CalSoc 2015

caledonian society for endocrinology and diabetes

Dunkeld Hilton
November 27th/28th

calsoc.org

Contents

Programme of Events

Friday 27th November

13.30 – 14.30 Registration

Session 1

Chair: Dr David Carty
Consultant Endocrinologist
Glasgow Royal Infirmary

14.30 – 15.15 **Pituitary tumours: an update**
Professor John Wass
Professor of Endocrinology
Oxford Centre for Diabetes, Endocrinology and Metabolism

15.15 – 16.00 **Contemporary endocrine imaging**
Dr. Dilip Patel
Consultant Radiologist
Royal Infirmary of Edinburgh

16.00 – 16.15 Coffee

16.15 – 17.00 **Hyperthyroidism: diagnosis, management and long-term consequences**
Dr. Kristien Boelaert
Reader and Honorary Consultant Endocrinologist
University of Birmingham, Institute of Metabolism and Systems Research

17.00 – 17.45 **CalSoc Network Discussion**

17.00 – 19.00 Drinks

19.00 Dinner

Programme of Events

Saturday 28th November

08.45 – 09.00 CalSoc Annual General Meeting

Session 2

Chair: Dr Russell Drummond
Consultant Endocrinologist
Glasgow Royal Infirmary

09.00– 09.45 **Endocrine hypertension – molecules and genes**
Dr Marie Freel
Consultant Endocrinologist and Honorary Clinical Associate Professor
Queen Elizabeth University Hospital, Glasgow

09.45 – 10.45 **Abstract Presentations**
Dr Marcus Lyall, University of Edinburgh
Dr Nyo Nyo Tun, University of Edinburgh
Dr Anna White, University of Glasgow

10.45 – 11.00 Coffee

11.00 – 11.45 **Abstract Presentations**
Dr Anna Anderson, University of Edinburgh
Dr Natasha Sawhney, Aberdeen Royal Infirmary
Dr Tom Chambers, University of Edinburgh

11.45 – 12.30 **Clinical uncertainties in the management of MEN1**
Dr Paul Newey
Senior Lecturer and Honorary Consultant Physician
University of Dundee

12.30 – 13.30 Lunch

Welcome to CalSoc 2015

Thank you for joining us in Dunkeld for the 35th winter meeting of the Caledonian Society for Endocrinology. Last year's meeting proved a great success, with an impressive lineup of speakers from across the United Kingdom. This year's meeting promises to be equally stimulating with an exciting mix of updates from expert lecturers and research presentations from Scottish trainees.

You will see that time has been allocated, in this year's programme, to discuss potential clinical audit and research projects under the auspices of CalSoc. We would envisage the next step, having reestablished the annual meeting, is to realise the potential of CalSoc as a force for encouraging collaboration between Scottish centres, with a view towards improving endocrine care.

Finally, many thanks to our sponsors: BI/Lilly, MSD, Novo Nordisk and Sanofi for their continuing generous support.

Dr Fraser Gibb
On behalf of the CalSoc Committee

CalSoc Committee

Professor Graham Leese
Consultant Physician and Honorary Professor
Ninewells Hospital / University of Dundee

Dr Russell Drummond
Consultant Physician and Honorary Clinical Associate Professor
Glasgow Royal Infirmary / University of Glasgow

Dr Fraser Gibb (Secretary-Treasurer)
Consultant Physician and Honorary Senior Clinical Lecturer
Royal Infirmary of Edinburgh / University of Edinburgh

Dr Sam Philip
Consultant Physician and Honorary Clinical Lecturer
Aberdeen Royal Infirmary / University of Aberdeen

'Caledonian Society for Endocrinology & Diabetes Annual Meeting' has been approved by the Federation of the Royal Colleges of Physicians of the United Kingdom for 6 category 1 (external) CPD credits. Code 101583

Attendees

First name	Second name	Centre	Title
Anna	Anderson	Edinburgh	ST
Nick	Barwell	Forth Valley	Consultant
Kristien	Boelaert	Birmingham	Consultant
David	Carty	Glasgow	Consultant
Tom	Chambers	Edinburgh	ST
Zhuo Min	Chong	Glasgow	ST
Louise	Clark	Dumfries	Consultant
Catriona	Clarke	Edinburgh	Biochemist
Jenna	Cowan	Glasgow	ST
Marion	Devers	Monklands	Consultant
Kerri	Devine	Wishaw	CT
Anna	Dover	Edinburgh	Consultant
Jane	Dymott	Aberdeen	Consultant
Evgenia	Foteinopoulou	Aberdeen	ST
Marie	Freel	Glasgow	Consultant
Iona	Galloway	Glasgow	ST
Fraser	Gibb	Edinburgh	Consultant
Fiona	Green	Dumfries	Consultant
David	Hill	Wishaw	Consultant
Kate	Hughes	Glasgow	Consultant
Berit	Inkster	Edinburgh	ST
Alan	Jaap	Edinburgh	Consultant
Pauline	Jones	Edinburgh	Consultant
Chris	Jones	Inverclyde	Consultant
Chris	Kelly	Forth Valley	Consultant
Chris	Kueh	Glasgow	ST
Catriona	Kyle	Edinburgh	ST
Robert	Lindsay	Glasgow	Consultant
Marcus	Lyall	Edinburgh	Research Fellow
David	Macfarlane	Inverness	Consultant
Alison	Mackenzie	Forth Valley	Consultant
Alasdair	Mackie	Dundee	Consultant
Sharon	Mackin	Glasgow	ST4
Laura	McCreight	Glasgow	ST
David	McGrane	Glasgow	Consultant
Gerry	McKay	Glasgow	Consultant
Emily	McMurray	Edinburgh	Consultant
Kenneth	Muir	Aberdeen	ST
Bala	Muthukrishnan	Edinburgh	ST
Paul	Newey	Dundee	Consultant
Dilip	Patel	Edinburgh	Consultant
Colin	Perry	Glasgow	Consultant
Sam	Philip	Aberdeen	Consultant
Spurgeon	Rachaprolu	Aberdeen	Clinical Fellow
Laura	Reid	Edinburgh	ST
Stuart	Ritchie	Edinburgh	Consultant
Natasha	Sawhney	Aberdeen	CT
Cathy	Shearing	Edinburgh	Biochemist
Karen	Smith	Glasgow	Consultant
Chris	Smith	Paisley	Consultant
Mark	Strachan	Edinburgh	Professor
Maria	Talla	Glasgow	ST
Adnan	Tariq	Aberdeen	ST
Nyo Nyo	Tun	Edinburgh	ST
Liesbeth	Van Look	Edinburgh	Consultant
Brian	Walker	Edinburgh	Professor
John	Wass	Oxford	Consultant
Anna	White	Glasgow	ST
Rachel	Williamson	Borders	Consultant
Rohana	Wright	Edinburgh	Consultant
Nicola	Zammitt	Edinburgh	Consultant

Prof John Wass

Biography

John Wass is the Professor of Endocrinology at Oxford University and was Head of the Department of Endocrinology at the Oxford Centre for Diabetes, Endocrinology and Metabolism, Churchill Hospital Oxford, UK until 2012.

His research interests include all pituitary tumours, especially acromegaly, adrenal disease, angiogenesis in endocrinology, and the genetics of osteoporosis and thyroid disease.

Since 1975 he has published over 380 articles in scientific journals and as well as written many reviews and chapters in textbooks including the Oxford Textbook of Medicine and DeGroot's Textbook of Endocrinology. He has also edited a number of different textbooks including the Oxford Textbook of Endocrinology, Clinical Endocrine Oncology and the Oxford Handbook of Endocrinology (3 editions). He was President of the European Federation of Endocrine Societies from 2001-2003 and was Chairman of the Society for Endocrinology (2006-2009. He has also served as President of the Pituitary Society.

He has won a number of prizes and given named lectures including the Jubilee Prize of the Society for Endocrinology. He was recently in June last year awarded the Distinguished Physician of the Year Award by the American Endocrine Society; the first non American to ever receive this award.

Amongst his charitable activities, he is Patron of the St. Pauls Way School (with Professor Brian Cox) and he founded the Pituitary Foundation.

He was Academic Vice President of the Royal College of Physicians in London, from August 2012 until August 2015.

He chaired the Royal College of Physicians Working Party 'Action on Obesity: Comprehensive Care for All' published in January 2013, and has been involved improving services for patients with obesity.

Recently he presented the acclaimed documentary 'The Fantastical World of Hormones' on BBC4.

Abstract

Pituitary Tumours occur commonly and account for 10% of intracranial neoplasms. One person per thousand has a significant pituitary tumour either functioning or non-functioning.

The commonest of these are prolactinomas. In women these present with amenorrhoea or galactorrhoea and infertility and in men with impotence or loss of libido. These symptoms should be investigated by measuring prolactin in both men and women. Prolactinomas normally respond dopamine agonists but between 10-15% of them do not and this is a commoner occurrence in tumours that are large. Disconnection hyperprolactinaemia which refers to compression of the pituitary stalk by a non functioning tumour or craniopharyngioma causes prolactin elevation up to 3,000 mU/L but levels above this are likely to reflect a prolactinoma which therefore mostly responds to medical therapy. Prolactinomas may cause hypopituitarism and this rarely reverses with treatment apart from the gonadal axis. Attempts to stop treatment may be successful after two years for a microprolactinoma and five years for a macroprolactinoma. Cessation of treatment with dopamine agonists rarely is associated with long-term normality of prolactin.

Non-functioning pituitary tumours occur next most commonly. They may occur in all age groups and recently have been shown to be associated whether they are cured or not with a slightly decreased life expectancy. They tend to present in men and women with hypogonadism and in men this can be of longstanding because of the fact that

symptoms of low libido and impotence are rarely reported in men. Primary treatment is with surgery and recurrence rates vary according to the degree of tumour removal. If there is an empty sella postoperatively this is unlikely at ten years but if the sella has got some residual tumour some 50% of tumours recur at this time when radiotherapy may need to be given.

Acromegaly is a rare disease and is often diagnoses late. Primary treatment is with surgery and this is most importantly done by a surgeon with experience of 30 or 40 cases per year of pituitary tumours. Experience improves outcome. Post operatively cabergoline or somatostatin analogues can be used and if there is residual disease and non responsiveness to these two drugs radiotherapy may be helpful, over a prolonged period of time, to improve biochemical control.

The study of pituitary tumours has over the last 15 years been a very rapidly advancing field. New treatments are available for acromegaly but therapy is expensive and needs to be carried out in centres with experience in order to optimise outcomes.

81,449 Inhabitants
91% of study population

	PRL	NFA	ACRO	CD	TOTAL
Total No.	37	18	7	1	64
Prevalence (100,000)	45.6	22.2	8.6	1.2	78.8
Duration of symptoms (yrs)	0.5-12	0-8	1.5-15	7	

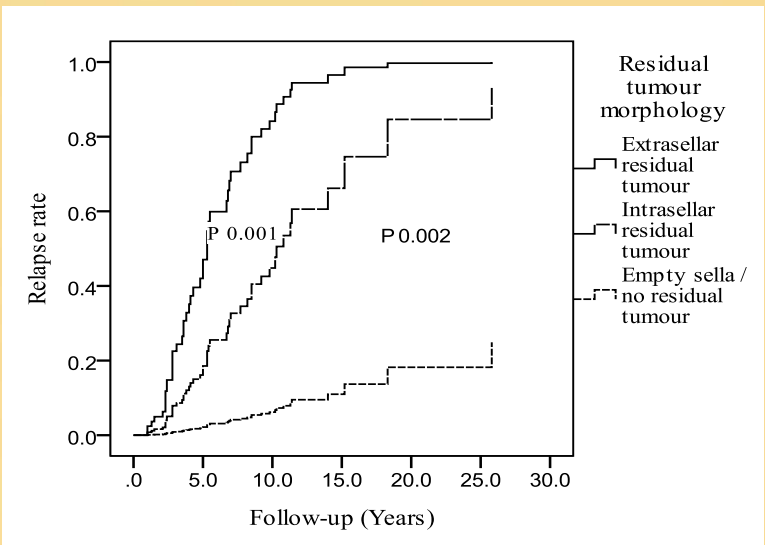
Prevalence 79/100,000

Prof John Wass

Table 3. Outcome of follow-up imaging

	Total tumours	Microadenomas	Macroadenomas
Mean follow-up, months (range)	42 (8–128)	41 (8–128)	43 (9–98)
Increase in size, *n* (%)	14/40 (35)	2/16 (12·5)	12/24 (50)
Mean time of detection, months (range)	34·3 (11–98)	21 (20–22)	36·5 (11–98)
Stable, *n* (%)	21/40 (52·5)	13/16 (81·3)	8/24 (33·3)
Decrease in size, *n* (%)	5/40 (12·5)	1/16 (6·3)	4/24 (16·7)
Mean time of detection, months (range)	24·6 (7–46)	19 (–)	26 (7–46)

Figure 1: Relapse rate according to postoperative scan classification



FOLLOW UP ALGORHITHM for NFAs

Operation (Euthyroid ± steroid cover)

Reassess post operatively @ 6 weeks All axes even if hypopituitarism pre-op

Synacthen + ITT + basals
- -T3 peri-operative
- -12% recovery

3 months post op scan

Little residual tumour + no cavernous sinus tumour
↓
Annual MRI pituitary
- 5 years
- then 2 yearly

Residual tumour + cavernous sinus involvement
↓
Adjuvant external beam pituitary irradiation
↓
Annual pituitary function tests + visual fields

Monitoring

Annual monitoring of
- GH - g.t.t.<1, basal <1.8ng/L
- IGF_1 - normal

+/- MRI pituitary

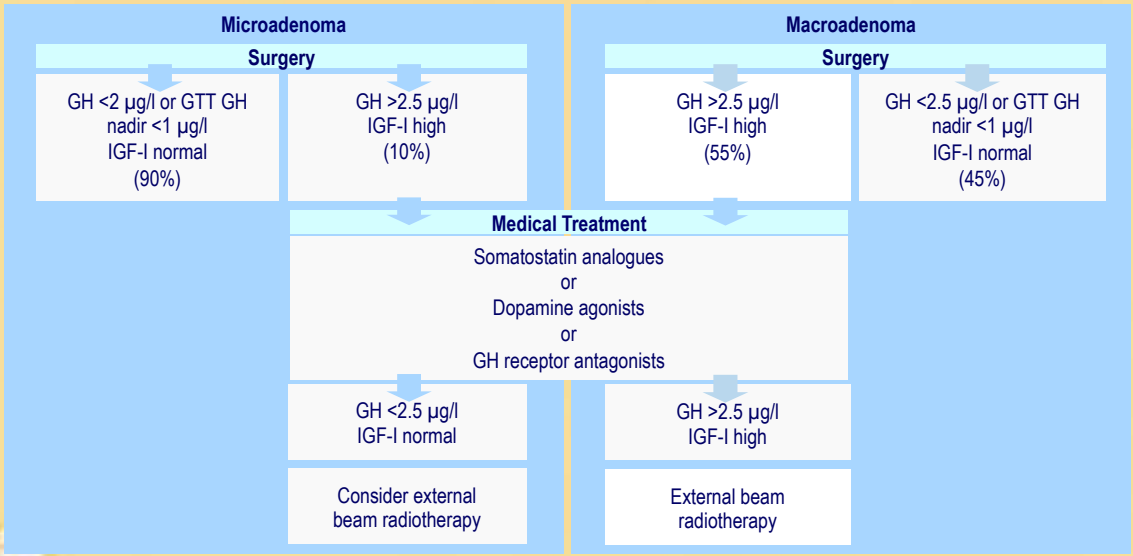
Cardiovascular
- blood pressure
- echo

Carbohydrate metabolism

Rheumatology

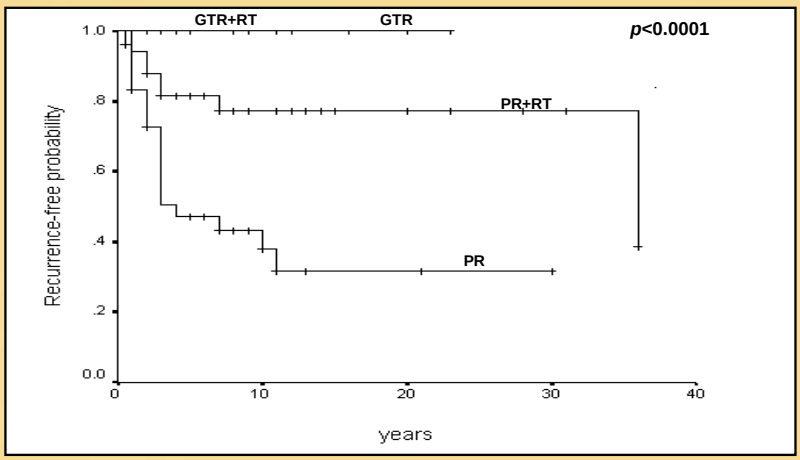
Colonoscopy/mammography/PSA

Treatment Paradigms in Acromegaly



From Wass, Lamberts & Melmed in *Handbook of Acromegaly*, edited by John Wass. Bristol: BioScientifica

Recurrence-free probability



	GTR	GTR+RT	PR	PR+RT
10-yrs	100%	100%	38%	77%

Median time of 1st recurrence: 2.5 yrs in both groups (0.5-36).

