range 17–38
HbA1c mmol/mol	Mean 46 mmol/mol	Range 32–79 mmol/mol

CFRD patients require careful management to optimise their glycaemic control. Their need to avoid exposure to microbial infections makes attendance at Diabetes clinics challenging. Multidisciplinary management at a combined Respiratory and Diabetes clinic is planned to improved management and overall health in our CFRD cohort.

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P52 The use of low dose Tolvaptan in the treatment of refractory SIADH in small cell lung cancer

Ryan D[1], Casey R[1], Blazcova S[2], O'Shea P[3], Bell M[1]

[1]Department of Endocrinology, University Hospital Galway; [2]Oncology Department, University Hospital Galway; [3]Department of Clinical Biochemistry, University Hospital Galway

Conventional approaches to the treatment of SIADH in malignancy include the use of hypertonic saline, fluid restriction and use of agents such as Demeclocycline. These approaches often result in suboptimal management of hyponatraemia, have variable efficacy, are frequently poorly tolerated and can have important side effects[1]. The "Vaptans" act by directly blocking the action of ADH at its receptor site. Vaptans are licensed for use in SIADH at a start dose of 15 mg. There is evidence however, that serum sodium levels can increase by over 12mmmol in 24 h in response to this dose and there is also evidence that lower doses used off licence can be similarly effective and less expensive. We report a case series on the use of low dose Tolvaptan (7.5 mg) to control refractory hyponatraemia in three patients with small cell lung cancer. Cases involved patients in their 60 s with a diagnosis of extensive stage small cell lung cancer (SCLC) with SIADH that failed to respond to conventional treatment. Patients had excellent responses to low dose Tolvaptan with normalisation of serum sodium levels without any side effects. In all cases, a lower dose of Tolvaptan was used which was effective at maintaining serum sodium at normal levels while the patients continued their palliative chemotherapy for extensive stage SCLC. This case series adds to the evidence that Tolvaptans used in smaller doses can be effective in the treatment of paraneoplastic SIADH in small cell lung cancer.

P53 Euglycemic DKA in a patient undergoing gastric bypass surgery: lessons learned! New recommendations

A 51 y/o woman, with DM2 (10 years) is referred 2 days post gastric bypass surgery with fever, nausea and abdominal pain. Her DM regime included dapagliflozin 10mgs, Metformin 2gms and Novomix 120 units BD. She had CKD stage 3a. Pre-op HbA1c was 71 mmol/l. Our 2-week pre-surgery protocol, includes a high protein, low carbohydrate diet: All medications and insulin were continued but recommending insulin titration reflecting glucose readings.

Surgery was uneventful. DM medications and insulin were held post-op, but to restart if sugars exceeded 10 mmol/l. She spiked a temperature 48 h postop, O2 sats fell (94 %,) CRP rose (200 mg/l) and CT confirmed pneumonia. Her anastomotic site was intact. GFR remained stable. ABGs confirmed PH 7.164, bicarb 7.3, PO_2 15.5 kPa, PCo_2 2.7 kPa, and lactate 1 mml/l. An anion gap of 19.8 mEq/l, confirmed metabolic acidosis. FBS day 1 post op was 8.7, and day 2 was 13 mmol/l. Glucose values in 48 h were <13. A diagnosis of eugylcaemic ketoacidosis was made, multifactorial in etiology BUT felt predominantly attributable to SGLT2 therapy. She started IV insulin, (240 units/day) for 5 days, subsequently converted to Glargine 20 units and Glucophage was recommenced. Glucose remained normal. Anti GAD antibodies were negative and C-peptide (pre Lantus dose) 1.12 ug/l (0.8–5.2).

In summary, the diet likely accelerated a ketogenic state, aggravated by SGLT2 therapy, and exaggerated in the postoperative fasting state with concomitant infection. Our pre-operative protocol has changed to specifically EXCLUDE SGLT2 therapy in the 2-weeks pre-surgery.

P54 Sunbeds and sarcoidosis

Kerr K[1], McElwaine F[2], Mullan K[1]

[1]Regional Centre for Endocrinology and Diabetes Royal Victoria Hospital Belfast; [2]Endocrine Unit Ulster Hospital Dundonald

A 50-year-old man presented acutely to hospital with a 5 day history of nausea, poor oral intake and polyuria. He had a history of type 2 diabetes, bipolar disease and outpatient investigations were underway for mild hypercalcaemia picked up incidentally (calcium corrected Ca(c) 2.69 mmol/l (2.2–2.6)). He had started using daily sunbeds 4 weeks previously. On examination he was tanned and had bilateral uveitis on slit lamp examination. He had an acute kidney injury (urea 18 mmol/L, creatinine 438 umol/l) and the following abnormal results: Ca(c) 3.74, phosphate 1.71 mmol/l (0.8–1.5), Serum Angiotensin Converting Enzyme (ACE) 136 U/l (12–68), Parathyroid hormone (PTH) 8 pg/ml (15–65) and urinary calcium output 178 mmol/24 h (2.5–7.5). Chest X-ray was normal but CT revealed mediastinal and retroperitoneal lymphadenopathy favouring sarcoidosis among the differentials. Pre-sunbed exposure 25OH Vitamin D was 25 nmol/l (n > 50) but on admission was 48 nmol/l and 1,25 vitamin D was 117 pmol/l (48–120). Whilst awaiting biopsy he was treated with intravenous fluids and oral prednisolone with rapid normalisation of calcium. Sunbeds mostly emit UVA and only low levels of the vitamin D forming UVB light (5 %). In healthy individuals hypercalcaemia has not been reported with sunbed use because of the diversion of metabolism of vitamin D to inert metabolites with prolonged exposure. In sarcoidosis, macrophages in the granuloma produce both PTH related peptide and 1αhydroxylase, the latter converting 25OH vitamin D to 1,25OH vitamin D. These changes, combined with the generation of vitamin D with sunbeds allows the development of hypercalcaemia in patients with sarcoidosis.

P55 Audit of thyroid status of patients post radioactive iodine treatment

Salehmohamed MR, Sweeney AM, Hatunic M

Diabetes and Endocrinology Unit, Mater Misericordiae University Hospital, Dublin

Radioactive iodine (RAI) has been used to treat overactive thyroid disorders since the 1940′s. RAI success rates vary in literature. Our aim was to assess the treatment outcomes in patients with hyperthyroidism after RAI treatment in Mater Misericordiae University Hospital (MMUH). A successful outcome was defined as euthyroidism or hypothyroidism by 1-year post treatment.

We identified 101 patients who had undergone RAI treatment between January 2010 and December 2014. Just under half (47) patients were followed up in MMUH while others (54) were referrals from outside hospitals. Most of the patients were females 36 (81 %) vs 9 (19 %) males. There were 30 (63 %) patients with Graves disease, 10 (21 %) with toxic multinodular goitre and 7 (15 %) with toxic single nodule. The average RAI dose was 471.6 (80) MBq. Overall the success rate was 83 % with 39/47 patients fulfilling the criteria for successful treatment after 1 year. The success rate in patients with Graves disease was 80 % (24/30), with MNG was 80 % (8/10) and with toxic nodule was 100 % (7/7). Male patients responded better than female -100 % vs 79 %. There was no significant difference in RAI doses received by those that had a successful outcome after 1 year comparing to patients

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who did not respond to the RAI treatment; 471.5 (80.0) MBq vs 471.5 (80.0) MBq. We found that our patients who had undergone RAI treatment consisted of a mixed cohort of hyperthyroid patients: Graves disease, multinodular goitre and toxic single nodule. Importantly 83 % of patients who underwent RAI treatment were euthyroid or hypothyroidism 1-year post treatment.

P56 Outcomes following fixed dose radioactive iodine therapy (RAI) in hyperthyroid patients attending Connolly Hospital Blanchardstown

Cheah SK, Nazri M, Kyaw Tun T, Sreenan S, McDermott J

Endocrinology Department, Connolly Hospital, Blanchardstown, Dublin 15

RAI is a definitive treatment for hyperthyroidism, but administered doses vary between institutions. We utilize a fixed dose RAI treatment protocol, administering 370 MBq to all patients unless there is a large goitre present. We retrospectively reviewed outcomes following RAI therapy in 168 hyperthyroid patients (Graves Disease N = 90 (48 %), Toxic Multinodular Goitre and Toxic Adenoma N = 70 (42 %) and unspecified N = 8 (5 %)) receiving 370 MBq RAI between January 2001 and March 2015 in order to determine treatment outcomes at 1 year post-RAI. Table 1 below details treatment outcomes at 1 year.

Table 1 RAI outcome at 1 year

	GD (N = 90)	TMG/TA (N = 70)
Age (mean ± SEM)$^{\alpha}$	45.93 ± 1.52 y	63.29 ± 1.39 y
Hypothyroid$^{\beta}$	48/90 **(53 %)**	12/70 **(17 %)**
Euthyroid$^{\beta}$	30/90 **(33 %)**	44/70 **(63 %)**
Hyperthyroid$^{\beta}$	10/90 **(11 %)**	14/70 **(20 %)**

$^{\alpha}$ t-test applied for age (GD group younger than TMG/TA by 17.35 y, $p = 0.000$)

$^{\beta}$ Chi Square test applied for proportions of RAI outcome, $X^2 = 23.235$ (df = 2, $p = 0.000$)

In summary, when compared to GD group, there were proportionally more TMG/TA patients who remained hyperthyroid a year following a single dose of 370Mbq RAI, although less likely to be rendered hypothyroid. These results suggest that a higher dose of RAI may be needed for TMG/TA.

P57 Malignancy risk stratification in multinodular Goitre: A retrospective review of sonographic features, histopathological results and cancer risk

Brendan Kelly[1], Pradeep Govender[2], Mark Sherlock[3], Michael Jeffers[4], Kinsella J[5], Gibney J[6], William Torreggiani[7]

[1]Dept of Radiology, AMNCH Dublin 24; [2]Dept of Radiology, AMNCH Dublin 24; [3]Dept of Endocrinology, AMNCH Dublin 24; [4]Dept of Pathology, AMNCH Dublin 24; [5]Dept of Otolaryngology, AMNCH Dublin 24; [6]Dept of Endocrinology, AMNCH Dublin 24; [7]Dept of Radiology, AMNCH Dublin 24

Aim: In the management of thyroid nodules it is understood that while the potential for malignancy exists, there is also the potential for over-treatment of sub-clinical disease. While the TI-RADs system outlines a risk stratification score based on suspicious ultrasound findings, it has not been universally accepted. Many "TI-RADS 2" patients proceed to fine needle aspiration biopsy (FNAB), potentially unnecessarily. The aim of our study was to examine whether the cytological results added to risk stratification of malignancy beyond the ultrasound findings alone.

Materials and method: We retrospectively analysed pathology records for proven multi nodular goitres (MNG) over a 5 year period. 289 cases in total were identified. FNAB and pre-biopsy ultrasound images and reports were identified for each case. Ultrasound images and reports were reviewed and assessed for sonographically suspicious criteria as outlined by the TI-RADS system. Logistic regression was applied to determine which if any sonographic features were associated with neoplasia and odds ratios with 95 % confidence intervals were calculated.

Results: Of 289 samples 14 (4.8 %) were neoplastic. Having no suspicious features on ultrasound (TI-RADS 2) conferred an average risk of 0.0339 (95 % CI 0.02831–0.04087) of having a thyroid neoplasm. Risk of neoplasm significantly increased by having 1 and >1 suspicious feature ($p < 0.001$). Regarding cytological results, of 237 patients with Thy-2 cytology 159 patients were followed up and 0.05 had a thyroid neoplasm.

Conclusion: Ultrasound features can be used to estimate risk of thyroid neoplasia in MNG. In the absence of suspicious radiological findings follow up with ultrasound rather than FNAB may be appropriate in patients with MNG who have a low clinical suspicion for neoplasia.

P58 Fine needle aspiration cytology of thyroid nodules: an institutional experience

Ahmed M[1], Jeffers M[2], Feeney J[3], Govender P[3], Sherlock M[1], Gibney J[1]

[1]Department of Endocrinology, The Adelaide and Meath Hospital Incorporating the National Children's Hospital (AMNCH), Tallaght, Dublin; [2]Department of Histopathology, AMNCH, Tallaght, Dublin; [3]Department of Radiology, AMNCH, Tallaght, Dublin

Fine needle aspiration cytology (FNAC) of the thyroid is a cost effective procedure that is valuable for distinguishing benign nodules from neoplastic lesions. The aim of this study was to determine the diagnostic accuracy of thyroid FNAC performed at our institution by correlating them to the histological outcomes. The cytological diagnoses of all thyroid FNAs performed between January 2013 and January 2014 in AMNCH-Tallaght were retrospectively retrieved from the Pathology Laboratory Information System. The cytological results were correlated with histological examination for those who underwent surgery. 179 FNACs were performed on 146 patients. The cytological diagnoses were as follows: Thy1 in 12 (6.7 %) cases, Thy2 in 147 (82.1 %) cases, Thy3 in 11 (6.2 %) cases, Thy4 in two (1.1 %), and Thy5 in 7 (3.9 %) cases. 98.3 % (n = 176) of FNACs were performed using US guidance and the inadequacy rate in this group (Thy1 rate) was 5.1 %. All 3 samples done using palpation-guidance only resulted in inadequate aspirates. 23 cases underwent surgery of which the final histology was benign in 15 (65 %) and malignant in 8 (35 %). Our false negative rate (malignant neoplasms reported as Thy2) was 0 %, and the false positive rate (benign histology reported as Thy4 or Thy5) was also 0 %. Complete sensitivity (including intermediate/Thy3 results) was 92.3 % with a specificity of 80 % and an overall accuracy of 87 %. In conclusion, thyroid FNAC

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is highly accurate procedure with low false negative and false positive rates. Findings from our institution compare favourably to those reported in published literature.

P59 Contrasting phenotypes in resistance to thyroid Hormone α correlate with divergent properties of thyroid hormone receptor α 1 mutant proteins

Anne McGowan[1], Carla Moran[1], Maura Agostini[1], Erik Schoenmakers[1], Greta Lyons[1], Odelia Rajanayagam[1], Laura Watson[2], Amaka Offiah[3], John Barton[4], Susan Price[5], Krishna Chatterjee[1]

Wellcome-MRC Institute of Metabolic Science[1] and NIHR/Wellcome Trust Clinical Research Facility[2]; University of Cambridge; Academic Unit of Child Health, University of Sheffield, Sheffield[3]; Department of Paediatric Endocrinology and Diabetes[4]; Bristol Royal Hospital for Children, Bristol and Department of Clinical Genetics, Northampton General Hospital, Northampton, UK[5]

Resistance to Thyroid Hormone alpha (RTHα) is characterised by tissue-selective hypothyroidism with near-normal thyroid function tests, and is due to thyroid receptor α gene mutations (1). We sought to define the characteristics and response to treatment of two RTHα patients and correlate these with properties of the *THRA* mutation. Clinical, biochemical and physiological parameters were assessed at baseline and after thyroxine therapy. Heterozygous *THRA* mutations were identified in a 17 year old male with mild pubertal and growth retardation (P1; A263 V mutation), and a 15 year old male (P2; L274P mutation) with short stature (0.4th centile), skeletal dysplasia, dysmorphic facies and global developmental delay. Both exhibited typical features of RTHα; macrocephaly, delayed dentition, constipation, low T4/T3 ratio, low reverse T3 levels and mild anaemia. *In vitro*, A263 V mutant TRα1 was transcriptionally impaired and inhibited the function of its wild type counterpart at low T3 levels, with higher T3 concentrations reversing dysfunction and such dominant negative inhibition. In contrast, L274P mutant TRα1 was transcriptionally inert, exerting significant dominant negative activity, only overcome with high concentrations of T3. Despite similar biochemical changes following thyroxine therapy in both patients, growth, dyspraxia, BMI and constipation improved in P1, whereas growth retardation and constipation in P2 were unchanged. We correlate a milder clinical phenotype and response to thyroxine therapy in an RTHα patient with heterozygosity for mutant TRα1 exhibiting partial, T3-reversible, loss-of-function; whereas skeletal dysplasia, developmental delay and growth retardation refractory to hormone therapy in another case are associated with a severe, virtually irreversible, dysfunction of mutant TRα1.

P60 Localisation studies in pre-operative workup for minimally invasive parathyroidiectomy

McKeever E[1], Kennedy R[2], Kirk S[2], Harper R[1], McLaughlin D[1], Mulligan C[1], Lynch T[3], Majury C[4], McHenry CM[1]

[1]Department of Endocrinology, Ulster Hospital, Belfast; [2]Department of Breast and Endocrine Surgery, Ulster Hospital, Belfast; [3]Department of Nuclear Medicine, Belfast City Hospital, Belfast; [4]Department of Radiology, Ulster Hospital, Belfast

Successful minimally invasive parathyroidectomy for primary hyperparathyroidism depends on accuracy of pre-operative localisation studies. Ultrasound (US) and sestimibi (SM) scanning remain the imaging modalities of choice. The aim of this study was to review the accuracy of US and SM in the pre-operative localisation of parathyroid adenomas.

We performed a retrospective review of 51 consecutive patients with a biochemical diagnosis of primary hyperparathyroidism who underwent surgery by one of two Endocrine Surgeons. We compared findings on ultrasound and ^{99m}Tc-sestamibi scintigraphy to histology results. Of the 51 patients who underwent parathyroid surgery over an 18 month period, complete data was available for 47 (M:F 12:35; median age 64 years, range 15–81). Primary hyperparathyroidism was confirmed biochemically with pre-operative calcium 2.85 ± 0.17 mmol/L and parathyroid hormone concentration 126.0 ± 113.0 pg/mL. 36 patients had a solitary parathyroid adenoma, 6 had parathyroid hyperplasia, 1 had multiple adenomas and 4 had inconclusive histological findings. Ultrasound was positive in 29 of 36 (80.6 %) adenomas with precise anatomical position found in 22 of the 29 (sensitivity, specificity and positive predictive value of 81, 64 and 88 %, respectively). Pre-operative ^{99m}Tc-sestamibi scintigraphy correctly identified 21 of 36 (58.3 %) adenomas (58.3 % sensitivity, 81.8 % specificity and 91.3 %. positive predictive value). US findings correlated with SM in 20 patients and were 85 % accurate (sensitivity 81.2 %, specificity 100 % and positive predictive value 100 %). US and SM scanning show good concordance with histology following parathyroid surgery and when combined provide accurate pre-operative localisation. They should remain the first line to guide minimally invasive parathyroidectomy.

P61 Growth hormone replacement in a hypopituitary female seeking fertility treatment: a clinical case

McKeever E[1], McCance DR[1], Agbaje I[2], Hunter SJ[1]

[1]Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast; [2]Regional Fertility Centre, Royal Victoria Hospital, Belfast

A 32-year-old female had a history of pituitary surgery for a non-functioning adenoma with subsequent external pituitary irradiation. Post-operative testing revealed panhypopituitarism and she was on standard replacement therapy. She was later noted to have Growth Hormone (GH) deficiency (IGF1 8.7 nmol/L (NR15–40 nmol/L), peak GH 0.3 ng/ml during Arginine Stimulation test) but despite an AGHDA (Assessment of GH Deficiency in Adults) score of 22 (NR <11) opted not to start GH treatment because of safety concerns regarding possible future pregnancy. 4 years post-surgery she sought fertility treatment. Investigations revealed a concomitant male infertility factor it was decided to proceed directly to Intracytoplasmic Sperm Injection (ICSI) treatment. Pre-treatment Anti-Mullerian Hormone levels were 31.9 pmol/L indicating satisfactory ovarian reserve. Following ovarian stimulation only one mature egg was obtained and following transfer a pregnancy test was negative. After discussion with Endocrinology she started GH replacement. After a further cycle of ICSI 6 suitable embryos were cryopreserved and subsequent frozen embryo transfer was undertaken following which a pregnancy test was positive. The patient remained on GH until 20 weeks gestation. She delivered a healthy baby girl weighing 3240 g by normal delivery at 38 weeks gestation. GH was restarted postpartum. Studies suggest that women with hypopituitarism have reduced success of ovulation induction, reduced pregnancy rates and reduced live birth rates. GH replacement therapy may be helpful in addition to standard pituitary hormone replacement. This case highlights the use of GH replacement in a hypopituitary woman during fertility treatment and early pregnancy leading to successful pregnancy outcome.

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P62 Nocturnal salivary cortisol in the diagnosis of cushings syndrome

McKeever E, Mc Cance DR, Hunter SJ, Courtney CH, Mullan KR, Graham UM

Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast

Nocturnal salivary cortisol (NSC), urinary free cortisol (UFC) and overnight dexamethasone suppression testing (ODS) are recommended screening tests for Cushing's syndrome (CS). Individual centers differ in their screening approach; UFC being the test of choice in Northern Ireland with ODS in patients with adrenal incidentalomas. NSC, which measures free cortisol, is not routinely used. The aims of this study were to 1. Evaluate the utility of NSC in the diagnosis of CS; and 2. Determine a NSC diagnostic threshold for CS. A retrospective study of all patients undergoing low dose dexamethasone suppression testing (LDDST) from 2010–2014 was performed. Patients were classified as "Cushing's" or "non-Cushing's" based on consultant clinical suspicion, biochemical results (UFC, ODS and LDDST) and clinical follow up. NSC samples, collected and stored over this time, were analysed using the ELISA technique. Diagnostic thresholds and test performance were determined using ROC curve analysis. Data was collected on 54 patients; 47 included in the study (20 Cushing's; 27 non-Cushing's). Seven patients were excluded (5 subclinical Cushing's, 1 cyclical Cushing's, 1 unclear diagnosis). NSC was the most effective diagnostic test for CS (AUC 0.928; $p < 0.001$) with a threshold of 10 nmol/l having a sensitivity of 94.4 %, specificity 88.5 % and diagnostic accuracy of 90.9 %. This was comparable to the LDDST (diagnostic accuracy 88.6 %). UFC, and ODS ($n = 14$; cut-off 50 nmol/l) were less effective with diagnostic accuracies of 72.3 and 42.9 %, respectively. In conclusion, NSC is an effective, easily performed screening test for CS, comparable to the LDDST and outperforming 24 h urinary collections.

P63 Fasting Plasma glucose and pregnancy outcomes: what is defined as gestational diabetes in one criterion is normal in another

Mohamed MI, Zia-UL-Hussnain HM, Higgins M, Hatunic M

Diabetes and Pregnancy Department, National Maternity Hospital, Dublin

Gestational diabetes (GDM) is a glucose abnormality diagnosed during pregnancy. Two main diagnostic criteria are used: Carpenter and Coustan (CC) criteria and the International Association for Diabetes in Pregnancy Study Group (IADPSG); these differ in fasting plasma glucose (FPG) levels. The aim of this study is to determine the association between (FPG) and pregnancy outcomes. Data was collected retrospectively for 110 pregnant women who underwent 50 gr glucose change (GCT) test then 100gr 3 h oral glucose tolerance test (OGTT) for GDM diagnosis in The National Maternity Hospital (NMH), Dublin. All of the women did not have GDM per CC criteria (FPG $\geq$ 5.3, 1 h $\geq$ 10, 2 h $\geq$ 8.6, 3 h $\geq$ 7.8 mmol/l). Women were assigned into two groups: group 1 ($n = 78$) with fasting FPG of 4.9–5.0 mmol/l, group 2 ($n = 32$) with FPG of 5.1–5.2 mmol/l. The groups were compared using t-test. There was no significant differences in baseline characteristics (age, parity, BMI, GCT). The age of participants was different; with group 1 age of 34.6 (±4.75), vs group 2, age 31.9 (±4.57), $p < 0.0008$. Glucose values did not differ in GCT and OGTT except for FPG. Birth weight was similar 3.73 (±0.49) kg vs 3.56 (±0.51) kg, p-value = 0.143. There were no documented fetal or maternal complications. Caesarean section (3 vs 8) and instrumental deliveries (1 vs 6) surprisingly was lower in group 2. Debate continues about the best screening and diagnostic method for GDM. We found that lowering cut-off point for FPG <5.3 mmol/l in diagnosis of GDM has no effect on fetal or maternal outcomes.

P64 Seasonal variation in insulin resistance during pregnancy

O'Brien EC[1], O'Sullivan EJ[1], Kilbane MT[2], Geraghty AA[1], McKenna MJ[3], McAuliffe FM[1]

UCD Obstetrics and Gynaecology[1]; School of Medicine and Medical Science, University College Dublin, National Maternity Hospital, Dublin, Departments of Clinical Chemistry[2]; and Endocrinology[3]; St Vincent's University Hospital, Dublin

Insulin resistance, above what is expected during pregnancy, is associated with pregnancy complications and adverse birth outcomes. In non-pregnant populations, insulin resistance is negatively associated with 25-hydroxyvitamin D (25OHD), but the literature regarding this association in pregnancy is inconsistent. We aimed to determine if gestation through winter and maternal 25OHD were associated with insulin resistance among euglycaemic pregnant women. Data came from an observational study of 334 pregnant women. Serum 25OHD, fasting glucose and insulin were measured in early pregnancy (13 weeks' gestation) and late pregnancy (28 weeks' gestation); HOMA-IR (marker of insulin resistance) was calculated. Participants were dichotomised into season of early pregnancy gestation; summer (May–October) or winter (November–April). 25OHD was lower among women who gestated through winter in early pregnancy compared with summer (32.8 and 43.8 nmol/L, respectively, $P < 0.001$). Exposure to winter was associated with significantly higher HOMA-IR in early pregnancy (winter 2.4, summer 1.7, $P = 0.004$). On multiple linear regression, after controlling for confounders (including 25OHD), early gestation through winter predicted a 30.9 % increase in early-pregnancy HOMA-IR compared to those exposed to summer in early pregnancy. Early-pregnancy 25OHD did not significantly predict HOMA-IR in the model. These findings suggest that seasonal variation in insulin resistance exists in early pregnancy, but the variation does not seem to be mediated through 25OHD. Further research into winter behaviours such as changes in dietary patterns, physical activity and wellbeing is required in order to explain seasonal variation in insulin resistance in early pregnancy.

P65 Predictors of babies weighing more than 4 kgs in pregnancies complicated by diabetes

Tadesse WG[1], Ramaiah S[1], Zibar D[1], Cooper A[1], Nazir SF[1], Dicker P[2], Kinsley B[1], Daly S[1]

Coombe Women and Infants University Hospital, Dublin, Republic of Ireland[2]; Department of Epidemiology and Public Health Medicine, Royal College of Ireland, Dublin, Republic of Ireland

The objective of this study was to evaluate predictors of babies weighing >4 kgs in pregnancies complicated by diabetes. It was a prospective cohort study of all diabetic pregnant women who delivered singleton live baby after 37 weeks of gestation in a large tertiary referral university hospital in the year 2014. We performed ultrasound examinations of fetal abdominal circumference at 27–28, 33–34 and

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37–38 weeks. We also documented other potential factors that are thought to influence birth weight. Abdominal Circumference (AC) measurements among other risk factors were compared between women who gave birth to babies weighing <4 kgs and those > 4 kgs. There were 567 women included for analysis. Logistic regression analysis showed that an increased AC measurement at either 33–34 weeks ($p = 0.003$) or 37–38 weeks ($p = 0.000$) was significantly associated with a birth weight of > 4 kgs. However, the ultrasound evaluation at 27–28 weeks was not useful in predicting babies whose birth weight was > 4 kgs ($p = 0.909$). Similarly, multiparity ($p = 0.001$), gestational age at delivery ($p = 0.0001$), birth weight of heaviest previous baby ($p < 0.001$), and maternal height ($p = 0.0001$) remained significantly associated after logistic regression analysis. We developed a prediction model for risk of weighing > 4kgs at birth using the logistic regression coefficients. Babies of diabetic mothers who are at risk of being large can be identified using a prediction model, which incorporates AC measurements at 33–34 and/or 37–38 weeks of gestation.

P66 Maternal diabetes in pregnancy and risk of autism spectrum disorder diagnosis in offspring

Brahm M[1], Egan AM[2], Carmondy L[2], Leader G[1], Dunne FP[2]

[1]School of Psychology, National University of Ireland, Galway; [2]Galway Diabetes Research Centre, School of Medicine, National University of Ireland Galway

Diabetes is the most prevalent chronic medical condition among pregnant women. Studies are now exploring the relationship of maternal diabetes to offspring neurological development. Observational recall studies suggest that diabetes (GDM, type 1 DM and type 2 DM) leads to a two-fold increased risk of Autism Spectrum Disorder (ASD) in offspring. These studies do not report objective evidence of metabolic status. This study evaluated the risk of a child being diagnosed with ASD when maternal diabetes was present during pregnancy using participants from the Atlantic Diabetes in Pregnancy (DIP) database. The study population comprised 97 mother-offspring pairs in women with Diabetes affecting pregnancy between 2005 and 2011. An ASD diagnosis was confirmed using the Social Communication Questionnaire. Rates of ASD among case participants were calculated and compared to reported general population prevalence rates of ASD from the literature. Preliminary results suggest an increased risk of ASD in case participants compared to the general population with prevalence rates of 5.7 vs 1 %, respectively. Increased paternal age and increased reporting of mental health conditions in case parents compared to non-case parents were reported. Analysis is ongoing to explore the demographic, metabolic, delivery and feeding patterns that may be contributing to the increased association of ASD with maternal diabetes. Further analysis will also compare outcomes to matched mother-offspring pairs from our database with objective evidence of normal glucose tolerance.

P67 Audit of retinopathy in young adults with type 1 diabetes mellitus

Melvin A, McQuaid SE

Department of Endocrinology, Mater Misericordiae University Hospital, University College Dublin, Dublin, Ireland

Background: Diabetic retinopathy remains a significant cause of visual impairment in patients with type 1 diabetes.
Objective: To determine the prevalence of diabetic retinopathy among patients attending a dedicated young adult diabetes clinic.
Methods: A retrospective analysis of 51 patients with type 1 diabetes registered to the young adult diabetes clinic was undertaken. Demographic and biochemical data was collected in addition to retinopathy rates based on retinal photography at first clinic attendance (2006–2010) and at 5 years follow up. Data is presented as Mean ± SD with a p value of <0.05 considered significant.
Results: Of 51 patients (57 % male), mean age at first clinic attendance was 17.6 ± 1.8 years with mean duration of diabetes of 6.3 ± 3.8 years. Mean HbA1c was significantly higher at first attendance (76.8 ± 22.3 mmol/mol v 69.7 ± 14.7 mmol/mol at 5 years ($p = 0.039$)). 76.5 % of patients received Multiple Daily Injections with 23.5 % utilisng Continuous Subcutaneous Insulin Infusion. 23.6 % (n = 12: $R_1M_1 = 11$, $R_3M_1 = 1$) had confirmed retinopathy at first attendance compared to 37.3 % (n = 19: $R_1M_0 = 16$, $R_1M_1 = 2$, $R_3M_1 = 1$) after 5 years ($p = 0.143$). Regression analysis identified HbA1c and duration of diabetes as independent risks for retinopathy at baseline ($p = 0.028$ and $p = 0.004$, respectively). Only duration of diabetes remained a determinant of retinopathy at follow-up ($p = 0.012$).
Conclusion: We report diabetic retinopathy rates within a dedicated Young Adult Diabetes Service. While retinopathy is prevalent, the majority of patients had non-proliferative changes. Duration of diabetes remained the strongest predictor of retinopathy after 5 years attendance.

P68 IL-1 beta production in obesity

Mat A[1], Tobin L[1], O'Brien A[1], Hogan A[1], O'Shea D[2]

[1]Education and Research Centre, St Vincent's University Hospital, Dublin 4; [2]Dept of Endocrinology, St Vincent's University Hospital, Dublin 4

Glucagon-like peptide-1 (GLP-1) receptor agonists are currently licensed for use in T2DM and Obesity. Previous reports showed that GLP-1 therapy reduces IL-1β levels in T2DM patients. IL-1β is a pro-inflammatory cytokine that has been implicated in the pathogenesis of T2DM and Obesity. The aim of the current study is to elucidate the mechanisms through which GLP-1 reduces the production of IL-1β. We recruited 47 patients who started GLP-1 therapy (liraglutide) for management of their T2DM or Obesity. Research samples were taken before commencement of therapy and after 12 weeks. Peripheral blood mononuclear cells (PBMC) were isolated and stimulated ex vivo with LPS for 24 h and the level of IL-1β was measured in the cell culture supernatants by ELISA. To investigate the impact of GLP-1 on IL-1β production in vitro, THP-1-derived macrophages were activated in the presence LPS and treated with varying concentrations of GLP-1. The levels of pro-IL-1β were analysed by real-time quantitative PCR, and active IL-1β was measured by ELISA. To date, 12 participants (58 % male; mean age 51.6 year) completed the study. GLP-1 therapy was associated with a reduction in mean BMI from 44.6 to 42.8 kg/m^2 ($p = 0.002$) and mean HbA1c from 52.5 to 47.8 mmol/mol ($p = 0.01$). FBG also decreased from 7.8 to 7.3 mmol/L ($p = 0.04$). Cholesterol profiles were not significantly affected. IL-1β production was reduced from mean of 3065.6 pg/ml pre-treatment to 392.6 pg/mL ($p = 0.02$). Our preliminary results show that IL-1β is reduced in T2DM patients 12 weeks post GLP-1 and this may be a direct cellular effect.

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P69 Investigating the insulinotropic mechanisms of Esculentin-2CHa-GA30 and its substituted analogues

Moffett RC, Vasu S, Flatt PR, Conlon JM, McGahon MK, Curtis TM*, Abdel-Wahab YHA*

SAAD Centre for Pharmacy and Diabetes, School of Biomedical Sciences, Ulster University, Coleraine, and *Centre for Experimental Medicine, Queen's University of Belfast, Northern Ireland, UK

We assessed the antidiabetic potential of esculentin-2CHa a peptide first isolated from skin secretions of the Chiricahua leopard frog Lithobates chiricahuensis (Ranidae). Analogues of esculentin-2CHa-GA30 were designed for ease of synthesis, plasma enzyme resistance and increased biological activity. Effects on insulin release were assessed using clonal insulin-releasing BRIN BD11 cells, human 1.1B4 cells and isolated mouse islets. Effects on membrane potential, intracellular Ca2 + and cAMP levels were determined. K-ATP currents were assessed using whole-cell mode of the patch clamp technique. Analogues [D-Arg7, D-Lys15, D-Lys23]-esculentin-2CHa-(GA30) and Lys15-octanoate-esculentin-2CHa-(GA30) (Peptides 7 and 10, respectively) stimulated glucose-dependent insulin release from mouse islets ($P < 0.01$) and stimulated insulin secretion by 1.5–3.5 fold ($P < 0.001$) from human 1.1B4 cells at concentrations as low as 1×10–11 M. Using chemical inhibitors of adenylate cyclase (30 uM), protein kinase C (10 nM) or phospholipase C (5 uM) pathways, involvement of PLC/PKC mediated insulin secretion was confirmed in BRIN BD11 cells with similar action to CCK-8. The analogues prompted weak plasma membrane depolarisation ($P < 0.05$) and small increase of intracellular Ca2 + ($P < 0.01$). Patch clamp experiments indicated lack of effect on K-ATP channels. These data suggest that multi-acting analogues of esculentin-2CHa-GA30 may prove useful for promotion of insulin secretion and glycaemic control in obesity-diabetes.

P70 Carbimazole induced ANCA positive vasculitis: a case report

Wallace HJ[1], Wilson C[2], Devine P[2], Guy S[3], Lindsay JR[1,2]

[1]Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast; [2]Department of Endocrinology and Diabetes, Mater Infirmorium Hospital, Belfast; [3]Department of Respiratory Medicine, Mater Infirmorium Hospital, Belfast

Vasculitis is a rare complication of thionamide medication. It is most commonly associated with propylthiouracil. We describe a patient who developed ANCA positive vasculitis while on carbimazole therapy.

A 68 year old lady was admitted with shortness of breath, diarrhoea and weight loss. Past medical history included COPD, fibromyalgia, polymyalgia rheumatica and a toxic multinodular goitre, for which she was taking carbimazole. On admission, she was clinically and biochemically thyrotoxic (FT4 41.0 pmol/l (12–22), TSH <0.01 mU/l (0.27–4.2)). Chest X-ray revealed bilateral infiltrates and she was commenced on antibiotics to treat community acquired pneumonia.

Investigation of weight loss 1 year previously included a CT and PET scan, which demonstrated a 1.5 cm right upper lobe lesion. The patient failed to attend for follow up scans and bronchoscopy. A repeat CT scan of chest during this admission revealed a new 2.5 cm lesion in the left lower lobe and complete resolution of the previously noted lesion. The migratory pattern of the opacification and the clinical picture raised the possibility of a non-infective pneumonia such as autoimmune disease, which may have been partially treated with the prednisolone she was taking for polymyalgia rheumatica. ANCA titres were elevated (c-ANCA 20 (0–19), p-ANCA 40 (0–19) and MPO-ANCA 2.5 (0–0.09)), suggesting ANCA positive vasculitis with pulmonary involvement. Our patient responded well to withdrawal of carbimazole, radioiodine (550 MBq) and a tapered dose of prednisiolone.

This case highlights awareness of this rare complication of antithyroid medication. Early identification and withdrawal of medication is important to prevent long-term complications of vasculitis.

P71 Relationship between eating breakfast, chronotype and metabolic profile in patients with type 2 diabetes

[1]Kgosidialwa O, [1]Wong M, [1]Barry C, [1]Kyaw Tun T, [1]Sreenan S, [2]Coogan A, [1]McDermott JH

[1]Department of Endocrinology, Connolly Hospital Blanchardstown, Dublin 15, Ireland; [2]Department of Psychology, Director of Chronobiology and Sleep Research Laboratory, National University of Ireland Maynooth, Maynooth, Co. Kildare

Skipping breakfast is associated with an adverse metabolic profile in type 2 diabetes (T2DM). Patients with a late chronotype may be more likely to skip breakfast. We aimed to examine the relationship between skipping breakfast, chronotype, and metabolic and clinical parameters in Irish patients with T2DM. Patients with T2DM attending routine clinic visits had a structured interview and completed questionnaires on chronotype (Munich Chronotype Questionnaire [MCTQ]), sleep quality (Pittsburgh Sleep Quality Index [PSQI] and Berlin Questionnaire for Sleep Apnoea) and diet. Physical examination was performed and clinical and anthropometric data were recorded. 88 patients were recruited (73 breakfast eaters (BE)). BE had: a lower body mass index (BMI 32 ± 6 v 36 ± 6 kg/m^2; $p < 0.05$); retinopathy (21.9 vs 26.7 %; $p < 0.01$) and cardiovascular disease rate (CVD) (23.3 vs 26.7 %; $p < 0.01$); and lower sleep apnoea risk (45.2 vs 80.0 %; $p < 0.05$). Later chronotype was associated with higher systolic blood pressure (136.8 ± 19.5 v 123.5 ± 11.1 mmHg) and poor sleep quality (72.7 vs 35.5 %). BE had an earlier chronotype but this did not reach statistical significance. BE with T2DM had lower BMI, sleep apnoea risk and retinopathy/CVD risk. BE tended to have an earlier chronotype, suggesting that a preference for breakfast eating may be genetically determined. Larger studies are needed to explore these relationships further, and to determine if interventions to encourage breakfast eating are beneficial in T2DM.

P72 Diabetes in adulthood following near total pancreatectomy for congenital hyperinsulinism

[1]Kgosidialwa O, [2]Frizelle I, [1]Malik Ali RA, [3]Murphy N, [2]O'Halloran DJ, [1]Sreenan S

[1]Department of Diabetes and Endocrinology, Connolly Hospital Blanchardstown, Dublin; [2]Department of Diabetes and Endocrinology, Cork University Hospital, Cork; [3]Department of Endocrinology, Children's University Hospital, Temple St, Dublin

Data on diabetes pathogenesis after surgical treatment for congenital hyperinsulinism (CHI) are lacking. We describe the cases of patients A (female, 19 year, HbA1c 99 mmol/mol) and B (male, 18 year, HbA1c 105 mmol/mol), who both had CHI diagnosed within the first

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year of life due to heterogenous ABBC8 mutations inherited from their unaffected fathers. Both underwent 95 % pancreatectomy; histology showing focal CHI. Patient A had a family history of type 2 diabetes. Both patients had normal BMI and negative autoantibodies. Unexpectedly, with a fasting glucose of 11 mmol/L, patient A's c peptide and insulin were 1.44 μg/L and 5.7 mU/L, respectively and 2 h after a mixed meal were 2.84 μg/L and 19.8 mU/L, respectively with a glucose of 14.8 mmol/L. Patient B's fasting glucose, c peptide and insulin 11 mmol/L, 2.2 μg/L and 16.0 mU/L. The development of diabetes despite apparent adequate insulin reserve leads us to hypothesize that the pathogenesis of diabetes in patients post pancreatectomy for CHI is not purely due to the surgical reduction in beta cell mass. To support this, a previous study found that a heterogeneous mutation in the SUR1 gene caused CHI in infancy but loss of insulin secretory capacity in early adulthood and diabetes in middle age[1]. More research is needed to explore the likely multifactorial cause of diabetes in this patient group and this may help tailor appropriate diabetes treatment.

P73 Insulin errors in an Irish teaching hospital

*Ring C[1], *Varley V[1], Marsden E[2], Callanan I[3], Crowley RK[1,4]

[1]UCD School of Medicine, Belfield, Dublin 4; [2]Department of Clinical Pharmacy, St Vincent's University Hospital; [3]Department of Clinical Audit, St Vincent's University Hospital; [4]Department of Endocrinology and Diabetes, St Vincent's University Hospital, Elm Park, Dublin 4

*joint first authorship; these authors contributed equally to the study

Omission of prescribed insulin is associated with hyperglycaemia, ketosis and hyperosmolar state; international studies report insulin error rates of up to 30 % of prescribed doses. In order to assess the prevalence of insulin errors in an Irish tertiary referral centre, an audit was conducted of subcutaneous insulin administration over a 1 week period in April 2016. The audit was conducted by 2 medical students who identified patients receiving subcutaneous insulin from nursing staff, and recorded prescriptions and administration records from the hospital insulin prescription sheet. Patients in the cystic fibrosis unit, emergency department, day ward and intensive care unit were excluded, as were patients receiving IV insulin. 345 doses of insulin were prescribed to 18 inpatients (75 % medical) and 332 (96.2 %) were administered. Four of the 13 omitted doses were basal insulin glargine or detemir. A further 11 doses were not administered at the dose prescribed; these were mealtime bolus doses prescribed in a sliding scale that was mis-interpreted by the administering nurse. There was an overall insulin error rate of 7.1 %. Auditing insulin administration in itself had an impact on errors; 84 % of errors occurred in the first and second day and there were no errors in the last 2 days of the audit week. Insulin error rates at SVUH compare with international reports. The audit was a positive trigger to reduce insulin error. These findings suggest that the error rate could be reduced by using less sliding scale prescriptions.

P74 Prevalence of dysglycaemia in a hospital-based oncology population

Corcoran L[1], Bird B[2], Murphy C[2], O'Sullivan EP[3]

[1]Department of Medicine, University College Cork; [2]Department of Oncology, Bon Secours Hospital, Cork; [3]Department of Endocrinology, Bon Secours Hospital, Cork

In-patient hyperglycaemia is relatively common. Risk factors include increasing age and steroid use. Oncology patients are a particularly susceptible group. The prevalence of dysglycaemia within this group is poorly defined. The aims of our study were to determine the prevalence of dysglycaemia within an oncology day-ward setting, and identify any predicting factors. Ethical approval was obtained from local Ethics Board.

All patients admitted to the oncology day-ward of the Bon Secours Hospital Cork over a 4-week period were prospectively evaluated. A full clinical history and physical characteristics were obtained. All patients had a plasma glucose and HbA1c measured month (n = 208). Statistical analysis was then performed using the statistical package SPSS. Dysglycaemia was found to be present in 29.3 % of the 208 patients. Of these 12.5 % had pre-existing diabetes. Statistically significant predictors of dysglycaemia included age > 65 (odds ratio = 3.51, p-value = 0.001), steroid use (2.01, 0.036), male gender (3.04, 0.002) and solid cell cancers (2.44, 0039). Further analysis showed the significance was due to prostate and GI cancers. The prevalence of dysglycaemia in an oncology day case population is significant. Consideration should be given to screening this group for dysglycaemia. This could be focused on older patients on steroids with prostate or GI malignancies. Further work is necessary to follow up on this group to ascertain whether the dysglycaemia tends to resolve or require ongoing clinical intervention.

P75 Metformin monotherapy versus dual therapy with metformin and a dipeptidyl peptidase-IV inhibitor for treatment of type 2 diabetes mellitus: a systematic review and meta-analysis

Tobin-Schnittger P[1], Ong G[2], O'Brien T[2,4], Liew A[2,3,4]

[1]Graduate Entry Medical School, University of Limerick; [2]Galway University Hospital; [3]Portiuncula University Hospital; [4]National University of Ireland Galway

Background: Initial metformin monotherapy is often insufficient to achieve or sustain a glycaemic target. Dual therapy with metformin and a dipeptidyl peptidase-IV (DPP-IV) inhibitor is effective and safe. We hypothesised that dual therapy with metformin and a DPP-IV inhibitor would be more effective than metformin monotherapy at reducing patients' HbA1c and fasting plasma glucose (FPG) with no significant differences in side effect profiles.

Methods: Randomised controlled trials (RCTs) comparing combined metformin with a DPP-IV inhibitor and metformin monotherapy were searched for using PubMed and http://www.ClinicalTrials.gov. Inclusion criteria were: (1) RCTs, (2) comparing between dual therapy with metformin (1000 mg BID) and a DPP-IV inhibitor versus metformin monotherapy (1000 mg BID), for a (3) duration of treatment ≥18 weeks. Studies with a DPP-IV inhibitor as an add-on therapy to metformin monotherapy were excluded.