Karavitaki *et al.*, 2005

Dr Dilip Patel

Biography

Dilip Patel graduated from the University of Newcastle Upon Tyne in 1988. After initially training in General and Respiratory medicine he completed Radiology training in Perth, Western Australia and Edinburgh.
He has been a Consultant Radiologist at the Royal Infirmary of Edinburgh since 1999 and is the Lead Radiologist for Radionuclide Imaging at the RIE and Clinical Lead for PET/CT, NHS Lothian.
His clinical and research interests include Endocrine, NET, Hepatobiliary and Upper GI Imaging and he is the Lead Radiologist for the Lothian Endocrine, Neuroendocrine Tumour and Upper GI cancer MDTs.

Abstract

The past twenty years has seen spectacular changes in imaging technology with major advances made in ultrasound, CT and MRI. Functional imaging is now a firmly established clinical tool with SPECT/CT and PET/CT combining the unique physiological information obtained from nuclear medicine techniques with the anatomical detail obtained from CT in the form of hybrid imaging.

This lecture will outline the current role of the various imaging modalities in the investigation of thyroid, parathyroid and adrenal disease and neuroendocrine neoplastic disease. Current opinion regarding the investigation of the adrenal incidentaloma and a radiological perspective of the BTA guidelines on ultrasonic assessment of thyroid nodules will also be discussed.

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Nuclear imaging in the diagnosis of primary aldosteronism.
Curr Opin Endocrinol Diabetes Obes. 2015 Jun; 22(3): 150-6.

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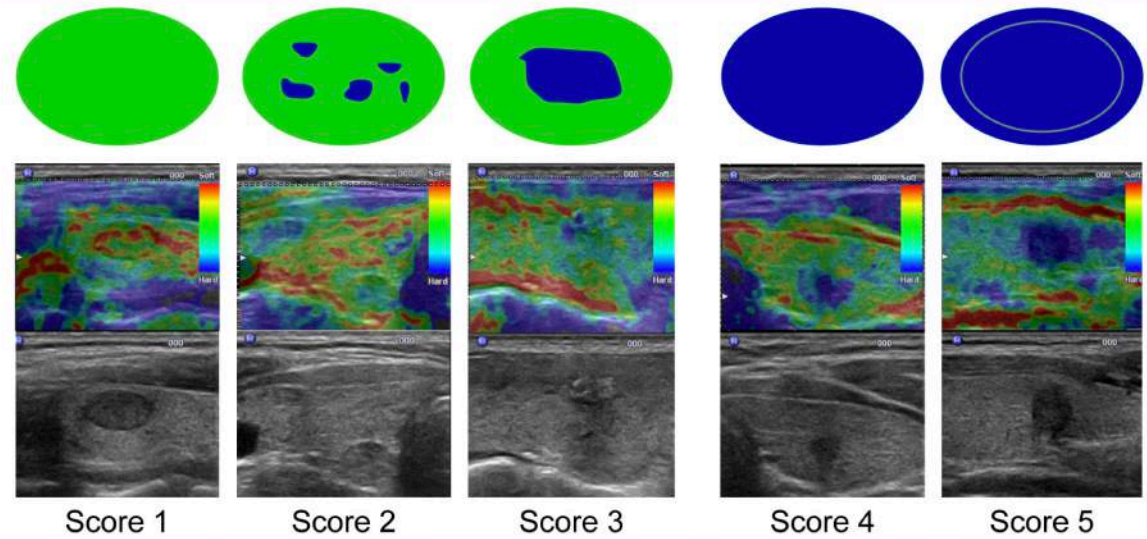
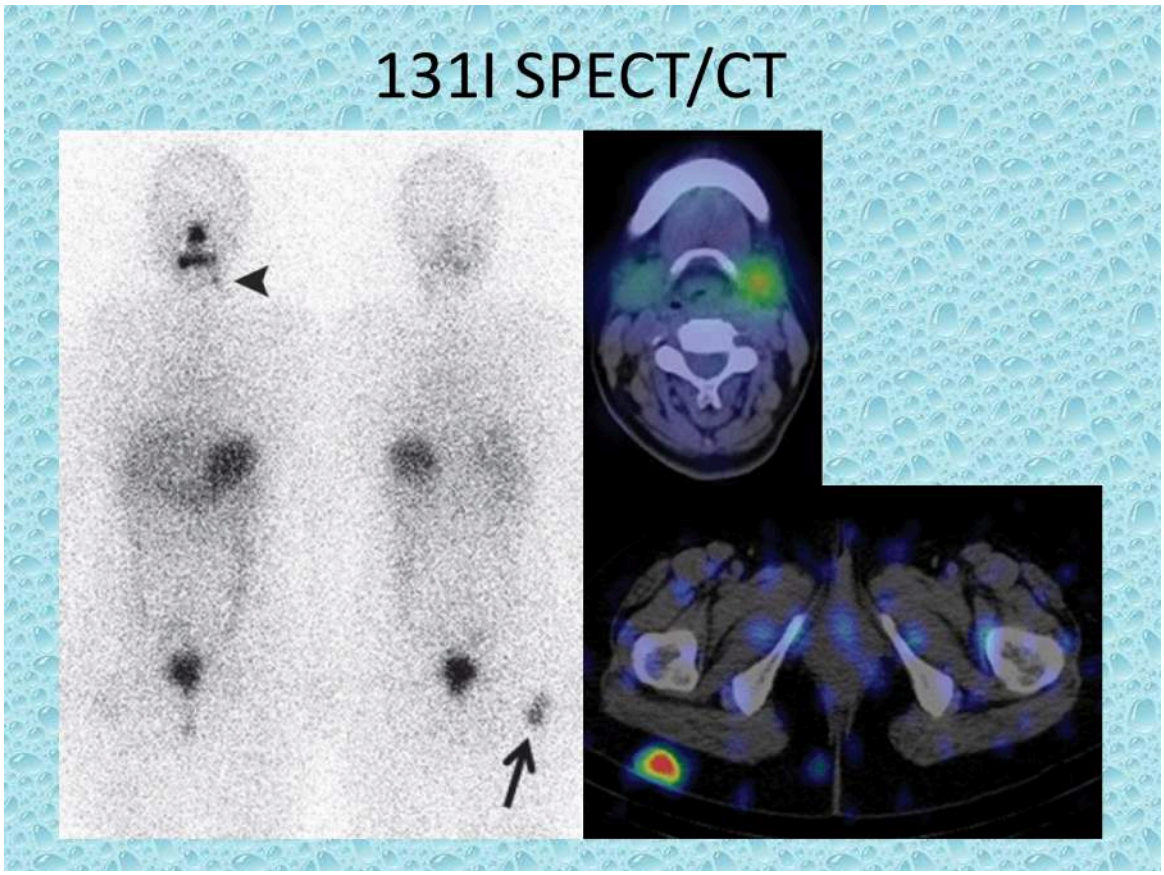
Gastroenteropancreatic neuroendocrine tumors: role of imaging in diagnosis and management.
Radiology. 2013; 266(1): 38-61.

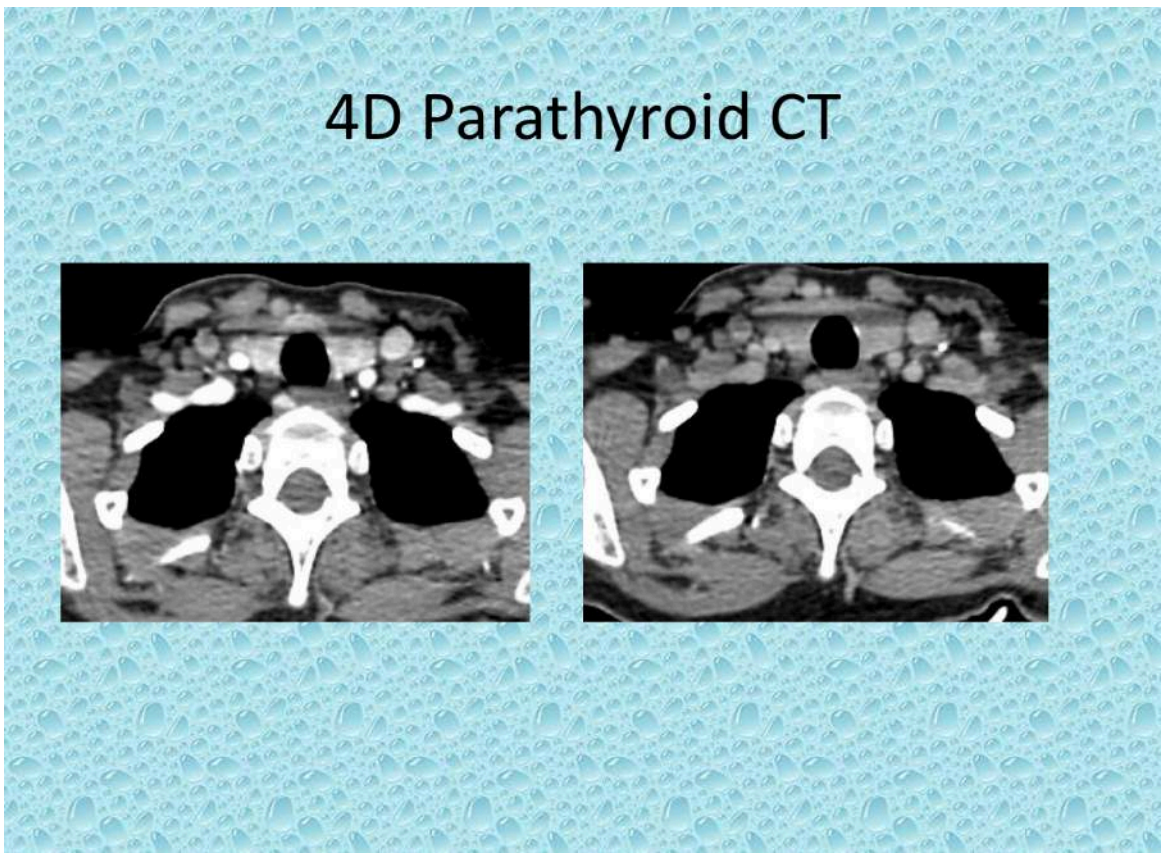
Contemporary Endocrine Imaging

- Ultrasound- Elastography/ARFI
- CT- 4D CT
- MRI
- Radionuclide Imaging- SPECT/CT
- PET/CT- 18F FDG/ C11 Methionine/ 68Ga DOTA

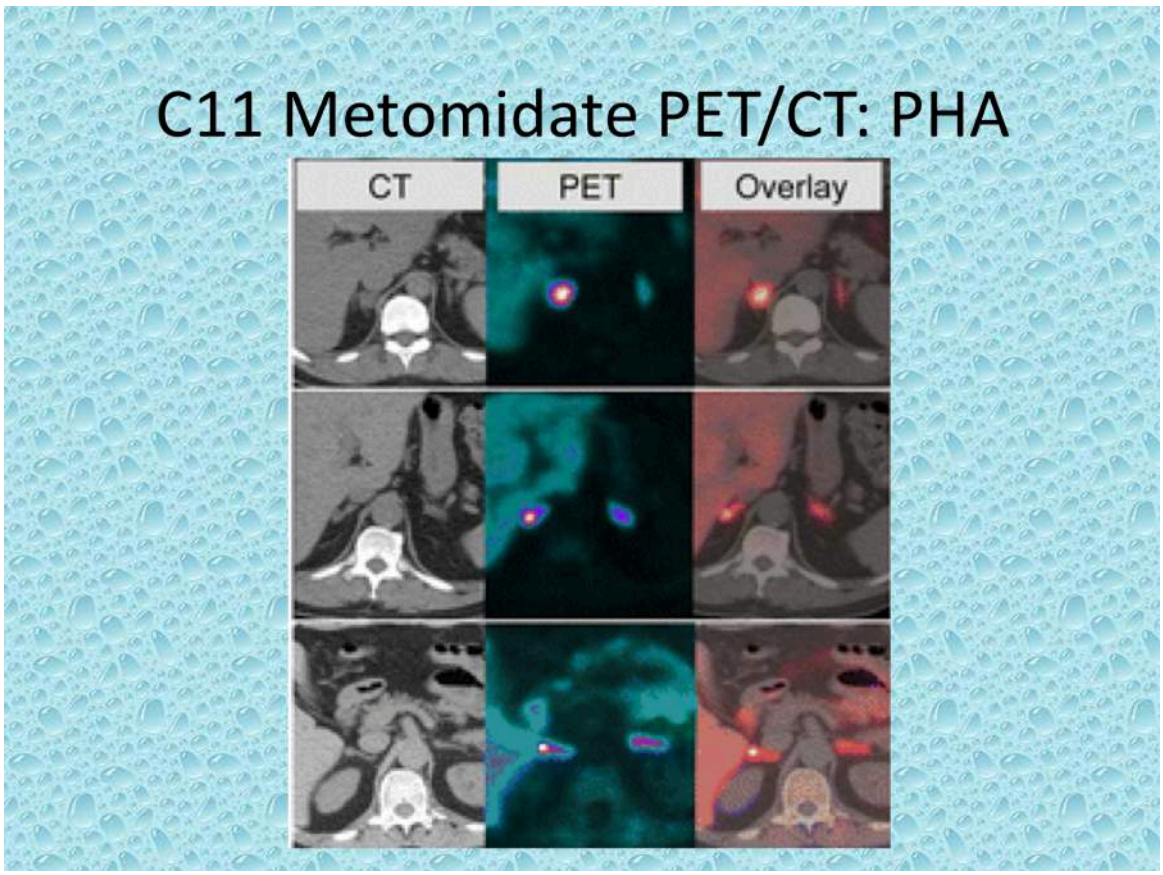
Thyroid Elastography

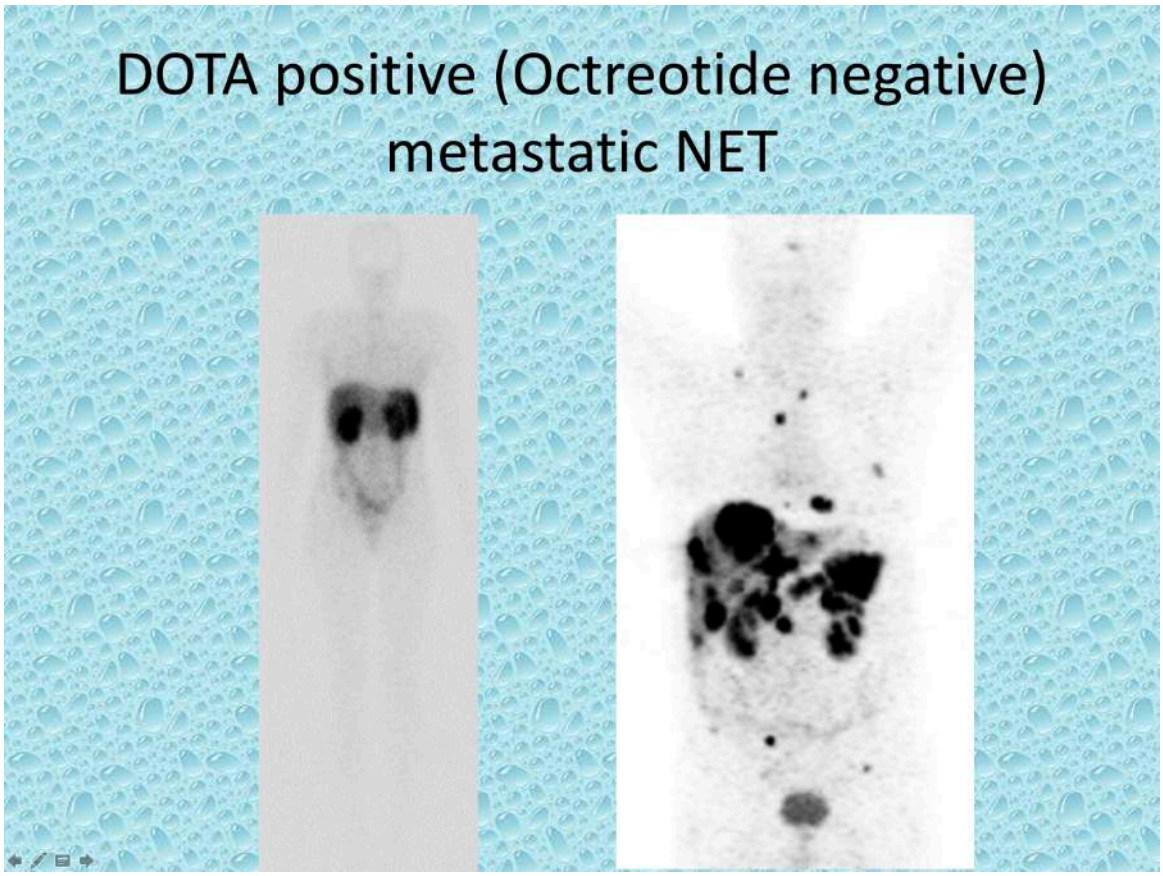



131I SPECT/CT


4D Parathyroid CT

Dr Dilip Patel





Dr Kristien Boelaert

Biography

Kristien is a Reader in Endocrinology at the University of Birmingham and a Consultant Endocrinologist at the Queen Elizabeth Hospital in Birmingham. Kristien obtained her MD from the Catholic University Leuven, Belgium and her Wellcome Trust-funded PhD from the University of Birmingham. Subsequently, she was successful in obtaining a prestigious MRC Clinician Scientist Fellowship in 2007. Her clinical research interests include the management of thyroid dysfunction, thyroid nodules and endocrine disorders in pregnancy. Her laboratory research programme focuses on the pathogenesis of goitre and thyroid cancer. Kristien's contribution to the field of thyroid disease has been recognised by awards from several national and international societies and by regular invitations to speak at national and international meetings. She held a Visiting Clinician Fellowship at the Mayo Clinic in 2011 and was the RCP representative on the recent national UK thyroid cancer guidelines committee (2014). Kristien's research continues to attract funding from major grant awarding bodies and is evidenced by a rapidly growing list of peer-reviewed research papers, reviews and book chapters. Kristien is a Senior Editor for Endocrine Connections and serves on the Editorial Boards of Lancet Diabetes & Endocrinology, Thyroid and the Journal of Endocrinological Investigation as well as on the British Thyroid Association Executive Committee and the RCP Specialist Certificate Examination Board.

Abstract

Hyperthyroidism: diagnosis, management and long-term consequences

Hyperthyroidism is common especially in women. The most common causes include Graves' disease and toxic nodular hyperthyroidism. We found that almost half of people with Graves' hyperthyroidism have a family history of thyroid dysfunction, consistent with a strong genetic influence. Moreover, we quantified the risk of diagnosis of coexisting autoimmune diseases in more than 3000 index cases with well-characterised Graves' disease and demonstrated significantly increased relative risks for almost all autoimmune diseases in index cases as well as their parents.

Excess thyroid hormones affect every physiological system and symptoms and signs can vary widely. Cardiovascular features often predominate and in general the severity and frequency of symptoms is associated with the biochemical severity of hyperthyroidism. A large study demonstrated that older people have fewer classical features and are more likely to present with cardiovascular complications such as atrial fibrillation and heart failure.
Three main treatments exist: administration of antithyroid drugs, radioactive iodine therapy and surgery. The treatment is best tailored to the individual, although opinions regarding what constitutes optimal therapy vary widely. Overall long term remission rates following antithyroid drugs are less than 50% whereas radioiodine treatment is associated with cure rates of up to 85%, although there are significant risks of developing permanent hypothyroidism.

Increased cardiovascular morbidity and mortality following treatment for hyperthyroidism has been demonstrated repeatedly. Furthermore we found that, among hyperthyroid subjects aged 40 years or older, mortality was increased during periods of thionamide treatment and after radioiodine not resulting in hypothyroidism, but not during follow-up after radioiodine-induced hypothyroidism. Independent associations of mortality with atrial fibrillation and incomplete biochemical control during treatment indicate potential causative links with poor outcome.

Whilst weight loss is one of the most frequent presenting symptoms of hyperthyroidism, weight gain is common following treatment. We found that patients with hyperthyroidism are less likely to have a BMI > 25 kg/m^2 at presentation but have a higher chance of being overweight or obese at discharge, when compared with the

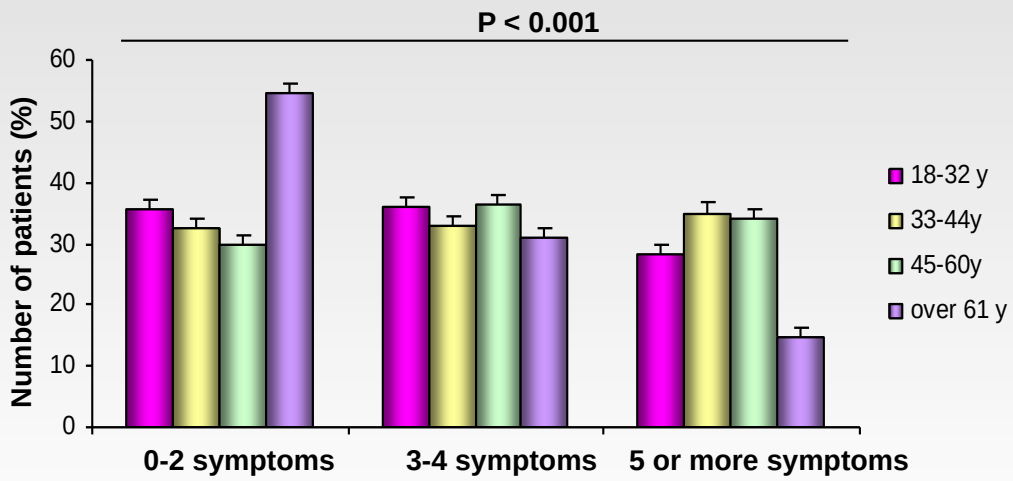
Dr Kristien Boelaert

Abstract (continued)

background population. Importantly, a statistical predictive model demonstrated that patients undergoing radioiodine treatment are more likely to have more weight gain than those treated with antithyroid drugs, although in absolute terms the amount of excess weight gain was small and development of radioiodine induced hypothyroidism was not associated with significant weight increases.

The diagnosis of thyroid dysfunction is especially difficult in patients who are hospitalised, when thyroid function test results may be influenced by non-thyroidal illness. Our most recent studies have evaluated data from a hospital-wide electronic prescribing and administration system, extracting 269,388 admissions of 147,693 inpatients between January 2007 and December 2011. Based on the ICD-10 coding and/or record or appropriate medication prescription during at least one hospital stay, patients were categorized as hyperthyroid (n=673), hypothyroid (n=8,037) or euthyroid (n=138,983). Hyperthyroid patients were matched with hypo- and euthyroid patients based on age, gender and the year of first admission. Hyperthyroid patients were more likely to be rehospitalised and spent longer times in hospital than hypothyroid and euthyroid matched patients. Moreover we found increased cardiovascular morbidity, in particular atrial fibrillation and heart failure, in hyperthyroid subjects. Further prospective studies may identify if early diagnosis, appropriate management and follow-up of hospitalised patients with hyperthyroidism are likely to alleviate this significant health and financial burden.

Number of reported symptoms of hyperthyroidism according to age



Boelaert et al. (2010) JCEM 95, 2715

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Hyperthyroidism and associated autoimmune diseases

- **2791 subjects with Graves' disease**

	Diagnosis of Graves' Disease in Female Index Case		
Associated Autoimmune Disease	Relative Risk	95% CI	*P* Value
Type 1 diabetes	2.29	1.36-3.60	.005
Rheumatoid arthritis	3.07	2.42-3.82	<.001
Pernicious anemia	11.29	7.83-15.72	<.001
Systemic lupus erythematosus	11.69	6.23-20.0	<.001
Addison's disease	14.39	2.97-41.99	.001
Celiac disease	19.98	12.95-29.42	<.001
Vitiligo	11.77	7.96-16.76	<.001
Multiple sclerosis	1.38	0.60-2.72	.398
Myasthenia gravis	2.15	0.06-12.01	1.00
Inflammatory bowel disease	4.14	2.69-6.11	<.001

Boelaert et al. (2010) Am J Med 123, 183.e1

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Dr Kristien Boelaert

Hyperthyroidism and mortality

Cause of death	Overall	Whilst on Thionamide Rx		Following ^{131}I Not hypothyroid		Following ^{131}I Hypothyroid	
	SMR	SMR	P	SMR	P	SMR	P
All causes	**1.15**	**1.30**	**0.006**	**1.24**	**0.02**	1.02	0.85
Males	**1.26**	1.36	0.10	1.34	0.11	1.1	0.57
Females	1.11	1.27	0.07	1.21	0.06	0.95	0.60
Comorbidity absent	0.95	1.03	0.84	1.09	0.48	0.81	0.08
Comorbidity present	**1.52**	**1.68**	**<0.001**	**1.48**	**0.002**	**1.43**	**0.01**
Sinus Rhythm	1.07	1.18	0.18	1.17	0.11	0.92	0.43
Atrial fibrillation	**1.59**	**1.74**	**0.006**	**1.53**	**0.02**	1.51	0.08
Circulatory deaths	**1.20**	**1.37**	**0.05**	1.19	0.22	1.12	0.45

Boelaert et al. (2013) JCEM 98,1869

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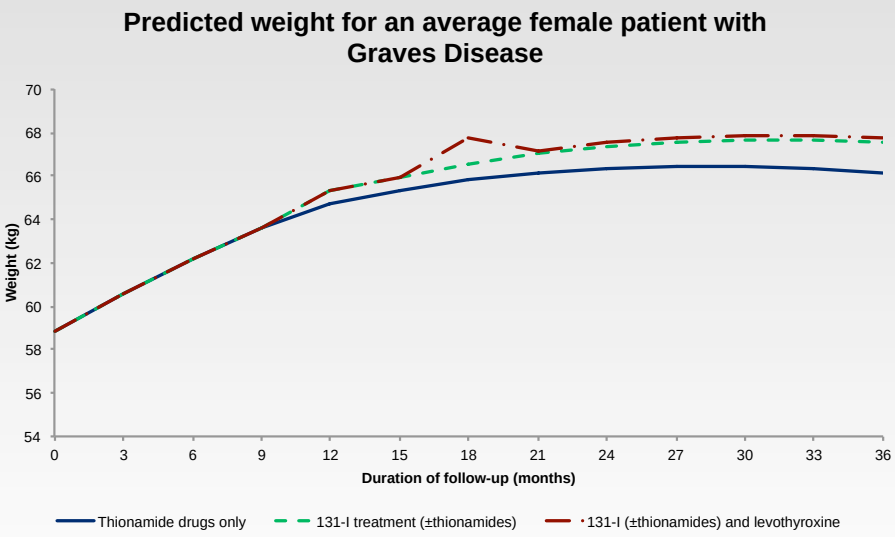
Weight gain following treatment for hyperthyroidism



Boelaert et al. (2015) in preparation

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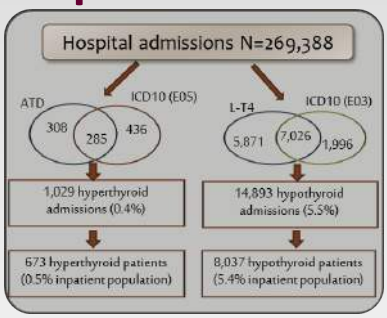
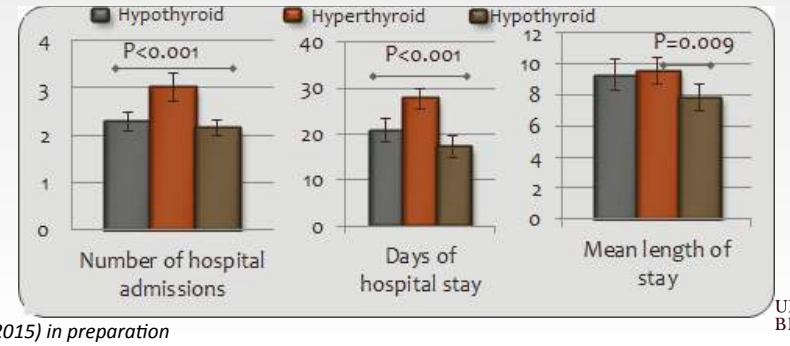
Hyperthyroidism in hospitalised patients