Results: Nine RCTs were included in the meta-analysis. Dual therapy was associated with a significant reduction in HbA1c (Mean difference (MD) −0.48 % (95 % CI −0.55, −0.42; p = 0.00001) and FPG (MD −0.82 mmol/L; 95 % CI -1.09, −0.56; p = 0.00001). There was no significant difference between the two treatment approaches regarding risk of hypoglycaemia (RR 0.98; 95 % CI 0.71, 1.35; p = 0.89), discontinuation due to non-serious adverse drug reactions (RR 0.90; 95 % CI 0.66, 1.22; p = 0.51), or adverse cardiovascular events (RR 0.57; 95 % CI 0.30, 1.07; p = 0.08).

Conclusion: Dual therapy with metformin and a DPP-IV inhibitor is more effective than metformin monotherapy at reducing HbA1c and fasting plasma glucose with no significant differences in side effect profiles.

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P76 A case of TSH suppression secondary to Bexarotene therapy for folliculotropic subtype mycosis fungoides

Todd A, Lewis A

Department of Endocrinology and Diabetes, Belfast City Hospital, Belfast Health and Social Care Trust

A 42 year old male with a diagnosis of folliculotropic subtype mycosis fungoides was commenced on Bexarotene 150 mg/m^2 and increased to 300 mg/m^2 in October 2013. He was commenced on levothyroxine concurrently at a dose of 50mcg daily due to the recognised complication of hypothyroidism from TSH suppression. Thyroid function and lipid profile were monitored closely throughout treatment. Pituitary profile was carried out and was normal. On starting Bexarotene his TSH suppressed to <0.01mIU/L with a FT4 of 11.1 pmol/L in keeping with secondary hypothyroidism. For the duration of the treatment he received levothyroxine replacement increased to a maximum dose of 175mcg daily. Bexarotene was then discontinued due to refractory hypertriglyceridaemia. Under close monitoring thyroid function normalised over the next 6 months with gradual reduction in levothyroxine dose until a complete stop in June 2015. Lipid profile normalised off bexarotene. This case demonstrates a common side effect of a rare treatment. The TSH suppression secondary to bexarotene was reversible and normalised with removal of the drug and titration of levothyroxine. Although not completely understood the effect is thought to be related to the down-regulation of the TSH*B* gene and through lesser effects on αTSH and TRH genes. Although not currently a commonly used drug Bexarotene commonly interferes with the thyroid axis affecting nearly all patients who are treated with the drug. Routine concomitant levothyroxine treatment is required and normalisation of thyroid axis is observed off treatment with appropriate titration and withdrawal of levothyroxine dose.

P77 A case of thyroid assay interference secondary to biotin supplementation

Todd A, Lewis A

Department of Endocrinology and Diabetes, Belfast City Hospital, Belfast Health and Social Care Trust

A 51 year old woman with a background of Non-Hodgkin's lymphoma and subsequent post radiation myelopathy was referred with abnormal thyroid function tests. She was well known to the neurology service and had previously been commenced on L-T4 100mcg for hypothyroidism by her GP. She had remained on this dose for the last 8 years. Thyroid function tests from primary care indicated free T4 > 100 pmol/L and TSH 0.05 mIU/L and the GP had commenced her on carbimazole 5 mg tid. On assessment she had no symptoms of hyperthyroidism and she was clinically euthyroid with no palpable goitre. Repeat thyroid function confirmed the previous findings with free T4 > 100 pmol/L and TSH 0.02mIU/L. On further questioning she was taking a Biotin supplement for perceived improvement in her neurological symptoms. Thyroid function was repeated off Biotin for 24 h and results had normalised with a free T4 of 20.1 pmol/L and TSH 1.72 mIU/L.

Biotin is a water soluble vitamin found in plants, liver, egg yolk and soya. It is an essential component of several enzyme complexes involved in carbohydrate and lipid metabolism. Deficiency can result in non-specific symptoms including sensory abnormality, the reason for which this patient was taking it as a supplement. At high doses (>5 mg/day) it can interfere with thyroid assays giving abnormal results. It should be held for at least 8 h prior to repeat testing. This case demonstrates the importance of identifying potential interfering medication including unprescribed supplements when assessing thyroid function.

P78 Spontaneous pneumomediastinum complicating diabetic ketoacidosis: a case report and literature review

Ahmed M[1], McCarthy C[1], Healy ML[2], Reynolds J[3], O'Shea D[1,4], Crowley R[1,4]

Department of Endocrinology and Diabetes, St Vincent's University Hospital, Elm park, Dublin 4; [2]Department of Endocrinology and Diabetes, St James's Hospital, James's street, Dublin 8; [3]Department of surgery, St James's Hospital, James's street, Dublin 8; [4]University College Dublin, Ireland

A 19 year old woman with type 1 diabetes mellitus presented to the emergency department with vomiting and neck pain. She omitted her insulin the day prior to admission. On examination she was dehydrated, with rapid shallow Kussmaul breathing. She was tachycardic and drowsy, opening her eyes only to commands. She had palpable cervical crepitus. Capillary blood glucose was 24 mmol/L and ketones were 5.9 mmol/L, blood gases showed acidosis with pH of 7.24 and bicarbonate of 12.3 mmol/L. Chest radiograph demonstrated a pneumomediastinum as well as cervical subcutaneous emphysema. Computed tomography of the thorax confirmed a pneumomediastinum and revealed epidural pneumatosis. Oesophageal contrast studies showed no perforation of the oesophagus. DKA was managed with fluids and insulin as per protocol and her symptoms resolved within 48 h of admission. Spontaneous pneumomediastinum (SPM) complicating DKA is rarely reported in medical literature. The exact pathophysiology is unknown; however, it is believed that Kussmaul respiration leads to a significant 20–30 mmHg rise in intra-alveolar pressure which may result in alveolar rupture. Furthermore, vomiting can predispose to alveolar rupture through increasing intra-thoracic pressure. More recently, alveolar histological changes and fibrosis have been described as part of the "diabetic lung'' in patients with poorly controlled diabetes. Whether these changes can predispose to alveolar rupture is not yet known, but may help explain this phenomenon. SPM is asymptomatic and resolve with conservative management in most cases, however in cases presenting with persistent vomiting and chest pain, more sinister conditions such as Boerhaave's syndrome should be excluded.

P79 Diabetic ketoacidosis in patients with type 2 diabetes recently commenced on SGLT2 inhibitors: a case series

Ahmed M[1], Slattery D[1], O'shea D[1,2], McKenna MJ[1,2], Crowley RK[1,2]

[1]Department of Endocrinology and Diabetes, St Vincent's University Hospital, Elm park, Dublin 4; [2]University College Dublin, Dublin, Ireland

Sodium–glucose co-transporter 2 (SGLT2) inhibitors have been associated with diabetic ketoacidosis (DKA). Clinical trials involving these agents claims that DKA incidence did not exceed that

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reported in the general diabetes population, and mostly occurred in patients on insulin, or were misdiagnosed with type 1 diabetes/LADA. In our recent practice, we encountered 3 episodes of DKA that all occurred in subjects with type 2 diabetes (T2D) recently commenced on SGLT2 inhibitors. The first patient was a 76 year old man with T2D. 3 weeks after canagliflozin was added, he presented with nausea and vomiting. Blood glucose was 11.7 mmol/L, serum ketones 3.4 mmol/L and pH 7.26. The second patient was a 60 year old man, who started canagliflozin 1 week before admission. He was admitted with abdominal pain and vomiting. His blood glucose was 18.4mmo/L, serum ketones of 4.1 mmol/L and pH of 6.88. He required intensive care monitoring and inotropic support. The third patient was a 75 years old man. 4 weeks after dapagliflozin was commenced, he presented with nausea and confusion. His blood glucose was 19.8 mmo/L with serum ketones of 5.8 and a pH of 7.29. His ketoacidosis resolved 24 h after initiating fluids and insulin. All 3 patients had documented follow-up for long standingT2D, were not on insulin, and none of them was previously admitted for DKA. This case series raises the question regarding the true incidence of DKA in this group in real world experience. Larger studies are required to examine the incidence and mechanisms leading to this complication.

P80 Experience in adrenocortical carcinoma (ACC) management in an Irish Tertiary referal Centre

Gunness A[1], Govender P[2], Feeney J[2], Walsh J[4], Crowther S[5], Crowley R[6], Behan LA[1], Gibney J[1], Conlon K[3], Sherlock M[1]

[1]Department of Endocrinology; [2]Department of Radiology; [3]Department of Surgery; [4]Department of Oncology and [5]Department of Histopathology, Adelaide and Meath Hospital, Tallaght, Dublin 24; [6]Department of Endocrinology, St Vincent's University Hospital, Elm Park, Merrion Road, Dublin 4

Adrenocortical Carcinomas (ACC) are rare with an estimated incidence of 1 per million/year. Prognosis is poor, with 5 year survival of 45–60 % for early stage and 10–25 % in advanced stage disease. International best practice is that these patients be managed in a dedicated MDT environment. We report all cases of ACC refered to our centre over the last 8 year (2008–2016). 14 patients, (9 males) with ACC were identified. 8/14 were referred from endocrinologists in other hospitals. Age of presentation was 40 (17–60 years). 9/14 patients had a functional tumour and 7/9 presented with symptoms of hormonal oversecretion. All functional tumours had Cushing's syndrome and 4/9 had co-existing hyperandrogenaemia. Mean tumour size was 10.9 cm (3.5–24). At diagnosis, 5/14 had evidence of metastatic disease. 12/14 patients proceeded to surgical resection. 2/14 patients who did not have surgery had evidence of metastatic disease at presentation and were deemed inoperable. 5/9 patients with functional tumours required medical therapy prior to surgery. The mean Weiss score was 6.3 (range 3–9). 9 patients received mitotane treatment and 4 patients are initiating or planning to start mitotane treatment. 7/9 achieved mitotane levels within the therapeutic target during their follow up. Drug toxicity was the main barrier to achieveing target range and 4/9 patients required hospitalisation due to side-effects of mitotane treatment. 6/14 patients also received cytotoxic chemotherapy. 5/14 patients died within 12 months of diagnosis. Of the 9 surviving patients, 4 are now more than 2 years post initial diagnosis.

P81 Androgen profiling by liquid chromatography-mass spectrometry (LC–MS) in reproductive-age women with and without diabetes

Gunness A[1], Pazderska A[1], Ahmed M[1], Phelan N[1], Boran G[2], Taylor AE[3], O'Reilly MW[3], Arlt W[3], Moore K[1], Behan LA[1], Sherlock M[1], Gibney J[1]

[1]Department of Endocrinology and [2]Clinical Chemistry, Adelaide and Meath Hospital, Tallaght, Dublin 24; [3]Institute of Metabolism and Systems Research (IMSR), University of Birmingham, Edgbaston, Birmingham B15 2TT, UK

The prevalence of hyperandrogenism has been reported to be increased in reproductive-age women with type-1 diabetes (T1DM). This observation however is based on findings using inaccurate immunoassays. No studies have been reported in diabetes using liquid-chromatography-mass-spectrometry (LCMS). We compared LCMS-measured androgens in T1DM-women with age-/BMI-matched normal women, and compared findings with those in women with type-2 diabetes (T2DM) also compared to a matched control group.

	TID (N = 63; median age = 32; median BMI = 25.5)	Non-diabetic (N = 42; median age = 34.5; median BMI = 27.4)	T2D TID (N = 32; median age = 38; median BMI = 36)	Non-diabetic (N = 55; median age = 34; median BMI = 35.1)
Androstendione (nM)	5.1 (1.4–13.1) p = 0.0005	3.6 (0.0–16.9)	2.5 (0.0–14.1) p = 0.0035	3.8 (0.4–15.5)
DHEA-OX (nM)	10.1 (2.0–44.O)	12.0 (1.3–43.7)	5.7 (0.0–15.3) p < 0.0001	13.5 (1.1–51.0)
DHEAS (uM)	5 (1.3–14.3)	5.0 (1.1–14.7)	6.0 (2.2–13.9) p = 0.0045	4.3 (1.3–13.1)
FT (%)	1.1 (±SEM 0.05)	p = 0.0015	1.4 (±SEM 0.07)	2.0 (±SEM 0.11) p = 0.0005
	1.6 (±SEM 0.056)			

Mean (±SEM); P-value vsmatched non-diabetic

Median (range); P-value vs matched non-diabetic

Compared to non-diabetic women, androstenedione and SHBG were greater in T1DM while estimated free-testosterone was lower. In contrast, compared to non-diabetic women, androstenedione, DHEA-OX and SHBG levels were lower in T2DM while free-testosterone and DHEAS were greater. Total testosterone did not differ between groups in either comparison. T1DM and T2DM are associated with differing effects on androgen levels. These differences are likely to reflect differences in insulin sensitivity and differing effects of exogenous insulin administration. Their clinical significance requires further investigation.

P82 Lipoprotein particle size in women with type one diabetes mellitus (TIDM) and its relationship to carotid intima-media thickness

Gunness A[1], Ahmed M[1], Pazderska A[1], Phelan N[1], Boran G[2], Moore K[1], Behan LA[1], Sherlock M[1], Gibney J[1]

[1]Departments of Endocrinology and [2]Clinical Chemistry, Adelaide and Meath Hospital, Tallaght, Dublin 24

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Although cardiovascular disease (CVD) is greatly increased in type 1 diabetes (T1DM), patients typically have apparently healthy lipid profiles. Simple measurement of plasma lipids however does not provide information regarding lipoprotein particle size which in the nondiabetic population is independently predictive of CVD. Plasma lipids and lipoprotein subclasses (using polyacrylamide gel-tube electrophoresis) were studied in reproductive age women with T1DM and compared to a matched control group. Outcomes were correlated with carotid intima-media thickeness (CIMT), a validated marker of atherosclerosis. Compared to nondiabetic women, T1DM women were younger (29 vs 34 years) and of lower BMI (24.7 vs 31.3 kg/m^2), with all data reported as median. Total (TC) and LDL-cholesterol (LDL-C) did not differ between groups. Triglyceride (TG) levels were lower (0.76 vs 0.91 mmol/l, $p = 0.0331$) and HDL-cholesterol (HDL-C) greater (1.65 vs 1.49 mmol/l, $p = 0.00331$) in T1DM. T1DM women had a greater proportion (46 % vs 5 %, $p < 0.0001$) of small LDL-C particles, lower mean LDL particle size (269 vs 272 Å, $p < 0.0001$) and a greater percentage of small-dense-LDL particles (%SDLDL; 3 vs 0 %, $p < 0.0001$). CIMT correlated positively in T1DM with %SDLDL (r 0.2983, $p = 0.0098$) and negatively with LDL size (r−0.3118, $p = 0.0068$), but did not correlate with TC, HDL-C, LDL-C or TG. Despite apparently healthy lipid profiles, women with T1DM have a greater proportion than nondiabetic women of atherogenic small LDL particles. The likelihood that this is clinically relevant is strengthened by the observed correlation of CIMT with particle size and lack of correlation with standard lipid profile. Further studies are needed to explore the mechanisms underlying these abnormalities.

P83 Biochemical and clinical characteristics of polysystic ovarian syndrome (PCOS) in women with and without type 1 diabetes (TID)

Gunness A[1], Pazderska A[1], Ahmed M[1], Phelan N[1], Boran G[2], Taylor AE[3], O'Reilly MW[3], Arlt W[3], Moore K[1], Behan LA[1], Sherlock M[1], Gibney J[1]

[1]Department of Endocrinology and [2]Clinical Chemistry, Adelaide and Meath Hospital, Tallaght, Dublin 24; [3]Institute of Metabolism and Systems Research (IMSR), University of Birmingham, Edgbaston, Birmingham B15 2TT, UK

PCOS prevalence is reported to be increased in reproductive-age women with type-1 diabetes (T1DM) but measurement of androgens, crucial for diagnosis, has been with inaccurate immunoassays. No studies have been reported using liquid-chromatography-mass-spectrometry (LCMS). Reproductive-age T1DM women attending a single centre were evaluated for PCOS (NIH criteria). Women with T1DM and PCOS (T1/PCOS) were compared to T1DM women without hyperandrogenism (T1/no HA), and to two groups of non-diabetic women with PCOS—one group BMI-matched (PCOS-lean) and the other overweight (PCOS-overweight)0.16 (18 %) of T1DM women had PCOS. TIDM women with PCOS compared to the overall group were younger (26.5 vs 29) and had a lower BMI (23.4 vs 25.3). Compared to T1/no HA, testosterone (1.3 vs 0.8 nM, $p = 0.004$) and androstenedione (7.1 vs 4.6 nM $p = 0.0016$) were elevated but no differences in DHEA-OX, DHEAS, SHBG or free testosterone was noted. They had an older age of menarche (13 vs 12.5 years, $p = 0.024$), and were more likely ($p = 0.024$) to have a positive family history of PCOS. There were no differences in androgen levels between T1/PCOS and PCOS-lean women, but both of these groups demonstrated greater androstenedione levels (7.1 vs 5.5 nM, $p = 0.0247$) than PCOS-overweight women. In summary, PCOS is common in T1DM. Women with T1/PCOS are leaner than T1 women without PCOS but are more likely to have a family history of PCOS. They have a similar biochemical phenotype to lean women with PCOS but differ from overweight women with PCOS. The mechanisms underlying PCOS in T1DM and its clinical significance are unknown.

P84 A case report of septic thyroiditis in a patient with infective endocarditis

Awang MH[1], Fahy E[2], Murphy MS[1]

[1]Department of Endocrinology, South Infirmary Victoria University Hospital, Cork, Ireland; [2]Department of Cardiology, Mercy University Hospital, Cork, Ireland

A 69 year old lady presented as an emergency with a 3 week history of general fatigue, dyspnoea, weight loss, neck pain, and pyrexia. She had a past history of aortic valve replacement and hypothyroidism treated with replacement doses of levothyroxine. On examination, there was a splinter haemorrhage seen on right hand. No focus of infection noted on physical examination. A small, non-tender goitre was noted on examination. On admission her thyroid function tests revealed fully suppressed TSH <0.01 mIU/l (reference range 0.4–3.8) and markedly elevated free T4 76.2 pmol/l (reference range 12–22) and free T3 19.59 pmol/l (reference range 2.63–5.70).

Given the past history of aortic valve replacement, investigation for infective endocarditis was sought early. Blood cultures were positive for Enterococcus and treatment for infective endocarditis was initiated. Thyroid ultrasound showed moderately sized multinodular goitre. Nuclear medicine isotope scan of thyroid revealed a diffuse symmetrical uptake with no focal hot or cold nodule. Overall, the presentation was consistent with septic thyroiditis. She responded very well to intravenous antibiotics and her TFTs improved over the following four weeks without introduction of anti-thyroid drugs. However, later in her admission she became infected with Influenza H1N1 and she died in the intensive care unit. Septic thyroiditis related to infectious endocarditis is a rare condition with two cases reported previously in the English language literature. The mechanism of the onset of thyroiditis is unclear and postulated to be due to mycotic infection of the thyroid gland and/or immune complex deposition.

P85 Post-traumatic amnesia, but not acute CT findings is predictive of pituitary dysfunction following traumatic brain injury

O'Shea T, Feeney C, Wise R, Sharp D, Goldstone A

Computational Cognitive and Clinical Neuroimaging Laboratory, Division of Brain Sciences Imperial College London, Hammersmith Hospital, London

Pituitary dysfunction is a common, treatable consequence of traumatic brain injury (TBI), and is associated with poorer outcomes. Identifying prognostic factors that allow targeted endocrine testing will ensure that patients at higher risk of pituitary dysfunction are identified and screened. Audit of 176 survivors of TBI who attended the multidisciplinary Imperial TBI clinic found a prevalence of pituitary dysfunction of 13.7 % (deficiency of growth hormone 7.4 %,

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gonadotrophins 3.7 %, ACTH 1.1 %, hyperprolactinaemia 2.5 %, syndrome of inappropriate anti-diuretic hormone secretion 0.6 %). Using the Mayo classification for TBI severity the prevalence of post-traumatic pituitary dysfunction was 15.7 % after moderate-severe TBI versus 7.1 % after possible-mild TBI. We retrospectively analysed demographic, imaging and clinical data. Post traumatic amnesia (PTA) > 24 h was recorded in 65 % of patients with pituitary dysfunction versus 37.9 % without ($p = 0.02$). PTA > 1 week occurred in 30 % of those with pituitary dysfunction versus 12.9 % without ($p = 0.04$). Facial fractures were also associated with an increased risk, recorded in 35.7 % with versus 14.5 % without pituitary dysfunction ($p = 0.05$). Other findings on CT including basal skull fracture, cerebral oedema, subdural haemorrhage, subarachnoid haemorrhage, intraventricular haemorrhage and cerebral contusions were not significantly associated with pituitary dysfunction following TBI. 17.8 % of patients with pituitary dysfunction had a normal CT brain initially versus 20 % without ($p = 0.78$). Male sex, the need for craniotomy, post TBI epilepsy and treatment for mental illness at first clinic visit were not significantly associated with post-traumatic pituitary dysfunction.

P86 Postnatal lifestyle intervention for overweight women with previous gestational diabetes mellitus (PAIGE): a pilot randomised controlled trial

McCance DR[1], Draffin C[2], Patterson CC[2], Francis L[1], Irwin J[1], McConnell M[3], Farrell B[4], Brennan S[2], McSorley O[2], Davies M[1], Holmes VA[2]

[1]Regional Centre for Endocrinology and Diabetes, Belfast Health and Social Care Trust; [2]Centre for Public Health, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast; [3]Craigavon Area Hospital, Southern Health and Social Care Trust; [4]Public Health Agency, Northern Ireland

Obesity is a risk factor for Gestational Diabetes Mellitus (GDM) and subsequent type 2 diabetes. Lifestyle modification can prevent type 2 diabetes. Our aim was to determine the effectiveness of a postnatal lifestyle intervention for overweight women with a history of GDM. A pragmatic randomised controlled trial with two parallel arms was conducted in two metabolic-obstetric clinics in Northern Ireland. Participants were overweight women with a history of GDM in their most recent pregnancy. The intervention included a 1 h education session with accompanying booklet based on the Diabetes Prevention Programme, delivered during the postnatal oral glucose tolerance test by a health educator using motivational interview techniques. Two individualised goals were set: 5 % weight loss over a 6 month period; 150 min of brisk physical activity each week. The intervention group received free 3 month membership to a commercial weight management organisation (Slimming World); a pedometer and structured telephone and text support. The primary outcome was weight loss at 6 months. Of the 404 women screened, 220 women met the inclusion criteria. In total, sixty women were randomised to intervention ($n = 31$) or usual care (control, $n = 29$). Weight loss data was available on 45 women (intervention, $n = 20$; control, $n = 25$). Women in the intervention group lost significantly more weight than women in the control group [mean (standard deviation) 3.8 (7.0)kg vs −0.7 (3.8)kg; mean difference 4.5 kg (95 % confidence intervals 0.9; 8.1), $p = 0.02$]. Findings suggests that this pragmatic multi-component lifestyle intervention is effective in helping overweight women with a history of GDM to lose weight.

P87 A challenging case of metastatic Insulinoma in pregnancy

Keane F[1], Bogdanet D[1], Leonard G[2], Gaffney G[3], O'Shea P[4], Bell M[1]

[1]Department of Endocrinology, Galway University Hospital; [2]Department of Oncology, Galway University Hospital; [3]Department of Obstetrics and Gynaecology, Galway University Hospital; [4]Department of Biochemsitry, Galway University Hospital

A 35 year-old female at 9 weeks gestation, presented following a "blackout" with loss of consciousness and amnesia. Family and friends confirmed intermittent episodes of uncharacteristic behaviour over the preceding 6 months. A blood glucose level en-route to hospital was 1.1 mmol/L. The patient responded rapidly to intravenous dextrose. On admission to hospital the patient had a further spontaneous episode of hypoglycaemia and investigations revealed the following; serum blood glucose 1.8 mmol/L, Insulin 141.2 pmol/L, C-peptide 915 pmol/L, proinsulin 53 pmol/L. A Sulphonylurea screen, Beta-hydroxybutyrate, IGF-I, IGF-II and IGF-II:IGF-I ratio were all within normal levels. Based on initial clinical and biochemical information a working diagnosis of a functional insulinoma was reached. The patient was dependant on intravenous dextrose. Due to pregnancy, radiological workup to identify the location of the tumour was limited. An Ultrasound did not locate a pancreatic lesion but suggested hepatic metastases. This was then confirmed by non-contrast MRI. Endoscopic ultrasound identified a mass of the pancreatic tail. Histological analysis of the liver metastases confirmed metastatic insulinoma. A hemi-hepatectomy and distal pancreatectomy was performed at week-12 gestation. The patient was managed conservatively throughout pregnancy until she delivered vaginally a healthy baby at full-term. Postpartum investigations included CT Thorax/Abdomen/Pelvis, Octreotide and MIBG scans. Surveillance via clinical and biochemical assessment, and radiological restaging at regular intervals were performed. Disease progression was observed despite treatment with long-acting somatostatin analogues, mTOR Inhibition, chemotherapy and targeted Radionuclide therapy. This rare case highlights the complex diagnostic and management challenges associated with metastatic Insulinomas, particularly in the context of pregnancy.

P88 Maternal vitamin D status and development of childhood atopy: findings from the ROLO study

Smith M[1], O'Brien E[1], Kilbane M[2], McKenna MJ[3], McAuliffe F[1]

UCD Obstetrics and Gynaecology[1]; School of Medicine and Medical Science, University College Dublin, National Maternity Hospital, Dublin. Departments of Clinical Chemistry[2]; and of Endocrinology[3]; St Vincent's University Hospital, Dublin

Vitamin D status may play a role in the development of atopic diseases due to its effect on the lung development, immune system development and function. There is conflicting evidence about the relationship between maternal vitamin D status and atopy in offspring. Our objective was to assess whether 25-hydroxyvitamin D (25OHD) in maternal or fetal blood was associated with atopy in children at 5 years. This was an analysis of 293 mother–child pairs from the ROLO study. 25OHD was measured in blood samples taken at 13 and 28 weeks, and in fetal blood from the cord at delivery. Development of childhood atopy (asthma or eczema) was self-reported by mothers at 5 years. The average (SD) 25OHD in early and

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late pregnancy was 45.0 (19.2)nmol/L and 40.2 (21.5)nmol/L, and in fetal blood was 44.7 (26.7)nmol/L. Those who developed an atopic disease at 5 years had significantly lower levels of 25OHD in cord blood than those who did not (24 nmol/L vs 42 nmol/L, $p < 0.05$). Fetal levels of 25OHD were associated with a non-significant reduction in risk of atopy at 5 years, (OR: 0.990, 95 % CI 0.969–1.012). No association was observed between maternal 25OHD in pregnancy and childhood atopic disease at any time point.

The development of atopy at 5 years might be associated with reduced 25OHD in cord blood at birth. Further research is required to explore the relationship between vitamin D and atopy, and whether vitamin D supplementation should be prioritised in pregnancy to reduce childhood atopy.

P89 Iodine nutrition and gestational changes in pregnant women living in Northern Ireland (NI)

McMullan PA[1], Woodside JV[2], Hamill LA[3], McCance DR[1], Mullan K[1]

[1]Regional Centre for Endocrinology, Royal Victoria Hospital, Belfast; [2]Centre for Public Health, Queens University, Belfast

Iodine deficiency remains the most preventable cause of mental impairment worldwide. Recent evidence suggests a re-emergence of iodine deficiency in the United Kingdom. Pregnant women are most at risk of the consequences of iodine deficiency yet studies looking specifically at this group are lacking in the UK. Thyroglobulin (Tg) has been suggested as an alternative marker of iodine status but its value in pregnancy is not well established.

Participants (n = 241) were recruited at their booking visit at the Royal Jubilee Maternity Hospital, Belfast. Urinary iodine concentration (UIC) was measured by Sandel-Kolthoff colorimetry. Current cut off values for median UIC from the World Health Organisation for iodine sufficiency were used (≥ 150 μg/L). Cut off values for Tg in pregnancy do not currently exist. A recent study in children defined iodine sufficiency as a median Tg <13 μg/L and/or <3 % of Tg values > 40 μg/L.

Median UIC were 71.7 μg/L, 94.2 μg/L and 115.6 μg/L at first, second and third trimesters, respectively. A total of 88 participants (37 %) had a urinary iodine concentration of <50 μg/L at first trimester when optimal thyroid function is most critical. The median Tg level was 19 μg/L with 18.4 % of participants having a Tg concentration > 40 μg/L.

Our study suggests that pregnant women living in NI are iodine deficient. This is of concern as currently there is no food iodine fortification program in the UK. Women in NI are not routinely advised on how to optimise iodine intake during pregnancy and public health initiatives are required.

P90 Selenium nutrition and thyroid function in pregnant women living in Northern Ireland (NI)

McMullan PA[1], Woodside JV[2], Hamill LA[3], McCance DR[1], Mullan K[1]

[1]Regional Centre for Endocrinology, Royal Victoria Hospital, Belfast; [2]Centre for Public Health, Queens University, Belfast

Selenium (Se) is an essential micronutrient required for the production of selenoproteins. These are involved in conversion of thyroxine (T4) to triiodothyronine (T3) and protect the thyroid from oxidative stress. Studies have shown low levels to be associated with thyroid autoimmunity and poor pregnancy outcomes. The effect of combined deficiencies of Se and iodine during pregnancy is poorly understood. Participants (n = 241) were recruited from the Royal Jubilee Maternity Hospital in Belfast and followed through pregnancy. First trimester fT4, TSH, TPO antibodies, urinary iodine concentration (UIC) and plasma Se levels were analysed. Se was measured by inductively coupled plasma mass spectrometry (ICP-MS). Our assay reference range for non-pregnant adults is 0.60–1.30umol/L with no specific reference range in pregnancy established. A higher reference range of 1.47–1.85 umol/L during the first trimester has been suggested[1]. Se levels were normally distributed with a mean of 0.95 ± 0.16 umol/L, indicating adequate status. However, only one participant had a level above the suggested pregnancy specific reference range. Median UIC was 71.2 μg/L indicating Iodine deficiency by World Health Organisation criteria which uses a cut off value of 150 μg/L. There was no statistically significant association between plasma Se and UIC concentrations. Twenty-eight participants (13 %) were positive for TPO antibody which is at a level expected in pregnant cohort. There was no significant difference in Se concentrations between thyroid antibody positive and negative women. Further evaluation of this cohort is ongoing and may contribute to our understanding the role of selenium nutrition and defining adequate status in pregnancy.

P91 Iodine nutrition knowledge amongst pregnant women living in Northern Ireland (NI)

McMullan PA[1], Woodside JV[2], Hamill LA[3], McCance DR[1], Mullan K[1]

[1]Regional Centre for Endocrinology, Royal Victoria Hospital, Belfast; [2]Centre for Public Health, Queens University, Belfast

Iodine is an essential micronutrient important for foetal nerve and brain development, especially in the early stages of pregnancy. The re-emergence of mild to moderate iodine deficiency has been reported in the UK, while data from the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort suggests that there may be a dose-dependent association between sub-optimal iodine status in pregnancy and childhood cognitive scores. The levels of knowledge pregnant women have regarding iodine nutrition and the link with infant health and child development is not well established.

We assessed current iodine knowledge among pregnant women (n = 183) living in NI. Pregnant women attending routine clinic visits to the Royal Jubilee Maternity Hospital in Belfast were asked to complete a short questionnaire assessing iodine nutrition and health knowledge. Of these, 45 % were unable to identify any foods they thought were iodine-rich, 30 % were aware that seafood was a good source but only 9.3 % and 14.8 % answered dairy or eggs as good sources, respectively. Only 20 % were aware of the increased iodine requirements during pregnancy and breast feeding. Five per cent of women felt they had been given sufficient nutritional advice about iodine during pregnancy, in contrast to 90 % when asked about folate. This study highlights the lack of knowledge among pregnant women living in NI regarding iodine, its major food sources and intake requirements during pregnancy. Evidence-based public health strategies are needed to boost iodine knowledge among pregnant women.

P92 Cycle of care: is primary care ready in the midland area?

Soong E, Hoashi S

Diabetes and Endocrine Centre, Midland Regional Hospital Mullingar and UCD Medical School

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Background: Cycle of Care is a new model of care for type 2 Diabetic patients in primary care. An online survey was conducted to evaluate primary care access to component of diabetes services and willingness of GP to manage type 2 Diabetic patients in primary care.

Methods: GP in Westmeath and Longford were surveyed anonymously on access to podiatry, dietician, Diabetic Nurse Specialist, structured diabetes education programme and prescribing of glucose lowering medications in the community.

Results: A total of 18 GP responded to the survey. Although all GP see diabetic patients in their setting, 76.9 % (10) prefer shared care with their secondary care center. 78.6 % (11) of GP see diabetic patients every 3 months and the other 21.4 % (3) see them every 6 months. In terms of access to services, only 53.8 % (7) of GP have access to dietician as compare to podiatry (76.9 %, 10) and Diabetes Nurse Services (84.6 %, 11). X-PERT is most easily accessible structured education in type 2 diabetes where 53.8 % (7) of the GP have access as compared to DESMOND and CODE. 30 % (4) of GP have no access to structured education in type 2 diabetes. All GP refer their patients to the National Diabetes Retinal Eye Screening. 75 % (9) of GP do not have access to 'point of care' HbA1c testing.

Conclusions: 1. Shared care is the preferred method of care in type 2 diabetes; 2. Cycle of care model required further investment in the community (e.g. access to dietician) to implement on a large scale.

P93 The need for ambulatory blood pressure monitoring to accurately assess blood pressure control in patients with type 2 diabetes

MohdArif N, Tuthill A

Department of Endocrinology, Cork University Hospital

Diabetes and hypertension are risk factors for cardiovascular disease. The prevalence of hypertension in diabetes is two-fold higher than in patients without diabetes. NICE guidelines propose 24-h Ambulatory Blood Pressure Monitoring (ABPM) as the gold standard for diagnosis of hypertension, although this has not been universally accepted. The aim of this study is to investigate whether all patients with type 2 diabetes (T2DM) should have blood pressure (BP) assessed using ABPM. BP was measured in 30 T2DM patients using clinic BP monitoring and ABPM. Patients were grouped into systolic blood pressure, SBP <140 mmHg and SBP $\geq$ 140 mmHg on clinic measurement. Subjects were asked to complete a questionnaire and biochemical profiles including cholesterol, *HbA1C*, creatinine, albumin, urine albumin/creatinine ratio and eGFR were recorded. 19/30 patients (63.3 %) had SBP <140 mmHg and 11 (36.7 %) had SBP $\geq$ 140 mmHg on clinic measurement. 5 patients with elevated clinic SBP had normal ABPM, and 6 who had normal clinic SBP demonstrated elevated BP on ABPM. Age, BMI, duration of T2DM, *HbA1C* albumin, creatinine and cholesterol were higher in patients with clinic SBP $\geq$ 140 mmHg, however these differences were not statistically significant ($p > 0.05$). Prevalence of patients on antihypertensive medication was 66.7 % (20/30); 3/10 patients who were not on medication had elevated BP on ABPM (undiagnosed hypertension). Due to the high rate of masked hypertension, and marked differences between clinic SBP and ABPM results, ABPM should be performed in all T2DM patients for accurate BP assessment, particularly those who are older and have longer duration of diabetes.

P94 Clinical findings on body mass index in an intellectual disability population and the effect of a healthy lifestyle intervention clinic

Woods CP[1], Boylan P[2], O Shea Donal[3]

[1]Naas General Hospital, Naas, Co. Kildare; [2]Cheeverstown House, Centre for Intellectual Disability, Templeogue Dublin 6 W; [3]St. Vincent's University Hospital, Elm park, Dublin 4

Data on weight status and weight loss interventions in persons with intellectual disability (ID) is scarce. We sought to ascertain the prevalence of obesity in an ID population and the impact of a 'healthy lifestyle' clinic.

We reviewed data on 149 adults (women = 69) attending an ID service. Prospective data was available on 23 adults (women = 22, baseline BMI = 39.1 $\pm$ 7.5kgs/m^2) attending a weekly 'healthy lifestyle' clinic where diet and lifestyle advice was available. Bi-annually, visits included food and exercise diary analysis, weight measurement, rationalisation of psychotropic/epileptic drugs by Psychiatry/Neurology and biochemical testing for diabetes and thyroid dysfunction. Baseline data showed 9.4 % (n = 14) were underweight (BMI <18), 25.5 % (n = 38) were normal weight (BMI = 18–25), 25.5 % (n = 38) were overweight (BMI = 25–30) and the remaining 39.6 % (n = 59) were obese (BMI >30). Women had a signficantly higher BMI compared to men (29.7 $\pm$ 7.8 vs 26.1 $\pm$ 7.3 kg/m^2, $p = 0.004$). Women with Down Syndrome (DS) had a significantly higher BMI than women with ID only (31.9 $\pm$ 7.9 vs 24.7 $\pm$ 8.6 kg/m^2, $p = 0.003$). There was a difference between those persons with ID living in the community and those in residential care (25.9 $\pm$ 7.9 vs 28.4 $\pm$ 7.3 kg/m^2). 20/23 persons attending the healthy lifestyle clinic achieved weight loss of 6.1 $\pm$ 8.4kgs (93.9 $\pm$ 26.6 vs 87.9 $\pm$ 23.4kgs, $p = 0.001$). In this ID cohort, the prevalence of obesity is similar compared to the general public. Women with DS had a significantly higher BMI then women with ID only. Persons with ID living in the community had clinically higher BMI compared to those in residential care. Diet and Lifestyle interventions and medication rationalisation were successful in producing sustained weight loss.

P95 Demand management of monomeric prolactin

Spence K, Cross S, Burgess C, McDonnell M

Regional Endocrine Laboratory, Belfast Health and Social Care Trust, Belfast. BT12 6PA

The Regional Endocrine laboratory at Belfast Trust analysed 19,394 samples for prolactin in 2014. 1889 (9.7 %) of these had a total prolactin > 700 mIU/L, and hence had monomeric prolactin (the biologically active form of prolactin) determined. Since we receive several repeat requests for prolactin over the course of several months and years on the same patients we wanted to determine if it was essential to analyse macroprolactin on every repeat sample we received. We examined all prolactin results which had an accompanying monomeric prolactin over the preceding 6 years. We determined the ratio between the total and monomeric prolactin result and the percentage change over time for each patient. 228 patients had monomeric prolactin repeated within 1 month. The mean change in the ratio between total and monomeric was 4.4 % with a median of 4.0 %. There were 890 patients who had monomeric prolactin repeated within 12 months. The mean change in the ratio between total and monomeric was 6.2 % with a median of 5.3 %.

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Even up to 48 months, taking 1347 patients into account, the mean difference between total and monomeric was 7.5 % with a median of 6.2 %. This data suggests that repeatedly checking monomeric prolactin is unnecessary, and that total prolactin alone is sufficient to monitor these patients after an initial monomeric prolactin level has been measured within at least 48 months.

P96 The scramble to replace Siemens Coat-A-Count® 17-α-hydroxyprogesterone assay

Spence K, Irwin S, McDonnell M

Regional Endocrine Laboratory, Belfast Health and Social Care Trust, Belfast BT12 6PA

17-α-hydroxyprogesterone (17OHP) is measured routinely as part of our female adrenal androgen profile to aid in diagnosis of late onset congenital adrenal hyperplasia (CAH) and in children and new-born babies suspected of having CAH, the latter requiring a 48 h turn-around time (TAT).

We were alerted in March 2014 that Siemens were withdrawing their 17OHP assay. We needed to find a replacement assay to allow us to meet current TAT guidelines for diagnosis of CAH in newborns. DIASource provide a competitive radioimmunoassay which does not require an extraction step, requires only 50 µl serum and has a 3 h incubation time. Within batch and between batch CVs were <5.2 and <7.3 %, respectively for concentrations 3.0–21 nmol/L. Linearity was $y = 0.9383x + 0.2841$; $R2 = 0.9982$. Forty five samples were compared using Siemens and DIASource assays. Results were significantly different: $R2 = 0.8214$; $y = 0.764x - 0.0348$. Six samples (13 %) were at least 50 % lower using the DIASource assay compared to the Siemens assay. These were extracted using the dichloromethane procedure and reanalysed using Siemens. Results obtained were significantly less and in keeping with DIASource assay. This indicated that the DIASource antibodies were more specific than Siemens antibodies. Finally, 15 previously circulated samples from NEQAS were reanalysed using DIASource assay. Results indicated that the DIASource assay was well aligned to tandem mass spectrometry (TMS) with $y = 1.0172x - 0.5606$ and $R2 = 0.9936$. In our evaluation, the DIASource 17OHP assay is a good replacement for Siemens 17OHP assay producing results comparable to TMS due to the highly specific antibodies.

P97 Utility of screening for hereditary haemochromatosis (HH) in the diabetes new patient clinic

Cheah SK, Nevin K, Foster D, Baqer M, Kadadah I, Redha M, Alkhalfan N, Kyaw Tun T, Sreenan S, McDermott JH

Endocrinology Department, Connolly Hospital, Blanchardstown, Dublin 15

HH is the commonest inherited condition in the Irish population. Diabetes secondary to HH is the commonest endocrine manifestation of HH. Studies suggest a declining incidence of DM in HH patients but a number of international clinical guidelines recommend screening for HH in patients with DM. We screened 1158 consecutive newly-referred Irish DM patients >30 years old for HH, between 2009 and the present day. 51 patients (4.4 %) proceeded to HH genotyping on the basis of elevated ferritin (FER, 43 %, 22 cases), transferrin saturations (TS, 10 %, 5 cases) or both (47 %, 24 cases). 14 of 51 (1.2 % of total screened) were ultimately found to have a mutation in the HFE gene (mean FER 995 ± 253 ng/ml, mean TS 71.6 = ±5.8 %), C282Y homozygous (16 %, 8 cases), compound heterozygous (10 %, 5 cases), or H63D homozygous (2 %, 1 case). This HH rate approximates that of the general Irish population. In the modern era HH in DM may be co-incidental rather than causative. Targeting patients with DM for HH screening may not be appropriate.

P98 Pilot study of biomarkers in Diabetic Kidney Disease

Griffin TP[1,2], Islam MN[1]*, Martin WP[1,2,3], Cormican S[3], Naicker SD[1], Logue S[1], O'Shea PM[4], O'Brien T[1,2], Griffin MD[1,3]*

[1]Regenerative Medicine Institute (REMEDI), School of Medicine, National University of Ireland, Galway, Centre for Endocrinology; [2]Diabetes and Metabolism, Galway University Hospitals, Galway; [3]Department of Nephrology, Galway University Hospitals, Galway; [4]Department of Clinical Biochemistry, Galway University Hospitals, Galway

Introduction: A significant unmet clinical need is the identification of biomarkers that serve as predictors or early indicators of both disease progression and favourable therapeutic response in Diabetic Kidney Disease (DKD). The aim of this pilot study was to identify a panel of novel biomarkers which could be used to evaluate longitudinal trends of these biomarkers in DKD.

Methods: Study subjects with type 2 diabetes were identified from a prospectively maintained database/biobank. Subjects were divided into two groups: mild-to-moderate (eGFR 30–90 mL/min/1.73 m^2; $n = 24$) and severe (eGFR <30 mL/min/1.73 m^2; $n = 20$) DKD. Baseline demographics, metabolic and renal indices were recorded. The biomarkers selected for analysis were Neutrophil Gelatinase-Associated Lipocalin (NGAL), Kidney Injury Molecule-1 (KIM-1), Adiponectin, Leptin, Fibroblast Growth Factor-21 (FGF-21), Plasminogen Activator Inhibitor (PAI-1), soluble Tumour Necrosis Factor-1 and -2 (sTNFR-1/2), Interleukin-8 (IL-8) and Monocyte Chemoattractant Protein-1 (MCP-1). NGAL, KIM-1, Adiponectin, Leptin and FGF-21 were measured using respective ELISA. PAI-1, sTNFR-1, sTNFR-2, IL-8 and MCP-1 were measured using a Multiplex Immunoassay kit. Statistical analysis was performed using GraphPad Prism-6®.

Results: Mean (±SD) Leptin (11.6 ± 9.4 v 40.7 ± 29.3 ng/mL; $p < 0.001$), FGF-21 (218.9 ± 249.9 v 607.7 ± 766.3 pg/mL; $p = 0.001$), sTNFR-2 (238.7 ± 68.9 v 298.5 ± 49.7 pg/mL; $p = 0.030$) and NGAL (183.7 ± 100.9 v 232.4 ± 75.7 ng/mL; $p = 0.035$) distinguished subjects with different degrees of DKD. eGFR showed a significant correlation with s-TNFR-1 ($r = -0.682$, $p = 0.021$), NGAL ($r = -0.370$, $p = 0.022$), Leptin ($r = -0.367$, $p < 0.001$), FGF-21 ($r = -0.344$, $p = 0.028$) and Leptin:Adiponectin Ratio (LAR) ($r = -0.3124$, $p = 0.049$).

Conclusion: Leptin, FGF-21, sTNFR-1, sTNFR-2, NGAL and LAR may be useful biomarkers to measure in a study examining longitudinal trends of biomarkers in DKD.