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Boelaert et al. (2015) in preparation

Cardiovascular disease in inpatients with hyperthyroidism

	Hypothyroid	Hyperthyroid	Euthyroid	P value	Significant relation (MD or OR, P value)	
Number of hospital admissions	2.29 (±0.09, [2.11-2.48])	3.01 (±0.16, [2.70-3.31])	2.16 (±0.08, [2.00-2.33])	P<0.001	Hyper-/Hypo- Hyper/Eu-	0.7, P<0.001 0.8, P<0.001
Days of hospital stay	20.8 (±1.32, [18.23-23.42])	27.7 (±1.72, [24.29-31.0])	17.3 (±1.18, [14.98-19.60])	P<0.001	Hyper-/Hypo- Hyper/Eu-	6.8, P=0.002 10.4, P<0.001
Mean length of stay	9.29 (±0.53, [8.25-10.33])	9.58 (±0.44, [8.71-10.45])	7.85 (±0.44, [6.99-8.71])	P=0.009	Hyper/Eu-	1.7, P=0.009
Adm. primary reason:						
Cardiovascular	195 (29.0)	252 (37.4)	175 (26.0)	P=0.001	Hyper-/Hypo-	1.4, P=0.003
Nervous	242 (36.0)	236 (35.1)	254 (37.7)	P=0.58	Hyper/Eu-	1.7, P<0.001
Respiratory	101 (15.0)	107 (15.9)	86 (12.8)	P=0.22		
Digestive	141 (21.0)	139 (20.7)	156 (23.2)	P=0.46		
Recorded comorbidity:						
Cardiovascular	413 (61.4)	451 (67.0)	384 (57.1)	P<0.001	Hyper-/Hypo-	1.4, P=0.03
Nervous	234 (34.8)	230 (34.2)	242 (36.0)	P=0.78	Hyper/Eu-	1.8, P<0.001
Respiratory	225 (33.4)	234 (34.8)	213 (31.6)	P=0.46		
Digestive	231 (34.3)	220 (32.7)	217 (32.2)	P=0.68		
CVD comorbidities:						
Hypertension (I10)	259 (38.5)	253 (37.6)	231 (34.3)	P=0.20		
AF and flutter (I48)	94 (14.0)	195 (29.0)	94 (14.0)	P<0.001	Hyper-/Hypo- Hyper/Eu-	3.0, P<0.001 2.6, P<0.001
Ischemic heart disease (I25)	132 (19.6)	125 (18.6)	102 (15.2)	P=0.059		
Heart failure (I50)	61 (9.1)	85 (12.6)	46 (6.8)	P=0.001	Hyper/Eu-	2.0, P=0.001

UNIVERSITY OF BIRMINGHAM

Boelaert et al. (2015) in preparation

Dr Marie Freel

Biography

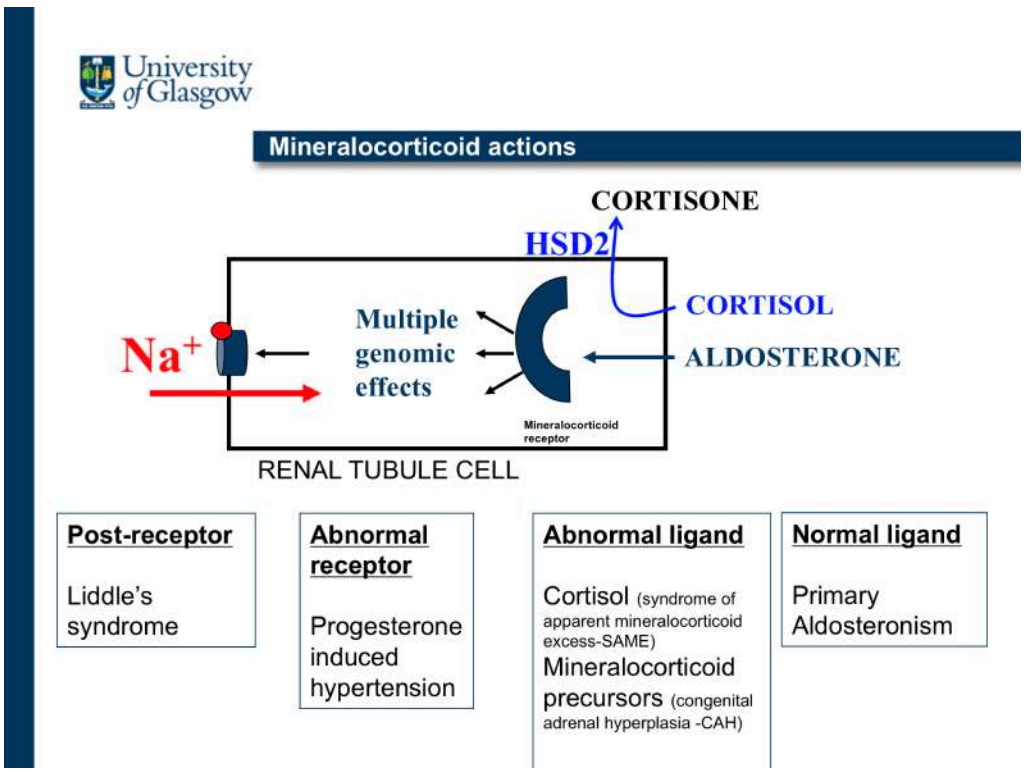
I am a research active Consultant Endocrinologist at the Queen Elizabeth University Hospital Glasgow and Glasgow University. I received both undergraduate degrees from Glasgow University (BSc Honours 1996 and MBChB Honours 1999) and was awarded a PhD in 2006.

I was awarded a MRC Clinician Scientist Fellowship in 2009 for a programme of work entitled 'Cardiovascular disease: investigating the expanding role of aldosterone.' My principal research interest remains in the role of corticosteroids (particularly aldosterone) in hypertension and cardiovascular disease. My Fellowship comprised a series of translational studies examining further the influence of aldosterone on end-organ (cardiac and renal) damage as well as basic science studies exploring the genetic basis of hypertension with aldosterone excess.
In 2009, I received a 'Clinical Department Visit Grant' from the Society of Endocrinology. This helped fund a visit to the Mayo Clinic, Rochester, Minnesota where I spent several months working with Professor Bill Young (current President of the American Endocrine Society).

I sit on the Editorial Board of Clinical Science and Hypertension, the National Scientific Advisory Committee for Tenovus, Scotland and NHS Greater Glasgow & Clyde Endowment Awards committee. In 2014, I returned to full time clinical work but maintain a research interest both by acting as local PI for pharmaceutical trials and a Horizon 2020 programme grant investigating endocrine hypertension.

Abstract

This talk will address why accurate diagnosis of aldosterone excess is important and how best to do this. In addition, there will be an overview of the recent advances in the genetic basis of adenomatous Primary Aldosteronism.



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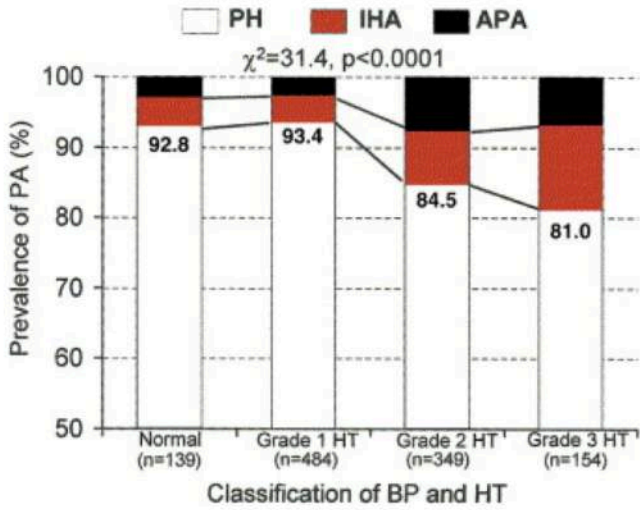
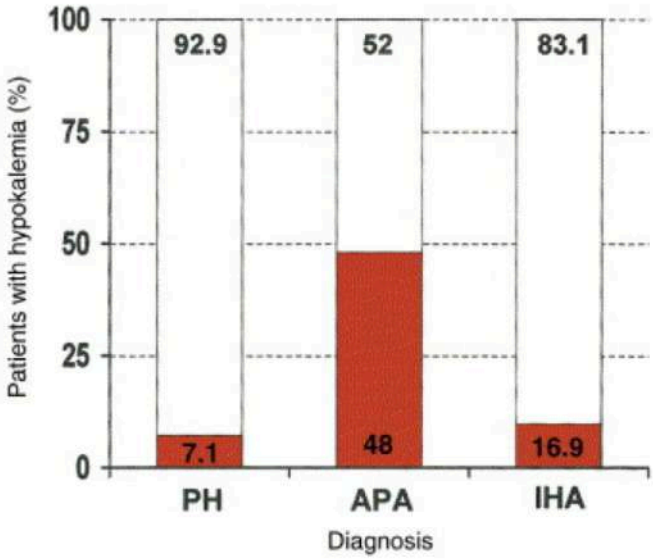
Prevalence of Primary Aldosteronism



Rossi et al. J Am Coll Cardiol 2006

University of Glasgow

Hypokalaemia and Primary Aldosteronism

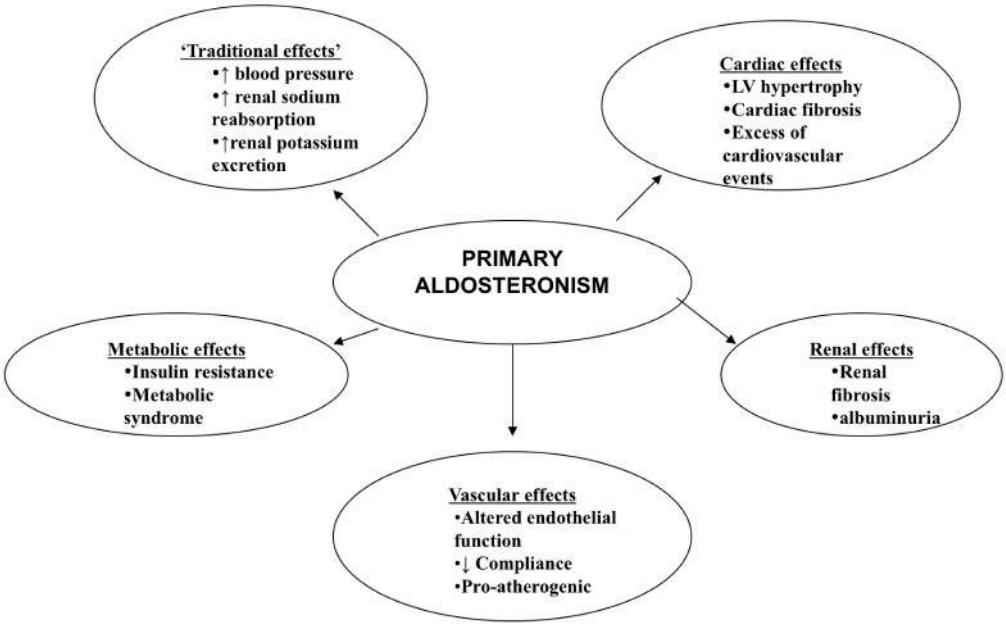


Rossi et al. J Am Coll Cardiol 2006

Dr Marie Freel

University of Glasgow

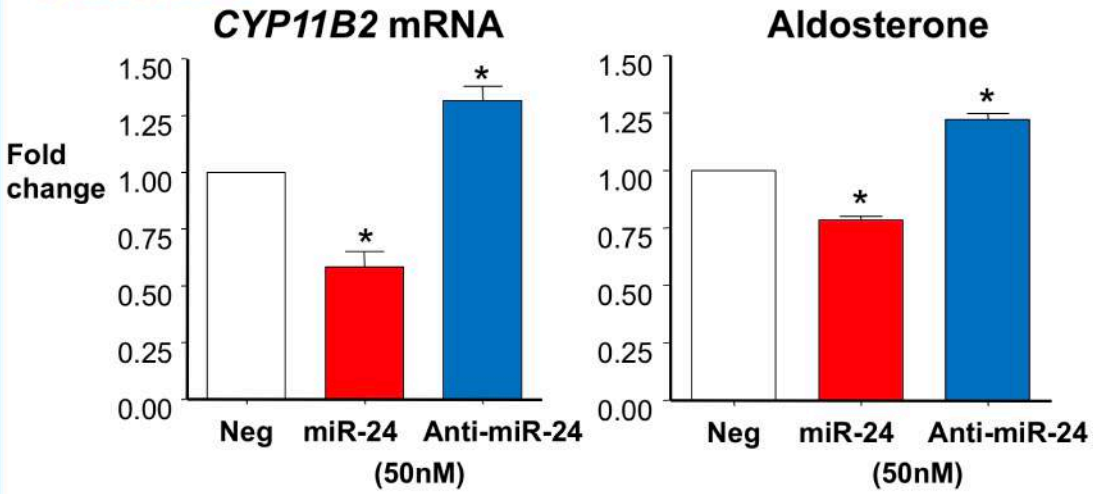
Multiple end organ effects of aldosterone excess



University of Glasgow

Role of micro RNA in modulation of aldosterone production

H295R cells



Decreased expression of miRNA-24 may contribute to increased aldosterone production in APA

Dr Paul Newey

Biography

Dr Paul Newey is a Senior Lecturer and Honorary Consultant Physician at the University of Dundee, Scotland. He undertook his medical studies at the University of Edinburgh before moving to Oxford for his Specialty Training. During this period he was awarded a DPhil for his studies on hereditary endocrine disorders including Multiple Endocrine Neoplasia Type 1 (MEN1) in the laboratory of Professor Rajesh Thakker. He was subsequently appointed a NIHR Clinical Lecturer in Endocrinology in Oxford undertaking post-doctoral research in the field of endocrine tumourigenesis. In 2014, Dr Newey moved to the University of Dundee to establish his own research group continuing his interest in endocrine tumourigenesis. In 2015, he was awarded a NRS Scottish Senior Clinical Fellowship.

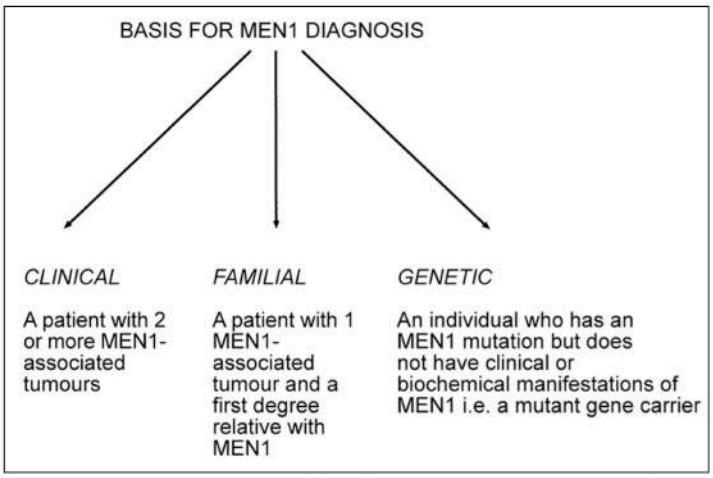
Dr Paul Newey has developed a specialist interest in neuroendocrine tumours and in particular the clinical management of Multiple Endocrine Neoplasia Type 1 (MEN1). He is one of the co-authors on Clinical Practice Guidelines for MEN1 published in 2012.