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P99 The importance of standardised diagnostic protocols for plasma metanephrines to ensure the highest diagnostic accuracy for investigation of Phaeochromocytoma and Paraganglioma

Griffin TP[1], Bogdanet D[1], Navin P[2], Drake WM[3], Callagy G[4], O'Shea PM[5], Bell M[1]

[1]Centre for Endocrinology, Diabetes and Metabolism, Galway University Hospitals, Galway; [2]Department of Radiology, Galway University Hospitals, Galway; [3]Department of Endocrinology, St Bartholomew's Hospital, London, UK; [4]Department of Pathology, Galway University Hospitals, Galway; [5]Department of Clinical Biochemistry, Galway University Hospitals, Galway

A 51-year old male presented 30 years ago with excessive sweating and haematuria. Blood pressure was labile. Intravenous pyelogram suggested a right-sided suprarenal mass displacing the right kidney caudally. A 24-h urine collection showed elevated urinary catecholamines. Right adrenal resection was performed; a phaeochromocytoma was confirmed histologically. 20 years later, he represented complaining of excessive sweating and measured variable blood pressure readings. Laboratory results showed elevated plasma normetanephrines (NMN) [50,250 (0–1180)pmol/L] and metanephrines (MN) [1030 (0–510)pmol/L]. Computerised Tomography (CT) abdomen showed a 10*9*6.3 cm enhancing mass. Curative resection was undertaken confirming recurrent phaeochromocytoma. Follow-up post-resection, plasma metanephrines (PMets) were sampled (intravenous cannula following 30/40 min seated-rest). Plasma NMN were 1,314 pmol/L (above decision threshold) at 30 min and 911 pmol/L (below decision threshold) at 40 min. Plasma MN were <40 pmol/L at both time points. Due to clinical suspicion of residual phaeochromocytoma, CT and MIBG scans were performed. Residual tissue was identified in the right upper quadrant, consistent with residual phaeochromocytoma. This case of incomplete resection could potentially have been missed if only seated-sampling Upper Reference Limits (URLs) were applied to the sample collected at 40 min. This case triggered a review of our PMets sampling strategy. Our review showed there were no statistically significant differences in PMets sampled at 30 and at 40 min seated-rest.[1] We adopted the Endocrine Society Clinical Practice Guideline of supine-sampling using URLs established in that position, at a single time point (30 min). This case highlights the importance of clinical acumen in the face of inconclusive biochemistry.

P100 Mechanistic insights into sulphonylurea- and glucose-induced insulin secretion in beta cell line models

McGuigan DH[1], Bjourson AJ[1], McClean P[1], Kelly C[1]

[1]N Ireland Centre for Stratified Medicine, Ulster University, Derry, Ireland

Type 2 diabetes is a disease characterised by a variety of metabolic defects (impaired insulin secretion; increased hepatic glucose production; decreased glucose uptake), which contribute to a hyperglycaemic state. Population studies suggest that variation in ABCC8, KCNJ11, KCNQ1, HNF1α affect response to front-line therapies such as sulphonylureas. The aim of this study was to assess the role of each of these genes in sulphonylurea- and glucose-induced insulin secretion. BRIN-BD11 and MIN6 cells were used for all experiments. mRNA (qPCR) and protein (western blot) expression of each gene was confirmed in both cell lines. siRNA (100 nm, Qiagen) against ABCC8, KCNJ11, KCNQ1 and HNF1α was transfected into each cell line using lipofectamine (Invitrogen) over 48–72 h and gene silencing confirmed by qPCR. The effect of the transfection process on cell viability was assessed by MTT. Insulin secretion in response to 20 min exposure to D-glucose (16.7 mm) and sulphonylureas (Tolbutamide, Glibenclamide; 200 μm) was assessed by ELISA. Transfection efficiency exceeding 60 % was achieved in all instances. Transfection-associated reductions in cell viability were not observed. Significant increases ($P < 0.001$) in insulin secretion were observed after exposure to Tolbutamide and Glibenclamide. A significant reduction ($P < 0.001$) in sulphonylurea-induced insulin secretion following ABCC8 and KCNJ11 silencing was observed. While this effect was not mirrored following HNF1α silencing, glucose-induced secretion was significantly impaired. Sulphonylurea- and glucose-induced insulin secretion was not impacted by KCNQ1 silencing in these models. Our data suggests that only ABCC8 and KCNJ11 are directly involved in sulphonylurea-induced insulin secretion in these cell models.

P101 Blue whiting protein hydrolysates display potent in vitro secretory effects upon insulin and glucagon-like peptide-1 release and acute glucose lowering effects in mice

McLaughlin CM[1], Parthsarathy V[1], Harnedy PA[2], Allsopp PJ[1], McSorley EM[1], Fitzgerald RJ[2], O'Harte FPM[1]

[1]School of Biomedical Sciences, Ulster University, Coleraine, N. Ireland; [2]Department of Life Sciences, University of Limerick, Limerick, Ireland

Underutilized marine protein sources could potentially be integrated as ingredients for functional food development with health promotion benefits. Marine protein hydrolysates derived from Blue whiting (*Micromesistius poutassou*), abundant in small molecular weight peptides, were used for acute in vitro and in vivo screening. Blue whiting protein hydrolysates were generated with food grade enzymes (Alcalase 2.4L/Flavourzyme 500L) alone, as well as being subjected to stimulated gastrointestinal digestion (SGID). Hydrolysate concentrations (2.5 mg/ml–0.01 mg/ml) combined with a fixed dose of glucose (5.6 mmol/l) promoted a 1.8 to 4–fold increase in insulin secretion from pancreatic BRIN-BD11 cells versus 5.6 mmol/L glucose control (Students t-test, $p < 0.001$). Hydrolysates displayed a 50 % increase in membrane potential via activation of intracellular calcium signalling pathways versus glucose control in cultured BRIN-BD11 cells ($p < 0.001$). Alc/Flav and the SGID hydrolysates displayed a 1.3-fold ($p < 0.01$) and 1.7-fold ($p < 0.001$) increase in secretion of the incretin hormone GLP-1 with 2.0 mmol/l glucose from murine enteroendocrine GLUTag cells. Using a lactate dehydrogenase assay (Promega, UK) no loss of cellular viability was observed in acute secretion studies with either cultured BRIN-BD11 or GLUTag cells. Following an OGTT, healthy NIH Swiss mice ($n = 8$) challenged with 100 mg/kg body weight of hydrolysate (Alc/Flav) displayed significantly lower blood glucose concentrations from 90 to 120 min ($p < 0.01$) versus glucose controls (2 g/kg). In conclusion, protein hydrolysates derived from Blue whiting displayed potent in vitro and in vivo bioactivities. Incorporation into functional foods could potentially provide a novel approach for the management of hyperglycaemia in type 2 diabetes.

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P102 Thyrotoxicosis induced reversible cardiomyopathy

Dineen R, Silva C, Hannon MJ

Department of Medicine, Bantry General Hospital, Bantry, Co. Cork, Ireland

Graves' thyrotoxicosis has profound cardiovascular effects; the most frequent complication being atrial fibrillation. Less than 1 % develop dilated cardiomyopathy with impaired left ventricular systolic function. We report a case of Graves' hyperthyroidism-induced reversible cardiomyopathy in a 35 year old female without primary heart disease. A 35 year old woman presented to the outpatients' department with sweating, 7 kg weight loss, and palpitations, despite therapy with carbimazole 20 mg twice daily in primary care. Clinical examination revealed marked exophthalmos, a large diffuse goitre, and an incidental finding of fast atrial fibrillation, with no clinical signs of decompensated cardiac failure. Laboratory investigations revealed Thyroid Stimulating Hormone (TSH) <0.03 mIU/L, Free Thyroxine (FT4) 96.6 pmol/L (12–22 pmol/L), a high Thyroid Peroxidase (TPO) antibody titre of 305.8 IU/mL and high TSH receptor antibody titre of 7.09 IU/L. Electrocardiogram confirmed the presence of atrial fibrillation. Transthoracic echocardiogram revealed a globally reduced ejection fraction of 35.4 %, biatrial enlargement and moderate mitral regurgitation. She was commenced on high dose beta blockade and maximum dose carbimazole, with little improvement in symptoms or biochemistry. She then underwent an urgent total thyroidectomy due to refractory thyrotoxicosis on maximal medical treatment. Postoperatively she reverted to sinus rhythm and was placed on replacement thyroxine. Repeat echocardiogram revealed interval improvement in systolic function to 58 % and normalization of atrial size, with improvement in valvular function to trival mitral regurgitation. Thyrotoxic cardiomyopathy should be considered even in young patients with Graves' thyrotoxicosis, especially in those with uncontrolled hyperthyroidism or a long duration of disease.

P103 10 years hidden in clinic: a case of secondary diabetes

Hannon AM, Hannon MJ

Department of Medicine, Bantry General Hospital, Bantry, Co. Cork, Ireland

Type 1 and type 2 diabetes mellitus are common. However, other specific causes of secondary diabetes should always be considered. We present a 79 year old man diagnosed with type 2 diabetes in 2006. During routine review in diabetes clinic in 2015 he was noted to have features of acromegaly. He had clinical features of hypogonadism with absent axillary hair. Furthermore he had poorly controlled diabetes—HbA1c 115 mmol/mol despite three oral hypoglycaemic agents and long acting insulin. His IGF-1 level was elevated at 649 μg/L (39–184 μg/L) with a random GH of 6.18 μg/L. Further investigations confirmed hypogonadotrophic hypogonadism, normal prolactin and intact TSH and ACTH axes. OGTT confirmed acromegaly with failure to suppress GH. MRI pituitary demonstrated a 9 mm pituitary microadenoma arising from the left side of the gland, extending into the left cavernous sinus and abutting but not encasing the internal carotid artery. After discussion with the patient, he was placed on primary medical therapy with octreotide LAR 30 mg monthly, with rapid improvement in IGF-1 (649 to 277 μg/L) and HbA1c (115 to 67 mmol/mol). The ADA recommends classification of diabetes into four categories: type 1, type 2, gestational and other specific types of diabetes. Correct classification is essential to initiate appropriate therapy. Previous studies have shown that classification is frequently incorrect, with under diagnosis of specific causes of diabetes. This case illustrates that although type 2 diabetes is by far the most common, it is important to consider alternative types when making the diagnosis, particularly in patients with atypical features.

P104 Hyperparathyroidism jaw tumour syndrome (HPT-JT)

Ahmed KS[1], Sherlock M[2], Stassen L[3], Timon C[4], Healy ML[1]

[1] St. James Hospital, Department of Endocrinology; [2]Adelaide and Meath Hospital, Department of Endocrinology; [3]St. James Hospital, Department of Maxillofacial surgery; [4]St. James Hospital, Department of Otorhinolaryngology

Hyperparathyroidism jaw tumour syndrome (HPT-JT) is an autosomal dominant disease with variable penetrance. Onset is typically in late adolescence or early adulthood. Primary hyperparathyroidism is typically caused by a single parathyroid adenoma but parathyroid carcinoma occurs in 10–15 %. Ossifying fibroma of the mandible or maxilla occurs in 30–40 %, and may be locally aggressive. 15 % of patients have renal manifestations which include polycystic kidney disease, Wilms tumour and renal cell carcinoma. In women there is an increased risk of uterine tumours. The gene causing HPT-JT, HRPT2, is located on chromosome 1q31.2a, coding for parafibromin (tumour suppressor gene) found in 50–75 %. We recently identified a patient with HPT-JT which led to detection of a kindred with the CDC73 pathogenic variant. A 54 year old male presented to the maxillofacial services for surgical removal of a jaw tumour. Histology confirmed an ossifying fibroma of the maxilla. During his admission he was noted to have hypercalcaemia (Ca^{++} 3.2 mmol/l, PTH 110 pmol/l).

On review of previous history, he described poor dentition since the age of 20, and he reported that his sister had died at the age of 35 from metastatic parathyroid carcinoma. Diagnosis of primary hyperparathyroidism was established and he underwent parathyroid surgery with normalisation of Ca^{++} and PTH. Histology was consistent with parathyroid adenoma. His genetic analysis detected a mutation in the CDC73 gene (Exon 7 c.664 C to T leading to protein PArg222Ter). Family members were screened, which confirmed CDC73 mutation in one daughter and one son, and 1 son was mutation negative.

P105 Ectopic lipoadenoma of the parathyroid

Melvin A, Kinsley B

Department of Endocrinology, Mater Misericordiae University Hospital, Dublin, Ireland

A 50-year-old woman noted to have asymptomatic hypercalcaemia was referred for Endocrine assessment. At the time of referral the patient's corrected calcium level was 2.94 mmol/L (2.15–2.52 mmol/L) and inorganic phosphate 0.55 mmol/L (0.80–1.58 mmol/L). A smoking history warranted a chest radiograph which revealed a mediastinal mass. CT imaging confirmed a 14 cm lobulated mass at in the middle mediastinum. Biochemically the hypercalcaemia was Parathyroid Hormone (PTH) mediated. SPECT Sestamibi imaging evaluating the lesion for parathyroid tissue showed mild accumulation of tracer within the mediastinal mass supporting ectopic PTH secretion from the lesion. The degree of hypercalcaemia coupled with the uncertain nature of this PTH producing tumour necessitated surgical resection. Histology confirmed a 14 cm benign lipoadenoma of

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parathyroid origin weighing 176.4 g. Post operatively Calcium and PTH levels normalised. We report a case of ectopic lipoadenoma of the parathyroid, a rare presentation of primary hyperparathyroidism at less than 1 % of all cases. Lipoadenoma of the parathyroid is a tumor composed of fibrofatty lobules and parathyroid chief cells, with stromal fat represents greater than fifty percent of the volume. Most Parathyroid lipoadenoma reside in the neck, however ectopic locations owing to the embryological origin should be considered. The high stromal fat content may make localisation with Sestamibi challenging. Lipoadenomas are described as benign tumors histologically however reports of atypical histopathological features have caused uncertainty as to the potential for malignant transformation. All reported cases thus far have been histologically benign and there are no reported cases of recurrence in the literature.

P106 Case report: management of primary hyperparathyroidism in a pregnant patient with MEN 1

Divilly P, Crowely R

Department of Endocrinology, St Vincent's University Hospital, Dublin 4

AF is a 34 yr old female with MEN 1 syndrome complicated with Zollinger-Ellison syndrome and primary hyperparathyroidism. Shortly after her diagnosis of hyperparathyroidism she became pregnant for the first time. Given the concerns with regards to the safety of cinacalcet in pregnancy and her rising ionised calcium levels it was decided to that she showed undergo a parathyroidectomy in the second trimester, due to the risks of her elevated calcium to mother and foetus. Post-surgery it was difficult to maintain AF's ionised calcium off intravenous calcium infusion. She was treated with high dose oral calcium carbonate, however she quickly become symptomatic with low calcium levels upon stopping intravenous calcium infusions. Calcium carbonate is the standard oral calcium preparation in Irish hospitals. Due to the treatment of her Zollinger-Ellison syndrome with high dose proton pump inhibitors, she had been rendered achlorhydric and thus the bio-availability of the calcium carbonate was greatly reduced (from 25 % to 4 % approximately). Bioavailablity of calcium citrate is maintained in achlorhydric patients. Calcium citrate was procured by the hospital pharmacy and ionised calcium improved upon starting the preparation. AF's baby was born healthy at 37 weeks with no complication of mother or baby.

P107 Treatment of diarrhoea predominant irritable bowel syndrome with glucagon-like peptide-1 receptor agonist Liraglutide

Divilly P, Rowan C, Doherty G, O'Shea D

Departments of Endocrinology and Gastroenterology, St Vincent's University Hospital, Dublin 4

RB is 39 year old female with a background history of diarrhoea predominant irritable bowel syndrome, paphypopituitarism secondary to hypophysectomy and radiotherapy for Cushing's disease and obesity. Prior to starting Liraglutide for her treatment of her obesity, she weighted 87 kg, had a body-mass index of 37.3 kg/m^2 and had bowel motions on average 8 times a day with consistency of 6 or 7 on the Bristol stool chart. RB identified that the frequency of bowel motions in particular was a barrier to exercise. Endoscopy prior to treatment was normal. Hormone profile was within treatment targets. After 12 weeks of treatment with Liraglutide, RB lost 4 kg in weight, had reduction in bowel frequency to one a day, with a Bristol stool score of 4 and an improvement in IBS-severity score questionnaire. This case opens the possibility that glucagon-like peptide-1 receptor agonists may have a role in treating diarrhoea predominant irritable bowel syndrome and should be studied further.

P108 Venous thromboembolism prophylaxis prescribing practice in patients over 100 kg in St Vincent's University Hospital

Divilly P, Vermeulen D, O'Hanlon N, Crowely R, O'Shea D

Department of Endocrinology, St Vincent's University Hospital, Dublin 4

The aim of this audit was to assess compliance of low molecular weight heparin (LMWH) prescribing in St Vincent's University Hospital with the current venous thromboembolism prophylaxis guidelines for patients that weight greater then 100 kg. The data was collected from all ward based in-patients from the 4/2/16 to the 22/2/16. Patients were identified through the hospital pharmacy department. Data was manually collected on data sheets using drug kardex's and clinical notes. Renal function was obtained from the hospital lab results system with estimate glomerular filtration rates calculated from the patients most recent renal function tests. Clinical notes were used to indicate if there were any contraindications to LMWH. 26 suitable patients were identified during the audit. 7 patients were on therapeutic anti-coagulation. Of the remaining 19 patients, 8 were on appropriate LMWH thromboembolic prophylaxis for their weight and renal function, meaning 11 were not optimally managed, leaving them at increased risk of thromboembolic events (no patients were under anti-coagulated). Despite the increasing levels of obesity in the general population, under treatment of thromboembolism risk with weight adjusted LMWH remains common in in-patients who weight over 100 kg. With the results of the audit the Vincent's Hospital group have revised the hospital guidelines and started an education campaign directed at NCHD's. We hope to re-audit in February 2017 to complete the audit cycle.

P109 A theory-based qualitative approach to the development of an intervention to improve outcomes among young adults with type 1 diabetes

Hynes L[1], O'Hara MC[2,3], Casey D[4], Murphy K[4], Dinneen SF[2,3], Byrne M[1]

[1]School of Psychology, NUI Galway, Galway; [2]School of Medicine, Clinical Science Institute, NUI Galway, Galway; [3]Endocrinology and Diabetes Centre, Galway University Hospitals, Galway; [4]School of Nursing and Midwifery, NUI Galway, Galway

Background and aims: Young adulthood is characterised by transition and unpredictability and may hinder consistent engagement in constructive self-management behaviours amongst those with type 1 diabetes (T1D). The aim of this study was to explore barriers and facilitators associated with T1D self-management using a theoretical model of behaviour change (Capability, Opportunity, Motivation-Behaviour/COM-B).
Materials and methods: Interviews were conducted with parents of young adults with T1D ($n = 10$) and healthcare providers

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($n = 15$). Focus groups ($n = 3$) were conducted with young adults at 3 sites. Topic guides were developed by the study's Young Adult Panel (8 service-users between 18 and 25 years old). Thematic analysis was used to analyse the data using the framework of the COM-B model.

Results: Self-management of T1D comprises tasks that are driven by capability, opportunity and motivation in an inter-related system. Diabetes education and regular, informal access to diabetes-related information is considered vital to capability to engage in diabetes self-management. However, self-management behaviour appeared to be determined to a greater extent, by external physical and social factors such as access to a supportive diabetes team. External factors may directly drive self-management behaviour or influence motivation. Where resources such as diabetes devices and peer networks were available, self-management was enhanced.

Conclusion: Barriers and facilitators associated with T1D self-management exist at multiple levels, including environmental and cognitive. External resources, i.e., access to information and support emerged strongly as determinants of self-management. Interventions should target environmental factors to positively influence capability and motivation to better engage young adult with T1D in self-management.

P110 Potential of a novel GLP-1/Xenin hybrid peptide to restore GIP insulinotropic action in an in vitro beta-cell model of impaired incretin action

Hasib A, Ng MT, Gault VA, Flatt PR, Irwin N

School of Biomedical Sciences, University of Ulster, Coleraine, United Kingdom

The insulin secretory response of the incretin hormone, glucose-dependent insulinotropic peptide (GIP), is severely impaired in type 2 diabetes. In this regard, we have previously shown that prolonged glucotoxic culture of pancreatic clonal BRIN-BD11 beta-cells recapitulates this impaired insulinotropic response. Both glucagon-like peptide-1 (GLP-1) and xenin-25 are known to potentiate insulin releasing effects of GIP. As such, the present study investigated the ability of a novel GLP-1/xenin hybrid peptide to overcome GIP resistance in BRIN-BD11 cells. As expected, prolonged (48 h) glucotoxic (22.2 mM) culture of BRIN-BD11 cells impaired the insulin-releasing action of GIP (10^{-12} to 10^{-6} M; $P < 0.05$ to $P < 0.01$). However, culture in presence of GLP-1/xenin (10^{-7} M) significantly ($P < 0.05$ to $P < 0.01$) improved the insulinotropic activity of GIP under these glucotoxic conditions. Additionally, GLP-1/xenin co-culture normalised the significant ($P < 0.05$) reduction of BRIN-BD11 cells insulin content under hyperglycaemic conditions. Incubation of BRIN-BD11 cells for 48 h at 22.2 mM glucose also resulted in reduced cell viability, which was reversed by co-culture with the GLP-1/xenin hybrid peptide. In agreement with this, GLP-1/xenin increased ($P < 0.001$) beta-cell proliferation when compared to control glucotoxic cultures, as demonstrated by Ki-67 staining. Observations were verified in isolated mouse islets, where islets co-cultured with GLP-1/xenin under hyperglycaemic conditions (22.2 mM glucose; 48 h) demonstrated significantly enhanced ($P < 0.01$ to $P < 0.001$) GIP-mediated insulin secretory function compared to controls. In conclusion, the novel GLP-1/xenin hybrid peptide restored the insulinotropic effectiveness of GIP in an in vitro model of impaired incretin action, suggesting its therapeutic potential for overcoming GIP resistance in T2DM.

P111 Record of bone health assessment in cholestatic liver disease

Gan KJ[1], Hanley B[1], Armstrong P[1], McKenna MJ[1,3], Hoti E[2], Houlihan DD[2,3], Crowley RK[1,3]

[1]Department of Endocrinology, St Vincent's University Hospital, Elm Park, Dublin 4; [2]National Liver Transplant Unit, St Vincent's University Hospital, Elm Park, Dublin 4; [3]UCD School of Medicine, Belfield, Dublin 4

Chronic liver disease and liver transplant are recognised risk factors for low bone density and fracture; this risk is elevated in patients with cholestatic liver disease because of associated malabsorption and inadequate calcium absorption from the gut. Records of 152 patients attending the St Vincent's University Hospital liver transplant unit with either primary biliary cirrhosis (86) or primary sclerosing cholangitis, and a liver transplant, were reviewed to assess whether bone health was being investigated and managed appropriately in this cohort. Medical charts, electronically-scanned health care records and radiology systems were used for ascertainment and records could be assessed for 107 patients. Twenty seven patients had had more than one transplant. Fifty percent of patients had a record of a DXA assessment, although results were available for only 22 % because scans were done elsewhere. Twelve percent of subjects had a record of a clinical fracture. Calcium and vitamin D supplements were prescribed to 81 % of this patient cohort; 38 % of whom also received a bisphosphonate (including 3 who received IV zoledronate). This review demonstrated that inadequate information was available to the transplant physicians to assist decision making regarding the bone health of their transplant cohort with cholestatic liver disease. Prescription rates for calcium and vitamin D were high. Centralisation of DXA scanning to SVUH, implementation of a bone health pathway with a chart proforma for completion at clinic and regular follow up audit are planned to inform decision making and improve bone health for this patient group.

P112 Clinical fracture prevalence in an Irish Orthotopic Liver Transplant Cohort

Ryan DM[1], Houlihan DD[1,2], Crowley RK[1,3]

[1]UCD School of Medicine, Belfield, Dublin 4; [2]The National Liver Transplant Unit, St Vincent's University Hospital, Dublin 4; [3]Department of Endocrinology, St Vincent's University Hospital, Dublin 4

Chronic liver disease (CLD) is a recognized risk factor for low bone density and fracture and after orthotopic liver transplant (OLT) the risk of fracture is increased. International guidelines recommend DXA measurement pre-OLT and supplementation of vitamin D and calcium but do not provide guidance on further treatment. Patients attending the Liver Transplant Clinic at SVUH were invited to complete a questionnaire regarding their bone health, with the aim of establishing the prevalence of clinical fractures and of risk factors for fracture in an Irish cohort. Forty-four patients completed the questionnaire, 1–24 years post-OLT; 18 were on tacrolimus, 2 on ciclosporin, 13 on mycophenolate and 14 on a glucocorticoid at the time of the survey. Three were prescribed an oral bisphosphonate and 18 were receiving a calcium or calcium and vitamin D supplement. Median body mass index was 25.8 kg/m^2. Twelve patients reported having had a DXA scan. Sixteen patients reported fractures (9 of

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whom had fractures at more than 1 site) and 5 required surgical fixation. Only 1 patient reported a vertebral fracture. A further 5 patients had fractures before their diagnosis of liver disease. We have demonstrated a high clinical fracture rate in this high-risk Irish cohort, which is similar to that seen in international studies, and have also observed low rates of prescription of anti-osteoporotic therapy. Further studies are indicated to establish the incidence of fracture, the prevalence of asymptomatic vertebral fractures, and to identify fracture prevention strategies in this population.

P113 Adrenal insufficiency secondary to ipilimumab induced hypophysitis: the Northern Irish experience

Todd A[1], Wallace I[1], Thiraviaraj A[2], Oladipo B[3], Nugent A[1]

[1]Department of Endocrinology and Diabetes, Belfast City Hospital, Belfast; [2]Department of Endocrinology and Diabetes, Altnagelvin Area Hospital, Londonderry; [3]Regional Cancer Centre, Belfast City Hospital, Belfast

Ipilimumab is a fully humanised monoclonal antibody used in the treatment of malignant melanoma. Endocrinopathies are amongst its known side-effects, in particular hypophysitis and thyroiditis. We describe our regional experience of 7 cases of hypophysitis (4 male, 3 female with a mean age of 62.1 years).

Cases presented with a spectrum of symptoms ranging from lethargy and headache to adrenal crisis. All patients presented after cycle 3 or 4. All patients had low serum cortisol concentration or undetectable ACTH and secondary hypothyroidism. In addition 5 patients had suppressed gonadotropins and 2 suppressed prolactin levels. In contrast to the literature only one patient demonstrated the classical finding of an enlarged pituitary or pituitary stalk. The first 4 patients were managed with high dose steroids in the form of prednisolone 1 mg/kg, slowly weaned to replacement doses. Levothyroxine and testosterone replacement was prescibed as required. Pituitary function was not regained in these 4 patients and 2 patients experienced significant deterioration in pre-existing type 2 diabetes control, 1 requiring admission. The subsequent 3 patients were treated with replacement hydrocortisone, levothyroxine and testosterone as appropriate. Outcomes in both groups were similar but the replacement dose group did not experience side-effects associated with high dose steroids. From our experience high dose steroid replacement does not improve pituitary recovery and therefore replacement hydrocortisone is more appropriate and appears to offer the same outcome. While only a small proportion of patients will suffer hypophysitis it is important to raise awareness as prompt diagnosis and treatment is potentially life-saving.

P114 The modulation of platelet function by growth hormone in growth hormone deficient hypopituitary patients

Slattery D[1], Oglesby I[2]*, Glynn N[1], Gupta S[1], Duggan K[1], Cuesta M[1], Rehill N[2], Dunne E[2], Garrahy A[1] Toner S[1], Kenny D[2], Agha A[1]*

Department of Endocrinology[1]; Beaumont Hospital and Department of Molecular and Cellular Therapeutics[2]; The Royal College of Surgeons in Ireland, Dublin, Ireland

*Both authors contributed equally to the research

Growth hormone deficiency (GHD) has been implicated in the increased risk of cardiovascular and cerebrovascular disease seen in hypopituitarism but the mechanism remains speculative. We hypothesise that platelet abnormalities may play a contributory role. This research aims to study platelet function in GHD hypopituitary patients and to assess the effect of growth hormone (GH) replacement. Thirteen hypopituitary adults (7 males) with GHD and 13 healthy matched controls were studied. Patients were assessed before and 3 months after GH treatment. All other pituitary replacements were optimised before the study. In addition to a full endocrine profile, whole blood was labelled and perfused over immobilised von Willibrand factor (VWF). Dynamic platelet-protein interactions, namely, the numbers of platelet tacks, stably-adhered platelets, translocating platelets, median speed and distance travelled and platelet coverage on the final analysis frame (PCFF) were tracked. Before GH treatment and compared to controls, GHD subjects, had a significantly altered profile of platelet-VWF interactions, specifically, increased numbers of platelet tracks ($p = 0.0035$), translocating platelets ($p = 0.0035$), stably-adhered platelets ($p = 0.03$) and PCFF ($p = 0.02$). The speed and distance platelets travelled across VWF was similar between the control group and pre-therapy GHD patients, however, this significantly decreased post treatment, ($p = 0.0108$ and 0.015, respectively). No significant difference in the other parameters were observed with GH treatment. We have demonstrated differential platelet behaviour in GHD individuals versus healthy controls which may contribute to an increased risk of thrombosis. Additional research with a larger number of subjects is needed to further evaluate the effect of GH on platelet function.

P115 Characteristics and outcomes of 153 patients consecutively reviewed by a dedicated adrenal multidisciplinary team

Ahmed KS[1], Kumar L[1], Morrow J[1], Gibney J[1], Gunness A[1], Govender P[2], Feeney J[2], Conlon K[3], Sherlock M[1]

[1]Adelaide and Meath Hospital, Department of Endocrinology; [2]Adelaide and Meath Hospital, Department of Radiology; [3]Adelaide and Meath Hospital, Department of Surgery.

Adrenal tumours (in particular incidentalomas) are increasingly common due to the increase use of cross sectional imaging. The majority of these lesions are benign but detailed radiology and endocrine studies are required to exclude hypersecretion/malignancy and to facilitate. We assessed the imaging and biochemical characteristics of 151 consecutively reviewed adrenal lesions in a dedicated adrenal MDT between January 2013 and May 2016.130/151 (86.1 %) lesions were incidentally discovered, 21/151 (13.9 %) were discovered on dedicated adrenal imaging due to symptoms or signs of endocrine excess. CT was the only imaging modality in 101/151, MRI the only imaging modality in 9 and 41 had a combination of CT/MRI imaging. Non-contrast HU were available in 88 and were <10 (a cut off deemed to reassure for benign behaviour) in 53/88. 34 patients had a HU > 10. The median size of tumours was 25 mm (range 5 to 240 mm). 99/151 had a 1 mg ODST of these 44/99 had a cortisol > 50 nmol/l and 8/99 patients had a cortisol > 138 nmol. 122/151 (80.7 %) had matched PRA and aldosterone. 116/151 (76.8 %) had assessment for catecholamine excess (no patients with HU <10 had catecholamine excess). 10/116 had positive catecholamine studies.

In total 25/151 (16.5 %) patients were recommended for surgery and 24/151 (15.8 %) patients required no further follow up and were discharged, 102/151 (67.5 %) required ongoing review by either biochemistry and/or imaging. Final diagnosis included 5 Myelolipoma, 12 Adrenocortical carcinoma, 12 phaeochromocytoma/paraganglioma, 1 adrenal lymphoma and 121 adenoma. Assessment in an MDT setting

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enables appropriate diagnosis and also facilitates discharge of patients, thus avoiding the need for prolonged follow up.

P116 Adrenal haemorrhagic infarction in antiphospholipid syndrome despite therapeutic anticoagulation

Wong E, Watts M, O'Hare JA

Department of Endocrinology and Medicine, University Hospital Limerick Group and UL Graduate Entry Medical School, Ireland

A 64-year-old man presented with vomiting and abdominal discomfort. Temperature was 37.8 °C, pulse 85/min and BP 100/63 mmHg. There was generalized hyperpigmentation. He has had two episodes of lower limb deep venous thrombosis and was on warfarin. He was previously diagnosed with primary antiphospholipid syndrome with a strongly positive anticardiolipin IgG antibody. Serum sodium was 127 mmol/l, and serum potassium was 5.7 mmol/l, urea: 9.8 mmol/l and Creatinine 103 μmol/l. Haemoglobin was 12.6 g/dl, white cell count of 7.3×10^9, INR was 3.1 on warfarin, APTT 133 secs and PT 32.7 secs. Primary adrenal insufficiency was suspected. The Tetracosactrin (250 micrograms) test had a maximum stimulated cortisol of 43 nmol/l (normal >550 nmol/l) confirming adrenal insufficiency. CT of Abdomen revealed bilateral adrenal enlargement (3.1 cm × 2.5 cm, each). Tuberculosis was considered and treated for several months though no bacteriological nor clinical features were established after 5 year follow up. PET scan negative for evidence of malignancy. Anti Ds DNA and adrenal antibodies tested negative. Beta-2 glycoprotein was positive. CT Abdomen 4 months later showed that adrenal glands shrunk to 1.5 cm bilaterally and deduced he had haemorrhagic infarction initially. He made a good recovery on hydrocortisone and fludrocortisone. INR target was increased to 3.5. No further infarction over 5 year follow-up. Adrenal infarction can occur in antiphospholipid syndrome despite conventional anticoagulation, perhaps because the adrenal vascular has only single venous drainage but multiple arterial arcades making it more susceptible to thrombosis and haemorrhage.

P117 Reversible thyrotoxic pulmonary hypertension with heart failure: 2 cases

Khattak A, Wong E, Mak G, O'Hare JA

Departments of Endocrinology and Cardiology, University Limerick Hospital Group and UL Graduate Entry Medical School, Limerick, Ireland

Heart failure is a complication of thyrotoxicosis. We present 2 unusual cases presenting with pulmonary hypertension with isolated right heart failure that reversed after treatment. Case 1: A 55-year-old man presented with weight loss, dyspnoea and leg swelling. HR: atrial fibrillation 51/min. He had a raised JVP, tricuspid regurgitation and severe pitting oedema. Pro-BNP: 4995 pg/ml (N < 75), TSH: 0.06 mU/l, FT4: 54.1 pmol/l, FT3:10.5 pmol/l. TSH receptor stimulating antibodies were positive. CTPA: no pulmonary embolism but showed dilated right heart with impaired right ventricular function, and bilateral pleural effusions. Echo: PAP 45 mmHg. LVEF preserved. IVC and hepatic veins were dilated. Carbimazole, diuretics, ACE inhibitors and Apixaban were commenced. Cardiac MRI highlighted overload of over right ventricle, pulmonary hypertension with normal left ventricle and no RV-LV shunting identified. Right heart catheterization showed non-obstructive coronary artery disease and pulmonary hypertension. Repeat ECHO 7 months later revealed normal right heart pressure and size when euthyroid. Tricuspid regurgitation and Pulmonary Hypertension were resolved. Case 2: A 34-year-old male presented with oedema and elevated JVP tricuspid regurgitation and atrial fibrillation 115/min. Pro-BNP: 2064 pg ml TSH: <0.05, Free T4: 72.6, TSHRSA positive. CTPA negative for PE. ECHO: PAP > 60 mmHg. Right cardiac catheterisation when euthyroid demonstrated a RVSP of 32 mm Hg, pulmonary artery systolic pressure of 27 mmHg and a wedge pressure of 14 mmHg indicating a resolution of his RHF. Raised pulmonary vascular resistance causing pulmonary hypertension with secondary TR might arise from endothelial injury due to increased cardiac output and accelerated metabolism of pulmonary vasodilators in thyrotoxicosis.

P118 Non-Hodgkin's B-Cell lymphoma presenting as acute adrenal crisis

Wong E, O'Hare JA

Department of Endocrinology, University Hospital Limerick Group and UL Graduate Entry Medical School, Limerick, Ireland

A 47-year-old woman presented with 1-month history of weight loss of 7 kg and vomiting. Shortly after admission she became hypotensive, BP 92/58 mmHg, heart rate 100/min and required volume resuscitation. On examination, she had generalised hyperpigmentation. Serum sodium was 130 mmol/l, serum potassium 5.1 mmol/l, creatinine 112 μmol/l and urea 7.1 mmol/l. Full blood count was normal. She had a history of depression on Escitalopram 10 mg daily and peptic ulcer disease. She had adrenal insufficiency: peak post-Tetracosactrin cortisol of 150 nmol/l (normal >550 nmol/l). CT scan abdomen revealed enlarged adrenals (Left: 8.6 cm × 5.7 cm and similar on the right) with polar masses in the kidneys with extrinsic compression of the inferior vena cava. She improved rapidly with hydrocortisone and fludrocortisone. Adrenal biopsy demonstrated a diffuse large B-cell lymphoma (non-germinal center subtype). Proliferation fraction was 60 %. PET scan demonstrated uptake in the right rib, bone marrow aspiration showed no evidence of infiltration. Staging was 4b. She was treated with Rituximab, Cyclophosphamide, Doxorubicin and Vincristine (CHOP). Antiphospholipid screen IgG antibody was negative. Partial remission was achieved with a modest reduction in adrenal dimensions. Lymphoma with partial adrenal hypofunction has been reported to involve the adrenals in 3 % of cases. Adrenal crisis from lymphoma is rare but is life threatening if missed. Replacement therapy was critical for toleration of subsequent chemotherapy. Imaging of the adrenals is advisable in all cases of primary adrenal insufficiency.

P119 Vitamin D demand management initiative

Spence K[1], Aldworth G[2], Burgess C[1], Hamilton P[2], Roberts B[2], McDonnell M[1]

[1]Regional Endocrine Laboratory, Belfast Health and Social Care Trust, Belfast BT12 6PA; [2]Clinical Biochemistry Department, Belfast Health and Social Care Trust, Belfast, BT12 6PA

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There has been a 30 fold increase in vitamin D requests from GPs over the last 5 years in Northern Ireland. We developed a 7 week Demand Management Initiative (DMI) in 2014 whereby GPs had to complete a form with each request with information including previous vitamin D results and reason for request.

During the DMI period we noted a 35 % drop in monthly requests from GPs and 30 % (392/1301) of samples received were not analysed as no DMI form received. Signs/symptoms of vitamin D deficiency accounted for 65 % of requests and 21 % were due to housebound/elderly/dark skinned. Repeat requests were sent for. 467 (36 %) patients and 41.5 % of these requests were within a 3 month period. We subsequently determined an acceptable list of criteria upon which the decision to accept or reject a request would be based. All NI GP were contacted, informing them that we were starting a strict gating policy for vitamin D requests based on the provision of appropriate clinical justification. GP Vitamin D requests dropped from approximately 1100 to 350 per month. Over 12 months only 75 % of GP requests were analysed. Vitamin D analysis costs £13.42/sample so the reduction in GP samples analysed from 10,100 to 4700 amounted to a saving of approximately £63,000 last year. This sum would pay for treatment of approximately 6300 patients over the same time period. A 3 month minimum retest interval for all vitamin D requests is to be introduced shortly.

P120 Audit of short Synacthen test results: is the 60-minute sample necessary?

Shaamile F[1], McGing PG[2], Mohammed MI[1], McQuaid SE[1,3]

[1]Department of Endocrinology; [2]Clinical Biochemistry, Mater Misericordiae University Hospital, Dublin 7; [3]University College Dublin

Introduction: Short synacthen test (SST) is widely used to assess adrenal function. Controversy remains concerning sample timing and diagnostic cut-offs.

Methods: A retrospective analysis of SST results for the 30-month period 1-1-13 to 30-6-15 was undertaken. Normal SST response in use during that period was peak cortisol (Abbott Architect assay) $\geq$ 500 nmol/L at 30 or 60 min with an increment from baseline of $\geq$ 180 nmol/L. 'Normal adrenal function' was determined clinically based on subsequent clinical follow-up (range 11–41 months).

Results: Of 299 total SSTs, this audit focuses on Endocrinology Department requests (97 tests in 87 patients, 34 males). Median age was 48 years (range17–86). Indications for testing: type I DM patients with suggestive symptoms (22 %), hyponatraemia (14 %), rule out congenital adrenal hyperplasia (10 %), autoimmune conditions (7 %), and other suggestive symptoms (31 %). Of 97 tests 67 (69 %) passed (i.e. met criteria at 30 or 60 min). 30 (31 %) failed at 60 min compared to 51 (53 %) failures at 30 min. Of the 21 (22 %) patients who passed at 60 but not 30 min, 15 had clearly normal adrenal function, 5 were re-tested and had normal response, and one patient had no clinical data available. No patient passed at 30 min and failed at 60 min.

Conclusion: Our results suggest that a number of patients undergoing SSTs may be inappropriately deemed as adrenally insufficient if the 60 min sample is not analysed. We propose continuing to include the 60 min sample in our SST protocol.

P121 A review of diagnosis, management and outcomes of congenital hypothyroidism in a cohort of 68 children and adolescents under active follow-up in an Irish regional Paediatric Endocrinology unit

Rafferty S[1], Morrissey R[1], O'Riordan[1] SMP, Mayne P[2], ÓConnell SM[1]

[1]Department of Paediatrics and Child Health, Cork University Hospital, Wilton, Cork; [2]National Newborn Screening Program, Metabolic Unit, Children's University Hospital, Temple Street, Dublin 1A

Congenital hypothyroidism (CHT) is estimated to affect 1 in 2500 newborns in Ireland. Severe untreated CHT is a preventable cause of intellectual disability. The National newborn screening program (NNSP) and early treatment have greatly improved outcomes. The European Society of Paediatric Endocrinology (ESPE) consensus guidelines for CHT were published in 2014. The aims of this study were to characterise a large Irish paediatric cohort with CHT and to determine if the management follows current guidelines. A retrospective chart review was conducted following local ethics committee approval. All cases of CHT under current follow-up, born between January 1997 and August 2015, were included. Results were cross referenced with the NNSP records. Data were analysed using SPSS V.18. Sixty eight cases fulfilled study inclusion criteria; 39 (57 %) female, 29 (43 %) male. Median time from diagnosis to treatment was 1 day. Thirty (54.5 %) patients received an initial thyroxine dose with the range 10–15mcg/kg/day (n = 55). High levels of pre-treatment free T4 were associated with lower current dose of thyroxine (rho = −0.462, n = 59, p = <0.001). Fifty nine (90.8 %) patients met the expected developmental targets for their age. In conclusion, the characteristics of this Irish cohort compare to international cohorts with CHT. This review of treatment supports the use of an initiation dose close to 10mcg/kg/day with close adjustment and monitoring of thyroid function and growth. Management of this cohort follow the standard set by the 2014 ESPE consensus guidelines.

P122 Activation of GPR55 regulates glucose homeostasis and incretin secretion from intestinal L cells

Miskelly MG, Flatt PR, McKillop AM

Diabetes Research Group, Biomedical Sciences Research Institute, Ulster University, Northern Ireland

G-protein coupled receptors (GPCRs) are the largest family of membrane receptors in mammals. GPR55 agonists have previously exhibited insulinotropic ability and this study has investigated the role of GPR55 in the regulation of glucose homeostasis and as a new therapeutic target for type-2 diabetes. Effects of GPR55 agonists (OEA, PEA, Abn-CBD, AM251) on insulin and GLP-1 secretion from BRIN-BD11 and GLUTag cells, respectively, were measured using radioimmunoassay and ELISA. MTT and Alamar Blue determined cell viability. Histochemistry and qPCR examined GPR55 expression in high fat fed (HFF) mice, an insulin resistant model of diabetes. qPCR measured agonist effects on GPR55 gene expression

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in GLUTag cells. OEA increased insulin secretion 1.4–2.2 fold ($p < 0.05$–$p < 0.001$) at 10^{-8} to 10^{-4}M and 1.1–1.7 fold ($p < 0.05$–$p < 0.001$) at 10^{-10} to 10^{-4}M in normal and hyperglycaemic conditions. GLP-1 secretion increased 1.8–2.0 fold ($p < 0.001$) at 10^{-6} to 10^{-4}M. PEA enhanced insulin secretion 1.1–1.5 fold at 10^{-8} to 10^{-4}M ($p < 0.05$–$p < 0.001$) in normoglycaemic and 1.2–1.7 fold ($p < 0.05$–$p < 0.001$) at 10^{-8} to 10^{-4}M in hyperglycaemic conditions while increasing GLP-1 secretion 1.9 fold ($p < 0.01$) at 10^{-4}M. AM251 elevated insulin secretion 1.4–1.7 fold at 10^{-8} to 10^{-4}M ($p < 0.05$–$p < 0.001$) in 5.6 mM glucose and 1.4–2.2 fold at 10^{-7} to 10^{-4}M in 16.7 mM glucose ($p < 0.05$–$p < 0.001$). GLP-1 secretion increased 1.4–1.7 fold ($p < 0.01$–$p < 0.001$). Abn-CBD increased GLP-1 secretion 1.7–2.4 fold ($p < 0.05$) at 10^{-8} to 10^{-4}M. Histochemistry and qPCR confirmed GPR55 expression in lean and HFF mouse small intestine and GLUTag cells. Abn-CBD ($p < 0.01$), AM251 ($p < 0.01$) and OEA ($p < 0.05$) increased GPR55 gene expression in GLUTag cells. These results indicate that GPR55, present in intestinal L-cell, increases GLP-1 secretion suggesting therapeutic potential for type-2 diabetes.

P123 Audit of presentation and genetic testing of patients with phaeochromocytoma and paraganglioma

Slattery LM[1], Doherty J[1], Prichard RS[2,4], O'Shea D[1,4], Swan N[3], Crowley RK[1,4]

[1]Department of Endocrinology, St Vincent's University Hospital, Elm Park, Dublin 4; [2]Department of Endocrine Surgery, St Vincent's University Hospital; [3]Department of Pathology, St Vincent's University Hospital; [4]UCD School of Medicine, Belfield, Dublin 4

Phaeochromocytomas and paragangliomas (PPGL) are rare neuroendocrine tumours that have the potential to secrete catecholamines. PPGL may present clinically, may be detected incidentally during imaging for another indication or in the screening of a patient from a recognized family with a PPGL syndrome germline mutation. A chart review was conducted to profile PPGL patients attending SVUH. Cases were identified from clinic letters, surgical database and pathology records. Thirty-eight PPGL cases (19 male; mean age 49 years at presentation) were identified of which 20 were paragangliomas (14 intra-abdominal; 4 neck; 2 thoracic). Eighteen presented with symptoms (pain or hypertension); 13 were incidentalomas; 6 from screening; and 1 from investigation of a PGL metastasis found on lung imaging. Three other PGL cases developed metastases; 2 to bone and 1 to liver. Fifty percent of PPGL lesions were functional. One patient has a clinical diagnosis of neurofibromatosis. A mother and daughter have a known RET mutation causing MEN2A. Since 2014 all patients with new diagnoses or still attending follow up with endocrinology have been offered genetic testing: this has identified 1 SDHB and 1 TMEM127 mutation not known to be pathogenic; 5 pathogenic mutations in SDHB; and 1 SDHD mutation. Twenty four percent of this heterogenous clinical cohort of PPGL have a recognized PPGL genetic syndrome (69 % of those offered testing); which illustrates the high prevalence of genetic syndromes in this patient group and which will inform future management planning and identification of PPGL kindreds at SVUH.