Abstract

Multiple Endocrine Neoplasia type 1 (MEN1) is an autosomal dominant disorder due to germline mutation of the *MEN1* gene and is characterized by the combined occurrence of parathyroid, pituitary and pancreatic neuroendocrine tumours. In addition, a variety of other tumour types are observed which include bronchial and thymic carcinoids, adrenal tumours, lipomas, and meningiomas. Germline *MEN1* mutations are highly penetrant and lead to tumour development in >95% of affected individuals by the age of 45 years. Such early disease onset is associated with premature mortality, predominantly due to pancreatic neuroendocrine tumours and foregut carcinoids. Thus, for affected individuals or those at risk of disease, interval clinical, biochemical and radiological screening has been recommended with the aim of early tumour detection. However, the management of MEN1-related disease present a number of specific challenges, which reflect their early age of onset, frequent multi-focality, and the concomitant presence of other tumours. This presentation will discuss several areas of uncertainty and / or controversy in field of MEN1. In particular, it will focus on: the role and timing of genetic testing; avoiding diagnostic pitfalls due to phenocopies; the challenges in biochemical and radiological screening; and the complex management of pancreatic neuroendocrine tumours.

1. Thakker RV, Newey PJ, Walls GV, Bilezikian JP, Dralle H, Ebeling PR, Melmed S, Sakurai A, Tonelli F, Brandi M. Clinical practice guidelines for Multiple Endocrine Neoplasia Type 1 (MEN1). *J Clin Endocrinol Metab* 2012; 97:2990-3011
2. Newey PJ & Thakker RV. Role of Multiple Endocrine Neoplasia type 1 (MEN1) Mutational Analysis in Clinical Practice. *Endocrine Practice* 2011;17:S3: 8-17Yates CJ, Newey PJ, Thakker RV.
3. Challenges and controversies in management of pancreatic neuroendocrine tumours in patients with MEN1. *Lancet Diabetes & Endocrinol* 2015;3:895-905

MEN1 - Diagnosis

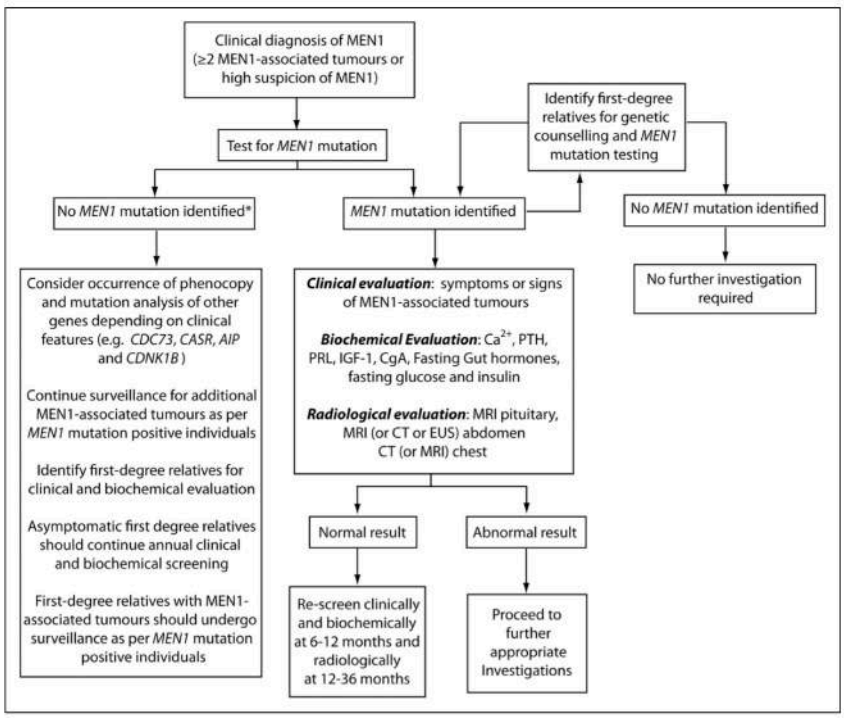


- MEN1 may be diagnosed on one of 3 criteria
- Recommendation to undertake genetic testing in all potential individuals with MEN1 and their first degree relatives

J Clin Endocrinol Metab 2012 97(9):2990-3011

- A diagnosis of MEN1 based on clinical and familial criteria may be confounded by the occurrence of phenocopies

Suggested approach to genetic and clinical screening in MEN1 kindreds



J Clin Endocrinol Metab 2012 97(9):2990-3011

Suggested clinical, biochemical and radiological screening in MEN1

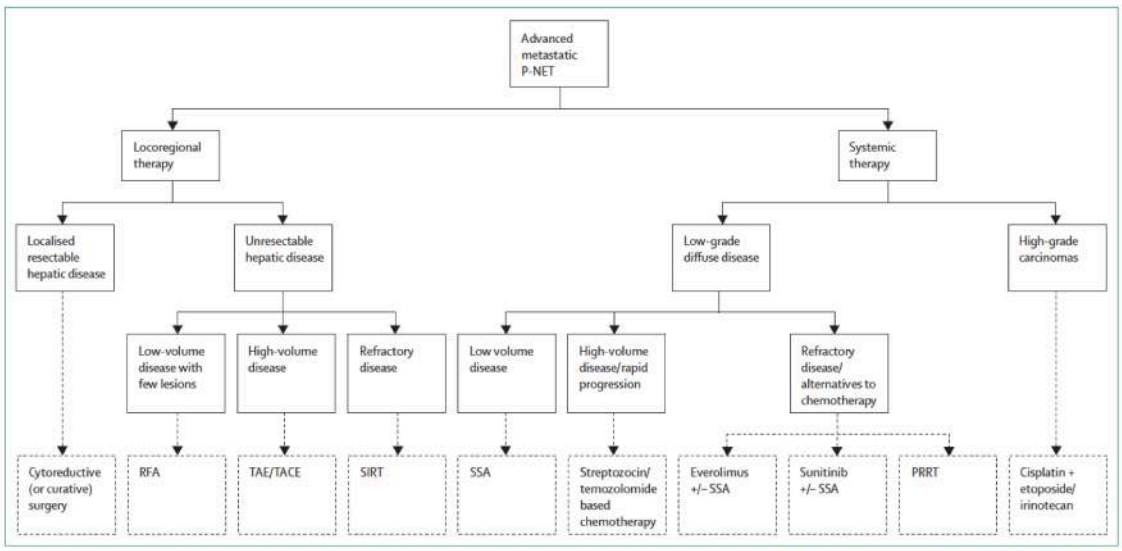
Tumor	Age to begin (yr)	Biochemical test (plasma or serum) annually	Imaging test (time interval)
Parathyroid	8	Calcium, PTH	None
Pancreatic NET			
Gastrinoma	20	Gastrin (± gastric pH)	None
Insulinoma	5	Fasting glucose, insulin	None
Other pancreatic NET	<10	Chromogranin-A; pancreatic polypeptide, glucagon, VIP	MRI, CT, or EUS (annually)
Anterior pituitary	5	Prolactin, IGF-I	MRI (every 3 yr)
Adrenal	<10	None unless symptoms or signs of functioning tumor and/or tumor >1 cm are identified on imaging	MRI or CT (annually with pancreatic imaging)
Thymic and bronchial carcinoid	15	None	CT or MRI (every 1–2 yr)

J Clin Endocrinol Metab 2012 97(9):2990-3011

Areas of uncertainty / controversy:

- Age to commence screening
- Imaging modalities (and interval) for screening of pancreatic NETs
- ?Routine screening for thymic carcinoid
- Utility of biomarkers for screening (low sensitivity and specificity)

Management of advanced pancreatic neuroendocrine tumours



Lancet Diabetes Endocrinol 2015, 3:895-905

- Large number of potential treatment options
- Lack of evidence base for their most effective use in MEN1 (and more generally)
- Role of multidisciplinary teams and availability of treatment modalities

Dr Marcus Lyall

Biography

Marcus Lyall is Clinical Research Fellow at the BHF Centre for Cardiovascular Science and MRC Institute of Genetics and Molecular Medicine at the University of Edinburgh. Having graduated in biochemistry and then subsequently medicine from the University of Dundee, he took up a specialty training post in diabetes and endocrinology in Lothian in 2011 before obtaining a position on the Edinburgh Clinical Academic Training (ECAT) Scheme in 2012. His PhD research under the supervision of Dr Mandy Drake and Professor Richard Meehan, is focused on the interaction between glucose metabolism and the epigenome in metabolic liver disease.

Abstract

Tet mediated DNA Hydroxymethylation as a Novel Regulator in Metabolic Liver Disease.

Marcus J Lyall1, John P Thomson2, Jessy Cartier1, Raffaele Ottaviano2, Richard R Meehan2 and Amanda J Drake1

Introduction: Non-alcoholic fatty liver disease (NAFLD) associates strongly with insulin resistance and can progress to irreversible liver fibrosis and hepatocellular carcinoma (HCC). The underlying mechanisms are incompletely understood, however epigenetic dysregulation may play a role. 5-hydroxymethlycytosine (5hmC) is a recently identified epigenetic modification generated from 5-methylcytosine (5mC) by the Ten eleven translocase isoenzymes (Tets) as part of a demethylation process. Profiling studies indicate that 5hmC is largely present in the bodies of expressed genes as well as over enhancer elements and a cohort of promoter regions in many tissues, as such it is a sensitive indicator of tissue state. We hypothesised that active hydroxymethylation is important in NAFLD progression.

Methods: C57Bl6/j mice were fed 58% saturated fat (HFD) or control diet for 17 weeks before intraperitoneal glucose tolerance testing and analysis of liver histology. Genome-wide profiling of 5-hmC was undertaken using DNA immunoprecipitation combined with subsequent semiconductor proton sequencing. Hepatic transcriptomic analysis was performed using Illumina WG6 beadchip microarrays.

Results: HFD feeding induced obesity, fasting hyperglycaemia, glucose intolerance, insulin resistance and hepatic steatosis. 5hmC was preferentially located in enhancer, promoter and gene body regions as previously reported ($P<0.001$). Whilst the global 5hmC profile was not altered by HFD, there was a highly significant correlation between 5hmC enrichment over genic regions and transcriptional changes (R2 0.2442, $P<0.001$). Genes with greater than 2-fold increase in genic 5hmC were significantly over represented in pathways of gluconeogenesis ($p = 0.026$), insulin-like growth factor binding ($p = 0.032$), mitochondrial inner membrane transport ($p = 0.0032$), and chemokine activity ($p= 0.009$). Notably, 5hmC genic enrichment was present in upregulated mediators of cholesterol biosynthesis (Lss, Sc4mol, Fdps, Hsd17b7, Cyp17a1, Mvd, Cyp1a2 and Dhcr7) and lost in the downregulated HCC tumour suppressor genes Osgin1 and Txnip.

Conclusion: HFD induces Tet-mediated genic hydroxymethylation with concurrent transcriptional activation of genes driving cholesterol biosynthesis. In contrast, HFD associates with a reduction in 5hmC with concurrent suppression of HCC-related tumour suppressor genes. Clinically, these pathways are highly relevant. Increased cholesterol biosynthesis exacerbates hepatic fat accumulation and increases cardiovascular mortality in the metabolic syndrome 1. Osgin1 and Txnip dysfunction are strongly implicated in HCC neoplastic transformation 2,3. This study supports a role for Tet activity and the dynamic regulation of cytosine modifications in the progression of NAFLD, and suggests 5hmC profiling may be a useful biomarker of disease state.

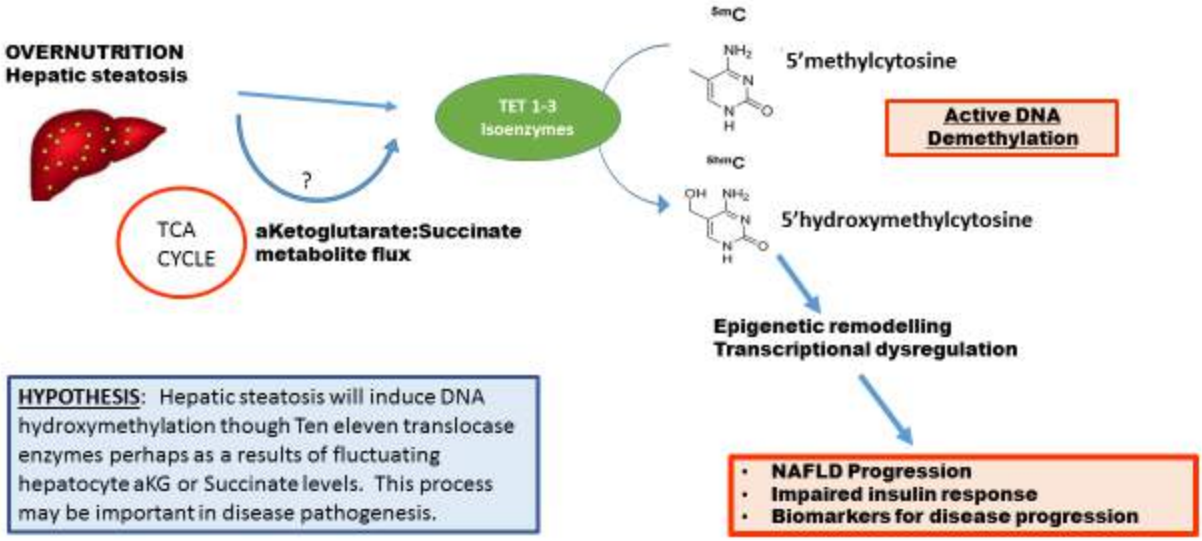
References: (1) Min, H. K. et al. Cell Metab. 15, 665–674 (2012). (2) Liu, M. et al. Gastroenterology 146, 1084–1096 (2014) (3) Sheth, S. S. et al Oncogene 25, 3528–3536 (2006). Laird A et al Epigenomics. 5(6), 655-69 (2013) . (4) Nestor, C. E. et al. Genome Res. 22(3), 467-77 (2012)

Sources of Research Support: MJL is supported by a Wellcome Trust PhD Fellowship as part of the Edinburgh Clinical Academic Track scheme (102839/Z/13/Z)

Dr Marcus Lyall

The University of Edinburgh

ECAT Edinburgh Clinical Academic Training



HYPOTHESIS: Hepatic steatosis will induce DNA hydroxymethylation though Ten eleven translocase enzymes perhaps as a results of fluctuating hepatocyte aKG or Succinate levels. This process may be important in disease pathogenesis.