P124 Thermal imaging as a novel assessment of neuropathic diabetic foot ulceration

O'Loughlin A[1], Flynn L[2], Watterson D[2], Gethin G[3]

[1]Diabetes Day Centre, Galway University Hospitals, Galway; [2]Department of Podiatry, Merlin Park University Hospital, Galway; [3]School of Nursing and Midwifery, National University of Ireland, Galway

Diabetic Foot ulceration (DFU) affects up to 25 % of patients with diabetes. There is a critical clinical need to develop objective, valid, reliable and easy to use biomarkers to assess the ulcer and ultimately improve decision-making, treatment planning and patient outcomes. This research project aims to pilot the use of thermal imaging as a biomarker for the assessment of DFU.

A prospective observational study was performed to map the changes in temperature and pH in neuropathic DFU over 12 weeks. Following consent, 50 consecutive patients attending a podiatry clinic with non-healing, non-infected neuropathic DFUs were assessed with a thermal imaging camera, wound tracings and pH of the wound bed.

Baseline temperature ranged from 23 to 36 °C and pH ranged from 5.5 to 8.7. More than half the ulcers had temperature <33 °C, the value below which it is proposed fibroblast activity is impaired. Mapping pH, temperature and size of DFUs demonstrated a moderate, positive correlation between temperature and pH, $r = 0.677$, $p = 0.016$. Initial findings provide unique insights to temperature profiles not previously identified. Assessment of inter-rater reliability (IRR) of temperature readings showed an intraclass correlation (ICC) of 0.998 indicating excellent consistency and no statistically significant difference between raters $p = 0.755$. Complete analysis is underway and will be presented. This preliminary data highlights a potential role for thermal imaging as a novel non-invasive assessment of a non-healing neuropathic DFU. The further development of thermal imaging as a biomarker of ulcer status may result in improved outcomes for DFU.

P125 The impact of Roux-en-Y gastric bypass on features of podocyte injury in an experimental model of diabetic kidney disease

Canney AL[1], Elliott JE[1,2], Eckhardt H[1], Jackson S[1], le Roux CW[1,3], Docherty NG[1,3]

[1]Diabetes Complications Research Centre, Conway Institute of Biomolecular and Biomedical Research, School of Medicine, University College Dublin; [2]Department of Surgery, Trinity Centre for Health Sciences, St. James's Hospital, Dublin, Ireland; [3]Gastrosurgical Laboratory, Sahlgrenska Academy, University of Gothenburg, Sweden

Podocytes injury is implicated as a both a marker and pathogenic driver of diabetic kidney disease (DKD). We describe and quantify changes in podocyte architecture and gene expression in the Zucker Diabetic Fatty rat (ZDF) and assess the impact of Roux-en-Y gastric bypass on these parameters. Development of glomerular injury was tracked between 8 and 22 weeks in ZDF (fa/fa) rats with reference

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to normal lean fa/+ control animals. Renal outcomes were also compared at 19 weeks of age between animals undergoing either sham operation or RYGB at 12 weeks of age. Specific parameters studied were glycaemic control, albuminuria, glomerular basement membrane (GBM) thickness, podocyte number, density, foot process frequency (PFPF) and de novo desmin expression. ZDF rats developed significant albuminuria by 12 weeks of age. Glomerulomegaly and early podocyte injury were evident by 12 weeks of age, marked by increases in tuft size, evidence of reduced PFPF, desmin acquisition and a decrease in podocyte density but not absolute number. Reductions in PFPF were more marked at 22 weeks and accompanied by increases in GBM thickness. RYGB normalised hyperglycaemia, albuminuria and glomerular tuft size. Coherent improvements were seen in PFPF and were accompanied by reductions in podocyte associated desmin expression and evidence of the arrest of GBM thickening. Progressive development of podocyte injury occurs in the kidneys of ZDF rats in line with the development of diabetes. RYGB corrects the metabolic milieu and partially reverses podocyte injury.

P126 Elevated plasma soluble TNFR1 levels are associated with renal injury and reduced renal function in patients with diabetes

Doody A[1], Slattery D[2*], Jackson S[1], Canavan RJ[2] Twomey PJ[3] le Roux CW[1,4] McKenna MJ[2], Docherty NG[1,4], *Co-first authors*

[1]Diabetes Complications Research Centre, Conway Institute of Biomolecular and Biomedical Research, School of Medicine, University College Dublin; [2]Department of Endocrinology, St. Vincent's University Hospital, Dublin; [3]Clinical Chemistry, St. Vincent's University Hospital, Dublin; [4]Gastrosurgical Laboratory, Sahlgrenska Academy, University of Gothenburg, Sweden

Elevated plasma soluble tumour necrosis factor receptor 1 (sTNFR1) may be predictive of long term renal outcomes and mortality in diabetes. Herein we examine sTNFR1 in relation to renal disease in a study of samples from patients with diabetes registering a haemoglobin A1c (HbA1c) of > 48 mmol mol (6.5 % DCCT). Plasma samples were reflex assayed for sTNFR1 (n = 3444). Central tendencies for metabolic, inflammatory and renal end-points for sTNFR1 groups above and below the Q4 cut-off for sTNFR1 were calculated. Receiver Operator Characteristic analysis of elevated sTNFR1 as a predictor of CKD3 (GFR <60 ml/min/1.73 m^2) or worse was conducted. The independent predictive power of sTNFR1 in relation to CKD was examined by both multiple linear and logistic regression. Values of sTNFR1 above Q4 (2061 pg/ml) were associated with significant elevations in plasma c-reactive protein and leptin-adiponectin ratios as well as increased urinary albumin excretion. Estimated glomerular filtration rate (eGFR) was significantly depressed in patients within the Q4 group. Elevated sTNFR1 was associated with an independent odds ratio of 9.1 (95 % Confidence Interval 6.8–12.1) for the presence of CKD3 or worse. In 38 patients with CKD3a at baseline, 92 % of patients with high sTNFR1 (Q4 > 2061 pg/ml) showed progressive eGFR decline over 3 years versus 57 % in patients with sTNFR1 below the Q4 cut-off. Upper quartile plasma sTNFR1 is associated with systemic inflammation and renal structural and functional impairment in patients with sub-optimal glycaemic control. Elevated sTNFR1 may reflect a role for systemic inflammation in the pathogenesis of diabetic kidney disease and be of value in prognostics and management.

P127 Social Jetlag is more common in patients with type 2 diabetes mellitus compared to age and gender matched controls

Healy U[1], Coogan A[2], McDermott JH[1]

[1]Dept. Endocrinology and Diabetes, Connolly Hospital Blanchardstown, Dublin; [2]Dept. Psychology, NUI Maynooth, Co. Kildare

Social Jetlag is the misalignment between our internal circadian clock and the external social clock. It occurs chronically in a significant proportion of the population and disrupts the preferred sleep-wake cycle. Disruption of the sleep-wake cycle in shift workers is associated with an increased incidence of type 2 diabetes. We hypothesise that subtler misalignment, in the form of social jetlag could is associated with similar metabolic derangement in non-shift workers. We aimed to determine if social jetlag is more common in subjects with type 2 diabetes (T2DM) than in controls. A multilevel circadian and metabolic analysis was performed on 30 subjects with T2DM and 27 age- and gender-matched controls. Questionnaires were used to assess sleep timing on work nights and free nights. Social jetlag was calculated as: social jetlag (h) = [mid-sleep time free days] − [mid-sleep time work days]. The independent samples T-test was used to compare social jetlag between the two groups. Pearson's product-moment correlation coefficient was obtained when assessing for correlation or partial correlation. T2DM subjects displayed a later chronotype and greater social jetlag compared to the control group (0.99 h vs 0.54 h, $p < 0.05$). The degree of social jetlag did not correlate significantly with Hba1c, measures of insulin resistance or body mass index in T2DM subjects. Subjects with T2DM have a later chronotype and greater social jetlag than controls. Further trials will be needed to determine if these associations represent causation or association, and to determine if interventions to target social jetlag have therapeutic benefits.

P128 Diabetic ketoacidosis at Tallaght Hospital: biochemical and outcome measures of DKA presentations in 2015

Costello R[1], Brady C[1], Healy U[2], Widdowson M[2]

[1]School of Medicine, Trinity College, Dublin; [2]Acute Medical Unit, Tallaght Hospital, Dublin

Diabetic ketoacidosis (DKA) is potentially fatal. To better manage DKA we need to better understand the complexity of cases that present to our institution. As such we carried out an audit of all adult patients presenting to Tallaght Hospital with DKA 2015. Here we present the predominant biochemical features and outcomes. Patients who presented between 01/01/15 and 31/12/15, who had a primary discharge diagnosis of DKA on HIPE coding were included. Medical records were reviewed and patients were subsequently excluded if the diagnosis of T1DM or DKA was felt to be incorrect. Patients with multiple presentations were treated as separate episodes. Anonymised data were inputted into a Microsoft Excel codebook. Results were calculated using standard Excel functions. 48 episodes were included for analysis. 17 % of patient presented with serum. pH <7.0 and 5 patients required ICU admission (10 %). Long-acting insulin was continued in 67 % of patients. Average time on IV insulin was 28 h. Average length of stay was 6.6 days. Hypoglycaemia occurred in 29 % of patients at some stage during their admission, and hypokalaemia in 24.75 %. A significant proportion of patients presenting to our institution with DKA have

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severe metabolic derangement. With an average length of stay of 6.6 days and significant rates of treatment induced hypoglycaemia and hypokalaemia these cases place a significant burden on the patients involved and on the heath care system. These data should allow us to better plan for future service provision and give parameters to target in the ongoing effort for quality improvement.

P129 Diabetic ketoacidosis at Tallaght Hospital: Investigating the effectiveness of new guidelines

Costello R[1], Brady C[1], Healy U[2], Widdowson M[2]

[1]School of Medicine, Trinity College, Dublin; [2]Acute Medical Unit, Tallaght Hospital, Dublin

Diabetic ketoacidosis (DKA) is potentially fatal. Recent guidelines emphasize ketone target driven treatment utilizing fixed dose IV insulin. A protocol in our institution reflects these guideline. We performed an audit of all adult patients presenting to Tallaght Hospital with DKA 2015. Here we compare outcomes to a similar audit performed prior to the introduction of this protocol.

Patients who presented between 01/01/15 and 31/12/15, who had a primary discharge diagnosis of DKA on HIPE coding were included. Medical records were reviewed and patients were subsequently excluded if the diagnosis of T1DM or DKA was felt to be incorrect. Patients with multiple presentations were treated as separate episodes. Anonymised data were inputted into a Microsoft Excel codebook. Identical methods were previously used to gather similar data between 01/01/12 and 31/12/13. Results were calculated using standard Excel functions. An episode pool of 66 was used in the audit of 2012–2013 compared to a pool of 46 episodes included in the 2015 audit. Capillary ketone testing is now used in all cases (100 % vs 5 %). The average time spent on IV insulin has decreased significantly (28 h vs 41 h). Long acting insulin is now more commonly continued during the admission (67 % vs 28 %). Hypoglycemia (29 % vs 53 %) and hyperkalaemia (25 % vs 46 %) now occur in fewer patients. The new guidelines for DKA management have been integrated into our DKA protocol. This seems to have resulted in better management of patients with DKA.

P130 Diabetic ketoacidosis at Tallaght Hospital: demographics and presenting features of DKA in 2015

Brady C[1], Costello R[1], Healy U[2], Widdowson M[2]

[1]School of Medicine, Trinity College, Dublin; [2]Acute Medical Unit, Tallaght Hospital, Dublin

Diabetic ketoacidosis (DKA) is a potentially fatal condition. To reduce the incidence of DKA we need to better understand the precipitating factors in our patient cohort. As such we carried out an audit of all adult patients presenting to Tallaght Hospital with DKA 2015. Here we present the predominant demographic, clinical, and presenting features seen. Patients who presented between 01/01/15 and 31/12/15, who had a primary discharge diagnosis of DKA on HIPE coding were included. Medical records were reviewed and patients were subsequently excluded if the diagnosis of T1DM or DKA was felt to be incorrect. Patients with multiple presentations were treated as separate episodes. Anonymised data were inputted into a Microsoft Excel codebook. Data averages, means and ranges were calculated using standard Excel functions. 48 episodes were included for analysis. The mean age was 31.7 years. 54 % involved female patients. The average HbA1c was 9.6 %. The average duration of diabetes was 18.6 years. 70.8 % were taking basal bolus insulin, 8.3 % were on a twice daily mixed insulin, and 4.2 % used an insulin pump. The most common presenting symptom was nausea and vomiting (72.9 %). 16.7 % of patients presented with reduced GCS. Missed insulin doses precipitated DKA in 41.6 %, not uncommonly in association with alcohol (14.5 %). Infection was a factor in 29.1 % of cases. Missed insulin doses and alcohol consumption are a factor in a significant number of DKA presentations and likely represent the major target for intervention.

P131 Endocrine factors associated with postprandial hypoglycaemia in patients with cystic fibrosis: a pilot study

Elamin Y[1], Hatton S[1], Kearns S[2], Martin-Grace J[1], Mckone E[2], Twomey P[3,4], Crowley RK[1,4]

[1]Department of Endocrinology, St. Vincent's University Hospital, Dublin; [2]Department of Respiratory Medicine, St. Vincent's University Hospital, Dublin; [3]Department of Chemical pathology, St. Vincent University Hospital, Dublin; [4]UCD School of Medicine, Belfield, Dublin 4

Postprandial hypoglycaemia in patients with cystic fibrosis (PWCF) is frequently reported but poorly understood. The aim of this pilot study was to investigate the aetiology of postprandial hypoglycaemia in PWCF.

Serum cortisol, insulin and C-Peptide were measured at the 2 h timepoint of the annual glucose tolerance test in 32 PWCF not known to have CF-related diabetes. Hypoglycaemia was defined as glucose <3.3 mmol/l. Patients were classified as Normal glucose tolerance (NGT; n = 17), Post prandial hypoglycaemia (PPH; 6) and Abnormal glucose tolerance (AGT; 9–3 CF related diabetes, 4 impaired fasting glucose and 2 impaired glucose tolerance). There was a difference in insulin level at 2 h between groups ($p = 0.007$, Wilcoxon); sub-analysis showed a difference between AGT (mean 48.9mu/l) and PPH groups (16.6 mu/l) (p 0.003) and between AGT and NGT groups (28.4 mu/l) (p 0.015). Of the PPH cases none had symptomatic hypoglycaemia. Three PPH cases with cortisol <500 nmol/l underwent short synacthen test (SST); 2 had a cortisol post-SST > 550 nmol/l. One patient showed suboptimal response with a cortisol level at 416 nmol/l and is undergoing further investigation. There were no differences between groups in body mass index (median 22.1 kg/m^2) or lung function. PPH occurred in 19 % of the cohort and was associated with detectable insulin at the 2 h OGTT timepoint, suggesting the possibility of dysregulated insulin release. AGT patients had higher insulin levels than NGT cases, suggesting relative rather than absolute insulin deficiency in this cohort of PWCF.

P132 The identification of novel metabolites that track with improvements in glycaemia following a 12-week lifestyle intervention in high risk individuals

O'Gorman DJ[1], Kennedy A[1], Cobb J[2], O'Donoghue G[4], Anderson G[4], McCaffrey N[1], Cleary S[1], Durkan E[1], Kenny H[1], Adam K-P[2], Sinnot M[3], Carr B[3], Thybo T[4], Nolan JJ[4]

[1]3U Diabetes Partnership and School of Health and Human Performance, Dublin City University, Ireland; [2]Metabolon, Inc., 617 Davis Drive, Suite 400, Durham N. C., U. S; [3]Vhi Healthcare, Lower Abbey St., Dublin, Ireland; [4]Steno Diabetes Centre, Copenhagen, Denmark

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The purpose of this study was to identify metabolite biomarkers, linked to dysglycaemia, that track with improvements in plasma glucose following a lifestyle intervention in individuals at high risk of developing type 2 diabetes. A total of 104 subjects participated in a 12-week lifestyle intervention. Oral glucose tolerance, body composition and fitness were determined before and after the intervention. A set of 23 candidate biomarker metabolites previously linked to dysglycemia were measured using stable isotope dilution. After the 12-week intervention fasting levels of 12 of the 23 metabolites were significantly different ($p < 0.05$). In subjects where fasting glucose decreased by > 10 % there was a significant decrease in plasma tyrosine, α-ketoglutarate and phenyalanine ($p < 0.05$) as well as increased glycine and serine ($p < 0.05$). A > 10 % decrease in 2-hr glucose was associated with significant decreases in branched-chain amino acid catabolites ($p < 0.05$), in addition to insulin, α-ketoglutarate, tyrosine ($p < 0.05$) and increased glycine ($p < 0.05$). The fold change in body weight was positively associated with the fold change in phenylalanine, tyrosine, leucine, isoleucine, 3-methyl-2-oxopentanoic acid and insulin ($p < 0.05$) and negatively associated with glycine ($p < 0.05$). The changes in aerobic fitness and % body fat were not associated with any of the metabolites. In conclusion, a subset of metabolites linked to dysglycaemia track with improvements in fasting and 2-hr glucose following a 12-week lifestyle intervention in high risk individuals. These metabolites are sensitive to small changes in metabolic function and may be useful for monitoring diabetes prevention programmes.

P133 Effects of 21-day best rest on skeletal muscle mitochondrial function

Kenny HC[1], Rudwill F[2], Breen L[1], Heer M[3], Blanc S[2], O'Gorman DJ[1]

[1]3U Diabetes, Dublin City University, Ireland; [2]CNRS, University of Strasbourg, France; [3]University of Bonn, Germany

The aim of this study was to determine if 21-days of bed rest decreased total and intrinsic mitochondrial respiration and if the changes could be mitigated by performing a combined resistance vibration exercise (RVE) protocol. Subjects ($n = 9$) completed 21-days bed rest without (CON) and with RVE using a randomized crossover design. The physiological response to inactivity was measured by VO_2 max, a hyperinsulinemic euglycemic clamp, resting metabolic rate (RMR) and body composition. The O_2 flux capacity of saponin permeabilized skeletal muscle fibres from the vastus lateralis was measured in response to carbohydrate and lipid substrates. There was a significant reduction in body mass and lean tissue mass ($p < 0.05$) but no change in fat mass following the CON and RVE trials. Insulin sensitivity and VO_2max were decreased in the CON but not RVE group ($p < 0.05$). There was a reduction in uncoupled respiration (LEAK), oxidative phosphorylation and electron transport system capacity in the CON but not RVE group ($p < 0.05$). Skeletal muscle citrate synthase activity was significantly lower in both groups ($p < 0.05$) and when used to normalize the respiratory data, only LEAK respiration remained significantly reduced and correlated with VO_2max, RMR and insulin sensitivity ($p < 0.05$). In conclusion, our data indicate that skeletal muscle mitochondrial respiration is decreased with bed rest but most of the changes are related to decreased mitochondrial content. The reduction in LEAK respiration represents an attempt by the mitochondria to maintain efficiency by prioritising coupled respiration and may be an important compensatory mechanism for inactivity.

P134 The prevalence of chronic kidney disease and albuminuria in patients with type 1 and type 2 diabetes attending a single centre

Majeed MS[1], Boran G[2], Behan LA[1], Sherlock M[1], Gibney J[1]

Departments of Endocrinology[1]; and Chemical Pathology[2]; The Adelaide and Meath Hospital, Incorporating the National Children's Hospital, Tallaght, Dublin 24

Chronic kidney disease (CKD) is an important complication of diabetes and determinant of mortality. Albuminuria represents early diabetic nephropathy, and also indicates generalised vascular dysfunction. Understanding the epidemiology of CKD and albuminuria helps inform health planning and identify opportunities to prevent or delay progression of diabetic kidney disease. The last available serum creatinine and urine albumin/creatinine ratio (UACR) in patients with type 1 (T1DM) or Type 2 (T2DM) diabetes recorded on the DIAMOND database were used for analysis. Patients were divided into tertiles of age. CKD was defined as eGFR <90 ml/min; microalbuminuria as UACR > 2.5 mg/mmol (male), > 3.5 mg/mmol (female); macroalbuminuria as UACR > 20 mg/mmol.

	T1DM, CKD	T1DM, No CKD	T2DM, CKD	T2DM, No CKD
	Number/ % (%NA/ MA/A/ND)	Number/ % (% NA/ MA/A/ND)	Number/ % (%NA/ MA/A/ND)	Number/ % (%NA/ MA/ND)
Age 18–58 (n = 2702)	271/27 % (60/13/6/ 21)	732/73 % (51/10/1/ 38)	721/42 % (56/14/4/ 26)	978/58 % (60/13/6/ 21)
Age 58–71 (n = 2704)	106/75 % (56/19/5/ 20)	36/25 % (45/23/6/ 26)	1736/67 % (50/17/5/ 28)	826/33 % (50/17/5/ 28)
Age 71–107 (n = 2704)	54/85 % (20/31/6/ 43)	9/15 % (44/22/11/ 23)	2244/84 % (40/28/6/ 26)	397/16 % (47/20/5/ 28)

NA-normal albumin excretion; MA-microalbuminuria; A-macroalbuminuria; ND-not done

CKD was common and increased with age. Microalbuminuria also increased with age and was similar in patients with and without CKD. Macroalbuminuria was uncommon. In summary, CKD is common in hospital-based diabetic patients. The low prevalence of macroalbuminuria indicates that this mostly does not reflect classical diabetic nephropathy.

P135 A rare case of hypocalcaemia

Bogdanet D[1], Boran G[2], Behan LA[1], Sherlock M[1], Gibney J[1]

Departments of Endocrinology[1]; and Chemical Pathology[2], The Adelaide and Meath Hospital, Incorporating the National Children's Hospital, Tallaght, Dublin 24

Barakat syndrome also known as hypoparathyroidism, deafness and renal dysplasia (HDR), is a rare autosomal dominant disorder (less than 25 cases worldwide described). The defect in the majority of

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cases has mapped to chromosome 10p. Haploinsufficiency of zinc-finger transcription factor GATA3 or mutations in the GATA3 gene appear to be the underlying cause of this syndrome. A 57 year-old man was referred to the Endocrinology clinic with a history of primary hypoparathyroidism. Past medical history included longstanding chronic kidney disease, bilateral renal cysts, sensorineural deafness, seizures, hypertension, megaloblastic anemia, iron deficiency anemia and vitamin D deficiency. He reports his first seizure at 16 years old in the context of ethanol consumption but also recalls being told that he had a calcium abnormality since infant years. Since presentation to our service 5 years ago, renal function and indices of bone and mineral metabolism have been stable. Fluorescent sequencing and multiple ligation dependent probe amplification confirmed Barakat (HDR) syndrome with a heterozygous mutation for c.896G>A p.(Arg299Gin). Barakat (HDR) syndrome can be diagnosed at any age. Recent advances in the genetics of Endocrine conditions increasingly allow unifying diagnoses in patients with unusual constellations of clinical features.