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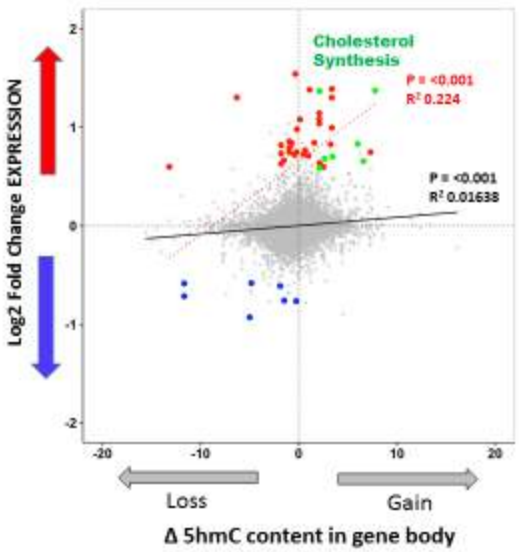


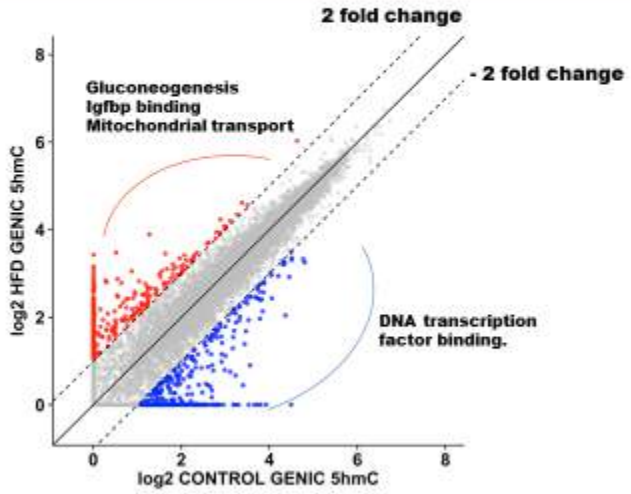
- **Liver transcriptome of control and high fat diet fed obese mice was analysed by microarray.**
- **The 5hmC content within the gene body each gene was analysed using DNA immunoprecipitation coupled with whole genome sequencing.**
- **Changes in genic 5hmC content correlates strongly with transcriptional change.**
- **Strongest enritchment was within upregulated genes of cholesterol synthesis.**
- **No such correlation was seen over promoter regions, enhancer regions or transcriptional start sites.**

Correlation was determined by linear regression analysis. Red line = correlation with significantly changed genes. Black line = correlation with all array probes. Significantly upregulated genes = Red, down regulated genes = Blue, induced genes of cholesterol synthesis = Green

Dr Marcus Lyall

The University of Edinburgh

ECAT Edinburgh Clinical Academic Training



- On determining an assoication between genic 5hmC and transcriptional activation, we went on to compare 5hmC content in all gene bodies between HFD and control animals.
- Genes with greater than 2-fold increase in genic 5hmC were significantly over represented in pathways of gluconeogenesis (p = 0.026), insulin-like growth factor binding (p = 0.032), mitochondrial inner membrane transport (p = 0.0032), and chemokine activity (p= 0.009).
- It is unclear whether 5hmC changes are causal or simply reflective of metabolic liver disease.
- 5hmC profiling shows potential as a method of assessing disease state in NAFLD.

Dr Nyo Nyo Tun

Biography

I graduated from the University of Edinburgh in 2007. I started my general medical training in North of Scotland before moving to Edinburgh in 2013 for my specialist training in Diabetes and Endocrinology. I am currently a clinical research fellow at the BHF Centre for Cardiovascular Science, University of Edinburgh under the supervision of Dr. Fraser GIbb and Dr. Dawn Livingstone looking into the metabolic effects of sex steroid hormones.

Abstract

Predicting Risk of Recurrent Thyrotoxicosis Following Thionamide Withdrawal in Graves' Disease

Dr Nyo Nyo Tun, Dr Nicola N Zammitt, Dr Geoff Beckett, Prof Mark W J Strachan, Dr Fraser W Gibb

Background/Aim: Thionamides are a safe and effective treatment for Graves' thyrotoxicosis. In the United States, primary therapy with thionamides has increased in popularity over the past two decades and remains the most popular primary treatment in Europe. Risk of recurrence following cessation of thionamides is high (up to 80%); although most studies tend to have short duration of follow up. The long-term predictive value of TSH receptor antibodies (TRAbs) has not been clearly defined. We aimed to establish the long-term natural history of Graves' thyrotoxicosis following thionamide withdrawal and the factors that best predict recurrence.

Methods: We undertook a review of all patients, with a first presentation of Graves' disease, who were prescribed (and completed) a course of thionamide as primary treatment (n = 266) at 2 large UK University hospitals. Age, gender, smoking status, free T4, total T3, TRAb at diagnosis, TRAb at cessation of thionamide and time to normalization of thyroid function were assessed as potential predictors of recurrence over 4 years of follow-up.

Results: Recurrent thyrotoxicosis was observed in 31% (n=82/266) at 1 year, 45% (n=111/247) at 2 years, 61% (n=125/205) at 3 years, and 70% (n=128/184) at 4 years. Logistic regression identified age, time to normalization of TSH and TRAb at cessation as independent predictors of recurrence. 1 year after thionamide withdrawal, cessation TRAb <0.9 mU/L was associated with a 22% risk of recurrence compared to 51% when TRAb was ≥ 2 mU/L (p <0.001). The corresponding figures for 4-year recurrence risk were 58% and 86%, respectively (p <0.001). TRAb at diagnosis >12 mU/L was associated with a 84% risk of recurrence over 4 years compared to 57% when diagnosis TRAbs were < 5mU/L (p = 0.002). Kaplan-Meir curves for relapse begin to plateau at approximately 30 months.

Conclusions: These data provide useful information to guide appropriate follow-up after withdrawal of thionamide therapy. Around 80% of patients with TRAbs >1.9 mU/L at cessation of treatment will relapse within 2 years; the same is true of patients with very high TRAbs (>12 mU/L) at diagnosis. In such patients, where the risks of recurrent thyrotoxicosis are unacceptably high (high cardiovascular risk, elderly), strong consideration should be given to primary radioiodine therapy.

Dr Nyo Nyo Tun

TRAbs at diagnosis

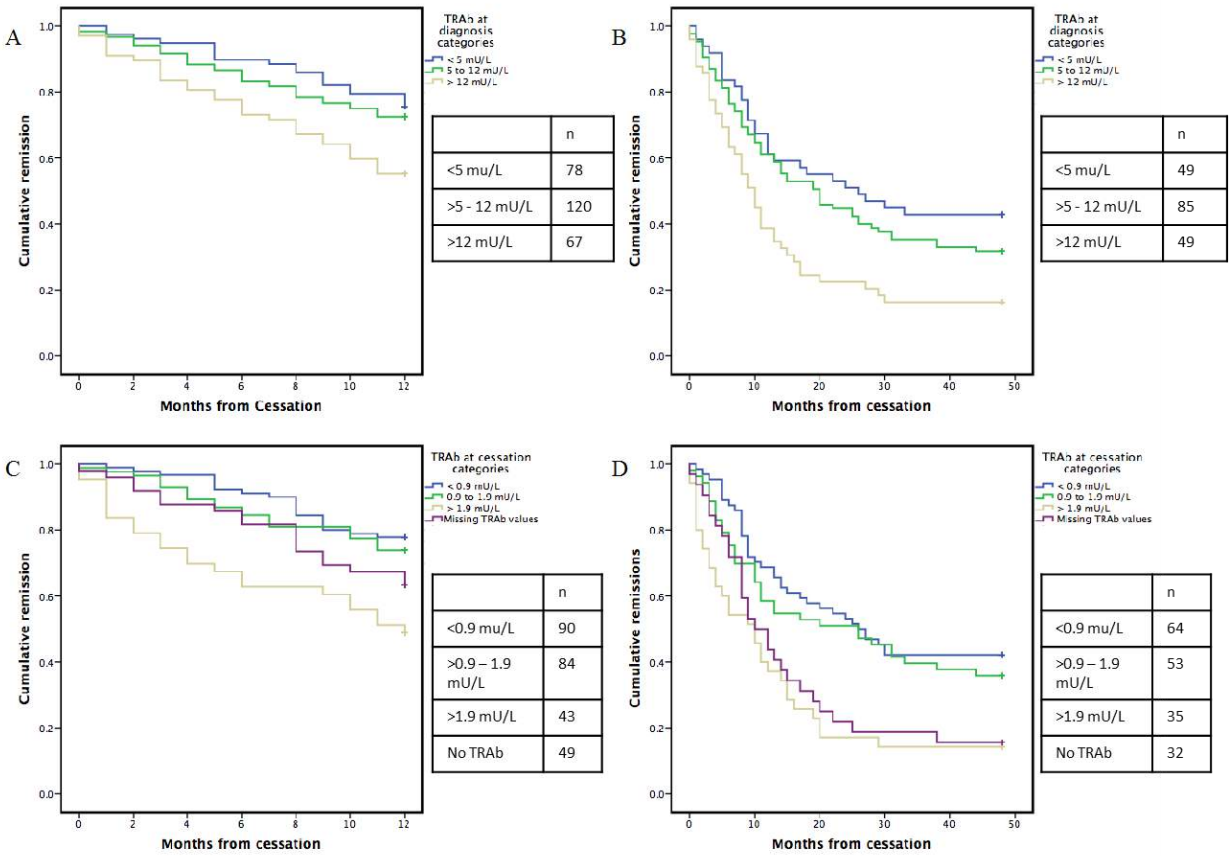
	1 year relapse rate*		2 year relapse rate**		3 year relapse rate***		4 year relapse rate****	
TRAb at diagnosis	%	n	%	n	%	n	%	n
< 5 mU/L	24	19/78	33	24/73	49	28/57	57	28/49
5.0 to 12.0 mU/L	28	33/120	44	48/109	59	55/93	68	58/85
> 12 mU/L	45	30/67	59	38/64	76	41/54	84	41/49

Relapse rate is shown by TRAb category at diagnosis. Log rank *p = 0.01, **p < 0.004, ***p = 0.003, ****p =0.002

TRAbs at cessation of thionamide

	1 year relapse rate*		2 year relapse rate**		3 year relapse rate*		4 year relapse rate*	
TRAb at cessation	%	n	%	n	%	n	%	n
< 0.9 mU/L	22	20/90	36	30/83	52	37/51	58	37/64
0.9 to 1.9 mU/L	26	22/84	35	27/77	52	32/61	62	33/53
≥ 2 mU/L	51	22/43	69	29/42	79	30/38	86	30/35

Relapse rate is shown by TRAb category at cessation of thionamide. Mantel-Cox *p < 0.001, **p = 0.001



Dr Anna White

Biography

Anna completed her medical training at the University of Glasgow graduating in 2006 with an additional intercalated BSc in Physiology. She has clinical experience in both the West of Scotland for foundation and specialty training and Northwest of England for core medical training. She is currently studying for a PhD in adipocyte biology related to obesity and diabetes supported by her Diabetes UK-funded clinical research training fellowship with supervision from Dr Ian Salt and Prof Rhian Touyz. Upon completion of her PhD she will take up a Clinical Lecturer position at the University of Glasgow.

Abstract

AMPK as a therapeutic target for metabolic disorders: interactions with the renin-angiotensin-aldosterone system in adipocytes.

Anna White, Sarah Mancini, Aurelie Nguyen Dinh Cat, Augusto Montezano, Ian Salt, Rhian M Touyz
Institute of Cardiovascular and Medical Sciences, University of Glasgow, United Kingdom.

Background

Upregulation of the renin-angiotensin-aldosterone system (RAAS) in adipocytes has been implicated in the chronic low-grade adipose tissue inflammation associated with obesity and insulin resistance. Adverse effects of the RAAS may be counter-regulated by the energy sensor AMP-activated protein kinase (AMPK), which has anti-inflammatory actions. We investigated the relationship between AMPK and the RAAS in adipocytes to determine whether AMPK activation ameliorates the injurious effects of angiotensin II.

Methods

Human liposarcoma-derived SW872 cells were differentiated into adipocytes then stimulated with either AMPK activators (AICAR, A769662 or metformin), angiotensins (II or 1-7) or pro-inflammatory cytokines (TNFα or IL-1β). RT-PCR, immunoblotting and ELISA were performed to evaluate expression/activation of the AMPK and pro-inflammatory signalling pathways.

Findings

AICAR, A769662 and metformin had anti-inflammatory effects in our human adipocyte model, additionally AICAR decreased angiotensinogen and mineralocorticoid receptor expression. Stimulation with angiotensin II activated the AMPK signalling pathway but not pro-inflammatory MAP-kinase or NFκB signalling. Gene expression of the AT1 receptor was not detected however the AT2 receptor was, in addition the AT2R antagonist PD123319 prevented angiotensin II mediated AMPK activation. Further characterisation of the alternative arm of the RAAS found expression of the angiotensin (1-7) receptor MAS, ACE and ACE2 genes, ACE expression was decreased by AICAR and ACE 2 expression was increased by A79662. We therefore evaluated effects of angiotensin (1-7) on AMPK activity and found significant increases in both AMPK phosphorylation and kinase activity.

Interpretation

These findings suggest an interaction between AMPK and the RAAS in adipocytes highlighting potentially beneficial metabolic effects of the alternative arm of the RAAS. This may be an explanation for the diabetes-preventing properties of ACE inhibitors and AT1R antagonists.