P136 Endocrine and metabolic status in a cohort of 24 adults with Prader–Willi Syndrome attending a single centre

Bogdanet D[1], Boran G[3], Behan LA[1], Sherlock M[1], Roche E[2], Gibney J[1]

Departments of Endocrinology[1]; Paediatric Endocrinology[2] and Chemical Pathology[3], The Adelaide and Meath Hospital, Incorporating the National Children's Hospital, Tallaght, Dublin 24

Prader-Willi syndrome (PWS) is a genetic condition usually diagnosed in childhood with reported prevalence ranging between 1 in 8000 and 1 in 45,000. Endocrine and metabolic abnormalities include hyperphagia and obesity, growth hormone deficiency and short stature, hypogonadism, osteoporosis, diabetes, hypertension and dyslipidaemia. It is likely that the phenotype of PWS in adulthood is changing due to changes in paediatric practice including intensive intervention to limit weight gain, and widespread use of sex steroid and growth hormone replacement. While most patients now live into adult life the majority of published data is from paediatric populations.

This was a retrospective observational study of endocrine and metabolic variables in adult patients with PWS performed in an Irish tertiary referral centre. Twenty-four adult patients (17 female) with a diagnosis of PWS were identified. Age, height and BMI (median (range)) were 25 (19–52) years, 154 (138–173) cm and 42 (17–69) kg/m^2, respectively. Eighteen had been assessed for growth hormone deficiency (GHD), 15 using the insulin tolerance test. Sixteen had severe GHD and fifteen had received GH therapy. All except one male were hypogonadal. Six (1 male) were receiving sex steroid replacement. Five of 10 who had a DXA scan had osteoporosis. Twelve were hypertensive and six had diabetes. Those with diabetes had a median (range) BMI of 47 (32–58) kg/m^2. In summary, endocrine and metabolic disorders are very prevalent in PWS adults. There is currently little evidence guiding optimal management of these disorders.

P137 A Phaeocrhomocytoma or not?

Frizelle I, Melvin A, Joyce C, O'Halloran DJ

Department of Endocrinology, Cork University Hospital

We report the case of fifty 4 year old lady referred for assessment of known right sided adrenal adenoma. She had a history of a left laparoscopic adrenalectomy for phaeochromocytoma in 2010 in Poland. She had a background history of hyperthyroidism due to a multinodular goitre, essential hypertension and bilateral nephrolithiasis. Medication consisted of a beta blocker, alpha blocker, thiazide diuretic and angiotensin- two antagonist, anti-inflammatories and levothyroxine. Serial radiological assessment showed the lesion was stable in size at four centimetres. Endocrine assessment showed normal overnight DST and plasma chromogranin A concentration. Twenty four hour urinary catecholamines measurements were normal. Twenty four urinary normetadrenaline levels were elevated on three occasions, up to twelve times the upper limit of normal, when measured by HPLC-ED while metadrenaline levels were normal. All other metanephrins were normal. A plasma sample measured by mass spectrometry in Newcastle showed normal metanephrin levels. An aliquot of the urine specimen was then sent to Birmingham for repeat metanephrin measures by mass spectrometry and the results were normal. Subsequently adrenal tissue blocks from 2010 were requested from Poland and reviewed by our pathology department who concluded the specimen was in keeping with a benign adrenal adenoma with no evidence of phaeochromocytoma. It is felt that drug interference by NSAIDs caused a false positive elevation in the urinary normetadrenaline levels measured by HPLC-ED. This case illustrates importance of critically evaluating all evidence in atypical neuroendocrine cases. Knowledge of methodology used in measurement of catecholamines and metanephrines is important in accurate interpretation of results in order to exclude assay interference. When the results aren't concordant, it is important to review the case, including accessing original tissue for review of the pathology. This case has important lessons in care of atypical adrenal lesions.

P138 Postmenopausal breast cancer, aromatase inhibitors, and bone health

Heneghan HM[1], McKenna M[2], Walshe J[3], Rothwell J[1], Evoy D[1], Geraghty J[1], McDermott E[1], Prichard RS[1]

[1]Department of Breast and Endocrine Surgery, St Vincent's University Hospital, Elm Park, Dublin 4, Dublin, Ireland; [2]Department of Endocrinology, St Michael's Hospital, Dun Laoghaire, Dublin, Ireland; [3]Department of Medical Oncology, St Vincent's University Hospital, Elm Park, Dublin 4, Dublin, Ireland

Background: Aromatase inhibitors (AIs) are the gold standard endocrine therapy for postmenopausal breast cancer (PBC) patients. However, they harbor side-effects due to near-complete estrogen suppression, most notably accelerated bone loss. Various guidelines exist for the management of bone health in AI-treated patients, however intervention strategies are not well-established. We aimed to evaluate adherence to such guidelines in an Irish cohort of AI-treated patients. **Methods:** All ER + PBC patients taking AIs were invited to complete a Bone Health Questionnaire as they attended SVUH for follow-up outpatient appointments. Patients' clinicopathologic data, including bone mineral density (BMD), were recorded. **Results:** Over a 4-week period, 48 AI-treated patients were reviewed (mean age 68.6 ± 10.8 years). Anastrozole was most commonly used (96 %) and mean duration of AI-therapy was 28 ± 18 months. Additional risk factors for BMD loss were noted in 65 %. No patient had a baseline DEXA scan prior to initiating AI-therapy, however a DEXA was performed in 25 % (n = 12) after a mean delay of 21 ± 12 months from initiation of AI-therapy. Of the 12 patients who had a delayed DEXA, 4 had normal BMD and 8 (66 %) were osteopenic or osteoporotic. Whilst oral calcium and Vitamin D

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supplements were prescribed in 85 %, only two patients were prescribed an antiresorptive agent (denosumab) at a mean time of 13 months after commencing AI. **Conclusion:** This data reflects our poor compliance with guidelines for bone health management in AI-treated PBC patients. Reasons for this are multifactorial and include restricted access to DEXA imaging and limited awareness of the benefits of antiresorptive agents in this population. Highlighting these issues will help improve management of bone health in our patients.

P139 A study comparing point of care testing to standard Oral Glucose Tolerance Test in the diagnosis of Gestational Diabetes

Hannon AM[1], Kennedy A[1], Tahriq S[1], O'Donovan A[1], Stapleton M[2], Joyce C[2], Butler M[2], O'Riordan M[3], Tuthill A[1]

[1]Department of Diabetes and Endcrinology, Cork University Hospital; [2]Department of Biochemisty, Cork University Hospital; [3]Department of Obstetrics and Gynaecology, Cork University Maternity Hospital

Gestational Diabetes is rapidly increasing in prevalence. With growing evidence for universal screening there is increasing interest in alternative cost-effective methods for screening. We collected fasting, 1 and 2 h samples from 64 women who attended the gestational diabetes screening clinic. All women were 24–28 weeks gestation. A standard 75 g 2 h OGTT was performed. A capillary sample was taken and analysed using a point of care device (POCT). A further fingerprick sample was analysed in the laboratory and this was compared to the venous plasma glucose. Gestational Diabetes was diagnosed using IADPSG criteria. 11 patients met the criteria for gestational diabetes according to the gold standard 2 h OGTT. When POCT was used, 22/60 patients met criteria—sensitivity 91 % and specificity of 76 %. 5/64 patients in the lab analysed capillary samples met criteria—sensitivity 45 % and specificity 100 %. The average fasting plasma glucose was 4.8 in the overall group and 5.6 in the patients who met diagnostic criteria. If fasting plasma glucose was combined with 1 and 2 h capillary point of care testing sensitivity rose to 100 % and specificity to 86 %. Previous studies have quoted that CBG testing can save up to 80 % of costs when compared to plasma samples. This pilot study would suggest POCT may be a viable initial screening option for gestational diabetes, is easy to perform, even in women with an elevated BMI, and provides immediate results, reducing costs of follow-up. Sensitivity was significantly improved combining fasting plasma glucose and capillary testing.

P140 Radioiodine induced pancytopenia in thyroid Cancer treatment

Kennedy A, Hannon AM, Tuthill A

Department of Endocrinology and Diaebtes, Cork University Hospital

Radioiodine is a commonly used treatment in thyroid disease. It is generally well tolerated, however with increased dose there are greater side effects.

We present the case of a 73 year old woman referred with an incidental finding of pulmonary nodules on a chest X-ray. She had a background of a right thyroid lobectomy for a benign multinodular goitre. Lung biopsy histology confirmed metastatic follicular thyroid carcinoma. She underwent a completion thyroidectomy and radio iodine ablation therapy (RAI). A haemangiomatous lesion on her forehead was noted in clinic. Histology confirmed further metastatic disease. Her thyroglobulin was > 1000 ug/L and a radioisotope scan showed uptake in the lung, thyroid bed and salivary glands. Further RAI was planned. She underwent five cycles of RAI ablation over a 3 year period. 6 weeks following her final course, pancytopenia was noted (WCC1.6 Hb 7.6 platlets 74). The presentation was concerning for marrow infiltration. Full Haematological screen was normal. Her previous FBCs were reviewed and a mild transient bone marrow suppression was noted post each RAI treatment. The most severe episode was following her fifth treatment with spontaneous recovery of counts over an 8 month period. Bone marrow suppresion is a rare but documented potential side effect of RAI. This typicaly occurs with higher doses of radiation. This case highlights bone marrow suppresion as a potential side effect of RAI. Secondly, it also demonstrates the importance to consider skin metastasis if a patient with follicular thyroid carcinoma presents with new skin lesions.

P141 Screening for obstructive sleep apnoea in high risk women attending for screening for gestational diabetes

Hannon AM[1], Kennedy A[1], Tariq S[1], O'Riordan M[2], Tuthill A[1]

[1]Department of Diabetes and Endocrinology, Cork University Hospital; [2]Department of Obstetrics and Gynaecology, Cork University Maternity Hospital

Excessive tiredness is a common problem in pregnant women. Previous literature has suggested an increased incidence of Obstructive Sleep Apnoea (OSA) in pregnant women. The association between OSA, obesity and diabetes is well established and is a predictor of poorer outcomes in pregnancy. We surveyed 60 women in the Gestational Diabetes screening clinic at our local maternity hospital. The Epworth Sleep Score (ESS) was used as a screening tool for Obstructive sleep apnoea. Women completed the ESS and basic demographic data from their booking visit was recorded e.g. height, weight, BMI and comorbidities. All women were between 24 and 28 weeks pregnant. Twin pregnancies were excluded. No patient had a previous diagnosis of Obstructive Sleep Apnoea (OSA). One patient was actively smoking. The average BMI was 28.49 with a range of 18.5 to 55.4. The average age was 34 years—range of 19–43 years. 44/60 were Irish ethnicity, 5/60 southeast Asia and 8/60 were Eastern European and 3/60 African ethnicity. 6 of the 60 women had an abnormal score (> 10 on the questionnaire), with 5 having borderline results (10–12). Only one woman had an abnormal reading of 13. The average BMI of those with an abnormal score was 30.8. Of the 60 women surveyed, 11 failed the OGTT. Of these 11 women, only one had an elevated ESS. This small pilot study does not suggest an association between OSA and gestational diabetes. It also suggests that the incidence of sleep apnoea is lower than expected in this high-risk pregnancy group.

P142 Comparison of 1- and 2-h plasma glucose in screening for gestational diabetes: sensitivity and cost

Hannon AM[1], Kennedy A[1], Tahriq S[1], O'Donovan A[1], Stapleton M[2], O'Riordan M[3], Butler M[2], Tuthill A[1]

[1]Department of Diabetes and Endocrinology, Cork University Hospital; [2]Department of Biochemistry, Cork University Hospital; [3]Department of Obstetrics and Gynaecology, Cork University Maternity Hospital

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There is increasing support for universal screening for gestational diabetes (GDM), however there is ongoing difficulty in providing this service in the community in our region due to lack of resources, particularly staff and time constraints. We wished to explore if a 1-h glucose reading was a better predictor of GDM than the 2-h value which would reduce the duration of time women needed to wait in a GP surgery/hospital clinic for testing with associated reduction in costs such as carparking and childcare.

We performed a 75 g 2 h Oral Glucose Tolerance Test (OGTT) on 68 women attending the GDM screening clinic at our centre. All women had been identified as high risk and referred for screening at 24–28 weeks. Fasting, 1 and 2 h samples were sent for analysis. IADPSG criteria were used for diagnosis. The average age was 34 and average BMI 28.4 (range of 18.5 -55.1). 11/68 women (16.2 %) tested met criteria for GDM. All 11 positive women had either abnormal fasting or 1 h glucose readings or both; none had abnormal 2 h values. This small pilot study would support the increased sensitivity of the 1-h plasma glucose check over the 2-h value on a standard OGTT for diagnosis of GDM. This should be associated with significant cost-savings when this test is performed in primary care and may increase the acceptability of this screening test to be performed in general practice.

P143 Does PCOS confer increased cardiometabolic risk after adjustment for simple measures of central adiposity?

Agnieszka Pazderska[1], Tommy Kyaw Tun[2], Niamh Phelan[3], Lucy Ann Behan[4], Gerard Boran[5], James Gibney[6]

[1]Department of Endocrinology, Adelaide and Meath Hospital, Dublin, Ireland; [2]Department of Endocrinology, Adelaide and Meath Hospital, Dublin, Ireland; [3]Department of Endocrinology, Adelaide and Meath Hospital, Dublin, Ireland; [4]Department of Endocrinology, Adelaide and Meath Hospital, Dublin, Ireland; [5]Department of Clinical Biochemistry, Adelaide and Meath Hospital, Dublin, Ireland; [6]Department of Endocrinology, Adelaide and Meath Hospital, Dublin, Ireland

Numerous cardiometabolic abnormalities are recognised in women with PCOS. However, over-emphasis on PCOS as a cardiometabolic risk factor potentially results in over-treatment of some women with, and under-recognition of risk in women without PCOS. A simple measure unifying cardiometabolic risk in women with and without PCOS would help overcome this problem. We conducted (Study-1); an exploratory cross-sectional study investigating the association of potential cardiometabolic risk markers (PCOS status, BMI, waist circumference (WC), hsCRP, HOMA-IR, SHBG) with indices of glucose (frequently-sampled-intravenous-glucose-tolerance-test (fsIVGT)) and lipid metabolism (post-prandial studies and lipoprotein particle size) in 29 PCOS women and 32 age-matched controls: (Study-2); a cross-sectional study in 103 PCOS women and 102 age- and BMI-matched controls to validate findings from Study-1. Stepwise regression modelling In Study-1 revealed WC to be the most promising marker, independently predicting insulin-sensitivity-index, glucose-effectiveness and disposition-index (all derived from fsIVGT); fasting and AUC HDL (from post-prandial studies); and HDL particle size. Before adjustment for WC in Study-2, plasma triglycerides, glucose and hsCRP, insulin resistance, serum amyloid A, HDL-associated phospholipid transfer protein and proportion non-A LDL pattern were greater, while fasting HDL, total and HMW adiponectin were lower in PCOS women compared with BMI-matched controls ($P < 0.05$). Following adjustment for WC, no differences were seen between groups. In summary, a number of cardiometabolic abnormalities in PCOS are intrinsically related to central obesity and following adjustment for WC do not differ from normal subjects. This provides preliminary evidence that measurement of WC should take precedence over PCOS status in determining cardiometabolic risk in reproductive-age women.

P144 Investigating the impact of a single nucleotide variant in NRG1 on thyroid cancer risk

Una McVeigh[1], Terri McVeigh[2], Patrick Owens[3], Derek Morris[4], Nicola Miller[5], Aoife Lowery[6], Michael Kerin[7]

[1]NUI Galway; [2]Our Lady\'s Children\'s Hospital Crumlin; [3]NUI Galway; [4]NUI Galway; [5]NUI Galway; [6]NUI Galway; [7]NUI Galway

Introduction: The Neuregulin1 (NRG1) gene is located on the short arm of chromosome 8(8p). NRG1 is known to interact with EGFR and HER2, and has an anti-proliferative function. An intronic variant (C > G) in NRG1(rs2439302), has been implicated in thyroid cancer in certain populations. The Irish population has relatively little admixture compared to more genetically heterogeneous populations, and the frequency of this variant in this cohort has not previously been investigated. Furthermore, the genetic architecture for non-medullary thyroid cancer has not been fully characterised.
Aim: We aimed to investigate the frequency and impact of rs2439302 in predisposition to differentiated thyroid cancer in Ireland.
Methods: A case–control study was undertaken. Patients with mutations in high-risk cancer susceptibility genes (e.g. RET/PTEN) were excluded. Controls included adults with no personal cancer history and no familial history of thyroid cancer. DNA was extracted from whole blood/buccal swabs by ethanol precipitation, and genotyped for the variant using a Taqman-based platfrom. Data was analysed using SPSS.
Results: The minor allele frequency in our cohort was 0.48. Significantly increased risk of disease was associated with the heterozygous genotype (CG), with odds ratio 1.75 (95 % CI 1.18–2.58), $p = 0.0048$, but bi-allelic mutations (GG) at this locus were not associated with disease in our cohort (OR 1.13 (0.74–1.74), $p = 0.57$).
Conclusion: In this series, a single copy of the G allele was associated with significantly increased risk of thyroid cancers, but this risk did not appear to be associated with the homozygous genotype.

P145 Diabetes management in hospitalised medical and surgical patients

Abdalla A, Abdalla S, Mawe E, Frizelle I, Tuthill A

Department of Endocrinology and Medicine, Cork University Hospital, Cork, Ireland

Background: Patients with type 1 or type 2 diabetes mellitus are frequently admitted to a hospital. Glycaemic control is likely to become unstable in these patients because of the stress of the illness or procedure, the concomitant changes in dietary intake and physical activity, and the frequent interruption of the patient's usual anti-hyperglycaemic regimen. The aim of this study was to evaluate the adequacy of glycaemic control in hospitalised medical and surgical patients in a tertiary care centre.
Methods: A prospective clinical audit between 22/2/2016 and 7/3/2016 was facilitated through a review of patient medical and drug records, laboratory and capillary blood glucose monitoring and

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results. The data was analysed using descriptive statistics and multi-group comparisons for categorical variables and continuous variables.
Results: Seventy-eight patients were included during the audit period. Mean age was 68 years SD (±15), 53 % were male, 80 % were admitted through the emergency department, with the majority (83 %) having type 2 diabetes. Approximately 10 % of patients during their stay were self-testing and self-adjusting insulin doses. Diabetic control defined by quartiles varied with 53 % of patients being hyperglycaemic at least 25 % of the time and 10 % not achieving glycaemic control during their entire stay. Only 20 % of the cohort was reviewed by the diabetic multidisciplinary team.
Conclusion: Diabetic patients are frequently admitted to hospital with only a small proportion achieving adequate glycaemic control during their stay and a minority benefitting from diabetic MDT input. Efforts at reducing length of stay in these complex patients should address these shortcomings.

P146 Forearm DEXA utility in primary hyperparathyroidism

Abdalla A, Abdalla S, Tuthill A

Department of Endocrinology and Medicine, Cork University Hospital, Cork, Ireland

Background: A reduction in bone mineral density (BMD) is common in primary hyperparathyroidism (PHPT), above all at cortical sites. Guidelines for the management of asymptomatic PHPT (aPHPT) recommend a BMD evaluation at the lumbar spine, hip, and forearm. Surgery is recommended for patients with a T-score _-2.5 at any of these sites. However, a BMD evaluation at the forearm is not routinely performed. The aim of this study was to evaluate the impact of measuring forearm BMD in the clinical management of PHPT.
Methods: We retrospectively analysed a prospective dataset of 185 patients with PHPT diagnosed in a tertiary care centre from 2000 to 2015. Data extracted included demographic details, dual X-ray absorptiometry (DEXA) results at all sites measured, surgical and biochemical data. The data was analysed using descriptive statistics and multi-group comparisons for categorical variables and continuous variables.
Results: One hundred and eighty-five patients were included in the analysis, 80 % of whom were female. Mean age was 69 years with SD ± 13. Of the entire cohort 40 % underwent parathyroidectomy. Mean Lumbar BMD was 1.05 g/cm3 (±0.2) corresponding to a T-score of -1.26 (±1.1). Forearm DEXA assessment was performed in 28 patients, with 10 patients meeting surgical criteria based on this score and only 3 patients having the lowest T score at the forearm alone.
Conclusion: Forearm DEXA assessment is infrequently utilised in patients with PHPT and in a minority of cases it may be the sole indication for surgical treatment.

P147 Systemic predictors of the function of small and large HDL particles in type 1 diabetes

Ahmed M[1], Guo W[2], McGillicuddy FC[2], Gibney J[1]

[1]Department of Endocrinology, The Adelaide and Meath Hospital, Incorporating the National Children's Hospital, Tallaght; [2]Diabetes Complications Research Centre, School of Medicine, University College Dublin, Belfield, Dublin

Individuals with type 1 diabetes (T1D) are at increased risk of cardiovascular disease (CVD), despite having normal-to-high levels of high-density lipoprotein (HDL)-cholesterol. HDL particles mediate cholesterol efflux from peripheral cells, including lipid laden foam-cells of atherosclerotic lesions, and deliver acquired lipid to the liver for excretion. Measurement of the efflux function of HDL particles in turn is a better predictor of CVD than HDL-C alone. Cellular efflux to small HDL particles is mediated via ABCA1 ('ABCA1-dependent efflux), while larger particles accept cholesterol via ABCG1 and SR-BI ('ABCA1-independent efflux'). This study evaluated total, ABCA1-dependent and ABCA1-independent efflux function of HDL particles in a female type 1 diabetic cohort (mean age 27.94 ± 12 years, BMI 25.73 ± 26, n-103) and correlated to measures of inflammation, body-weight and lipid parameters using Pearson's Correlation testing. Total cholesterol levels positively correlated with total ($r = 0.3$, $p < 0.01$), ABCA1-dependent ($r = 0.245$, $p < 0.05$) and ABCA1-independent ($r = .196$, $p < 0.05$) efflux. Interestingly only ABCA-1independent efflux correlated with HDL-C levels ($r = 0.633$, $p<0.001$) with no association to ABCA1-dependent efflux ($r = -0.117$, $p = 0.239$). By contrast a positive correlation was observed between plasma triglyceride concentrations and ABCA1-dependent efflux ($r = 0.235$, $p < 0.05$) with no association to ABCA1-independent efflux ($r = -0.039$, $p = 0.698$). No association was observed between HDL efflux function and BMI, age or HbA1c levels. These findings demonstrate that efflux to larger HDL particles, but not smaller HDL particles, is largely determined by HDL-C levels in type 1 diabetes. Interestingly the efflux function of smaller HDL particles, but not larger HDL particles, was increased under the setting of hypertriglyceridemia in type 1 diabetes.

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