Key References

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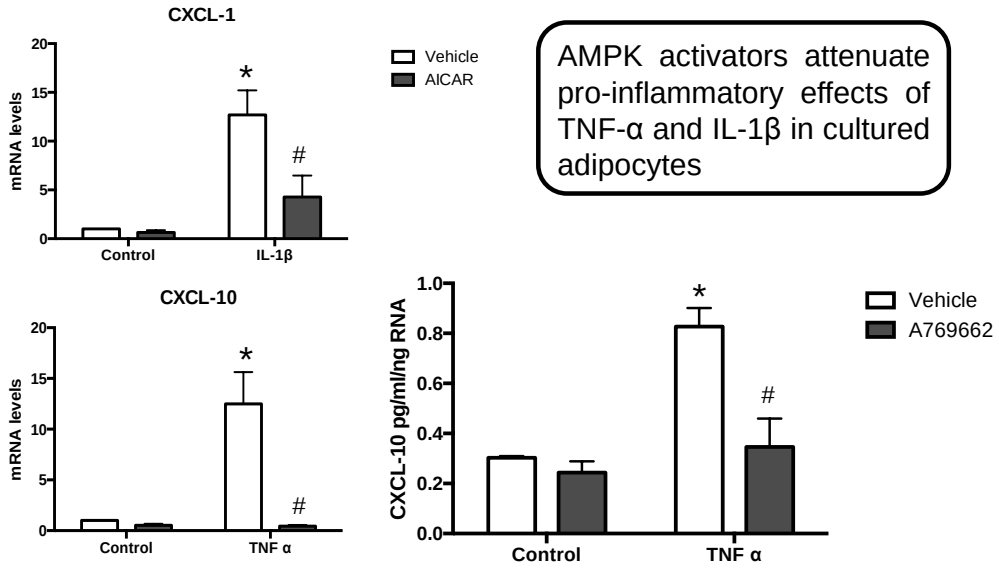
2. Kalupahana, N. S. et al. Overproduction of Angiotensinogen From Adipose Tissue Induces Adipose Inflammation, Glucose Intolerance, and Insulin Resistance. Obes. Silver Spring Md. 2011; 20, 48–56.
3. Lee, J. H. et al. AMP-activated protein kinase inhibits TGF-β-, angiotensin II-, aldosterone-, high glucose-, and albumin-induced epithelial-mesenchymal transition. Am. J. Physiol. Ren. Physiol. 2013; 304, F686–97

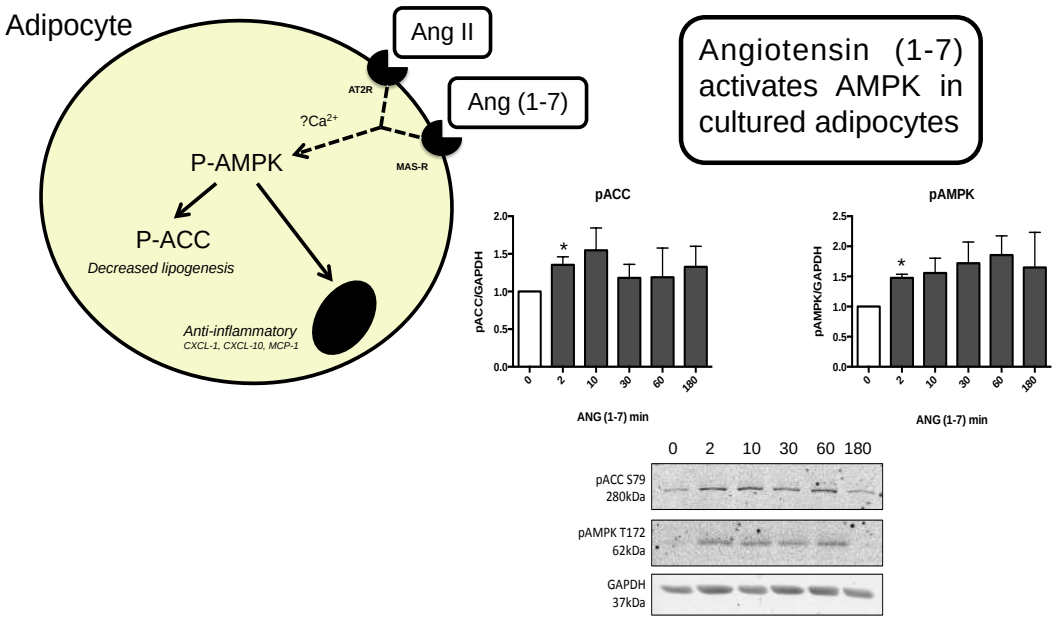
Dr Anna White

University of Glasgow | College of Medical, Veterinary & Life Sciences



AMPK activators attenuate pro-inflammatory effects of TNF-α and IL-1β in cultured adipocytes

University of Glasgow | College of Medical, Veterinary & Life Sciences



Angiotensin (1-7) activates AMPK in cultured adipocytes

Dr Anna Anderson

Biography

Anna Anderson graduated from the University of Edinburgh in 2005 and is currently a specialty trainee (ST5) in Diabetes and Endocrinology in South East Scotland. She is currently completing her PhD investigating the cellular regulation of cortisol in vivo by 11βHSD1.

Abstract

Metformin increases in vivo 11βHSD1 activity in obese men with and without type 2 diabetes mellitus

Anna J Anderson, Ruth Andrew, Gregory C Jones, Kenneth Smith, Natalie Z Homer, Dawn E Livingstone, Brian R Walker, Roland H Stimson.

Reducing cortisol regeneration using 11βHSD1 inhibitors in patients with type 2 diabetes (T2DM) improves glycaemic control, lipid profile, body weight and blood pressure, but these effects are of smaller magnitude than anticipated from pre-clinical studies. We hypothesized that metformin, which was administered to most participants in trials of 11bHSD1 inhibitors, down-regulates 11βHSD1, limiting the efficacy of 11βHSD1 inhibitors. We tested this in obese men with and without T2DM.

8 obese non diabetic men (OND) and 8 obese men with type 2 diabetes (ODM) (BMI 37.4 ± 2.6 v 34.7 ± 1.1 kg/m^2, respectively, p=ns) were recruited to a double-blind randomized crossover study. Subjects received 28 days of placebo or metformin, and the ODM group also received gliclazide in a third phase to control for effects mediated by glycaemic control. On day 28, participants attended after overnight fast for infusion of 9,11,12,12-$[^2H]_4$-cortisol (D4-cortisol)(20%) and unlabelled cortisol (80%) at 1.74mg/hr for 4 hours. Irreversible removal of ^2H from the 11C by 11βHSD2 converts D4-cortisol to D3-cortisone, which then forms 9,12,12-$[^2H]_3$-cortisol (D3-cortisol) when regenerated by 11βHSD1. In steady state (t+150-180 mins), dilution of D4-cortisol by D3-cortisol is a specific measure of cortisol regeneration by 11βHSD1. In the ODM group, to assess hepatic 11βHSD1 activity oral cortisone (5mg) was administered at t+180 mins and rate of appearance (Ra) of cortisol quantified by dilution of D4-cortisol. Data are mean ± SEM.

Metformin reduced fasting plasma glucose in the ODM (metformin 7.4 ± 0.6 v placebo 9.6 ± 1.0 mmol/L, p=0.01) but not OND group (5.3 ± 0.2 v 5.6 ± 0.6 mmol/L); in ODM, metformin and gliclazide lowered fasting glucose similarly. Ra D3-cortisol was increased in ODM vs OND ($p<0.05$). Metformin increased steady state Ra D3-cortisol in both OND (12.9 ± 1.2 v 11.4 ± 1.4 nmol/min, p=0.01) and ODM (metformin 15.8 ± 0.6 v placebo 14.2 ± 0.6 v gliclazide 14.2 ± 0.6 nmol/min (metformin v placebo/gliclazide both $p<0.05$). In the ODM group, metformin tended to increase Ra cortisol following cortisone (peak Ra cortisol metformin 136 ± 17 v placebo 108 ± 15 v gliclazide 100 ± 20 nmol/min (both $p<0.1$)). Cortisol and D4-cortisol clearance were similar in all phases.

Amongst obese men, whole body 11βHSD1 activity is increased in those with T2DM. Metformin further increases whole body, and most likely liver, cortisol regeneration by 11βHSD1 in obese men with and without T2DM. This effect is independent of improved glycaemic control, as gliclazide reduced glucose levels comparably to metformin without altering 11βHSD1 activity. We conclude that any interaction between metformin and selective 11βHSD1 inhibitors in T2DM is likely to potentiate, rather than attenuate, efficacy of both agents.

This work was funded by grants from the Medical Research Council, British Heart Foundation and the Edinburgh and Lothians Health Foundation.

Dr Anna Anderson

Metformin increases *in vivo* 11βHSD1 activity in obese men with and without Type 2 diabetes mellitus

8 obese non diabetic participants (OND)

Metformin (1G bd) or placebo for 28 days

Whole body 11βHSD1 activity measurement using D4 cortisol tracer

Hepatic 11βHSD1 activity measured using oral cortisone

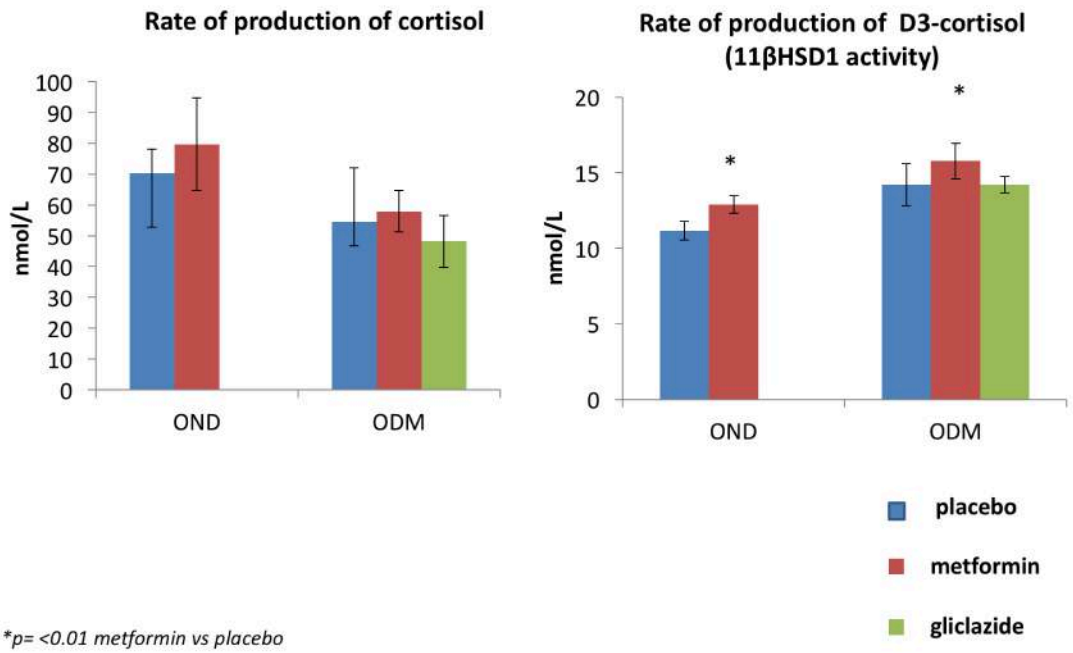
8 obese diabetic participants (ODM)

Metformin (1G bd) or gliclazide (80mg bd) or placebo for 28 days

Whole body 11βHSD1 activity measurement using D4 cortisol tracer

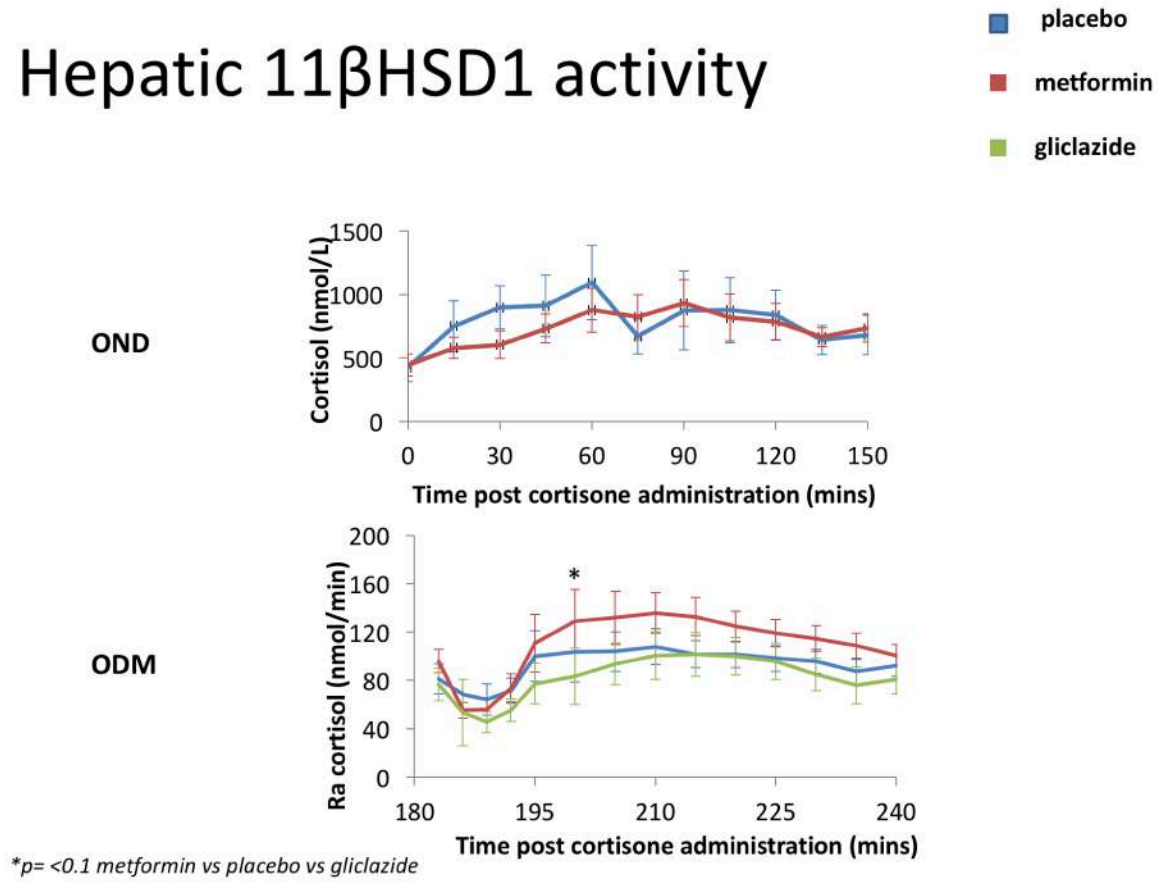
Oral cortisone administered t = 150 mins for measurement hepatic 11βHSD1 activity

Cortisol kinetics



*p= <0.01 metformin vs placebo

Hepatic 11βHSD1 activity



p= <0.1 metformin vs placebo vs gliclazide

Dr Natasha Sawhney

Biography

Natasha Sawhney graduated from the University of Aberdeen in 2011 having also completed an intercalated degree in Sports Science. During her degree and medical training she has been particularly interested in the role of the endocrine system in health and disease and the interaction with lifestyle, diet and exercise. She completed her foundation training in Edinburgh and is currently completing her 3rd year of the acute care common stem (acute medicine) training programme in Aberdeen. She will be applying for dual training in endocrinology, diabetes and general medicine next year.

Abstract

Outcomes after acute stroke in people with diabetes in NHS Grampian.

Natasha Sawhney, Mary Joan Macleod, Melanie Turner, Sam Philip

Introduction

Stroke is a leading cause of disability and the second most frequent cause of death worldwide. Diabetic patients have an increased risk of stroke with previous studies suggesting ranges from 1.8 to 6 times that of the non-diabetic population.1-3 Mortality is also increased.4 The number of people with diabetes diagnosed is estimated to increase 165% between 2000 and 2050.5 Enhanced awareness of the impact of diabetes on stroke risk and outcomes might influence both primary and secondary prevention strategies.

Aim

To examine the outcome of acute stroke in people with diabetes in NHS Grampian population between 2000 and 2011 .

Methods

Population-based linkage study using data extracted and linked from two datasets the NHS Grampian local stroke clinical audit and NHS Grampian Scottish Care Information-Diabetes Collaboration (SCI-DC) dataset for stroke patients admitted to hospital between 2000 and 2011 in NHS Grampian. Both datasets contain demographic and clinical data relevant to care. Descriptive and univariate statistics were generated.

Results

6747 index stroke events were recorded between 2000 and 2011. 897 (13.3%) had a diagnosis of diabetes before the stroke event. 803 (89.5%) had type II diabetes. 7.9% had diabetes for less than a year, 55.7% between 1-10 years, and 21.5% greater than 15 years, prior to the stroke event.

Diabetic patients were more likely to be diagnosed with ischaemic rather than haemorrhagic stroke (p=<0.001). Mortality at 7 days post stroke was 4.9% for stroke patients without diabetes compared to 4.8% for stroke patients with diabetes (p=0.86). By one year mortality was 19.0% and 22.7% respectively (p=0.01).

Conclusion

People with diabetes have worse outcomes at one year following acute stroke when compared to people without diabetes. This requires further exploration.

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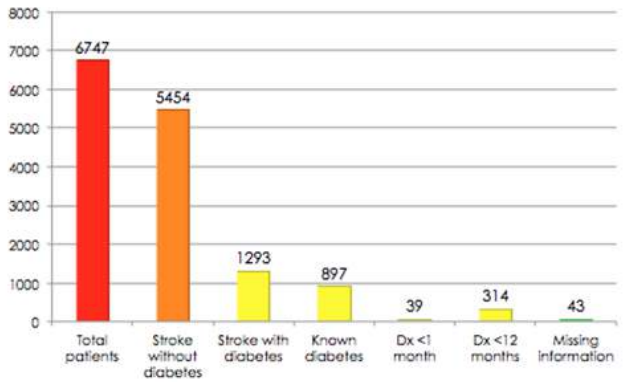
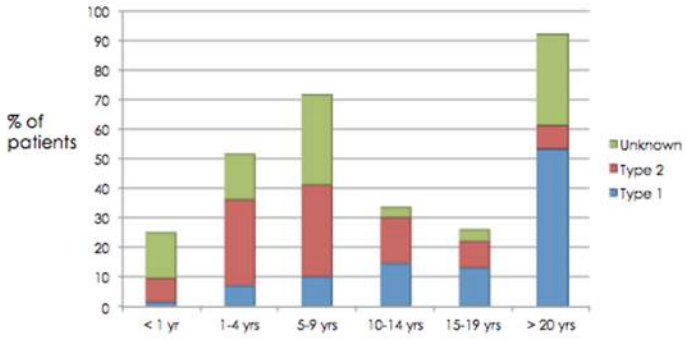
5. Narayan KM, Boyle JP, Thompson TJ et al. Lifetime risk for diabetes mellitus in the United States. JAMA 2003; 290:1884-1890.

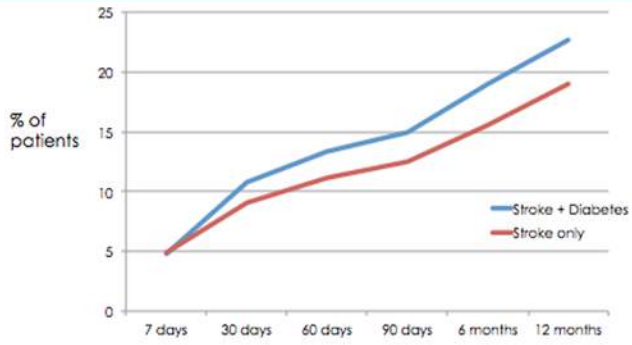
Study population



Duration of diabetes at time of stroke event



Mortality per patient group



Dr Tom Chambers

Biography

Tom Chambers graduated from the University of St Andrews-University of Manchester medical course in 2008. He intercalated to obtain an MRes investigating the role of Wnt signalling in oestrogen stimulated lactotroph proliferation under the supervision of Prof. Julian Davis. Following academic foundation training in Lancaster, he returned to Manchester to complete core medical training. He has recently completed his PhD, as an MRC clinical research training fellow, investigating the intergenerational effects of high fat diet exposure under the supervision of Prof. Richard Sharpe and Dr Mandy Drake. He has just started specialist training in Diabetes and Endocrinology in South East Scotland, currently based at the Western General Hospital in Edinburgh.

Abstract

High-fat diet disrupts metabolic function of two generations of rats in a parent-of-origin specific manner without affecting the germ cell transcriptome

Chambers TJG, Morgan M, Sharpe RM, Drake AJ.

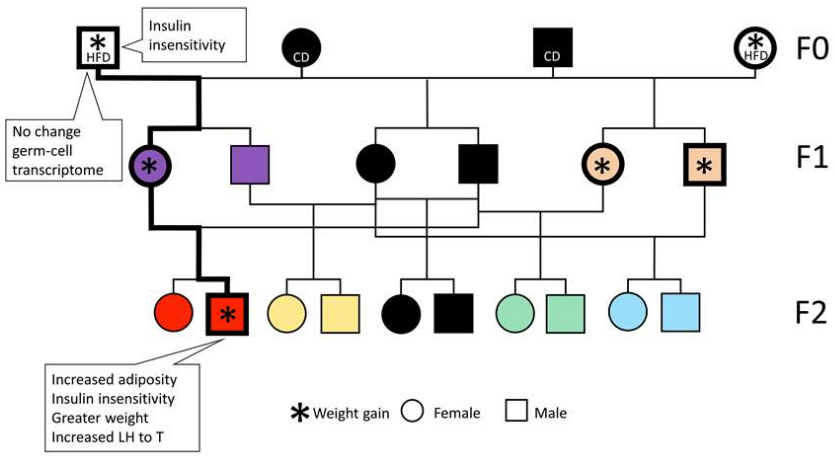
OBJECTIVES:

1. To examine if a parental high fat diet (HFD) influences metabolic health in two generations of offspring.
2. To examine if HFD exposure alters the male germ cell (GC) transcriptome.

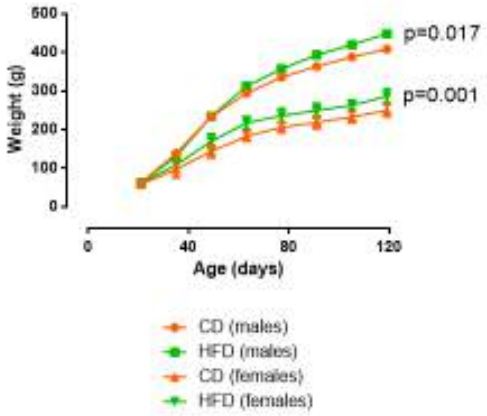
METHODS: Sprague Dawley rats were weaned onto HFD (45% fat) or Control Diet (CD; 10% fat), which they consumed for 14 weeks. After metabolic testing, founders (F0) were bred with controls, establishing the F1 generation. Germ cells from F0 males were isolated and their RNA sequenced. F1 rats were bred with control rats at 19 weeks to generate F2 offspring.

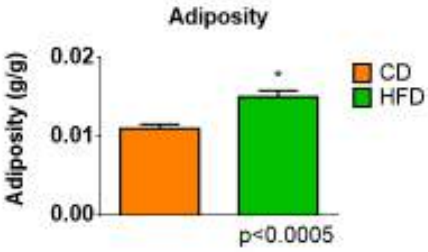
RESULTS: HFD resulted in 9.7% and 14.7% increased weight in male and female F0 respectively. F1 offspring of HFD mothers were heavier than controls. F1 daughters of HFD-fed males were also heavier. F2 male offspring derived from HFD-fed maternal grandfathers were 7.2% heavier, and exhibited increases of 31% in adiposity, 97% in plasma leptin and 300% in luteinising hormone to testosterone ratio. HFD exposure did not alter the F0 GC transcriptome.

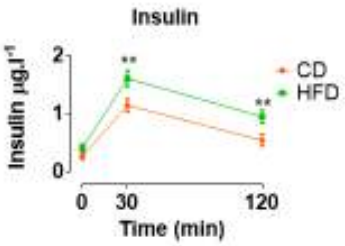
CONCLUSIONS: HFD consumption by maternal grandfathers results in a disrupted metabolic and reproductive hormone phenotype in grandsons. This effect is not mediated by alterations to the GC transcriptome.



Results F0





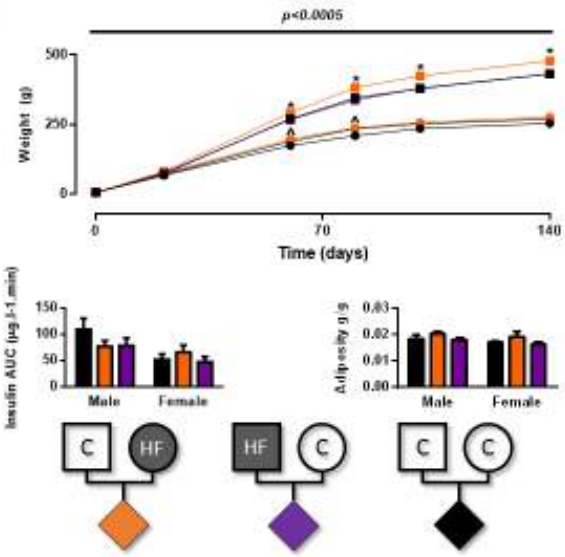


p<0.0005

Significance determined by RM ANOVA

n= 15 males from 2 cohorts and 6-12 females from one cohort
Male data compared by general linear model with diet as fixed factor and cohort as random factor

Results F1

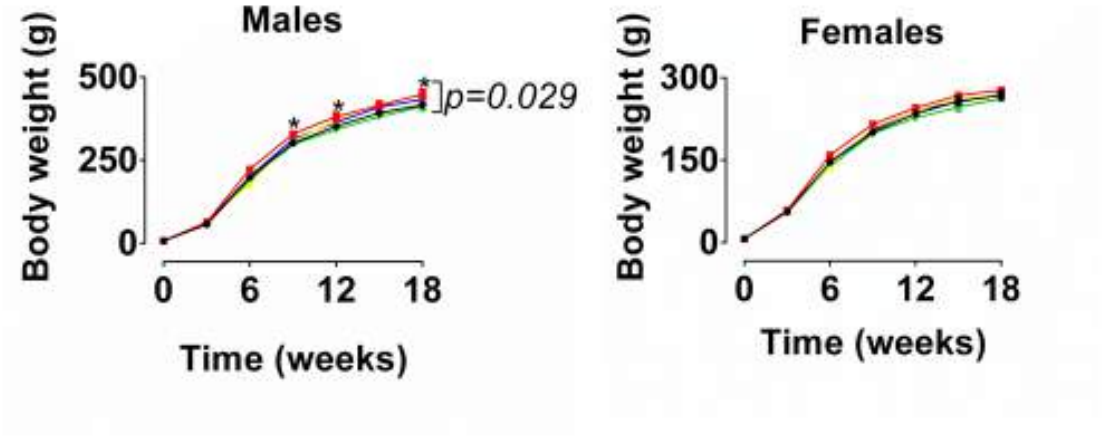


N=17-23 from 5 litters

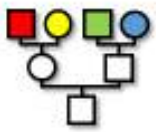
Significance tested by linear mixed model with group and sex (and time) as fixed factors and litter as random factor followed by Bonferroni *post hoc* test

Dr Tom Chambers

Results F2

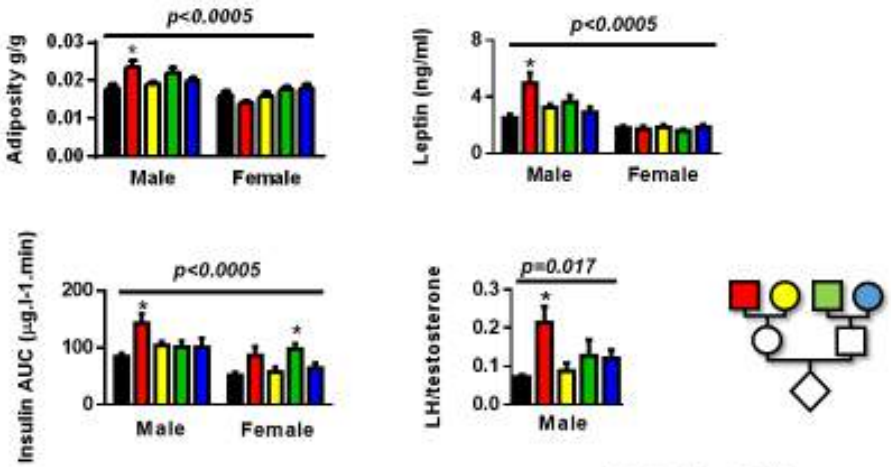


N= 8-14 in 4-7 litters



Significance tested by mixed linear model with group as fixed factor and litter as random factor and followed by Bonferroni *post hoc* test

Results F2



N= 8-14 in 4-7 litters

Significance tested by linear mixed model with group and sex as fixed factors and litter as random factor followed by Bonferroni *post hoc* test

CalSoc Network

One of the founding aims of CalSoc was to promote studies in clinical endocrinology. Recent UK-wide collaborative projects, such as the acromegaly register, dopamine agonist audit and PRAGMA radioiodine audit have contributed to shaping clinical practice. We feel that Scotland is ideally placed, in terms of both the size of population and endocrine community, to contribute similar collaborative projects to the knowledge base in clinical endocrinology.

Time has been allocated on Friday evening for members to discuss how best to proceed and the following potential projects are provided as a basis for discussion:

Possible topics include:

Addison's disease: A nationwide survey to determine variation in the management of Addison's disease. Consideration of compiling a register of Addison's patients with a view towards contributing to future studies of novel therapies, and looking at long-term outcomes by data linkage.

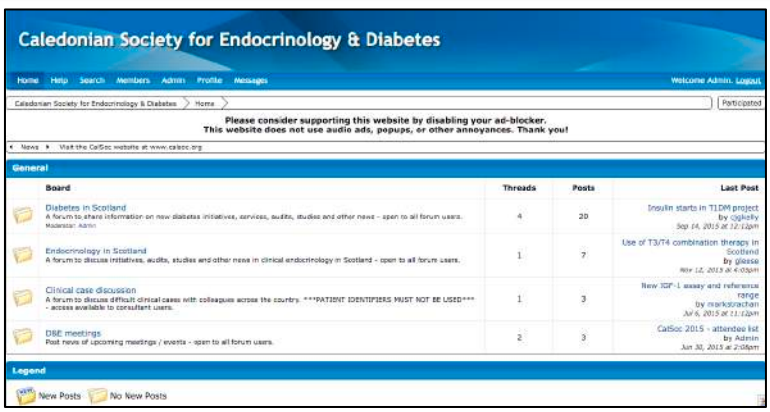
Hypoparathyroidism: A nationwide survey to determine variation in the management of hypoparathyroidism. Consideration of compiling a register of hypoparathyroid patients with a view towards contributing to future studies of PTH replacement.

Graves' disease: A prospective register of new Graves' thyrotoxicosis patients across a predefined period (perhaps 1 year) with collection of clinical, biochemical and treatment data. Opportunity to prospectively assess complications and linkto national morbidity / mortality registers in future.

Primary Hyperparathyroidism: Similar approach to Graves' project.

Male Hypogonadotrophic Hypogonadism: Retrospective review of pituitary imaging in men presenting with isolated hypogonadotrophic hypogonadism to help better define biochemical thresholds for imaging.

We would welcome any further suggestions at the meeting and would hope to take this forward in the early part of 2016.



Finally, a reminder that the CalSoc online forum is open to all D&E healthcare professionals in Scotland.

It is the ideal place to share initiatives, audits, pose clinical questions and advertise local meetings.

To succeed, it will require a 'critical mass' of users and we'd encourage you to sign up.

calsoc.proboards.com

caledonian society for endocrinology and diabetes

CalSoc 2015 registration, meals and accommodation were covered by unrestricted educational grants from our sponsors: